Chapter 17

Necropsy Findings in Ruminant Poisonings by Plant, Fungal, Cyanobacterial and Animal-Origin Toxins in Australia

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INTRODUCTION

Poisoning of ruminants affects virtually all body systems. These notes will deal with lesions detectable at necropsy of ruminants poisoned by natural toxins from (1) a clinical perspective and system by system and (2) a toxin perspective. Major toxin sources, pathology and appraoches to diagnosis are listed Suggestions for confirmation of diagnoses are also included. All data in this work are drawn from McKenzie RA (2002) *Toxicology for Australian Veterinarians.* (published by the author: 26 Cypress Drive, Ashgrove 4060; phone 07 3366 5038; e-mail yapunyah.house@bigpond.com) which should be consulted for more information on the syndromes and toxins included and references to the data.

CLINICAL CONSPECTUS

This section gives an overview of natural toxins and toxin sources affecting ruminants arranged by syndrome or affected organ system to help with differential diagnosis of cases.

Sudden death syndromes

'Sudden' death is defined as death occurring so rapidly that affected animals are **found dead** without being seen to be ill or **die within a few minutes to a few hours** of clinical signs being noticed. Of course, the transition from life to death itself is always sudden, that is, instantaneous.

Plants

- Cyanogenic glycosides [→ Cyanide, HCN or Prussic acid]
- Nitrate-nitrite
- Oxalates (acute poisoning)
- Fluoroacetate
- Cardiac glycosides
- Andromedotoxins (grayanotoxins)
- Taxine diterpenoid alkaloids
- *Erythrophleum* spp. (diterpenoid alkaloids & cinnamic acid derivatives)
- Pyrrolizidine alkaloids
- S-methylcysteine sulphoxide (SMCO) & N-propyl disulphide / thiosulphates

- Phytotoxin-induced cardiomyopathies (see below under Heart & Vascular disease for specific toxins)
- *Trachymene* spp. (wild parsnips)
- Galegine
- Phyto-oestrogens - bladder rupture (wethers)
- Ifforestine
- Diterpenoid alkaloids - *Delphinium* spp.
- Nicotine (pyridine) alkaloids
- Tropane alkaloids [scopolamine (=hyoscine), hyoscyamine, atropine and others]
- *Phalaris aquatica* poisoning – sudden death
- Cucurbitacins (tetracyclic triterpenes)
- Aliphatic nitro compounds (nitrotoxins)
- *Parsonsia* spp.
- Selenium

Fungi

- *Aflatoxins*
- *Corallocytostroma ornicopreoides toxicity (black soil blindness)*

Cyanobacteria

- Cyanobacterial alkaloid neurotoxins – paralytic shellfish poisoning (PSP) toxins and anatoxins

Acute liver necrosis:

Plants

- Diterpenoid (kaurene) glycosides - atractyloside, carboxyatractyloside, parquin, carboxyparquin & wedeloside
- Furanosesquiterpenes
- Methylazoxymethanol (MAM)
- Trema tomentosa [liver-necrosis-inducing phytotoxin]
- Gossypol
- Argentipallium blandowskianum [liver-necrosis-inducing phytotoxin]
- Ozothamnus diosmifolius [liver-necrosis-inducing phytotoxin]
- Cynosurus echinatus (rough dog's tail grass) [liver-necrosis-inducing phytotoxin]
- Lythrum *hyssopifolia (lesser loosestrife)*

Fungi

- Macrofungal peptides
- Aflatoxins
- Mouldy sprouted barley - suspected mycotoxicosis

Cyanobacteria

- Cyanobacterial hepatotoxic cyclic peptides – microcystins and nodularin
- Cylindrospermopsin

Animals

- Sawfly larval peptides

Nephrosis:

Plants
- Oxalates (acute poisoning)
- Tannins (hydrolysable)
- Pennisetum clandestinum (kikuyu -grass)
- Lythrum hyssopifolia (lesser loosestrife)
- Ifforestine

Fungi
- Corallocytostroma ornicopreoides toxicity (black soil blindness)

Photosensitisation:

Primary

Plants
- Dianthrone derivatives (hypericin, fagopyrin)
  - *Hypericum perforatum*
  - *Fagopyrum sagittatum*
- Furanocoumarins (furocoumarins, psoralens)
  - *Ammi majus*
  - *celery, parsley, parsnip*
  - *Cullen (Psoralea) patens*
  - *Citrus aurantifolia*

Secondary (hepatogenous)

Plants
- Lantadenes (pentacyclic triterpenes)
- Steroidal or lithogenic saponins
  - *Panicum spp.*
  - *Brachiaria spp.*
  - *Tribulus terrestris*
- Tannins (hydrolysable) - Terminalia oblongata ssp. oblongata

Fungi
- Sporidesmin
- Phomopsins

Sporadic - unknown toxins

Plants
- *oats, barley, wheat, millets*
- *lucerne, clovers, medics*
- *Sorghum sudanense*
- *Brassicaceae – Glucosinolates*
- *Polygonum spp.*

- Pyrrolizidine alkaloids
- Liver necrosis-inducing plants, cyanobacteria, mycotoxins
- Cynosurus echinatus (rough dog's tail grass) [liver-necrosis-inducing phytotoxin]

Haemorrhage (including haematuria)/Haemolysis/ ethaemoglobinaemia/Myoglobinuria/Red urine pigments (non-haem):

Widespread Haemorrhage

Plants

- Ptaquiloside
- Dihydroxycoumarin (dicoumarol)
  - mouldy Melilotus spp.
  - Anthoxanthum odoratus
  - Ferula communis
- Daphnoretin (presumed toxin in Wikstroemia indica)
- Colchicine and related alkaloidal amines

Fungi

- Aflatoxins
- Trichothecenes (Type A)

Haematuria

Plants

- Ptaquiloside (bovine enzootic haematuria)

Haemolysis

Plants

- Pyrrolizidine alkaloids
- Pyrrolizidine alkaloidosis + Copper
- S-methylcysteine sulphoxide (SMCO) & N-propyl disulphide / thiosulphates
- Glycosidic steroidal alkaloids (glycoalkaloids) of Solanum spp. (nightshades)
- Gossypol
- Acer spp. (maples)
- Berteroa incana (hoary alyssum)
- Raphanus raphanistrum (wild radish)

Fungi

- Gyromitra esculenta (false morel)

Methaemoglobinaemia

Plants

- Nitrate-nitrite
- Acer spp. (maples)

Myoglobinuria

Plants

- Senna spp. [= Cassia spp.]
- Malva parviflora (mallow, marsh mallow, small-flowered mallow)

Red Pigments (non-haem) in urine

Plants

- Xanthorrhoea minor (grasstree) - cattle
- Haloragis odontocarpa (mulga nettle) - sheep
- Trifolium pratense (red clover) – deer

Chronic ill-thrift:

Liver damage

Plants

- Pyrrolizidine alkaloids
- Heliotropium spp.
- Echium plantagineum
- Senecio spp.
- Crotalaria spp.
- Indospicine
- Glucosinolates
- Schinus spp.
- Raphanus raphanistrum (wild radish)

Fungi

- Aflatoxins
- Phomopsins
- Sporidesmin
- Mouldy sprouted barley - suspected mycotoxicosis

Kidney damage

Plants

- Tannins (hydrolysable)
  - *Quercus* spp.
  - *Terminalia oblongata*
- Oxalates
- Pyrrolizidine alkaloids - pigs
- Pennisetum clandestinum (kikuyu grass)
- Iforrestine
- 3-methoxy-2(5H)-furanone [Liliaceae nephrosis – cats, cattle, deer]
- Lythrum hyssopifolia (lesser loosestrife)
- Schotia brachypetala (drunken parrot tree)

Fungi

- Ochratoxins
- Citrinin

Alimentary tract damage

Plants

- Ptaquiloside - neoplasia
- Dittrichia graveolens enteritis (mechanical damage)

Connective tissue damage

Plants

- Plant calcinogenic glycosides

Thyroid damage

Plants

- Glucosinolates
- Mimosine
- Cyanogenic glycosides
- Pennisetum typhoides

Skin & appendage damage

Plants

- Selenium (chronic selenosis)
- Vicia spp. (vetch toxicity)
- Citrus pulp

Poor weight gain/Weight loss

Plants

- Swainsonine
- Swainsonine + calystegines (Ipomoea spp.)
- Cyanogenic glycosides - sulphur-responsive

Fungi

- Aflatoxins

Anaemia

Plants

- Irritant diterpenoids of Pimelea spp. – simplexin (& huratoxin)

Depressed wool growth in sheep

Bacteria

- Corynetoxins (tunicaminyl-uracils)

Nervous syndromes I (CNS): Convulsions, tremors, deranged behaviour, deep depression:

Convulsions (seizures) - clonic

Plants

- Fluoroacetate
- Thiaminase
- Terminalia oblongata (yellow-wood) - sheep
- Tropane alkaloids [scopolamine (=hyoscine), hyoscyamine, atropine and others]
- Cynanchosides
- Piperidine & nicotine (pyridine) alkaloids
- Sulphur (S-associated polioencephalomalacia of ruminants)

Fungi

- Cyclopiazonic acid

Bacteria

- Corynetoxins (tunicaminyluracils) (ARGT)

Convulsions (seizures) - tetanic

Plants

- Strychnine (& brucine)
- Alstonine, alstonidine and other indole alkaloids of Alstonia constricta
- Indole (pyrrolidinoindoline) alkaloids - calycanthine, chimonanthine, idiospermuline
- Cynanchosides
- Musa sp. (bananas) (?)

Tremors

- *Plants*
- Indole alkaloids of Phalaris spp (phalaris) - Phalaris staggers
- Pyridine (nicotine) and piperidine alkaloids
- Chamaecytisus proliferus

Fungi

- Lolitrems
- Paspalitrems (Claviceps paspali tremorgens)
- Aspergillus clavatus tremorgenic mycotoxins

Deranged behaviour (mania), deep depression

Plants

- Dianthrone derivatives (hypericin, fagopyrin)
- Prosopis juliflora (mesquite) – neuronal vacuolation in cranial nerve nuclei
- Avena sativa (oats) – "red-tipped" or "rusty" oats crops
- Swainsonine
- Swainsonine + calystegines (Ipomoea spp.)
- Calystegines (nortropane alkaloids) - probable aetiology of Solanum spp.-associated cerebellar degeneration
- Quinolizidine alkaloids of Lupinus spp.
- Hepatoencephalopathy
- Pyrrolizidine alkaloids
- Acute liver necrosis toxins
- Dendrocnide spp. (stinging trees)
- Glycosidic steroidal alkaloids (glycoalkaloids) of Solanum spp. (nightshades)
- Pisum sativum var. arvense (field pea)
- Dialkylimidazoles (indole alkaloids) - Ammoniated forage toxicity
- Tetrahydrocannabinol - Cannabis sativa (marijuana)

Fungi

- Lysergic acid amide (ergot alkaloid)
- Ethanol (ethyl alcohol)

Nervous syndromes II (CNS/PNS):
Ataxias, paralyses, gait abnormalities:

Ataxias

Plants

- Cycads
- Xanthorrhoea spp. (grasstrees) –posterior ataxia syndrome
- Aliphatic nitro compounds (nitrotoxins)
- Indole alkaloids of Phalaris spp (phalaris) - Phalaris staggers
- ß-carboline alkaloids [indole alkaloids] – Coonabarabran staggers
- Swainsonine + calystegines (Ipomoea spp.)
- Calystegines (nortropane alkaloids) - probable aetiology of Solanum spp.-associated cerebellar degeneration
- Tribulus micrococcus (yellow vine)
- Pyridine (nicotine) and piperidine alkaloids
- Hoya australis (hoya, wax flower)

- Trachyandra spp.
- Cyanogenic glycosides - Sorghum spp. spinal cord damage
- Other plant staggers syndromes –
- Stachys arvensis
- Lamium amplexicaule
- Malva parviflora
- Echinopogon spp.
- Gomphrena celosioides (gomphrena weed, soft khaki weed)
- Tetrahydrocannabinol - Cannabis sativa (marijuana)
- Solanum spp.-associated cerebellar degeneration
- Cumulative bufadienolide cardiac glycosides (cotyledonosis)
- Chamaecytisus proliferus (tagasaste)
- Humpyback of sheep
- "Scrub ataxia" of suckling calves in south-eastern Queensland

Fungi

- Aspergillus clavatus tremorgenic mycotoxins
- Cyclopiazonic acid
- Diplodia maydis neurotoxin

Paralysis/paresis

Plants

- Tropane alkaloids [scopolamine (=hyoscine), hyoscyamine, atropine and others]
- Aliphatic nitro compounds (Nitrotoxins)
- Cumulative bufadienolide cardiac glycosides (cotyledonosis)

Fungi

- Diplodia maydis neurotoxin

Gait abnormality

Plants

- Swainsonine
- Swainsonine + calystegines (Ipomoea spp.)
- Indole alkaloids of Phalaris spp (phalaris)
- Phalaris staggers

Fungi

- Paspalitrems (Claviceps paspali tremorgens)
- Lolitrems
- Diplodia maydis neurotoxin

Blindness:

Retinal ± optic nerve degeneration

- Plants
- Stypandrol
- Ptaquiloside – "bright blindness"
- Rhodomyrtus macroparpa (finger cherry)

Cataracts

Plants

- Mimosine
- Xanthorrhoea johnsonii (northern forest grasstree)

Corneal opacity

Plants

- Furanocoumarins (furocoumarins, psoralens)
- Glucosinolates

Fungi

- Ramaria flavo-brunnescens (a coral fungus)

CNS Damage

Plants

- Swainsonine
- Swainsonine + calystegines (*Ipomoea* spp.)

Polioencephalomalacia

Plants

- Thiaminase
- Sulphur (S-associated polioencephalomalacia of ruminants)

Hepatoencephalopathies

Plants

- Pyrrolizidine alkaloids
- Acute liver necrosis

Unknown mechanism

- Fungi
- Corallocytostroma ornicopreoides toxicity (black soil blindness)

Respiratory syndromes:

Pneumonitis

Plants

- Andromedotoxins (grayanotoxins)
- Zieria arborescens (stinkwood)
- Glucosinolates

Fungi

- Furans - Mouldy sweet potatoes

Pulmonary oedema (dominant sign)

Plants

- Galegine
- Aliphatic nitro compounds (Nitrotoxins)

Pyrexia, hyperpnoea

Plants

- Ptaquiloside
- Dianthrone derivatives (hypericin, fagopyrin)

Fungi

- Ergot alkaloids (ergopeptide alkaloids)- ergotism
- Balansia sp. in Paspalidium jubiflorum (Warrego summer grass)

Heart & vascular disease:

Phytotoxin-induced cardiomyopathies – sudden death

Plants

- Fluoroacetate
- Gossypol

- Unsaturated fatty acids, particularly crepenynic acid
- Persin
- Theobromine (a xanthine alkaloid)
- Senna spp.
- Trachymene spp. (wild parsnips)
- Castanospermum australe (Moreton Bay chestnut, black bean) (rare)

Heart failure

Syndromes including jugular vein distension, subcutaneous oedema (head, brisket, limbs), ascites, hydrothorax, cardiac dilation. There may be some overlap with cardiomyopathies producing sudden death.

Plants

- Irritant diterpenoids of Pimelea spp. – simplexin (& huratoxin)
- Gossypol
- Persin
- Isoquinoline alkaloids - Argemone spp. (Mexican poppy)
- Parsonsia spp.

Vascular disease

Fungi

- Ergot alkaloids (ergopeptide alkaloids)- ergotism

Diarrhoea and other alimentary syndromes:

Diarrhoea

Diarrhoea is a common sign attributed to plant and other poisonings. The main syndromes included here are the better characterised ones and are *not inclusive of all plants or other toxins capable of producing diarrhoea.*

Plants

- Cardiac glycosides
- Irritant diterpenoids of Pimelea spp. – simplexin (& huratoxin)
- Irritant diterpenoids of Families
- Thymeleaceae & Euphorbiaceae
- Glycosidic steroidal alkaloids (glycoalkaloids) of Solanum spp. (nightshades)
- Cucurbitacins (tetracyclic triterpenes)
- Castanospermum australe (Moreton Bay chestnut, black bean)
- Senna spp. [= Cassia spp.]
- Meliatoxins (tetranortriterpenes)
- Trachymene spp. (wild parsnips)
- Phytolacca spp.
- Avena sativa (oats) – "red-tipped" or "rusty" oats crops
- Schinus spp.
- Dittrichia graveolens enteritis (mechanical damage)
- Pyrrolizidine alkaloids
- Colchicine and related alkaloidal amines
- Terpenoids of Pachyrhizus erosus (yam bean)
- Berteroa incana (hoary alyssum)
- Raphanus raphanistrum (wild radish)

Fungi
- Ramaria flavo-brunnescens (a coral fungus)
- Trichothecenes (Type A)

Buccal irritation (stomatitis) or ptyalism (excessive salivation, sialorrhoea)
Plants
- Calcium oxalate raphide crystals
- Mimosine
- Protoanemonin
- Grass awns

Fungi
- Ramaria flavo-brunnescens (a coral fungus)
- Trichothecenes (Type A)
- Slaframine
- Diplodia maydis neurotoxin

Forestomach lesions
Plants
- Pennisetum clandestinum (kikuyu grass)
- Cucurbitacins
- Glucosinolates

Fungi
- Corallocytostroma ornicopreoides toxicity (black soil blindness)

Vomiting/regurgitation (ruminants, horses)
Plants
- Andromedotoxins (grayanotoxins)

Phytobezoars (plant fibre balls)
Plants
- Romulea rosea var. australis (onion grass, Guildford grass)
- Anemone patens (pasque flower)

Neoplasia
Plants
- Ptaquiloside – upper alimentary tract (cattle), intestines (sheep)

Hair loss or dermatitis:

Hair loss
Plants
- Mimosine
- Selenium (chronic selenosis)

Fungi
- Ramaria flavo-brunnescens (a coral fungus)

Dermatitis
Plants
- Vicia spp. (vetch toxicity)
- Grass awns
- Schinus spp.
- Parsonsia spp.

- Citrus pulp
- "Scrub ataxia" of suckling calves in south-eastern Queensland

Fungi
- Trichothecenes Type A

Goitre:

Plants
- Cyanogenic glycosides – congenital goitre
- Mimosine
- Glucosinolates
- Pennisetum typhoides (pearl millet seed) – goats; Africa

Skeletal muscle syndromes:

Plants
- Unsaturated fatty acids, particularly crepenynic acid
- Senna spp. [= Cassia spp.]
- Malva parviflora (mallow, marsh mallow, small-flowered mallow)

Fungi
- Phomopsins

Bone syndromes:

Plants
- Trachymene spp. (wild parsnips)

Reproductive syndromes:

Congenital abnormalities

Plants
- Cyanogenic glycosides (putative agent) - Sorghum sudanense hybrids
- Cyanogenic glycosides – congenital goitre
- Trachymene spp. (wild parsnips)
- Piperidine, pyridine (nicotine) & quinolizidine alkaloids - *Conium,* Lupinus, Nicotiana teratogens
- Steroidal alkaloids- Veratrum, Solanum tuberosum
- Chamaecytisus proliferus (tagasaste)

Mastitis/Agalactia

Plants
- Persin (Persea americana)

Fungi
- Ergot alkaloids (ergopeptide alkaloids)- ergotism

Reduced fertility

Plants
- Phyto-oestrogens
- Gossypol
- Swainsonine
- Romulea rosea var. australis

Fungi
- Zearalenone - cattle
- Trichothecenes (Type A)

Abortion/premature birth

Plants
- Isocupressic acid (bicyclic labdane diterpene acids) and/or Vasoactive lipids
- Swainsonine
- Gossypol
- Nitrate-nitrite
- Salvia coccinea (red salvia, Texas sage)
- Trigonella foenum-graecum (fenugreek)
- Mentha longifolia (horse mint)
- Mentha saturioides (native pennyroyal)
- Tanacetum vulgare (tansy)
- Indospicine (Indigofera spicata)
- Raphanus raphanistrum (wild radish)
- Romulea rosea var. australis
- Verbena spp.
- Ranunculus repens (creeping buttercup)
- Berteroa incana (hoary alyssum)
- Leucaena leucocephala

Fungi
- Ergot alkaloids (ergopeptide alkaloids)- ergotism
- Trichothecenes (Type A)

Neoplasia:

Plants
- Ptaquiloside

Fungi
- Aflatoxins

Immunological suppression:

Fungi
- Aflatoxins
- Trichothecenes (Type A)

PHYTOTOXINS (*TOXINS* OF VASCULAR PLANT ORIGIN)

INORGANIC TOXINS

Nitrate-nitrite

Common sources:

- Avena sativa (oats)
- Sorghum spp. (sorghum)
- Lolium spp. (rye grasses)
- Portulaca spp. (pig weed)
- Salvia reflexa (mint weed)
- Silybum marianum (variegated thistle)
- Arctotheca calendula (cape weed)

+ many others

Pathology:
At necropsy, **chocolate-brown blood** (methaemoglobin) is usually seen. Note that the colour fades with time after death as methaemoglobin is reconverted to haemoglobin and the abnormality is not always observed.

Diagnosis:
The **diphenylamine test for nitrate** may be applied to **plants, aqueous humour** (up to 6-12 hrs after death) and rumen contents. Note that microbial action after sampling can decrease nitrate content, so chill aqueous humour samples for transport to a laboratory and test rumen contents very soon after death.

Plants with greater than 1.5% KNO_3 equivalent in their dry matter are regarded as potentially toxic to ruminants.

Aqueous humour nitrate concentrations in normal cattle are about 5 mg/L. In poisoned cattle they can be 100-150 mg/L. Interpretation of aqueous humour nitrate concentrations in aborted foetuses suspected of being associated with dam exposure to toxic pasture have been suggested as: <25 ppm = definite negative; 25-50 ppm = probable negative; >50 ppm = suspicious. Cases associated with a source of nitrate and with no infectious agent or inflammatory change demonstrated in foetal tissues usually have aqueous humour nitrate >>50 ppm.

Post mortem blood samples may also be tested for nitrate content (half-lives in blood: nitrate = 5.0 hr; nitrite = 0.5 hr), but *post mortem* bacterial decomposition may destroy it more rapidly than aqueous humour nitrate, so negative results must be interpreted with caution.

Diphenylamine spot test for nitrate in plants or body fluids

Reagent
0.5 g diphenylamine in 20 ml distilled water with enough sulphuric acid added to bring the total volume to 100 ml. Cool and store in a brown bottle. Dilute with 80% sulphuric acid to half strength to make the test solution.

Procedure
Place 1 drop of test solution on the cut surface of a plant,
OR place a drop of serum, urine or other body fluid on a white plate and add 3 drops of test solution.
A green to blue colour is a positive test.

Alternatively
Commercial test strips for nitrate testing are available from Merck [Merckoquant® Nitrate Test in packs of 100 or 25 test strips]; [Note: work well for plants and water, but seriously under-estimate nitrate concentrations in ocular fluids (MP Carlson, personal communication, VETTOX discussion list 1997)]

Urinalysis test strips (Combur 9 test strips; Boehringer) may be used to test aqueous humour as well as urine for nitrate/nitrite (Montgomery & Hum 1995)

Garlic press field spot test method for use on plant samples

Use garlic press + Merckoquant strips + fresh plant

Squeeze fresh plant in garlic press; place a drop of sap on the end pad of test strip, shake gently to remove excess sap; time for 1 min; compare colour with NO_3 scale on strip container

Result: 500 mg/L nitrate or more (= 0.8% KNO_3) may be hazardous to ruminants. Confirm hazardous concentrations by submitting samples to a laboratory.

Selenium (chronic selenosis)
Common sources:

- *Morinda reticulata* (mapoon, ad-a)
- *Neptunia amplexicaulis* (selenium weed)

Syndrome names:

- *chronic selenosis*
- *alkali disease (USA) ("the alkali", "bob tail disease")*

So-called "blind staggers", attributed to Se intoxication in USA for decades, is now recognised not to be a Se intoxication, but most commonly polioencephalomalacia (S-associated) (*q.v.*) or due to other encephalopathies. The geochemistry associated with Se-accumulator plants often produces water with a high S content in the same landscape.

Pathology:
Cattle (natural cases are rare)

- dystrophic hoof lesions: separation of horn from lamellar and coronary epidermis
- tubules in the stratum medium of hooves replaced by island of parakeratotic cellular debris separated by more normal hoof matrix ± hyperplasia, acanthosis, parakeratosis and disorganised germinal epithelium of varying severity in hoof epithelium, particularly at the tips of epidermal lamellae. Distinguished from chronic laminitis which has predominantly dermal (chorial) lesions

- loss of tail switch: follicles atrophic and devoid of hair shafts, dyskeratosis and mild superficial follicular keratosis.
- no lesions outside the integument

Diagnosis:
Assay liver, kidney [hair, hoof] for Se

SIMPLE ORGANIC TOXINS

Fluoroacetate

Common sources:

- *Gastrolobium* spp. (poison bushes) – 34 known and 8 suspected toxic species in south-western Australia, central Australia (2 species) and central Queensland (1 species)
- *Acacia georginae* (Georgina gidyea) – western Queensland, eastern Northern Territory

Pathology:

- hyperglycaemia, acidosis
- increased citrate concentrations in blood, kidney
- rapid onset of *rigor mortis* similar to cases of strychnine toxicity (*q.v.*)
- multifocal myocardial degeneration and necrosis has been seen in sheep and myocardial scarring is reported in survivors of *Acacia georginae* poisoning.

Diagnosis:
Assays for fluoroacetate may be done on stomach/rumen contents, liver, kidney, plants and suspected baits. A modified HPLC method has been developed in South Africa. The recommended sampling protocol from necropsies is: Collect 100g each of liver & kidney & stomach/rumen contents into separate scrupulously-clean glass or plastic containers as soon after death as possible and freeze immediately. Submit to the laboratory frozen (to be assayed within 14 days of collection). If samples are not frozen, assay within 7 days of collection. In rumen samples spiked with fluoroacetate and held at room temperature (10-27°C), the concentration after 83 days was 85% of the starting concentration. In spiked liver samples, concentration decreased to 52% after 104 days. Further time lapse revealed no further decreases. A fluoroacetate assay is available from Queensland Department of Natural Resources, Alan Fletcher Research Station, 27 Magazine Street (PO Box 36), Sherwood 4075; Phone 07 3375 0700. Samples are tested in batches, usually monthly at a cost about $70 per sample (2001).

Botanical examination of rumen contents for the presence of source plants is useful, given that herbovores die rapidly from intoxication.

Histopathology of the myocardium may be helpful in ruminants. Lesions may be present if the animal survives more than 24 hrs.

The difficulty of field diagnosis of fluoroacetate poisoning due to the lack of unequivocal clinical signs and lesions may lead to over-diagnosis

(misdiagnosis) of this intoxication in endemic areas. In the endemic area for *Gastrolobium granidflorum* toxicity in Queensland, introduction of vaccination of cattle against botulism virtually halved the number of deaths in cattle in vaccinated herds. All these deaths had been previously ascribed by owners to fluoroacetate poisoning.

Oxalates (acute poisoning)

Common sources:

- *Oxalis pes-caprae* (soursob)
- *Portulaca* spp. (pigweed)
- *Setaria sphacelata* (setaria)

+ others

Pathology:

Acute oxalate poisoning: Clinical pathology reveals **hypocalcaemia** and **azotaemia** (increased concentrations of serum urea and creatinine). Necropsy may reveal minimal changes. In severe cases there may be pulmonary congestion and oedema, hyperaemia of forestomach walls or rumenitis. Kidneys are pale and swollen and may have petechial or ecchymotic haemorrhages. Histopathology reveals **nephrosis with rosettes of calcium oxalate crystals** in tubular lumens.

Chronic oxalate poisoning: Clinical chemistry reveals azotaemia and hypoproteinaemia. Kidneys are shrunken and fibrotic.

Diagnosis:

Acute oxalate poisoning:

- access + hypocalcaemia + calcium oxalate crystals in kidney tubules
- assay plants for soluble oxalate content. Hazardous plants contain over 2.0 - 2.5% soluble oxalate in dry matter. N.B. the other conditions of poisoning must be satisfied before poisoning can take place.

ALKALOIDS

Pyrrolizidine alkaloids

Common sources:

- Senecio spp. (groundsels, fireweeds)
- Heliotropium spp. (common & blue heliotropes)
- Echium spp. (Paterson's curse, viper's bugloss)
- Crotalaria spp. (rattlepods)

Pathology:

Hepatotoxic syndrome

Clinical pathology findings are variable. There may be increased plasma concentrations of bilirubin and liver-associated enzymes and decreased plasma concentrations of albumin and urea. **The most consistent finding is hyopalbuminaemia.** Anaemia may be found also. Pyrrolic metabolites can be detected on haemoglobin by TLC techniques.

The major lesion is a **chronic hepatopathy** characterised by atrophy of hepatic parenchyma (reduced numbers of hepatocytes) with

megalocytosis of the survivors, bile ductule proliferation and fibrosis (usually periportal, less commonly centrilobular). Multiple regeneration nodules of hepatocytes may occur. Pyrrolic metabolites can be detected in liver by TLC techniques.

Secondary and minor lesions may include ascites, status spongiosis of cerebral white matter (sometimes also grey matter), pulmonary emphysema and interstitial fibrosis, and megalocytosis of renal or pulmonary epithelium.

Acute pneumotoxicity - ruminants
Pulmonary oedema with tracheobronchial foam and distension of interlobular septa with fluid is the main lesion. Hydrothorax, hydropericardium and sub-pleural haemorrhages are also seen. Fibrin is present in the thoracic fluid and it coagulates on exposure to air. Histologically, there is proteinaceous fluid and some haemorrhage in alveoli. No significant hepatic lesions are seen.

Diagnosis:
Field tests are available to detect PAs and PA N-oxides in plants. Results obtained should be confirmed by laboratory assays.

Plant access by affected animals can be difficult to establish due to the lag between ingestion and the onset of signs weeks to months later.

Hepatotoxicity

Liver histopathology: **megalocytosis**, biliary ductular hyperplasia, fibrosis (note differential diagnosis includes aflatoxicosis)

Serum γGT may be used as a screening test for subclinical liver damage in horses.

Pyrrolic metabolites (PM) bound to tissue macromolecules may be detected in liver or blood using TLC (thin layer chromatography), but only in specialised laboratories.

Conditions for successful PM detection by this means include

- large sample sizes (at least 10 g liver or 20 ml whole blood in EDTA) are required to detect the small concentrations involved, so liver samples obtained by biopsy are unsuitable for testing.
- blood sample collection during or within about 2 weeks of access to the PA source so that sufficient PMs remain bound to haemoglobin of circulating erythrocytes for detection. As erythrocytes turn over (normal 120 day lifespan), dilution of the PM concentration occurs.
- liver samples fixed in formalin are suitable for PM detection

Jaagsiekte
Lung histopathology is characteristic.
Acute pneumotoxicity - ruminants
Plant access & pathology. Differential diagnoses should include poisoning by galegine (*q.v.*).

Indole (pyrrolidinoindoline) alkaloids - calycanthine, chimonanthine, idiospermuline

Idiospermum australiense is a rare lowland rainforest tree of northern Queensland in the monotypic Family Idiospermaceae. Its "seeds" are 3-6 cm in diameter and comprise naked embryos each with 3-4 massive fleshy cotyledons.

Pathology:
Numerous "seeds" in rumen contents (> 1kg in the field case), haemorrhages in epicardium, rumen, abomasum and upper small intestine with free blood in the lumen of the small intestine in one case.

Diagnosis:
Syndrome + access + seeds in rumen. Differential diagnoses include strychnine poisoning (hypersensitivity leading to tetanic spasms) and arsenic poisoning (alimentary haemorrhages)

Taxine diterpenoid alkaloids

Common source:
Taxus spp. (yew trees)

Pathology:
- plant in mouth and rumen/stomach
- **no significant lesions**
- gastric congestion (if death delayed for a few hours)

Diagnosis:
- access + sudden death + plant demonstrated in mouth/stomach [more likely in ruminants than monogastrics]
- assay of stomach contents for taxine alkaloids or other chemical markers of *Taxus* spp. is available in some labs; stomach contents preserved with ethanol are suitable for some assays

Swainsonine [an indolizidine alkaloid]

Common sources:
- Swainsona spp. (Darling peas)

Pathology:
- no specific lesions at necropsy; emaciation
- yellow discoloration of brainstem in chronically-emaciated sheep
- cytoplasmic vacuolation of circulating lymphocytes
- fine cytoplasmic vacuolation of neurones and visceral parenchyma (liver, kidney, pancreas, thyroid, placenta)
- persistent eosinophilic spheroids in axons

Diagnosis:
Access + pathology

Swainsonine + calystegines (Ipomoea spp.)

Sources:

- Ipomoea sp. aff. calobra (Weir vine) confined to the Maranoa district, Q;
- Ipomoea muelleri (poison morning glory) widespread in tropics (WA, NT, Q)

Pathology:

- nephrosis
- cytoplasmic vacuolation of neurones, persistent spheroids in axons (cerebellum particularly susceptible)

Diagnosis: pathology

Calystegines (nortropane alkaloids) - probable aetiology of Solanum spp.-associated cerebellar degeneration

Sources:

- Solanum dimidiatum Raf. [= S. carolinense L.] (potato weed, western horsenettle). Naturalised in Australia in the Bundaberg area of Queensland. No poisoning cases recorded in Australia.
- Solanum cinereum (Narrawa burr) - goats, sheep

Pathology:

Cattle

- *cerebellar atrophy at necropsy*
- *paucity or absence of Purkinje cells in cerebellar cortex*
- *foamy cytoplasmic vacuolation of remaining Purkinje cells*
- *swollen axons of Purkinje cells*

Goats

- cerebellum: deficit of grey matter compared with white matter; lesion only in cerebellum; other organs normal at necropsy
- brain weights and cerebellar weights similar to normal goats
- absence of Purkinje cells in many cerebellar folia
- some remaining Purkinje cells degenerative and some with fine foamy cytoplasmic vacuolation
- similar but milder vacuolation in hippocampus and choroid plexus
- proximal portions of Purkinje cell axons swollen and degenerate ("torpedoes")
- limited spheroidal neuroaxonal dystrophy scattered through brain
- mild Wallerian degeneration in white matter of cerebellum and spinal cord

Diagnosis: syndrome + plant access

Indole alkaloids of Phalaris spp (phalaris) - Phalaris staggers

Common sources:

- Phalaris aquatica

Pathology:

- **greenish pigmentation** in CNS (brain, spinal cord & dorsal root ganglia) and kidney medulla = indole-like pigments
- pigments thought to indicate neurones affected by the syndrome, but pigments themselves not responsible for dysfunction; stored in lysosomes
- CNS pigment distribution: neurones in brain stem nuclei (thalamus to caudal medulla), cerebellum and in spinal cord dorsal root ganglia and dorsal and ventral horn cells

Diagnosis:
Access + syndrome, pathology

ß-carboline alkaloids [indole alkaloids] – Coonabarabran staggers

Source: *Tribulus terrestris* (caltrop)

Pathology:
± demyelination of some peripheral nerves
± Wallerian degeneration of spinal cord white matter
± neurogenic degeneration skeletal muscles
Diagnosis: syndrome + access

Piperidine, pyridine (nicotine) & quinolizidine alkaloids - Conium, Lupinus, Nicotiana teratogens

Common sources:

- *Conium maculatum* (hemlock) – coniine (piperidine)
- *Lupinus spp. (lupins) – anagyrine (quinolizidine), ammodendrine (piperidine)*

Pathology:
congenital arthrogryposis (± brachygnathia, palatoschisis, torticollis, scoliosis, lordosis)

Diagnosis: pathology + access

Pyridine (nicotine) and piperidine alkaloids

Common sources:

- *Nicotiana spp. (tobaccos)*
- *Duboisia hopwoodii (pituri)*
- *Conium maculatum (hemlock)*

Pathology:
alimentary tract congestion in cases with diarrhoea

Diagnosis: access + clinical signs

Erythrophleum spp. (diterpenoid alkaloids & cinnamic acid derivatives)

Common source:

- *Erythrophleum chlorostachys (Cooktown ironwood); northern Australia*

Pathology:

- *recognisable leaves (or other plant parts) present in rumen contents (whole in some cases)*
- *gastrointestinal congestion*
- *± haemorrhagic colitis*
- *subepicardial, subendocardial and myocardial haemorrhage*

Diagnosis: history of access + sudden death + identify plant in ingesta

Glycosidic steroidal alkaloids (glycoalkaloids) of Solanum spp. (nightshades)

Pathology: gastroenteritis

Diagnosis: syndrome + access

Isoquinoline alkaloids - Argemone spp. (Mexican poppy)

Cattle fed whole plants in hay in South Africa and Australia develop ventral subcutaneous oedema, ascites, hydrothorax, cardiomyopathy.

Isoquinoline alkaloids - Papaver spp.

Pathology:
Sheep (*P. nudicaule*): No significant lesions were seen, but the plant could be recognisedin the rumen

Diagnosis:
History of access + syndrome + identification of plants in rumen contents

Iforrestine

Sources:

- ***Isotropis*** spp. (Family Fabaceae) 14 species in Australia, 7 associated with poisoning

Pathology:
- ↑ serum urea & creatinine
- perirenal oedema
- pale kidneys
- necrosis of proximal renal convoluted tubules
- oedema of abomasal wall
- ± liver necrosis

Diagnosis: access + pathology

Colchicine and related alkaloidal amines

Sources:

- *Colchicum autumnale L. (meadow saffron, autumn crocus, naked ladies, naked boys)*
- *Gloriosa superba L. (glory lily, flame lily, gloriosa).*

Pathology:

- *acute gastrointestinal inflammation*
- *widespread haemorrhages*
- *lysis of lymphocytes in lymphoid organs*

Diagnosis:

- *Access + syndrome + plant parts in rumen (difficult to identify)*
- *Assay rumen contents for colchicine*

AMINO ACIDS & PROTEINS

Thiaminase

Common sources:

- *Marsilea drummondii (nardoo)*
- *Cheilanthes sieberi (mulga or rock fern)*
- *Pteridium esculentum (bracken) - insufficient thiaminase to threaten ruminants*

Pathology:
Sheep

- *large amount of fern in the rumen*
- *polioencephalomalacia: all cerebral lobes affected, sometimes sparing the temporal lobes*
- *autofluorescence of lesions under UV illumination @ 365 nm wavelength*

Diagnosis:
Sheep: access + pathology

Mimosine

Common sources:

- *Leucaena leucocephala*
- *Mimosa pudica*

Clinical signs & Pathology:
Cattle
Rapid effects (days):

- *stomatitis, mucosal erosions (mouth, pharynx, tongue), drool saliva*
- *hair loss (tail switch, other parts of coat)*

Chronic effects (months):

- *hyperplastic goitre*
- *oesophageal erosion*
- *↓ fertility, low birth weight, congenital goitre*
- *bilateral cataracts*

Sheep

- *fleece shedding*

Diagnosis: syndrome + access

S-methylcysteine sulphoxide (SMCO) & N-propyl disulphide / thiosulphates

Common sources:

- SMCO: *Brassica* spp. (kale, rape, canola, cabbage, swede)
- N-propyl disulphide & thiosulphates: *Allium* spp. (onions, garlic)

Pathology:

Clinical pathology

- Heinz body anaemia, ± eccentrocytes (erythrocytes with haemoglobin contracted to one side of the cell)
- ± azoturia
- ± increased concentrations of liver-associated enzymes & bilirubin

Necropsy

- haemoglobinuria (dark red-brown urine in bladder; red-brown-black kidneys)
- ± jaundiced carcase
- ± strong small of onions from the carcase (if fed onions)

Histopathology

- haemoglobinuric nephrosis
- ± periacinar hepatocyte necrosis (hypoxia)
- splenic haemosiderosis

Diagnosis:

- access + Heinz bodies in erythrocytes
- assays for SMCO in plants are available in some laboratories

Indospicine

Common sources:

- Indigofera spicata (creeping indigo)
- Indigofera linnaei (Birdsville indigo)
- indigofera suffruticosa

Cattle, sheep: hepatotoxicity, abortion. Feeding experiments in Hawaii and Fiji caused abortions in sheep and cattle; rations contained 25-50% *Indigofera spicata.*

Toxalbumins (lectins)

Common sources:

- seeds of *Ricinus communis, Abrus precatorius, Robinia pseudoacacia*
- bark of *R. pseudoacacia*

Pathology:

- severe **gastroenteritis**
- ± liver & kidney degeneration/necrosis

Diagnosis: syndrome + access

GLYCOSIDES

Cyanogenic glycosides [sources of Cyanide (HCN) = Prussic acid]

Common sources:

- Acute poisoning
  - *Sorghum* spp. (sorghum)
  - Numerous other plants
- Chronic poisonings
  - *Sorghum spp.*
  - *Cynodon spp. – congenital goitre, sheep*
  - *Sorghum sudanense and hybrids – foetal arthrogryposis*

Pathology:

Acute poisoning (sudden death):

- **bright red blood**
- **non-specific** lesions related to respiratory and circulatory failure such as agonal haemorrhage and congested organs.
- a fleeting "bitter almond" odour may be noticed immediately on opening the stomach. Benzaldehyde, a break-down product of amygdalin (the cyanogenic glycoside in bitter almond (*Prunus amygdalus* var. *amara*) kernels and some other plants), is responsible for the odour. Benzaldehyde is readily oxidised in air to benzoic acid, rendering the odour fleeting. About 40-60% of humans are thought genetically unable to detect the odour.
- leucoencephalomalacia may occur in some of the rare cases where animals (including humans) survive sufficiently long.

Posterior ataxia & urinary incontinence:

- cystitis
- **spinal cord white matter degeneration**

Sheep grazing *Sorghum* that develop a variant neurological syndrome have pathology including axonal spheroids throughout the brain (most numerous adjacent to the cerebellar roof nuclei) and focal Wallerian degeneration in cerebellar white matter and spheroids in ventral grey matter of cervical cord. Mild neurological damage has been produced experimentally in the

brainstem, spinal cord and cerebellum (mild axonal swelling, gliosis, reduction in Purkinje cell numbers) by PO administration of 1.2 or 3.0 mg KCN/kg/day for 5 months.

Foetal arthrogryposis:

- fixation of foetal limb joints (arthrogryposis)
- Wallerian degeneration of foetal white matter of spinal cord, medulla, pons and cerebellum
- cerebral oedema

Diagnosis:
Acute poisoning (sudden death):

- Assay suspected source plants for HCN potential
- Assay skeletal muscle, liver and rumen contents (in descending order of usefulness) for HCN. Continued microbial activity in rumen samples will produce a negative result very soon after death.

A rapid field spot test, the **picric acid test for free HCN** (also called the Henrici test), can be used on **plants, rumen contents, liver or skeletal muscle**. The test papers are yellow, turning brown-red if positive (details are given below). Using these spot tests, which do not include an exogenous β glucosidase, on hays may indicate a falsely small HCN potential because haymaking can destroy the enzyme but not the glycoside. This *caveat* also applies to the testing of plants that do not naturally contain β glucosidase.

The smallest concentration *in plants* to suggest toxicity is 200mg HCN/kg plant dry matter (0.02%) (> 7.5 μmol/g fresh weight). Plant material subjected to assay for HCN production **must be unwilted at the time of testing**. When submitting plants to a laboratory for testing, collect the whole plant with a clump of soil enclosing the roots; wrap the root ball and soil in damp paper and send the whole plant to arrive as soon as possible to try to prevent wilting. Carefully and gently packing it into an insulated container with freezer bricks is acceptable for short transport periods.

Muscle samples can be usefully analysed up to 20 hr after death, liver samples 4-5 hr and rumen samples < 1 hr. The smallest concentration *in skeletal muscle* suggestive of toxicity is 0.63 μg HCN/g tissue.

Blood cyanide concentrations in a cow that survived poisoning have been reported as 60 – 173 μ*M*. Reference ranges for HCN in cattle determined by GC-MS method are: serum <0.7 to 35.0 μ*M*; rumen fluid < 0.7 to 28.1 μ*M*. In humans, cyanide concentrations of > 40 μ*M* in blood are considered toxic and 100-200 μ*M* are considered lethal.

Foetal arthrogryposis:

- pathology + access
- differentiate from viral and genetic aetiologies

Picric acid spot test for cyanide (Henrici test) in rumen contents or plants

Test papers

0.5 g sodium bicarbonate + 0.5 g picric acid dissolved in 100 ml distilled water - solution keeps for 4 months if well-stoppered and kept cool.
Saturate strips of filter paper in the solution and allow to almost dry before use.
Strips may be dried and stored in a stoppered container, but lose sensitivity in about 1 week. Moisten before use.

Procedure

Place rumen contents in a flask and add enough water to make contents slushy,
OR a couple of grams of moist shredded plant material in the flask and add 4 drops of chloroform.
Fix a picric acid filter paper strip above the sample by jamming it into the neck of the flask with a stopper - do not let the paper touch the sides of the flask or the sample. Run a negative control sample (a blank) simultaneously. Incubate in a warm place.
Positive test = red/brown to violet colour. Incubate test for at least 24 h before declaring it negative.

Cardiac glycosides

Common sources:

- *Nerium oleander* (oleander)
- *Cascabela thevetia* [= *Thevetia peruviana*] (yellow oleander)
- *Cryptostegia grandiflora* (rubber vine)
- *Bryophyllum* spp. (mother-of-millions)
- *Homeria* spp. (cape tulips)
- *Adonis microcarpa* (pheasant's eye) - plants in hay, seeds in grain
- *Digitalis purpurea* (foxglove)
- *Corchorus olitorius* (jute) - seeds in grain

+ others

Pathology:

- increasing plasma urea, creatinine and glucose concentrations with time after ingestion
- **cardiomyopathy** (multifocal degeneration & necrosis). Lesions can be expected in animals that survive for over 24 hours. Animals dying earlier may not have had time for lesions to develop to a stage that is detectable microscopically.
- **haemorrhage into alimentary tract** or congested, fluid-filled alimentary tract
- pulmonary atelectasis (associated with dyspnoeic cases) and/or pulmonary oedema
- omasal ulceration (in cases surviving several days - related to uraemia)

Diagnosis:

- Access to plants, including seeds
- ± recognise plant fragments in rumen contents
- Cardiac arrhythmia + diarrhoea + azotaemia

- Myocardial histopathology (collect multiple samples: both ventricles, both atria & interventricular septum)
- Assay stomach contents/faeces for some toxins [limited availability of chromatographic assay: TLC, HPLC]
- Radioimmunoassay has been used to confirm the presence of cardiac glycosides in serum of intoxication cases. In human medicine this technique is used to monitor the therapeutic use of cardenolides and medical laboratories may provide assays in veterinary cases.

Ptaquiloside

Common sources:

- *Pteridium esculentum* (bracken)
- *Cheilanthes sieberi* (mulga or rock fern)

Pathology:

'Bracken' poisoning:

- thrombocytopaenia
- leucopaenia
- anaemia
- multiple haemorrhages (subcutaneous, intramuscular, subserosal, subepicardial etc.)
- ulceration of intestine (over Peyer's patches)
- ± oedema of larynx (calves)
- ± liver septicaemic infarcts

Bovine enzootic haematuria:

- anaemia
- usually normal leucocyte and platelet numbers
- various bladder mucosa lesions: chronic cystitis with various neoplasms. Haemangiomas, haemangiosarcomas or both are usually present. Transitional cell carcinomas, adenomas, adenocarcinomas or other types of neoplasms may also be present.

Bright blindness: Not reported in Australia. Sheep in UK only.

- leucopaenia
- retinal atrophy (loss of rods & cones)

Alimentary neoplasia: Not reported in Australia. Cattle in South America & UK

- Squamous cell carcinoma of the pharynx and oesophagus

Diagnosis:

'Bracken' poisoning:

- access to above fern species
- haemorrhagic disease
- + thrombocytopaenia, leucopaenia
    - ❖ live: blood smear assessment
    - ❖ dead: bone marrow histopathology [Hint: take sample from the sternum rather than a rib or long bone]

Bovine enzootic haematuria:

- live: access to ferns + clinical syndrome (microurine to differentiate haematuria from haemoglobinuria or other pigments). Transrectal ultrasonography of the urinary bladder may be an adjunct to diagnosis.
- dead: bladder pathology

Bright blindness:

- Syndrome + chronic bracken access

Alimentary neoplasia:

- Syndrome + chronic fern access

Diterpenoid (kaurene) glycosides - atractyloside, carboxyatractyloside, parquin, carboxyparquin & wedeloside

Common sources:

- Cestrum parqui (green cestrum)
- Xanthium occidentale (Noogoora burr) - only burrs or cotyledonary leaves toxic
- Wedelia asperrima (sunflower daisy)

Pathology:

- Ruminants: Acute hepatic necrosis (q.v.)

Diagnosis:

- Access to plants; plants detected in stomach contents
- Ruminants: Acute hepatic necrosis (q.v.)

Plant calcinogenic glycosides (cholecalciferol, vitamin D_3)

Cestrum diurnum, *Solanum torvum*, *Solanum linnaeanum* and *Trisetum flavescens* occur in Australia, but poisoning of this sort has not been reported. *Solanum torvum* (devil's fig) has been reported to produce the syndrome in New Guinea.

Pathology:

- serum Ca & P ↑ 20-25%
- anaemia
- anasarca, ascites
- calcification of blood vessels & endocardium, pleura, lungs, tendons & ligaments

Diagnosis: access + pathology

Glucosinolates

Common sources:

Plants in the Family Brassicaceae -

- Brassica spp.
- Sinapis spp.
- Raphanus raphanistrum (wild radish)
- Rapistrum rugosum (turnip weed)

Pathology:
Goitre
- Hypertrophy and hyperplasia of the thyroid glands

Atypical interstitial pneumonia
- Pulmonary oedema and emphysema (interstitial)
- ± subcutaneous emphysema
- ± liver necrosis (presumably hypoxic in origin)

Rumenitis
- Acute rumenitis with marked oedema of the wall attributed to damage to submucosal and intramuscular blood vessels.

Diagnosis:
Goitre
- Syndrome + pathology + access to sources either directly or through placenta/milk

Atypical interstitial pneumonia
- Syndrome + access to lush source plants

Rumenitis
- Differential diagnosis should include other forms of chemical rumenitis such as inorganic arsenic, cucurbitacins (*q.v.*)

Aliphatic nitro compounds (Nitrotoxins)

Toxicity not recorded in Australia to date.
Common sources (North America): *Astragalus* spp., *Lotus* spp., *Coronillia* spp., *Indigofera* spp. + others (some of which occur in Australia)

Pathology:
Acute intoxication
- pulmonary oedema, hydrothorax, tracheal petechiae
- methaemoglobinaemia

Chronic intoxication (ruminants)
- congested liver
- ulceration of cardiac region of abomasum
- pulmonary emphysema, bronchoconstriction ± bronchopneumonia
- Wallerian degeneration of spinal cord & peripheral nerve white matter
- focal brain haemorrhage

Diagnosis:
- access + syndrome + pathology
- assay methods available for miserotoxin, NPA and NPOH in plants

Cynanchosides

Common source (suspected):
- Sarcostemma brevipedicellatum [= Sarcostemma australe] (caustic vine, caustic creeper, pencil caustic)

Pathology: no significant lesions reported

Diagnosis: access + syndrome

Dihydroxycoumarin (dicoumarol)

Common sources:
mouldy hays/silage of

- *Melilotus* spp. (sweet clovers)
- *Anthoxanthum odoratum* (sweet vernal grass)

Pathology

- *↑↑ prothrombin time, APTT & clotting time*
- *platelet numbers are normal*
- *anaemia*
- *extensive haemorrhages & haematomas*

Diagnosis: clinical pathology; serum & feed dicoumarol assay

Daphnoretin (presumed toxin in Wikstroemia indica*)*

Wikstroemia indica (tie bush) [Family Thymeleaceae] is suspected of producing a haemorrhagic syndrome in farmed deer in Queensland on one occasion. Widespread haemorrhage occurred, but circulating platelet and leucocyte numbers remained normal. Daphnoretin has been isolated from the plant stems (Kato *et al.* 1979).

Furanocoumarins (furocoumarins, psoralens)

Common sources:

- *Ammi majus* (bishop's weed)
- *Apium graveolens* (celery) ± infected with microbes
- *Petroselinum crispum* (parsley)
- *Pastinaca sativa* (parsnip) ± infected with fungus

Pathology:

- Photosensitisation
- Corneal oedema/keratoconjunctivitis is a feature of furanocoumarin photosensitisation (uncommon in other kinds)
- Skin vesication or bulla formation is seen in white pigs (snout, forelegs), but has not been described in ruminants. It may possibly occur on the muzzle from direct contact with source plants.

Diagnosis:
skin lesions of photosensitisation (± corneal oedema) + absence of liver damage determined by clinical examination for jaundice and confirmed by clinical chemistry (liver function tests on serum or plasma).

Phyto-oestrogens

Common sources:

- isoflavones in *Trifolium subterraneum* (subterranean clover), *Trifolium pratense* (red clover)
- coumestans in *Medicago* spp. (medics including lucerne)

Pathology:
Classical clover disease (ewes)

- uterine prolapse

- hydrops uteri
- cystic hyperplasia of endometrium
- permanent `defeminisation' after 1-2 years high intake → reduction in uterine size, metaplasia of mucosa of cervix →↓ flock fertility

Classical clover disease (wethers)

- enlarged teats
- bulbo-urethral gland cysts
- blockage of urethra → bladder rupture
- Diagnosis: syndrome + access

TERPENES AND TERPENOIDS

Furanosesquiterpenes

Common sources:

- Eremophila deserti [= Myoporum deserti] (Ellangowan poison bush)
- some Myoporum spp. (boobiala, water bush)

Pathology: See acute hepatic necrosis

- Lesions may vary in location within the hepatic acinus from periacinar to periportal depending on the metabolic state of the xenobiotic biotransformation enzyme systems.

Diagnosis: See acute hepatic necrosis

Lantadenes (pentacyclic triterpenes)

Common source:

- Lantana camara - toxic flower-colour forms: red & orange, Helidon white, pink (only north of Rockhampton)

Pathology

- *jaundice*
- *swollen, yellow-orange liver*
- *severe distension of gall bladder with watery bile, sometimes to as much as 30 times normal, due to smooth muscle paralysis.*
- *swollen pale kidneys (nephrosis)*
- *colon contents dehydrated*

Andromedotoxins (grayanotoxins)

Common sources:

- *Rhododendron spp. (rhododendrons, azaleas)*

Pathology:

- *gastroenteritis*
- *± aspiration pneumonia*

Diagnosis:

- *syndrome + access*
- *assay rumen contents/faeces [limited availability of test]*

Irritant diterpenoids of Pimelea *spp. – simplexin (& huratoxin)*

Syndrome names:

- *Pimelea* poisoning of cattle
- St.George disease
- Marree disease

Common sources:
- *Pimelea trichostachya*
- *Pimelea simplex*
- *Pimelea elongata*

Pathology:
- dilation of right ventricle
- hydrothorax
- subcutaneous oedema of brisket and submandibular space
- liver: peliosis hepatis = swollen blue-black liver engorged with blood in massively dilated sinusoids
- capillary dilation in adrenal glands and kidney

Diagnosis:
- Diagnosis is based on clinical syndrome + pathology. It is important to note that the responsible Pimelea sp. is likely to be absent from pastures when animals are affected; winter plant growth precedes summer poisoning.

Irritant diterpenoids of Families Thymeleaceae & Euphorbiaceae

Common sources:
- *Pimelea* spp. (flaxweeds)
- *Euphorbia* spp. (spurges)
- *Jatropha* spp.

Pathology:
- *alimentary tract congestion*
- *haemorrhagic, necrotising gastroenteritis*

Diagnosis: syndrome + access

Cucurbitacins (tetracyclic triterpenes)

Common sources:
- *Cucumis spp.*
- *Citrullus spp.*

Pathology:
- *congestion/haemorrhage of alimentary tract*
- *oedema of forestomach walls*
- *seeds numerous in rumen contents*
- *microscopic rumenitis*
- *± focal myocardial degeneration & necrosis*

Diagnosis: syndrome + access

Meliatoxins (tetranortriterpenes)

Common sources:

- *Melia azedarach var. australasica (white cedar) - fruits of some trees toxic*

Pathology:

- *severe gastroenteritis*
- *fatty degeneration of liver & kidneys; scattered or periacinar hepatocyte necrosis in experimental cattle*
- *necrosis of lymphoid follicles in alimentary tract*
- *myodegeneration and necrosis of skeletal muscles were reported in experimental cattle*

Diagnosis: syndrome + access

LIPIDS, OILS, GLYCERIDES, FATTY ACIDS

Unsaturated fatty acids, particularly crepenynic acid

Common sources:

- *Ixiolaena brevicompta seedheads*

Pathology:

- *skeletal muscle pallor*
- *muscle fibre degeneration* and necrosis in skeletal muscle and heart

Diagnosis:

- *pathology + access*
- *identify seeds in rumen contents*

Isocupressic acid (bicyclic labdane diterpene acids) and/or Vasoactive lipids

Common sources:

- *Pinus ponderosa (Ponderosa pine)*
- *Cupressus macrocarpa (Monterey cypress, macrocarpa*)

Pathology:

- *late-term abortion*
- *serosal haemorrhages, oedema and flaccidity of uterus; no gross lesions in the foetus*
- *histologically, a profound constriction of the caruncular arterial bed in the uterus*
- *± cerebral leucoencephalomalacia in bovine foetus - ? anoxia*

Diagnosis: syndrome + access

Persin

- Common sources:
- *Persea americana* (avocado) - Guatemalan & Guatemalan x Mexican hybrid cultivars (not pure Mexican)

Pathology:
Cardiotoxic syndrome:

- cardiac muscle necrosis
- hydrothorax
- pulmonary oedema

Mammary gland syndrome:

- sterile mastitis with necrosis of the acinar epithelium of the mammary gland

Diagnosis: syndrome + access

Protoanemonin

Common sources:

- *Ranunculus spp.*

Pathology:

- *inflammation of the alimentary tract, sometimes with ulceration*

Diagnosis:

- *access + syndrome*
- *detection of plants* in rumen

PHENOLIC COMPOUNDS

Gossypol

Common sources:

- *pigment glands of cotton seeds (Gossypium spp.)*

Pathology:
Cardiac and associated effects:

- cardiomyopathy (cardiac dilation ± pale myocardial streaking; histologically cardiac muscle necrosis)
- pulmonary oedema, fluid in thorax and abdomen
- periacinar hepatic congestion and necrosis
- mild nephrosis

Reproductive effects:

- testicular cessation of spermatogenesis

Diagnosis:

- access + pathology
- assay feed for free gossypol (note that the relevant feed batch may no longer be available)

Dianthrone derivatives (hypericin, fagopyrin)

Common sources:

- Hypericum perforatum (St.John's wort)

Pathology:

- primary photosensitisation (q.v.)

Diagnosis:

- syndrome + plant access

Steroidal or lithogenic saponins

Common sources:

- Panicum spp. (French millet, Bambatsi panic, etc.)
- Brachiaria spp. (signal grass)
- Tribulus terrestris (caltrop)

Pathology:

- ± jaundice
- ± swollen yellow-orange liver
- diffuse hepatocellular hydropic degeneration and hyperplasia of smooth endoplasmic reticulum indicative of prolonged cholestasis.
- crystals in hepatocytes, small bile ducts & Kupffer cells
- ± crystals in renal tubules
- ± crystals in macrophages are reported in intestinal submucosa, liver, spleen, mesenteric and hepatic lymph nodes in cases of weight loss without photosensitisation.

Diagnosis: access + pathology

Tannins (hydrolysable)

Common source:

- Terminalia oblongata ssp. oblongata (yellow-wood)
- Quercus spp. (oaks)

Pathology:

Oak poisoning

- serum ↑ urea & creatinine, ↑ protein, Na, Cl & Ca
- perirenal oedema
- pale swollen kidneys - tubular necrosis
- alimentary mucosal erosions/ulcers
- ± numerous acorns in rumen contents

Yellow-wood poisoning

Acute toxicity

- multiple erosions of abomasal mucosa
- swollen greenish-grey kidneys
- swollen pale to orange liver

Chronic toxicity

- fibrotic greenish-grey kidneys - pigment in nephrotic kidneys
- distended thickened bladder
- abomasal ulcers

Diagnosis: access + pathology

Methylazoxymethanol (MAM)

Common sources:
Cycads in the genera

- Cycas
- Macrozamia

Pathology: See acute hepatic necrosis

Diagnosis: See acute hepatic necrosis

Stypandrol

Common sources:

- Stypandra glauca (blind grass, Candyup poison, nodding blue lily)

Pathology:

- vacuolation (oedema) of CNS white matter → resolves in 6-8 weeks
- optic nerve axonal degeneration → complete atrophy, sclerosis
- 12 weeks → retinal atrophy

Diagnosis: access + histopathology (eye, optic nerve, brain)

Galegine

Common sources:

- Galega officinalis (goat's rue, French lilac)
- Verbesina encelioides (crownbeard)
- Schoenus asperocarpus (poison sedge)
- Schoenus rigens

Pathology:

- fluid from nostrils
- severe pulmonary oedema & hydrothorax
- thoracic fluid clots rapidly on exposure to air

Diagnosis: access + pathology

Tetrahydrocannabinol - **Cannabis sativa** *(marijuana)*

Pathology: Nil

Diagnosis:

- history often incomplete or misleading
- ± identify plant in rumen contents
- ± assay plasma, urine for THC (only at certain laboratories)

MECHANICAL DAMAGE BY PLANT PARTS

Dittrichia graveolens *enteritis (mechanical damage)*
Pathology:

- dark bristles embedded in the intestinal mucosa (grossly visible)
- intestinal wall oedema & haemorrhage with multiple white nodules
- pyogranulomatous enteritis; histologically, bristles + bacteria in the mucosa and submucosa with neutrophils, macrophages & foreign body giant cells

Diagnosis:

- differentiation from common causes of diarrhoea is required
- access + intestinal pathology/histopathology

Grass awns
Strictly-speaking a mechanical injury, not an intoxication, but included for convenience.
Examples include:

- Triticale (variously classified as X *Triticosecale,* X *Triticale* or *Triticum aestivum* x *Secale cereale*) fed as hay after seedhead maturation causing stomatitis through the penetration of the buccal mucosa by the awns on the seeds
- *Stipa neesiana* (Chilean needle grass) [present in NSW] seed awns penetrate the skin causing subcutaneous and intramuscular abscesses and granulomas.

PLANTS WITH UNKNOWN OR UNCHARACTERISED TOXINS
[Plants are listed by syndrome/organ system affected, then by plant family]

LUNG
Lung – Family Rutaceae
Zieria arborescens *(stinkwood)*
Pathology

- pulmonary oedema & emphysema
- degeneration of pulmonary arteriole walls

LIVER

Liver – Family Asteraceae
Argentipallium blandowskianum *(woolly everlasting)*
Pathology: As for acute hepatic necrosis syndromes (*q.v.*)
Diagnosis: As for acute hepatic necrosis syndromes (*q.v.*)
Liver – Family Poaceae

Cynosurus echinatus (*rough dog's tail grass)-associated liver necrosis*
Pathology:
As for acute hepatic necrosis syndromes (*q.v.*).

Clinical pathology results are variable, often including increased activities of serum GLDH, γGT and an increased concentrations of bilirubin; less

frequently, increased values for AST, creatinine, urea, chloride, bicarbonate, phosphorus and magnesium may occur (Gunn & Clarke 2003).

Necropsy reveals an enlarged, grey, friable liver with massive distension of the gall bladder which has thickened walls and contains black bile. Subcutaneous oedema and jaundice occur. Ecchymotic or petechial haemorrhages occur in many tissues including the subcutis, omentum, peritoneum, gall bladder, epicardium, myocardium abomasum, duodenum and kidney capsules.

Massive hepatocyte necrosis has been reported in Tasmanian and South Australian cases, severe acute periportal hepatocyte necrosis with early biliary ductular hyperplasia and necrosis of portal veins is more typical of South Australian cases and necrosis of scattered individual and small groups of hepatocytes with no distinct zonal pattern was seen in the Western Australian case.

Diagnosis:
As for acute hepatic necrosis syndromes (*q.v.*). Differential diagnoses should include sporidesmin (*q.v.*) toxicity and other causes of secondary photosensitisation (*q.v.*). Clinical and environmental examinations should be supplemented by clinical pathology and liver biopsy of affected and in-contact animals, as currently, confirmation of cases requires histopathology as well as other evidence.

Liver – Family Ulmaceae

Trema tomentosa *(poison peach)*
Pathology: acute periacinar hepatic necrosis
Diagnosis: As for acute hepatic necrosis syndromes (*q.v.*)

KIDNEY

Kidney – Family Caesalpiniaceae
Schotia brachypetala *(drunken parrot tree, boer bean)*
Associated with nephrosis in cattle which browsed on flowering branches at Maryborough in September 1998. 80 2-3 year-old Brahman cattle introduced to a paddock with branches of *S. brachypetala* overhanging the fence line; onset of illness 2 weeks after introduction; 6 died; clinical signs – loss of weight, crusty nasal exudate, pale mucous membranes, tarry faeces; clinical pathology (2 steers) – dehydration with either slight leucopaenia or slight absolute neutrophilia + increased concentrations of creatinine, urea & Mg, decreased Ca; necropsy (1 steer) – pale kidneys, haemorrhages throughout the alimentary tract, swollen liver, congested lungs; histopathology – severe subacute diffuse necrosis of epithelium of proximal renal cortical tubules, no oxalate crystals detected.

Kidney – Family Lythraceae
Lythrum hyssopifolia *(lesser loosestrife)*
Pathology:
Clinical pathology
- ↑ serum creatinine & urea ± ↑ serum bilirubin & liver-associated enzymes (including GLDH)

Necropsy
- scattered petechial haemorrhages (subcutis, kidneys, diaphragm, thoracic wall, omentum, mediastinum, heart)
- perirenal oedema, mild ascites
- pale swollen kidneys
- ± jaundice
- ± tan or orange-coloured swollen liver

Histopathology
- renal tubular necrosis: coagulation necrosis of tubular epithelium, hyaline casts
    - ❖ interstitial fibrosis & loss of tubules (cases with access > 5 days)
    - ❖ dilated ascending loops of Henle & distal convoluted tubules + some tubular regeneration (cases with access > 10 days)
    - ❖ ± slight to moderate haemoglobinuric nephrosis and/or renal haemosiderosis
- ± hepatocellular damage
    - ❖ ± periacinar or mid-zonal hepatocyte necrosis + biliary hyperplasia
    - ❖ ± hepatocyte fatty change
    - ❖ ± individual hepatocyte necrosis

Diagnosis: access + pathology

NERVOUS – ATAXIA

Nervous – Ataxia – Families Cycadaceae & Zamiaceae
Cycads
Common sources:
- *Cycas* spp.
- *Macrozamia* spp.
- *Bowenia* spp.

Pathology:
- **Degeneration of spinal cord white matter** occurs in the fasciculus gracilis, dorsal spinocerebellar & corticospinal tracts.
- Chronic liver damage (fibrosis, enlarged hepatocytes) may result in ataxic cattle from the action of MAM

Diagnosis: access + pathology

Nervous – Ataxia – Family Fabaceae
Chamaecytisus proliferus *(tagasaste)*

Pathology:
Congenital leucoencephalopathy:

- histological lesions of CNS white matter: vacuoles and faintly eosinophilic plaques 40-50 μm in diameter (H&E), plaques slightly pink (PAS) or non-staining (LFB) with special stains; some plaques contained peripheral nuclei resembling those of oligodendroglia; plaques contained normal axon segments demonstrated in LFB-Holmes silver stained sections; occasional microglial phagocyte in empty axonal tubes but no other inflammation; glial cell reaction limited to occasional isolated dense shrunken microglial nuclei near injured axons
- moderate-severe lesions of white matter in internal capsule, midbrain, medulla and cerebellum; severity increasing towards the mid and hindbrain
- lesions present in optic tracts and chiasma, but not optic nerves or retina
- severe lesions in spinal cord white matter, but not cauda equina or peripheral nerves
- lesions similar to those of progressive ataxia of Charolais cattle in which signs occur at 8-24 months of age and progress over 1-2 years
- ultrastructure of CNS lesions: plaques = intramyelinic expansions containing numerous vesicular membranous profiles and myelin bodies dispersed throughout a granular matrix possibly containing remnants of microtubules; remnant myelin sheaths around these foci and very thin with only a few lamellae. Around the plaques, numerous glial cells and their processes are similarly affected with numerous vesicular profiles; oligodendrocytes and possibly astrocytes affected. Some smaller diameter myelinated fibres have periaxonal vesiculation, apparently from the inner lamellae of myelin sheathes. Some brains have focal plaques of disorganised and tangled myelin.

Diagnosis:
Congenital leucoencephalopathy: syndrome + dam access

Nervous – Ataxia – Family Iridaceae
Romulea rosea *var.* australis *(onion grass, Guildford grass)*
Pathology:

Romulosis (reproductive effects)
fluid accumulation noted in non-pregnant uteri

Romulosis (ataxia/paralysis)
Histological lesions attributed to this disease included degeneration of myelin with axonal swelling and fragmentation, particularly of motor nerve roots. Peripheral nerves were less affected. There was usually a light infiltration of lymphocytes (rarely more than one cell layer deep)

about blood vessels in the brain stem. There was mild swelling of axons and nerve sheaths in the ventro-medial columns of the spinal cord white matter. In more chronic cases, macrophages containing golden-brown lipochrome pigment were found in perivascular spaces in the brain stem, cerebellar white matter and spinal cord. Rarely, there was also fine vacuolation of the white matter of the cerebrum, brain stem and cerebellum.

Phytobezoars
Bezoars in stomach/abomasum or blocking the tract downstream of these sites.

Diagnosis:
Syndrome + association with a pasture dominated by the plant.

Nervous – Ataxia – Family Liliaceae
Trachyandra divaricata *(branched onion weed)*
Pathology:

- no lesions at necropsy
- intense **lipofuscin pigment granule deposition in neurones** (brain, cord, ganglia)
- spheroids in spinal cord grey matter and brain stem
- axonal degeneration, demyelination, lipid storage by Schwann cells

Diagnosis: histopathology

Nervous – Ataxia – Family Mimosaceae
Prosopis juliflora *(mesquite) – neuronal vacuolation in cranial nerve nuclei*
No cases recorded in Australia to date.
Pathology:

- rumen full of mesquite pods & seeds
- denervation atrophy of masseter, temporal, hyoglossus, genioglossus, styloglossus, medial pterygoid, lateral pterygoid and mylohyoid muscles: marked variation in muscle fibre diameter, some myofibre degeneration, some fibrous replacement
- spongiosis & gliosis of CNS
- trigeminal motor nuclei neuronal lesions
- loss of Nissl substance
- fine cytoplasmic vacuolation of pericaryon or one pole of cell
- trigeminal ganglion lesions
- loss of neurones
- proliferation of satellite cells & neuronophagia
- Wallerian degeneration in trigeminal & mandibular nerves

Diagnosis:

- prolonged access + pathology
- differentiate from transmissible spongiform encephalopathies, lysosomal storage diseases, swainsonine & calystegine intoxication

Nervous – Ataxia – Family Xanthorrhaceae
Xanthorrhoea *spp. (grasstrees) – posterior ataxia syndrome*
Species associated with toxicity:

- *Xanthorrhoea johnsonii* (northern forest grasstree - Q)
- *Xanthorrhoea fulva* [= *X. resinosa, X. hastile*] (swamp grasstree - Q)
- *Xanthorrhoea australis* (yacca - Tas)
- *Xanthorrhoea quadrangulata* or *Xanthorrhoea semiplana* (SA)

Pathology:
± degeneration of spinal cord, brain stem and cerebellar white matter. Lesions are usually slight.

Diagnosis: syndrome + access

ALIMENTARY

Alimentary – Family Fabaceae
Castanospermum australe *(Moreton Bay chestnut, black bean)*
Pathology:

- cytoplasmic vacuolation of 1-5% of lymphocytes in peripheral blood; cytoplasmic PAS-positive granules present in 78-92% of lymphocytes (15-20% positive in unexposed animals)
- haemorrhagic gastroenteritis
- ± focal myocardial necrosis
- ± nephrosis (vacuolation of renal cortical tubular epithelium, hyaline casts, dilation of collecting ducts)

Diagnosis: syndrome + access to ripe seeds in large amounts

Alimentary – Family Phytolaccaceae
Phytolacca *spp.*
Phytolacca dioica (packalacca, bella sombra): A tree native to South America with separate sexes; cultivated for shade and fodder in south-eastern Australia, NSW, Vic; Leaves are very palatable to cattle. Ingestion of fruit & leaves by cattle and fowls in Australia has been associated with enteritis.

Alimentary – Family Poaceae
Avena sativa *(oats) – "red-tipped" or "rusty" oats crops*
Sources: stressed *Avena sativa* (oats) used as fodder crops

Pathology:
Cattle

- ↓ plasma concentrations of P
- lesser decreases in plasma Ca, Mg
- ruminal acidosis: rumen pH of 5 or less and urine pH of less than 7; serum D-lactate concentrations increased (9.18-15.15 mmol/L in 3 cows; normal <0.4)
- no necropsy findings reported

Diagnosis:

- access to "red-tipped" oats + syndrome
- rule out nitrate-nitrite toxicity, hypomagnesaemia

Pennisetum clandestinum *(kikuyu grass) – "kikuyu poisoning"*
Pathology:
- dehydration (↑ PCV)
- ↑ serum urea & creatinine, ↓ serum Cl
- ruminal contents fluid (pH may be acid)
- ruminal and abomasal distension & hyperaemia
- histological lesions
  - ❖ **microvesication of forestomach mucosa** with neutrophil infiltration
  - ❖ **renal tubular necrosis**

Diagnosis: syndrome + access

MUSCLE

Muscle – Family Caesalpiniaceae
☑ Senna *spp. [= Cassia spp.]*
Sources:
- *Senna occidentalis* (L.) Link [= *Cassia occidentalis* L.] (coffee senna, ant bush)
- *Senna obtusifolia* (L.) H.S.Irwin & Barneby [= *Cassia obtusifolia* L.] (sicklepod, Java bean)
- *Senna didymobotrya* (Fresen.) H.S.Irwin & Barneby [= *Cassia didymobotrya* Fresen.]

Pathology:
- ↑↑↑ serum creatine phosphokinase & AST concentrations
- myoglobinuria (red urine)
- skeletal & cardiac muscle pallor
- necrosis of muscle fibres

Diagnosis:
- pathology + access
- differential diagnoses include haemolytic diseases (babesiosis, Cu poisoning)

Muscle – Family Malvaceae
Malva parviflora *(mallow, marsh mallow, small-flowered mallow)*
Pathology:
- ↑ CPK , AST, urea, creatinine
- skeletal muscle oedema, degeneration ± necrosis (particularly in large muscle groups of hindlimbs)
- multifocal myocardial necrosis
- ± myogobinuric nephrosis
- Vitamin E & Se concentrations normal
- no CNS lesions detected

Diagnosis: access + pathology

BONE

Bone – Family Apiaceae
Trachymene *spp. (wild parsnips)*
Sources:

- *Trachymene ochracea* (wild parsnip)
- *Trachymene glaucifolia* (wild parsnip)
- *Trachymene cyanantha* (wild or blue parsnip)

Pathology:
Bent leg of lambs

- lateral and medial deviation of carpal joints
- posterior peromelia (deformity of the limbs) - reduction or absence of bones distal to metatarsals
- irregularity of epiphyseal plates

Sudden death, Diarrhoea

- No pathology has been described.

Diagnosis: syndrome + access

SKIN AND APPENDAGES

Skin & Appendages – Family Fabaceae
Vicia *spp. (vetch toxicity)*
Sources:

- *Vicia villosa* (woolly-pod vetch)
- *Vicia benghalensis* (Popany vetch)

Pathology:

- all lesions **eosinophilic granulomas**, often associated with blood vessels
- dermatitis (head, neck, shoulders, tail base, udder, perineum, ± trunk, ± limbs)
- pale foci in kidneys, heart
- enlarged adrenal glands & lymph nodes
- ± jaundice

Diagnosis:

- syndrome (pathology) + access
- differential diagnosis: photosensitisation, dermatomycosis, dermatophilosis
- similar syndrome seen in cattle fed citrus pulp

PHOTOSENSITISATION

Clinical signs (various combinations depending on species and toxin)

- abnormal **behaviour**
  - restlessness
  - head shaking
  - rubbing, scratching, kicking affected parts
  - seeking shade

- effects on the eyes
  - blepharospasm / photophobia
  - ocular discharge / conjunctivitis
  - corneal oedema / keratitis (`blue eye')
- skin
  - drooping swollen ears
  - swollen lips, head
  - raw muzzle
- skin **erythema**
- skin **necrosis**
  - ear tips curl up, lips become immobilised

ACUTE HEPATIC NECROSIS

Common effects of acute hepatotoxins from plants, mycotoxins, cyanobacteria, macrofungi and sawfly larvae

Pathology:

- liver-associated serum enzymes (AST, GLDH), ↑ serum bilirubin
- ± jaundice
- liver swollen, congested, zonally mottled
- **coagulation necrosis of hepatocytes** (periacinar; periportal; rarely midzonal), ± haemorrhage
- gall bladder oedema
- haemorrhage in the lower alimentary tract (?portal hypertension) and elsewhere (?exhaustion of clotting factors in damaged liver)

MYCOTOXINS (TOXINS OF FUNGAL ORIGIN)

MOULDS

Aflatoxins

Common sources:

- *Aspergillus flavus* growing in carbohydrate-rich feeds: peanuts, grain, bread

Pathology:

- Lesion manifestation depends on dose and duration od intake
- 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

Phomopsins

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

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
- 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.

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 <0.67□g/g d.m.; Se responsive)

Sporidesmin
Syndrome: facial eczema
Common source: spores of *Pithomyces chartarum* on *Lolium* sp. pasture litter

Pathology:

- Liver: cholangitis, fibrosis
- Severe chronic cases produce complete atrophy of the left liver lobe. The 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 is worse in left lobe leading in turn to portal fibrosis, reduced blood flow to worst-affected

parenchyma, deprivation of hepatotrophic factors and thus atrophy of the left lobe to a much greater extent than the right lobe.

Diagnosis:

- Spore count on pasture: > 70,000 spores/g pasture litter is hazardous. Spores may be detected in scrapings of the exudate from the gland just near the medial canthus of the eyes in sheep. An assay is available for sporidesmin in pasture.
- Clinical pathology: ↑ plasma GGT concentration
- Necropsy: Hepatic lesions

Confirmation of sporidesmin toxicity in areas where it is not commonly seen requires demonstration of

- hazardous spore counts
- sporidesmin production by *Pithomyces chartarum* isolates because many isolates outside New Zealand are atoxicgenic
- typical gross and histopathology of livers

Furans - Mouldy sweet potatoes

Common sources:

- *Ipomoea batatus* (sweet potato) tubers infected with *Fusarium* sp. or *Ceratocystis fimbriata*

Pathology:

- acute severe **interstitial pneumonia**, pulmonary oedema & emphysema

Diagnosis: access + pathology

Zearalenone

Common sources:

- *Fusarium graminearum* growing on maize, sorghum and other grains
- *Fusarium* spp. growing on pasture

Cattle (rarely-affected)
- decreased fertility
- prolonged oestrus, some with oestrus during mid-cycle
- vulval swelling

Aspergillus clavatus *tremorgenic mycotoxins*

Sources:

Sprouted grains infected with *Aspergillus clavatus*

- barley (malt, distiller's culms)
- wheat
- maize
- sorghum

Pathology:

No necropsy lesions are visible, but histological changes of **neuronal degeneration & necrosis** are seen in **brainstem** (midbrain, medulla oblongata), **spinal cord & spinal ganglia**. The larger neurones are affected, often in groups. There is central to complete chromatolysis, often

with intense cytoplasmic eosinophilia. There may be cytoplasmic vacuolation. Nuclei are frequently flattened, pyknotic and displaced peripherally or may undergo kayrolysis. Wallerian degeneration occurs in spinal cord white matter tracts.

Diagnosis: access + syndrome + pathology

Diplodia maydis *neurotoxin*

Source:

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* or other fungal infections of maize. *D. maydis* infects maize in Australia, but is not prominent or widespread.

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.

Mouldy sprouted barley - suspected mycotoxicosis

Cattle (late pregnant and recently-calved heifers) at Merredin, WA, fed sprouted barley produced in a hydroponic system were affected by a syndrome of weight loss, sore hind feet to hindquarter stagger to collapse and death. Severe liver damage was detected in about 33% of the herd by clinical chemistry (very high GLDH activity) 3-4 weeks after the sprouted barley was removed from the ration, but no necropsy material revealed any liver lesions. Removal of the barley from the ration resulted in recovery. The producers observed a blueish fungus unevenly distributed on the sprouted barley and also white material, probably fungal hyphae, on the green sprouts. *Aspergillus* spp. were cultured from the material. *Pyrenophora semeniperda* was common on barley grain in WA in 2002. This fungus is believed to be capable of producing mycotoxins that could produce a similar syndrome.

See *Aspergillus clavatus* tremorgenic mycotoxicosis and sprouted barley above.

ERGOTS

Ergot alkaloids (ergopeptide alkaloids)- ergotism

Common sources:

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

Pathology:
Hyperthermia:
- no specific lesions

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

Paspalitrems (*Claviceps paspali *tremorgens)
Common sources:
- *Claviceps paspali* ergots in seedheads of *Paspalum* spp.

Pathology: no significant lesions

Diagnosis: syndrome + ergotised pasture

GALL-FORMING FUNGI

Corallocytostroma ornicopreoides *toxicity (black soil blindness)*
Sources:
- ***Corallocytostroma ornicopreoides*** fungal growths ("corals"; sclerotia & conidiomata) on **Mitchell grasses (*Astrebla* spp.)** in the Kimberley (WA) & Victoria River (NT) districts. The fungus has also been seen on *Dicanthium* sp. (bundle bundle, blue grass) and *Iseilema vaginiflorum* (Flinders grass).

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

ENDOPHYTES

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

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

Diagnosis:

- **Poppi stain** of leaf sheath → presence and density of endophyte: > 20 hyphae/mm leaf sheath width in toxic swards.
- **Iolitrem B assay** (HPLC) of pasture: > 2mg/kg significant, > 4 mg/kg usually → clinical signs

MACROFUNGI (MYCETISM)

Ramaria flavo-brunnescens *(a coral fungus)*

Cases unrecorded in Australia to date.

Source:

- *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.

Pathology:

Cattle:

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

Sheep:

- 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

CYANOBACTERIAL TOXINS

TOXINS OF FRESH & BRACKISH WATER CYANOBACTERIA

☑ Cyanobacterial hepatotoxic cyclic peptides – microcystins and nodularin

Common sources:

- *Microcystis aeruginosa* [= *Anacystis cyanea*]
- *Nodularia spumigena*

Other sources include

- *Microcystis flos-aquae*
- *Microcystis viridis*
- *Anabaena flos-aquae*
- *Anabaena* spp.

- *Oscillatoria agardhii*
- *Oscillatoria limosa*
- *Nostoc* sp.
- *Anabaenopsis milleri*

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

Diagnosis:
- Evidence of access to blooms
- Identification of toxigenic cyanobacteria in bloom material (microscopic examination of bloom samples allows recognition of known toxigenic cyanobacterial species and justifies the expense of toxin assays, mouse toxicity tests or both)
  - For laboratory examination, two (2) samples are required from each bloom:
    - **For Identification of organisms**: 20 ml of bloom material + 1 ml 10% formalin for preservation [N.B. alcohol may produce distortion of cells, so formalin is preferred].
    - **For Toxicity testing**: 1 litre of the most concentrated bloom material (minimum useful quantity is 20 ml) chilled and transported as swiftly as possible; do **not** add preservative to this material.
- Mouse bioassay has been the standard toxicity testing method for cyanobacterial blooms, but is being superseded by assays for specific toxins. Mouse bioassay results should be expressed as LD_{50} or LD_{100} values in units of mg dry weight of cyanobacteria / kg mouse body weight.
- Assay methods for microcystin and nodularin are available for water and cyanobacterial bloom material
  - HPLC
  - ELISA - microcystins
- Gene probes are being developed to allow identification of potentially toxigenic strains of *Microcystis* without the need for toxicity testing.

Cyanobacterial alkaloid neurotoxins – paralytic shellfish poisoning (PSP) toxins and anatoxins

Common source:
- *Anabaena* spp.

Pathology: No significant lesions recorded

Diagnosis:
See section on cyanobacterial peptide toxins above.
Saxitoxins (paralytic shellfish poisoning toxins) assays available

Cylindrospermopsin

Common source:
- *Cylindrospermopsis raciborskii*

Pathology:
Cattle:
Necropsy: jaundice, pale liver, distended gall bladder

Histologically: liver, kidney and heart degeneration and necrosis

sub-acute cases: biliary ductular proliferation, swelling of hepatocytes with foamy vacuolation of cytoplasm, scattered individual hepatocyte necrosis in periacinar areas; foamy vacuolation and swelling of renal proximal tubular epithelium with protein and cellular casts in tubular lumens; scattered mild focal myocardial degeneration and necrosis

chronic case: extensive hepatic fibrosis and biliary ductule proliferation with marked reduction in hepatocyte numbers and foamy vacuolation of hepatocyte cytoplasm.

ZOOTOXINS (TOXINS OF ANIMAL ORIGIN)

ARTHROPODS - INSECTS

Sawfly larval peptides

Common sources:

- *Lophyrotoma interrupta* (Australian cattle-poisoning sawfly larvae)

Pathology :

As for acute hepatic necrosis (*q.v.*).
In many cases, the extent of hepatocyte necrosis is total (panacinar coagulation necrosis).

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

*Piperidine alkaloids (solenopsins) & peptide allergens of fire ant venom (*Solenopsis *spp.)*

Source:

- ***Solenopsis invicta*** Buren (red imported fire ant, RIFA [USA]), native to central Brazil, northern Argentina, Paraguay and (arguably) Uruguay in South America, invaded the southern USA in the early to mid 20th century (1918, 1940s), Mexico and the West Indies. They were confirmed in Brisbane, Queensland, in February 2001 and have probably been present in south-eastern Queensland for at least 5 years before detection.

Pathology: Pustules at sting sites

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