TERPENES AND TERPENOIDS

Definition [adapted from Lewis' Dictionary of Toxicology 1998]

Terpene: Any of a large class of naturally-occurring saturated hydrocarbons produced by plants that are formed completely by 5-carbon isopentyl (isoprene) C_5 units with the general formula $(C_5H_8)_n$. Small terpenes give plants their characteristic odours. Large terpenes include carotinoids, squalene, vitamin A and natural rubber.

Terpenoid: Any compound with an isoprenoid structure similar to that of terpenes. Camphor is a terpenoid.

Furanosesquiterpenes

Core data

Common sources:

- *Eremophila deserti* [= *Myoporum deserti*] (Ellangowan poison bush)
- some *Myoporum* spp.

Animals affected: ruminants
Mode of action:
Poisoning circumstances: travelling or hungry animals allowed access to plants
Main effects: acute hepatic necrosis (zonal lesion distribution depends on metabolic state of the xenobiotic biotransformation enzyme systems)
Diagnosis: pathology + plant access
Therapy: nil
Prevention: deny access

Chemical structure:

Sesquiterpenoids or furanoid ketones in the essential oils of source plants

Sources:

Family Myoporaceae

Eremophila deserti [=***Myoporum deserti***] (Ellangowan poison bush [Qld], dogwood poison bush [NSW]) [Se77,130; DM130] (Bailey & Gordon 1887, Albert 1934)

Eremophila deserti populations contain morphologically-indistinguishable chemical races, some of which are non-toxic (Sutherland & Park 1967)

Myoporum acuminatum [= *M. montanum*] (water bush, boobialla) [Se77; DM129; Legg & White 1941a,b]

Myoporum tetrandrum (boobialla) (Allen *et al.* 1978)

Myoporum laetum (ngaio) in New Zealand (Webster 1926, Connor 1977), Argentina, Brazil, Uruguay (Raposo *et al.* 1998a,b)

Eremophila deserti [= *Myoporum deserti*] whole plant [RAM Photo]

Eremophila deserti (= *Myoporum deserti*) [RAM Photo (left)]

Myoporum acuminatum (boobialla) flowering branch [RAM Photo]

Toxicity:

ruminants

Myoporum acuminatum toxic doses in sheep were 12-25 g fresh leaf/kg body weight (Legg & White 1941b)

Mode of action:

Conditions of poisoning:

travelling or hungry animals allowed access to plants

drought conditions leading to increased browsing of shrubs (Legg & White 1941a)

Clinical signs: See acute hepatic necrosis chapter

Pathology: See acute hepatic necrosis chapter

Lesions may vary in location within the hepatic acinus from periacinar to periportal depending on the metabolic state of the xenobiotic biotransformation enzyme systems. Experimental rats dosed with ngaione developed periacinar hepatocyte necrosis, but if rats were pre-treated with phenobarbitone to induce xenobiotic biotransformation enzymes before being given ngaione, they developed periportal necrosis (Seawright 1968)

Diagnosis: See acute hepatic necrosis chapter

Therapy: See acute hepatic necrosis chapter

Prevention & control: deny access to hungry animals

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💣☑ *Lantadenes (pentacyclic triterpenes)*

Core data

Common source: Lantana camara - toxic flower-colour forms: red & orange, Helidon white, pink (only north of Rockhampton)
Animals affected: ruminants
Poisoning circumstances: newly-introduced animals, lack of alternative feed
Main effects: hepatogenous photosensitisation + gall bladder paralysis + nephrosis
Diagnosis: access, pathology
Therapy: basic (as above) + activated charcoal or bentonite + fluids
Prevention: plant control - remove mechanically, burn, herbicides + pasture improvement

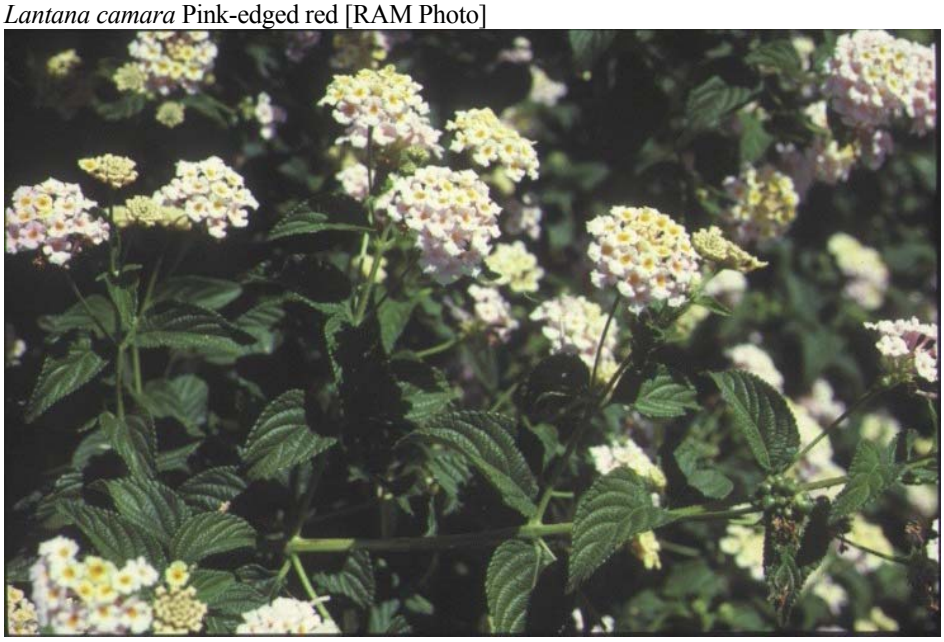
Syndrome name:
lantana poisoning
red nose, pink nose
secondary or hepatogenous photosensitisation

Chemical structure:
Lantadenes (includes rehmannic acid = lantadene A), icterogenins

Plant sources:
- ***Lantana camara*** (lantana) [Se68, DM136] → lantadenes A, B & reduced lantadene A
- *Lippia* spp. from southern Africa contain icterogenins and rehmannic acid capable of producing secondary photosensitisation, but are clinically unimportant. Secondary photosensitisation has been produced by experimental dosing of sheep with *Lippia rehmanni* and *L. pretoriensis* (Quin 1933). [Note: *Phyla nodiflora* (L.) Greene [=*Lippia nodiflora* L.] (lippia, no-mow lawn, fog-fruit) is a weed of pasture in southern Australia; no toxicity is recorded]

Lantana camara
- plants originate in Central & South America (Swarbrick 1986); listed as a Weed of National Significance for Australia
- 29 flower colour forms described as naturalised in eastern Australia (Smith & Smith 1982). Note that for identification of the biotype (colour form) of *L. camara,* a normal botanical specimen is needed, plus a coloured photograph of the mature flowerhead. Determination of the biotype can be difficult.
- + other garden-cultivated varieties

Lantana camara Pink-edged red [RAM Photo]



Lantana camara Helidon white [RAM Photo]

Toxicity:

Lantana poisoning: Australia, Southern Africa, Indonesia, India, Mexico, Central America

cattle (sheep, goats (Ide & Tutt 1998)) *Lantana camara* was first demonstrated to be toxic to cattle in experiments by Tucker in 1910 at Townsville (Tucker 1910-11) and subsequent experiments were done by Pound in Brisbane (Pound 1913-14).

lantadene A is the significant toxin in *Lantana camara* plants, with lantadene B being less toxic by some 2-3 times and reduced lantadene A being similarly toxic but present in only small amounts (Seawright & Hrdlicka 1977)

horses are *not* affected; no convincing clinical cases reported; a sheep lethal dose of lantadene A injected IV into a horse produced no detectable hepatic dysfunction, suggesting that horses do not metabolise lantadenes to toxic metabolites (Pass MA, Seawright AA, unpublished data)

Toxic forms (Seawright 1965)

Rule of thumb for recognising toxic colour forms of lantana

- most red & orange-flowered forms
- most pink-flowered forms north of Rockhampton
- Helidon white

Toxicity of *Lantana camara* biotypes (Smith & Smith 1982, NRM Facts Pest Series PP34 2001)

Dominant Flower colour form	Geographic Range	Toxicity
White		
Smith's snowflake	Near Laidley; Limestone Creek (north of Rockhampton); cultivated	Unknown
Pale Pink		
Bundaberg large-flowered pink	Bundaberg	Highly Toxic
Helidon white	Burnett-Moreton Districts	Toxic
Coolum pink	Coolum	Toxic
Bundaberg small-flowered pink	Bundaberg	Non-toxic
Mt.Berryman pink	Lockyer Valley (rare)	Unknown
Spiny orange-centred pink	Rockhampton eastward to the coast (infrequent)	Unknown
Pink		
Townsville red-centred pink	Ayr-Cooktown	Very toxic
Small-flowered red-centred pink	Brisbane-northern NSW	Toxic
Mackay red-centred pink	Cooktown-St.Lawrence	Toxic
Rockhampton red-centred pink	Rockhampton	Toxic
Pink Minnie Basil	Brisbane-Gatton-Beenleigh	Toxic
Common pink	Cooktown-northern NSW	Non-toxic
Hawaiian pink [= *L. camara* var. *aculeata* (L.) Moldenke]	Halifax & Ingham areas (locally common)	Unknown
Pink-edged red		
Common pink-edged red	Atherton Tableland-northern NSW	Very Toxic
Proserpine pink-edged red	Gordonvale-Brisbane	Toxic
Balnagowan pink-edged red	Mackay	Toxic
Broad-edged pink-edged red	North-west of Brisbane [The Gap, Ferny Grove, Samford] (locally common)	Unknown
Red		
Stafford red	Brisbane-northern NSW	Toxic

Toxicity of *Lantana camara* biotypes (Smith & Smith 1982, NRM Facts Pest Series PP34 2001)

Dominant Flower colour form	Geographic Range	Toxicity
Round red	Cooktown-northern NSW	Toxic
Pale Stafford red	Rockhampton-northern NSW	Unknown
Orange-red		
Large-flowered orange	Port Curtis-Moreton District	Toxic
Oblong red	Gatton-northern NSW	Unknown
Chelsea Gem	Cultivated; naturalised sparingly in SE Qld	Unknown
Hawaiian orange-red	Cairns-Atherton Tableland-Cooktown	Unknown
Orange Minnie Basil	Margate (rarely naturalised)	Unknown
Rockhampton large-flowered orange	Rockhampton eastward to the coast (locally abundant)	Unknown
Orange		
True orange	Bundaberg-northern NSW	Toxic
Townsville prickly orange	Mission Beach-Ayr	Non-toxic

Lantana montevidensis (creeping lantana), a weedy prostrate perennial plant with purple flowers, was **non-toxic** in feeding experiments with sheep dosed at 6 g dried leaf/kg with plant collected from the Ipswich region (Seawright 1965) and neither lantadene A nor lantadene B nor any significant amount of any triterpene were detected in two samples of the plant, one cultivated and the other field-collected (Hart *et al.* 1976a).

Circumstances of poisoning
- newly-introduced animals
- lack of alternative feed (drought, flood)

Pathogenesis
- **large reservoir of toxin in rumen**
- absorption of small amount from small intestine → hepatic damage
- → autonomic reflex slowing/atony of rumen
- → feedback loop maintaining the intoxication
- lantadenes damage hepatocyte biliary canalicular membranes → cholestasis.

Clinical signs- photosensitisation (see basic list above) +
- anorexia, depression, ruminal atony
- **jaundice**
- **frequent urination**
- dehydration
- constipation
- ± transient diarrhoea (severe cases)
- death in 2 days (severe cases) or 1-3 weeks

Pathology
- **jaundice**
- **swollen, yellow-orange liver**
  - histologically (Seawright & Allen 1972):
    - hepatocyte degeneration: pronounced hepatocyte enlargement with vesication & enlargement of nuclei, feathery degeneration (fine vacuolation and reticulated appearance, sometimes with brown pigmentation) of hepatocyte cytoplasm typical of biliary retention in hepatocytes, + multinucleated hepatocytes. In more severe cases, some or all of: periportal vacuolar degeneration of hepatocytes, midzonal foci of coagulative hepatocyte necrosis, fragmentation of hepatic cell plates with extensive shrinkage necrosis of individual hepatocytes

- cholestasis: deposits of bilirubin in hepatocyte cytoplasm, Kupffer cells and bile canaliculi
- mild biliary ductular hyperplasia and periportal fibrosis

severe distension of gall bladder (paralysis), watery bile (Pass & Heath 1977)

swollen pale kidneys (**nephrosis**)

histologically (Seawright & Allen 1972):

- vacuolar degeneration of renal tubular epithelium (coagulation necrosis in severe cases)
- cystic dilation of tubules
- hyaline and leucocyte casts

colon contents dehydrated

Therapy

inactivate rumen toxin reservoir → adsorbents (**activated charcoal** or **bentonite** [much cheaper]) - repeat adsorbent dose in 24 hours if required

rehydrate → electrolyte replacement solution- repeat electrolyte replacement fluids → full rehydration, stimulate rumen function

apply general case management measures (above)

Lantana camara therapeutic protocol

- Activated charcoal @ 5 g/kg orally in electrolyte replacement solution: Adult cattle: 2.5 kg in 20 litres. Sheep: 0.5 kg in 4 litres.
- OR Bentonite @ 5-10 g/kg substituted for the activated charcoal (much cheaper, somewhat slower effect)

Control

biological control of *L. camara* underway

28 insects have been introduced as biocontrol agents since 1914, with 17 species established; 4 are currently effective and causing significant damage to *L. camara* populations, 4 others approved for release, 3 others under study

widely-established insect agents (all from Brazil): leaf-mining beetles *Octotoma scabripennis* & *Uroplata girardi*, leaf-sucking bug *Teleonemia scrupulosa* and seed-mining fly *Ophiomyia lantanae*

insects under study: stem-sucking bug *Aconophora compressa* (from Mexico), stem-boring beetle *Aerenicopsis championi* from Mexico) and leaf-rolling moth *Ectaga garcia* (from Brazil)

combine **mechanical removal, fire & herbicides** to remove plants followed by **vigorous pasture improvement program**

protective immunisation may be possible (preliminary work only: Stewart *et al.* 1988)

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☙☑ *Andromedotoxins (grayanotoxins)*

Core data

Common sources: Rhododendron spp. (rhododendrons, azaleas)
Animals affected: ruminants, horses
Mode of action: modifies cell membrane Na channels
Poisoning circumstances: access to garden waste
Main effects:
- vomiting
- cardiac arrhythmia
- aspiration pneumonia

Diagnosis: syndrome + access
Therapy:
- remove from source
- rehydrate, adsorbents, antiarrhythmics

Prevention: careful garden waste disposal

Syndrome names: Rhododendron poisoning
Chemical structure:
Andromedotoxins (grayanotoxins) = water-soluble diterpenoid compounds
Sources:
garden plants (in Australia)
Family Ericaceae (the heath family):
Rhododendron spp. (rhododendrons, azaleas)
Andromeda spp. (bog rosemary)
Kalmia spp. (mountain laurels, lambkill, calfkill – USA)
Ledum spp. (black laurel, Labrador tea – USA)
Leucothoe spp.
Lyonia ligustrina
Menziesia ferruginea
Pieris spp.
Toxicity:
ruminants (cattle, goats), horses, kangaroos (Hough 1997)
humans (through honey from bees foraging on plants of family Ericaceae)
poisoning in Europe, India, North America, Australia
lethal dose of leaves = as little as 0.2% body weight
Mode of action:
bind to and modify the Na channels of cell membranes
→ prolonged depolarisation & excitation
→ ↑Ca movement into cells → positive inotropic effect (similar to cardiac glycosides)
Conditions of poisoning:
poisoning of ruminants (goats) with access to **garden waste** or gardens where shrubs may be browsed
honey produced from nectar of these plants contains andromedotoxins and can be toxic to humans
Clinical signs:
drooling saliva
vomiting
repeated swallowing, retching
diarrhoea, tenesmus
abdominal pain
cardiovascular effects

bradycardia
hypotension (through vasodilation)
atrioventricular block
± sudden death
± dyspnoea

Pathology:
gastroenteritis
± **aspiration pneumonia**

Diagnosis:
syndrome + access
assay rumen contents/faeces [limited availability of test] (Holstege *et al.* 2000)

Therapy:
remove from source
rehydrate + adsorbents + demulcents
for severe bradycardia: atropine
for heart block: isoprenaline hydrochloride (isoproterenol) or sodium channel blockers (e.g. lignocaine, phenytoin)

Prevention & control: deny access (proper disposal of garden refuse)

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

Core data

Syndrome names:
- *Pimelea* poisoning of cattle
- St.George disease
- Marree disease

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

Animals affected: cattle

Mode of action:
- constricted pulmonary venules
- alimentary irritation
- expanded plasma volume

Poisoning circumstances:
- dense *Pimelea* populations (overstocking, soil disturbance)
- above average winter rain followed by below average summer rain or drought
- dead plant fragments contaminating pasture/dust

Main effects:
- right-sided heart failure (distended jugular veins, subcutaneous oedema; dilated right ventricle, hydrothorax, distended hepatic sinusoids)
- diarrhoea
- anaemia

Diagnosis: syndrome + pathology

Therapy:
- no specific therapy
- remove cattle from toxic pasture

Prevention: avoid overstocking and soil disturbance

Syndrome names:
***Pimelea* poisoning of cattle**

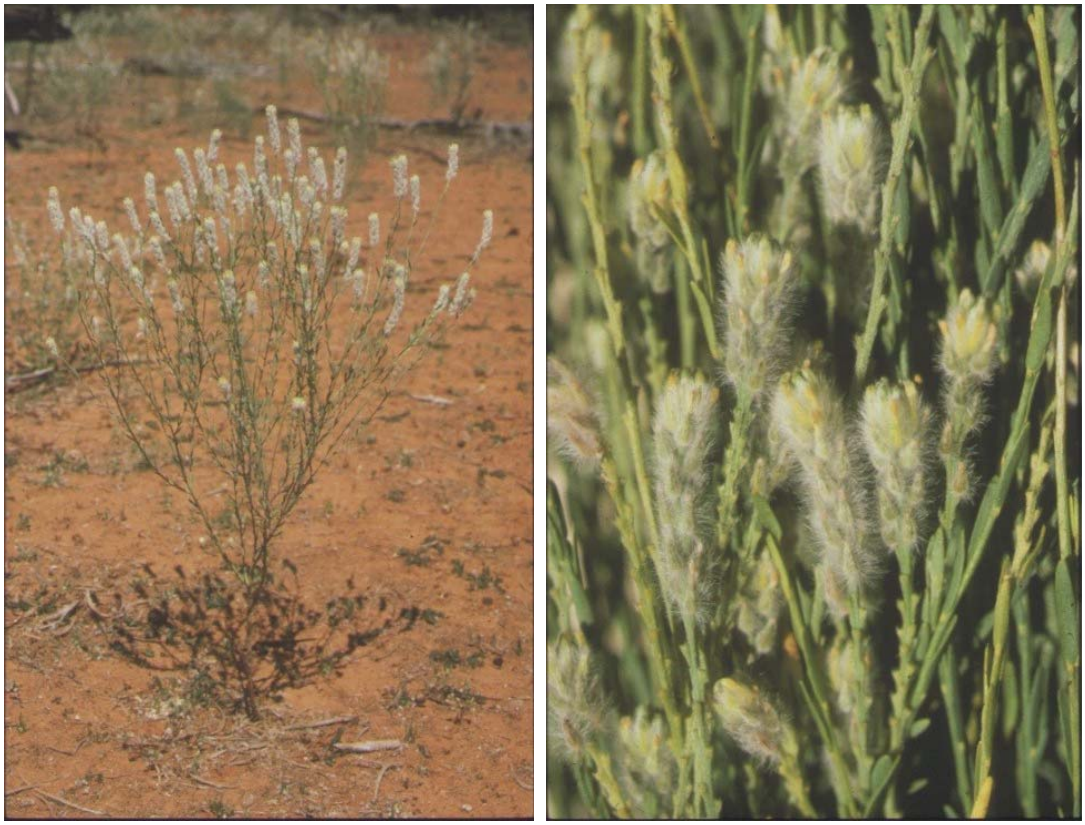
St.George disease [named after the town in southern Queensland, not the patron saint of England]
Marree disease [named after the town in northern South Australia]

Sources:

Pimelea spp. (rice flowers, flax weeds); Family Thymeleaceae. There are 90 species of *Pimelea* recognised in Australia, all endemic (Rye & Heads 1990).

major plants (associated with multiple poisoning incidents):

southern inland Queensland, north-western NSW, northern SA
winter-growing annual herbs
Pimelea trichostachya (flax weed, rice flower, broom bush, Borgia's bouquet) [DM101]
Pimelea simplex* ssp. *simplex (desert rice flower)
Pimelea simplex* ssp. *continua [DM102]
Pimelea elongata [DM102]



Pimelea trichostachya [RAM Photos]

Pimelea simplex ssp. *continua* [RAM Photos]

Pimelea elongata [RAM Photo]

minor plants (associated with single or a few poisoning incidents):
coastal or near-coastal Q
perennial small shrubs
Pimelea latifolia ssp. *altior* (Rogers & Roberts 1976)
Pimelea neoanglica (Storie *et al.* 1986)
Pimelea strigosa (RA McKenzie, unpublished data 1994)
Pimelea linifolia

Toxicity:

Only cattle are affected by the full syndrome. Other species develop only diarrhoea.
Dosing with simplexin (a daphnane ester) reproduces the disease (Roberts *et al.* 1975).
Pimelea plants are **very unpalatable**; living plants are only eaten as the very last resort (and will cause severe diarrhoea).
Toxin intake is by inhalation or ingestion of **fine dry particles of dead *Pimelea* plants** on other pasture components. Most inhaled particles are probably trapped in mucus and ultimately swallowed.
The toxins are diterpene esters related to phorbol esters (esters of the tetracyclic diterpene phorbol) from *Croton tiglium*, the source of croton oil. These constituents of croton oil are responsible for purgative, skin-irritant and tumour promoting (co-carcinogenic) properties.
Diterpene ester types include tigliane, daphnane and ingenane esters. They have been found only in plant families Euphorbiaceae and Thymeleaceae (Kinghorn 1991).

Mode of action:

The toxins are potent activators of protein kinase C (Pegg *et al.* 1994)
There are three facets to toxicity in cattle:

- persistent **constriction of pulmonary venules** causing chronic right-sided heart failure . Sheep and horses lack the powerful smooth muscle present in bovine pulmonary venule walls.
- **irritation of alimentary tract** causing persistent diarrhoea
- **expansion of the plasma volume** without stimulating erythropoiesis causing anaemia. The mechanism is unknown.

Conditions of poisoning:

Historically, widespread *Pimelea* poisoning of cattle emerged in 1960s after replacement of sheep with cattle on pastoral holdings with significant populations of the annual herbaceous *Pimelea* spp.
Annual herbaceous *Pimelea* spp. population density in pastures is boosted by
heavy grazing pressure on palatable pasture species (overstocking),
soil disturbance (abandoned cultivation) or fire
Cattle grazing in pastures with living annual herbaceous *Pimelea* plants do not eat them and very seldom develop poisoning
The greatest incidence of disease occurs after **above average winter rain** promotes the growth of annual *Pimelea* species and is **followed by below average summer rain** or **drought** preventing complete removal of dry *Pimelea* particles from the pastures by rain and the biodegradation of the toxins by soil microbes

Clinical signs:

usually > 3 weeks exposure before signs noted
diarrhoea (absent in some cases)
weight loss → emaciation
distended jugular veins
subcutaneous oedema of brisket & submandibular space → massive anasarca
anaemia
↓ exercise tolerance

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** (Seawright & Francis 1971)
capillary dilation in adrenal glands and kidney

Diagnosis:

syndrome + pathology

note that the responsible *Pimelea* sp. is likely to be absent from pastures when animals are affected (winter plant growth → summer poisoning)

Therapy:

no recognised specific therapy

supportive therapy with diuretics may be justified in valuable animals (e.g. bulls)

remove cattle from toxic pastures

→ ↓↓ diarrhoea, but heart failure signs and anaemia persist for months before eventual recovery, if death from circulatory collapse does not intervene

in practical terms, this can involve moving cattle to pastures on a different soil type where the local *Pimelea* sp. has not grown

cattle should not be returned to affected pastures until after significant rainfall (*Pimelea* plant fragments washed from the pasture and toxin biodegraded)

Control (after establishment of hazardous *Pimelea* populations):

reduce *Pimelea* population density in pastures (research is required on methods):

reduce grazing pressure (uncertain if large annual herbaceous *Pimelea* populations decline under low grazing pressure once they have become established)

fire regimens (unpredictable rainfall in affected areas makes it very difficult to reliably establish sufficient fuel loads in 2 successive growing seasons to allow burning of *Pimelea* plants before seeding)

herbicides: application restricted by cost and environmental considerations e.g. to abandoned cultivations; 1.5L atrazine + 0.5L 2,4-D/ha in 60 L water/ha with 250 ml Agral 60 kills 80-90% young *Pimelea* plants - $9/ha; 1L 2,4-D/ha also effective - $6/ha (Wells G, Queensland Wheat Research Institute, unpublished data 1995)

immunisation (failed): An attempt in the 1990s by CSIRO/University of Central Queensland to produce a protective immunogen against simplexin was not successful. Antibodies were produced by immunised cattle, but protection from poisoning was not demonstrated (Pegg *et al.* 1994).

Prevention:

avoid factors that favour increased density of annual herbaceous *Pimelea* spp., namely overstocking and soil disturbance

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Irritant diterpenoids of Families Thymeleaceae & Euphorbiaceae

Core data

Common sources:

- *Pimelea* spp.
- *Euphorbia* spp.
- *Jatropha* spp.

Animals affected: ruminants, horses
Mode of action: direct irritation of alimentary mucosa
Poisoning circumstances: plants unpalatable, eaten only as last resort
Main effects: severe diarrhoea
Diagnosis: syndrome + access
Therapy: remove from source, rehydrate, adsorbents, demulcents
Prevention: deny access

Chemical structure:

highly irritant tigliane, daphnane and ingenane diterpenoid esters

Sources:

Family Thymeleaceae

***Pimelea* spp.** (rice flowers, flax weeds) [DM99-103] 90 species in Australia (Rye & Heads 1990), 12 species associated with poisoning; some authorities regard all species as potentially toxic; examples include
Pimelea decora (Flinders poppy) - horses (Hill 1970)
Pimelea haematostachya (Pimelea poppy)
Pimelea trichostachya (flaxweed, broom bush, rice flower, Borgia's bouquet) (*q.v.*) - sheep (Legg & White 1940)

Pimelea decora [RAM Photo]

Pimelea haematostachya [RAM Photo]

Wikstroemia indica (tie bush) - cattle (Pound & White 1920) [DM133] *Wikstroemia* is a genus of about 70 species from tropical and eastern Asia to Australia with only 1 species native to Australia (Rye & Heads 1990).

Daphne spp. - cultivated in gardens

Daphne mezereum (mezereon)

Family Euphorbiaceae

***Euphorbia* spp.** (spurges) 30-40 species in Australia (including at least 10 naturalised), about 14 species associated with poisoning

Jatropha curcas (physic nut, Barbados nut, curcas bean, purge nut, purging nut, purgeerboontjie [S. Afr.], tuba [Philippines]) [see toxalbumins (lectins)]

Jatropha gossypifolia (bellyache bush, cotton-leaf physic nut)

Aleurites moluccana (candle nut tree) (Forster 1996) - native and cultivated in gardens and as a street tree

Toxicity:

ruminants and horses (humans)

Mode of action: direct irritation of alimentary mucosa

Conditions of poisoning:

plants are **unpalatable**, so **poisoning only under conditions of nutritional stress** (e.g. drought)

fruits of *Daphne mezereum* toxic to children (2-3 fruits can be fatal)

Clinical signs:

diarrhoea profuse

± blood in faeces

dehydration

abdominal pain (teeth grinding *etc.*)

death in ± 24 hours in severe cases

Pathology:

alimentary tract congestion

haemorrhagic, necrotising gastroenteritis

Diagnosis: syndrome + access
Therapy:
remove from source
rehydration + adsorbents + demulcents
Prevention & control: deny access (particularly when other feed is scarce or absent)
References:
Se102, 53, 146

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Cucurbitacins (tetracyclic triterpenes)

Core data

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

Animals affected: cattle, sheep
Mode of action:
- direct irritation of alimentary mucosa
- ↑ vascular permeability
- damage to heart muscle

Poisoning circumstances: avid consumption of ripe fruit
Main effects: rumenitis, enteritis, sudden death (myocardial damage)
Diagnosis: syndrome + access
Therapy:
- remove from source
- rumenotomy
- rehydrate, adsorbent, demulcent

Prevention: deny access to ripe fruit

Chemical structure:
Cucurbitacins (bitter principles of cucurbits) = tetracyclic triterpenes. These compounds are feeding deterrents for most insects, excluding the cucumber beetle which is attracted by them (Lavie 1971). They have some structural affinities with cardiac glycosides (*q.v.*) and some similar pathological effects.

Sources:
Family Cucurbitaceae (Telford 1982)
Cucumis myriocarpus (prickly paddymelon, paddy melon, gooseberry cucumber) - naturalised; native of southern Africa (Telford 1982); (cattle toxicity - McKenzie *et al.* 1988)
Cucumis melo ssp. *agrestis* (Ulcardo melon) - naturalised; native to Africa, Asia (Telford 1982); (cattle toxicity - Jubb *et al.* 1995)
Citrullus lanatus (wild, pie, bitter or camel melon) - naturalised; native to tropical and southern Africa (Telford 1982)
Citrullus colocynthis (colocynth) - naturalised; native to northern Africa & SW Asia (Telford 1982)
Ecballium elaterium (squirting cucumber) - naturalised; native to Mediterranean region & SW Asia (Telford 1982)

Family Scrophulariaceae
Stemodia kingii F.Muell. (Allen & Mitchell 1998)

Stemodia florulenta (Benth.) W.R.Barker [= *Morgania floribunda* Benth.]
(morganflower, bluerod) (?)

Toxicity:
ripe fruit of the cucurbits listed above are toxic
cattle, sheep
South Africa, Australia
Mode of action:
cucurbitacins → irritation of alimentary tract, ↑ permeability of blood vessels → oedema of stomach walls
Conditions of poisoning:
Cucurbitaceae
ripe fruits more toxic than unripe (have a larger cucurbitacin content)
poisoning from avid fruit consumption
Clinical signs:
sudden death
dehydration, haemoconcentration
diarrhoea
± jaundice
Pathology:
congestion/haemorrhage of alimentary tract
oedema of forestomach walls
seeds numerous in rumen contents
microscopic **rumenitis**
± focal myocardial degeneration & necrosis
Diagnosis: syndrome + access
Therapy:
remove from source
rumenotomy to remove fruits
rehydrate + adsorbents + demulcents
Prevention & control: deny access to ripe fruit of toxic species
References:

Allen JG, Mitchell AA (1998) A newly discovered toxic plant, *Stemodia kingii*, in Western Australia. Chapter 26 in Garland T, Barr AC (eds) *Toxic Plants and other Natural Toxicants.* CAB International, Wallingford UK, pp. 120-124.
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Meliatoxins (tetranortriterpenes)

Core data

Common sources: *Melia azedarach* var. *australasica*
Animals affected: pigs
Mode of action: undetermined
Poisoning circumstances: eating ripe fruit
Main effects: gastroenteritis
Diagnosis: syndrome + access
Therapy:
- remove from source
- rehydrate, adsorbents, demulcents

Prevention: deny access to ripe fruit

Chemical structure:
Meliatoxins are tetranortriterpenes of the limonoid class (Oelrichs *et al.* 1983)

Sources:

Melia azedarach* var. *australasica (white cedar, cape lilac, china berry, mindi [Indonesia]) [DM154] - native in rainforest and cultivated in gardens and as a street tree or shade tree

Toxicity:

pigs (ruminants, poultry)

dogs (Hare *et al.* 1997)

Experimental toxicity is reported with fruit in cattle in Brazil (Mendez *et al.* 2002). Toxic doses given were 5-30 g/kg PO. Fatal doses were 15-30 g/kg.

Mode of action: undescribed

Conditions of poisoning:

Ripe fruits are toxic. Some individual trees are non-toxic.

Clinical signs:

Pigs

vomiting
diarrhoea
± excitement
± depression
dyspnoea
cardiac arrhythmia

Dogs (Hare *et al.* 1997)

vomiting, hypersalivation
abdominal pain
diarrhoea
bradycardia
seizures

Cattle (experimental) (Mendez *et al.* 2002)

Anorexia, depression
Ruminal stasis
Diarrhoea
Incoordination, muscle tremors
Recumbency
Hypothermia
Dyspnoea

Pathology:

severe **gastroenteritis**

fatty degeneration of liver & kidneys; scattered or periacinar hepatocyte necrosis in experimental cattle (Mendez *et al.* 2002)

necrosis of lymphoid follicles in alimentary tract

myodegeneration and necrosis of skeletal muscles were reported in experimental rats (Bahri *et al.* 1992), and experimental cattle (Mendez *et al.* 2002)

Diagnosis: syndrome + access

Therapy:

remove from source

rehydrate + adsorbents + demulcents

Prevention & control: deny access to ripe fruit

References: Se76

Bahri S, Sani Y, Hooper PT (1992) Myodegeneration in rats fed *Melia azedarach*. *Aust. Vet. J.* **69**:33.

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Oelrichs PB, Hill MW, Vallely PJ, MacLeod JK, Molinski TF (1983) Toxic tetranortriterpenes of the fruit of *Melia azedarach*. *Phytochem.* **22**:531-534.

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Sesquiterpene lactones (probable aetiology) - nigropallidal encephalomalacia

Syndrome names:

- chewing disease (USA)
- nigropallidal encephalomalacia

Chemical structure:

toxins uncertain, probably sesquiterpene lactones

Sources:

Centaurea solstitialis (St.Barnaby's thistle, yellow burr, yellow star thistle)

Acroptilon repens [= *Centaurea repens*] (Russian knapweed, creeping knapweed, hard heads, hardhead thistle, blue weed, Russian centaurea)

Toxicity:

Horses only are affected, with young horses the more susceptible.

Cases are reported in North & South America and (rarely) from Australia (NSW, Q) (Gard *et al.* 1973)

Several weeks of feeding on the plants elapse before clinical signs occur. Experimental poisoning requires intakes of 60-70% of body weight for *A. repens* and 86-200% for *C. solstitialis*. A lethal dose of green *C. solstitialis* is 1.5-2.5 kg/100 kg body weight/day (Cordy 1978).

Mode of action:

Lesions are suggested as the result of dopamine deficiency in the dopaminergic nigrostriatal pathway after an initial massive release of stored neurotransmitter into the corpus striatum (Cordy 1978).

Conditions of poisoning:

Pasture dominated by young plants before flowering. Mature plants are very spiny and probably uneaten except under extreme conditions of nutritional stress. The interval between first access to plants and onset of the clinical syndrome is about 30 days (Cordy 1978).

Cases seen in New South Wales in 1971 and 1972 were associated with good summer rains producing a substantial crop of thistles in autumn, followed by a dry early winter in which the thistles were the only green feed available for the affected horses (Gard *et al.* 1973).

Clinical signs:

Most cases die, but some milder cases adapt to the neurological deficit and survive.

- abrupt onset
- head drooped
- aimless walking
- drowsy inactivity
- impaired prehension & mastication (swallowing normal)
- mouth held half open, tongue protruding (paresis)
- tongue lateral edges curled upwards

Pathology:

Necrosis of discrete foci of neurones in the globus pallidus & substantia nigra (usually bilateral) - thus **nigropallidal encephalomalacia**.

Smaller necrotic lesions have been described in nuclei of the inferior colliculus, dentate nucleus, the mesencephalic nucleus and the tract of the 5th cranial nerve.

Diagnosis:

Clinical syndrome in association with the known causative plants supports a tentative diagnosis. Confirmation requires brain histopathology.

Therapy: nil

Prevention & control: deny access

References: Se30

Cordy DR (1978) *Centaurea* spp. and equine nigropallidal encephalomalacia. In Keeler RF, van Kampen KR, James LF (eds.) *Effects of Poisonous Plants on Livestock.* Academic Press, New York. pp. 327-336.

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Stevens KL (1990) *J. Nat. Prod.* **53**:218. [cited by Harborne & Baxter 1996 p.317]

☑ *Vitamin A (hypervitaminosis A)* (q.v.)

Rabbit fed almost exclusively on carrots (*Daucus carota*) developed hyperostotic polyarthropathy after 4.5 years (Frater 2001).

See the account of hypervitaminosis A under Mammals.

Reference:

Frater JL (2001) Hyperostotic polyarthropathy in a rabbit – a suspected case of chronic hypervitaminosis A from a diet of carrots. *Aust. Vet. J.* **79**:608-611.

Terpenoids of Pachyrhizus erosus *(yam bean)*

Pachyrhizus Rich. ex DC. (Family Fabaceae) comprises 6 species from tropical America. *Pachyrhizus erosus* (L.) Urb. [= *P. angulatus* Rich. ex DC. , *P. palmatilobus* Benth. ex Hook.f.] (yam bean, chopsui potato, jicama), a perennial herbaceous vine, is cultivated in tropical gardens in Australia for its edible tubers, eaten raw of cooked. Its pods (legumes) may be eaten, but only after thorough cooking. Eating **uncooked pods** causes gastrointestinal irritation with mild to moderate **diarrhoea**. The pods contain terpenoids that are held responsible for the irritation. The seeds have been reported to contain rotenone and pachyrrhizid and have been used as fish poisons and insecticides (Blohm 1962, Burrows & Tyrl 2001). Young pods may be eaten, but mature seeds are poisonous (Vaughan & Geissler 1997).

References:

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