CLINICAL TOXICOLOGY

1: Phytotoxins (toxins of vascular plants) [Biological-origin toxins]

INORGANIC TOXINS

Nitrate-nitrite

Core data

Common sources:

- Plants:
  - *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
- water

Animals affected: ruminants

Poisoning circumstances:

- high soil nitrate + low light intensity, plant tissue damage (herbicide, virus)
- most nitrate in stems/stalks
- persists in hay
- rumen bacteria convert nitrate to nitrite
- rapid feed intake + unadapted rumen bacteria → nitrite absorption

Main effects:

- nitrite oxidises Hb to methaemoglobin, preventing oxygen carriage
- sudden death

Diagnosis:

- brown blood
- plant & aqueous humour nitrate assay

Therapy: methylene blue IV

Prevention:

- feed adequate carbohydrate (grain)
- check suspect crops

Haldane *et al.* (1897) first demonstrated the toxic properties of nitrite in mammals through the production of methaemoglobinaemia by intravenous injection of nitrite in mice. The discovery of plant nitrate converted to nitrite as toxic for grazing ruminants was made by Rimington & Quin (1933a,b) in South Africa while researching *Tribulus terrestris* 'geeldikop' toxicity (*q.v.*) and further established by Bradley *et al.* (1939a,b) in North America during investigations of poisonous oaten hay and by Williams & Hines (1940) in Queensland during investigations of poisoning incidents with cattle consuming *Salvia reflexa*.

Chemical structure:

nitrate ion = NO_3^-

nitrite ion = NO_2^-

Nitrate and nitrite are normal constituents of plants, being intermediate compounds on the pathway from soil nitrogen to plant proteins, driven by energy produced by photosynthesis. Interruption of this pathway in the plant may cause marked increases in NO_3 concentrations.

Sources:

Water

high-nitrate water in reservoirs created with explosives; 2 cases in cattle in Canada, water nitrate 4.8 & 7.0 g/L (Yong *et al.* 1990)

accidental contamination with fertilizer (e.g. ammonium nitrate) (Yeruham *et al.* 1997); containers used to transport fertilizer and subsequently used to transport water (MP Carlson, personal communication, VETTOX Discussion List, 2000)

Meat preservative

sodium nitrite used in excess has produced nitrite poisoning in cats and dogs (Worth *et al.* 1997)

Fertilisers

ingestion of lawn /garden fertilisers (Osmocoat®, Dynamic Lifter®) has produced nitrite poisoning in dogs (Carolyn Jones & Peter Alan, personal communication 3 Feb 1999)

Plant sources of potentially-toxic amounts of **nitrate** are **numerous** [Those included by Everist (1981) for Australia are indicated],

Examples (this is not an exhaustive list) include

Family Amaranthaceae

Amaranthus spp. (Ev888)

Amaranthus cruentus
Amaranthus macrocarpus
Amaranthus mitchellii
Amaranthus retroflexus
Amaranthus spinosus (needle burr)
Amaranthus viridis

Family Apiaceae

Apium graveolens (celery) (Ev889)

Family Asteraceae

Silybum marianum (variegated thistle) [DM92] (Ev914)
Arctotheca calendula (capeweed) (Ev890)
Acanthospermum hispidum (star burr) (Ev888)
Carduus pyncnocephalus (Ev892)
Verbesina encelioides (crownbeard) (Ev919) (*q.v.*) - toxicity of this plant is due to galegine, not nitrate
Wedelia asperrima (sunflower daisy) (Ev919) (*q.v.*) - toxicity of this plant is due to wedeloside, not nitrate
Chromolaena odorata (Siam weed) – young stems up to 11.6% KNO_3 (Sajise *et al.* 1974)

Family Brassicaceae

Brassica spp.

Brassica napus (canola, rape, kale) (sheep grazing rape in New Zealand - Bruere 1956; up to 5.25% KNO_3 - Ev211)
Brassica rapa (turnip) (stubble turnips, cattle, UK - Anon. 1996) (Ev891)

Capsella bursa-pastoris (shepherd's purse) (Wiese & Joubert 2001)

Family Chenopodiaceae

Atriplex muelleri (Ev890)
Beta vulgaris (beets) (Ev890)
Chenopodium spp. (Ev893)

Chenopodium album (fat hen)
Chenopodium ambrosioides
Chenopodium atriplicinum
Chenopodium hubbardii
Chenopodium murale
Chenopodium trigonon

Kochia spp. (Ev903)

Kochia brevifolia (suspected)

Kochia sedifolia
Trianthema triquetra (Ev918)
Family Convolvulaceae
Ipomoea spp. (Ev903)
Ipomoea plebia (bell vine)
Ipomoea purpurea (morning glory)
Family Fabaceae
Medicago sativa (lucerne, alfalfa) (Ev907)
Vigna catjang (Ev919)
Family Lamiaceae
***Salvia* spp.** (Ev913-914)
Salvia reflexa (mintweed) [DM89] (Williams & Hines 1940)
Salvia coccinea (red salvia)
Family Malvaceae
Malva parviflora (small-flowered mallow, marsh mallow) (Ev 906, Gordon & McKenzie 2000)
Family Papaveraceae
Argemone spp. (Mexican poppies) (Ev890) - toxicity of these plants is due to isoquinoline alkaloids, not nitrate
Argemone mexicana (*q.v.*)
Argemone ochroleuca (*q.v.*)
Family Poaceae (grasses including crops & pastures)
Avena sativa (oats) (Bradley *et al.* 1939a,b, Ev890)
***Lolium* spp.** (ryegrass) [DM52]
Lolium multiflorum (Italian ryegrass) (Ev904)
Lolium perenne (perennial ryegrass)
Lolium hybrids
***Sorghum* spp.** (sorghum) [DM55-57] (Ev917)
Sorghum arundinaceum (?)
Sorghum bicolor ("vulgare") (grain sorghum)
Sorghum dochna (?)
Sorghum drummondii (?)
Sorghum sudanense (Sudan grass)
Zea mays (maize) (Ev920)
Dactyloctenium radulans (button grass) [DM52] (Ev896; McKenzie *et al.* 2002)
Urochloa panicoides (liverseed grass) [DM59] (Ev918)
Echinochloa spp. (Ev897)
Echinochloa crus-galli
Echinochloa frumentacea (Japanese millet, Siberian millet, white panic) (Montgomery & Hum 1995; 6.5% KNO_3 in dry matter in hay - RA McKenzie & SR Daly unpublished data 2002)
Brachiaria gilesii (Ev891)
Bromus cathartica [= *B. unioloides*] (prairie grass) (Ev891)
Eleusine spp. (Ev897)
Eleusine indica (crow's-foot grass)
Eleusine tristachya
Pennisetum clandestinum (kikuyu grass) (Ev911)
Family Polygonaceae
Polygonum aviculare (wire weed) (Ev912)
Rumex brownii (swamp dock) (Ev913)
Family Portulacaceae
***Portulaca* spp.** (Ev912)
Portulaca oleracea (pigweed, purslane) [DM108]
Portulaca* sp. aff. *oleracea (inland pigweed, munyeroo) [DM108]
Family Proteaceae
Grevillea helmsiae (Ev901)
Family Solanaceae
Lycopersicon esculentum - dried tomato vines (Shlosberg *et al.* 1996)
Datura leichhardtii (native thornapple) (Ev896)
Nicotiana megalosiphon (long-flowered native tobacco) (Ev908)

Solanum spp. (Ev915)
Solanum esuriale (quena)
Solanum nigrum ssp. *nigrum*
Solanum nigrum ssp. *schultzii* (?)

Family Sterculiaceae
Brachychiton rupestre (bottle tree) (Ev891) – pith of the trunk cut for drought feeding may be toxic

Family Zygophyllaceae
Tribulus terrestris (caltrop) (Ev918)
Zygophyllum ammophilum (twin-leaf) (Ev921)

Dactyloctenium radulans (button grass). [RAM Photo]

Arctotheca calendula (cape weed) [RAM Photo]

Silybum marianum (variegated thistle). [RAM Photos]

Salvia reflexa (mint weed). [RAM Photo]

Salvia reflexa (mint weed). [RAM Photo]

Portulaca oleracea (pigweed). [RAM Photo]

Portulaca sp. aff. *oleracea* (munyeroo, inland pigweed). [RAM Photo]

Toxicity:
Ruminants are much more susceptible than monogastrics to plant nitrate, except after microbial conversion of nitrate to nitrite in food (e.g. swill, wet hay). Most nitrate in plants is concentrated in **stems** and **stalks**. Toxic amounts of nitrate **persist in hay** made from plants containing hazardous concentrations. As a general rule, **hazardous feed contains > 1.5% KNO_3 equivalent in plant dry matter** (see box below).

Conversion factors for different expressions of nitrate-nitrite content
Form A x Conversion Factor = Form B

			Form B		
Form A	N	NO_2	NO_3	KNO_3	$NaNO_3$
Nitrate-nitrogen (N)	1.0	3.3	4.4	7.2	6.1
Nitrite-nitrogen (N)	1.0	3.3	4.4	7.2	6.2
Nitrate (NO_3)	0.23	0.74	1.0	1.63	1.37
Nitrite (NO_2)	0.30	1.0	1.34	2.2	1.85
Potassium nitrate (KNO_3)	0.14	0.64	0.61	1.0	0.84
Sodium nitrate ($NaNO_3$)	0.16	0.54	0.72	1.2	1.0

Hazardous plant nitrate concentrations

Nitrate concentrations in plant dry matter greater than 1.5% KNO_3 (Bradley *et al.* 1940b) to 2% KNO_3 (O'Hara & Fraser 1975) are widely regarded as potentially hazardous to grazing ruminants. These guideline values were based initially on a measurement of the oral LD_{50} in cattle for NO_3 given as an aqueous solution of about 0.3g/kg (Bradley *et al.* 1940b). In contrast, the oral LD_{50} in cattle for NO_3 in plant material has been estimated as 1.0g/kg body weight (Crawford *et al.* 1966), which largely reflects the influence of the rate of intake of plant material compared with that of an aqueous drench. Calculation suggests that the corresponding lower limit of hazardous NO_3 concentration in *plant* dry matter is 5% KNO_3, but the whole issue is complicated by several factors influencing the rate of microbial metabolism of NO_3 and NO_2 in the rumen including recent feeding history (fasting animals are more susceptible), prior exposure to dietary nitrate, intake of readily-available carbohydrate, and particularly, the rate of intake of the plant (National Research Council 1972, O'Hara & Fraser 1975). Emphasising the imprecision of plant NO_3 toxicity guidelines is the finding from the original investigation of nitrate-nitrite poisoning that batches of *Tribulus terrestris* containing 1.2 to 3.39% KNO_3 in dry matter were toxic to sheep (Rimmington & Quin 1933). The association of greater NO_3 concentrations with plants growing in and around stockyards was noted originally for *T terrestris* (Rimmington & Quin 1933).

How much high nitrate grass or hay will kill a cow?

Assume: Cattle LD_{50} = 1.0 g nitrate/kg = 450 g for a 450 kg cow
If: Plant nitrate (in dry matter) = 2.4% (4.0% KNO_3) = 24 g nitrate/kg
Then: Plant dry matter LD_{50} for cows = 19 kg
Assume: Plant dry matter content = 20% (grass), 80% (hay)
Then: Plant wet weight LD_{50} for cows = 95 kg grass, 24 kg hay

Bradley WB, Eppson HF, Beath OA (1940b) Livestock poisoning by oat hay and other plants containing nitrate. *Wyoming Agricultural Experiment Station Bulletin* 241 [cited by Crawford *et al.* 1966]
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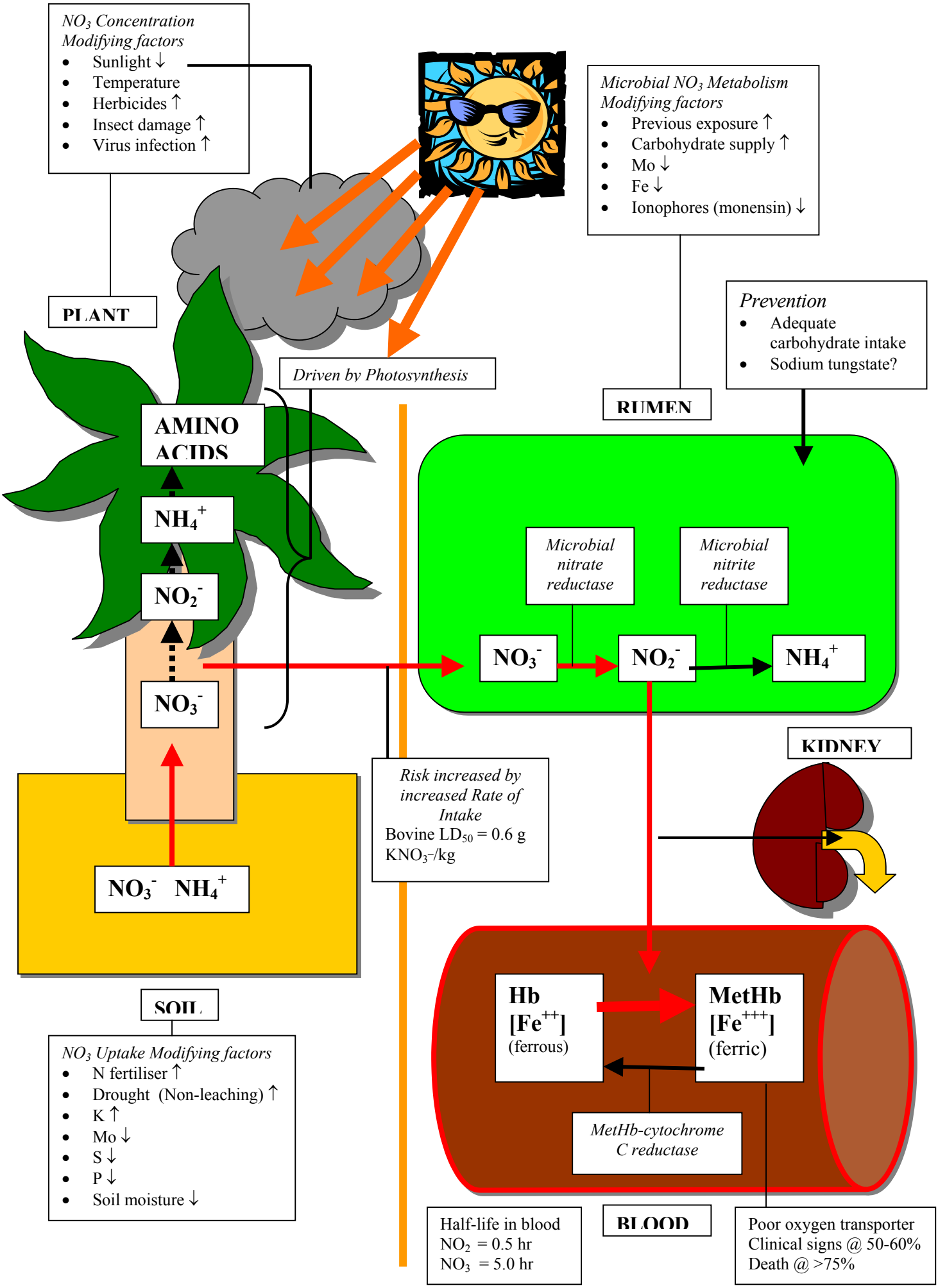
NO_3 Concentration Modifying factors
• Sunlight ↓
• Temperature
• Herbicides ↑
• Insect damage ↑
• Virus infection ↑
Microbial NO_3 Metabolism Modifying factors
• Previous exposure ↑
• Carbohydrate supply ↑
• Mo ↓
• Fe ↓
• Ionophores (monensin) ↓
Prevention
• Adequate carbohydrate intake
• Sodium tungstate?
PLANT
Driven by Photosynthesis
RUMEN
AMINO ACIDS
NH_4^+
NO_2^-
NO_3^-
Microbial nitrate reductase
Microbial nitrite reductase
NO_3^-
NO_2^-
NH_4^+
KIDNEY
Risk increased by increased Rate of Intake
Bovine LD_{50} = 0.6 g KNO_3-/kg
NO_3^- NH_4^+
SOIL
NO_3 Uptake Modifying factors
• N fertiliser ↑
• Drought (Non-leaching) ↑
• K ↑
• Mo ↓
• S ↓
• P ↓
• Soil moisture ↓
Hb $[Fe^{++}]$ (ferrous)
MetHb $[Fe^{+++}]$ (ferric)
MetHb-cytochrome C reductase
BLOOD
Half-life in blood
NO_2 = 0.5 hr
NO_3 = 5.0 hr
Poor oxygen transporter
Clinical signs @ 50-60%
Death @ >75%

Mode of action:
Microbial action in the rumen converts nitrate → nitrite → ammonia
Absorbed nitrite oxidises the iron in haemoglobin → **methaemoglobin** (an inefficient oxygen transporter, brown colour)
methaemoglobin @ 50-60% → clinical signs; @ >75% → death

Nitrite also causes **decreased blood pressure** through a direct relaxing effect of the nitrite ion on the smooth muscle of smaller blood vessels (sheep - Holtenius 1957, cattle - Asbury & Rhode 1964), but probably does not contribute significantly to death from nitite as its experimental reversal with noradrenaline did not change the course of illness (Asbury & Rhode 1964).

Bacterial nitrate reductase contains molybdenum (Mo); increased Mo in the diet promotes nitrite formation; tungsten (a metal of the same group as Mo) inhibits nitrate reductase formation; S also inhibits the formation of the enzyme through interaction with Mo (Takahashi *et al.* 1998)

Conditions of poisoning:
Factors that predispose to high nitrate concentrations in plants **promote nitrate uptake** from soil and **inhibit its conversion into protein**

- **high soil nitrate** concentration due to
  - nitrogen **fertilizer** application
  - manure deposited in **stockyard** soil (see McKenzie *et al.* 2002)
  - **fallow**, during which atmospheric N enters soil at a greater rate than it is leached by rain or taken up by plants
  - **drought**, during which atmospheric nitrogen entering the upper layers of the soil is not leached out by rain
- **low light intensity** (cloudy weather)
- **tissue damage**, e.g. herbicides, insects, rust fungus (Piening 1972), viruses
- low temperature
- water stress
- soil deficiencies, e.g. sulphur, molybdenum, phosphorus - increased soil potassium

Factors modifying poisoning in ruminants
Increased hazard:

- **rapid feed intake** (hungry animals)
- monensin feeding

Decreased hazard:

- **previous exposure** to plant nitrate allows the rumen bacteria to become adapted. The possible species differences in susceptibility (with cattle being more susceptible than sheep) may be related to the composition of the rumen flora and its capacity to reduce nitrite.
- an **adequate supply of available carbohydrate**

Clinical signs:
similar to acute cyanide poisoning
rapid deep breathing
irregular weak pulse
muscle weakness/spasms
coma, **rapid death**
± brown discoloration of mucosae

Suspected sublethal effects of chronic or subclinical intake in ruminants (with no clinical signs of nitrite intoxication in adults) include abortion, congenital defects, depressed production, vitamin A deficiency and goitre. A possible causal relationship is claimed for low forage vitamin A associated with high nitrate (Case 1957). Evidence for links to these outcomes is inconclusive (Norton & Hogan 1993, El Bahri *et al.* 1997; Kammerer & Pinault 1998). Evidence suggesting no long-term effects on ruminants exists (Baranova *et al.* 1999).

However, pregnant ruminants *clinically affected* by nitrate-nitrite poisoning do commonly abort (Bradley *et al.* 1933a). This occurs 3-7 days after the poisoning episode and is probably related to foetal hypoxia/anoxia from maternal methaemoglobinaemia, not foetal methaemoglobinaemia.

Abortion of malformed foetuses in pigs is reported on *Avena sativa* (oats)/ *Brassica napus* crop containing 5.25% KNO_3 in USA.

Nitrate combined with possible iodine deficiency is statistically associated with congenital deformities and hypothyroidism in foals in western Canada where mares were fed oaten hay or green oat forage during pregnancy (Allen *et al.* 1998).

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 (Carlson *et al.* 1994) 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 (see box above).

Aqueous humour nitrate concentrations in normal cattle are about 5 mg/L. In poisoned cattle they can be 100-150 mg/L (Boermans HJ 1990). 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 (Merl Raisbeck, personal communication VETTOX Discussion Group 21 June 2002).

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.

Therapy:
Methylene blue IV is the therapy of choice (Bradley *et al.* 1940a, Scott 1941, Burrows & Way 1975). It activates a normally-dormant reductase enzyme system in erythrocytes which reduces the methylene blue to leucomethylene blue. Leucomethylene blue then reduces methaemoglobin to haemoglobin.

In large doses, methylene blue can itself induce methaemoglobinaemia and haemolysis, but this may be only an *in vitro* phenomenon, as the LD_{50} of methylene blue in sheep is in the range 40-43 mg/kg with no deaths produced at 35 mg/kg and only 6% methaemoglobin produced in sheep by a dose of 22 mg MB/kg (Burrows & Way 1975).

MB is a mutagen and suspected carcinogen, so concerns about its use in food animals have (in part) caused cessation of sale as an antidote in USA and Australia; MB is rapidly excreted from the body but partitions into milk and is strongly recommended not to be used in lactating cows unless a withdrawal period after treatment of 180 days is imposed; animal testing of the carcinogenic potential of MB is underway in USA and the results will influence its long term availability as an antidote (Post & Keller 1999).

Therapeutic protocols for nitrate-nitrite poisoning

Principal therapy
IV **methylene blue** @ 2mg/kg as a 2-4% aqueous solution. Repeat doses may be required if nitrite continues to be absorbed from the rumen.

Overdosing with methylene blue itself will cause methaemoglobinaemia, but Burrows & Way (1975) reported that higher dose rates do not cause significant methaemoglobinaemia in ruminants and recommended using a rate of 20 mg/kg. However, the "standard" dose rate appeared to be adequate in the experiments of van Dijk *et al.* (1983).

A 180 day withholding period should be applied to milk (and other human food products) from cows treated with methylene blue (MB) because of its mutagenic and suspected carcinogenic properties (subject to change after further data generation).

2% MB solutions may be made up from crystalline or anhydrous MB by adding 20 g to each litre of sterile water or sterile saline. Heating the liquid component aids mixing. Gloves and face mask should be worn when handling anhydrous MB.

MB tends to crystallise out of solution. Means of overcoming or avoiding this include
- only making up the solution immediately before administration. For this, carry a zip/snap-lock plastic packet containing 10 g MB taped to the side of a 500 ml bottle of sterile water.
- vigorously shaking and warming the solution to dissolve crystals/precipitate before use.

MB solutions may run poorly through a flutter valve. Administration by large volume syringes is an alternative delivery method. Perivascular injection may cause sloughing.

Alternative therapies
Ascorbic acid IV @ 5-20 mg/kg as an aqueous solution was suggested by Radeleff (1964), but 20 mg/kg was tested experimentally by van Dijk *et al.* (1983) and found **ineffective**.
Menadione IV @ 1 & 2 mg/kg was also tested experimentally by van Dijk *et al.* (1983) and found **ineffective**.

A further suggested alternative is tolonium chloride (Cudd *et al* 1996).

Prevention & control:

Do *not* expose hungry ruminants to stockyards containing lush plants of known capacity to accumulate nitrate.

Check the nitrate content of susceptible crops under drought or cloudy conditions before allowing access by ruminants. Oats crops pose a high nitrate risk if they look very dark green, blue, stunted or frosted (Sneath *et al.* 1998).

Feed adequate amounts of grain (or other carbohydrate source) to dairy cattle before exposing them to crops or pastures of known capacity to accumulate nitrate. This will improve their ruminal microbial detoxification capacity and reduce the risk of intoxication.

Feed roughage to hungry stock before allowing them access to high-nitrate forage. This should reduced the rate of forage intake, giving more time for ruminal microbes to deal with the influx of nitrate and reduce the risk of intoxication.

Alternative preventive measures suggested include

- antibiotics to suppress ruminal flora (not recommended)
- tungsten feeding has been effective experimentally, but the effect is reversed by increased molybdenum intakes
- L-cysteine feeding is effective experimentally in preventing methaemoglobinaemia in sheep dosed with toxic amounts of nitrate (Takahashi *et al.* 1998)
- dose with *Propionibacterium* before exposure to hazardous pastures/crops (under development) (Muirhead 1992)

Boiling does not reduce the nitrate concentration of water (Dalefield & Oehme 1997).

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☑ *Selenium (chronic selenosis)*

Core data

Syndrome names: chronic selenosis
Common sources:

- plants (Australia)
  - *Morinda reticulata*
  - *Neptunia amplexicaulis*
- feed pre-mix
- localised high-Se soils

Animals affected:

- horses
- pigs

Mode of action: Se replaces S in amino acids, interferes with keratinisation
Poisoning circumstances:

- *Morinda* regrowth after pasture burn palatable & high Se (Cape York peninsula)
- *Neptunia* abundant on disturbed soil (Richmond-Hughenden, NQ)
- feed formulation error
- grazing pastures on high-Se soils

Main effects:

- mane & tail hair loss; alopecia
- "laminitis" (hoof cracking); necrosis of coronary band, claw loss

Diagnosis: assay hair, hoof, liver, kidney Se
Therapy: nil
Prevention/Control:

- supplementary feeding in hazardous periods
- correct feed formulation errors

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 (O'Toole *et al.* 1996). The geochemistry associated with Se-accumulator plants often produces water with a high S content in the same landscape (Raisbeck *et al.* 1993).

See also Selenium poisoning syndromes described under Industrial-origin toxins.

Chemical structure:

Selenium is accumulated in plants in **seleno-amino acids**. Australian selenium-accumulating plants contain selenocystathionine. Selenomethionine is the predominant chemical form of Se in plants in North America (O'Toole & Raisbeck 1995).

Sources:

- **selenium-accumulating plants** develop high plant Se content from soils with normal Se content
  - in Australia:
    - ***Morinda reticulata*** (mapoon, ada-a) Family Rubiaceae[DM135]
    - ***Neptunia amplexicaulis*** (selenium weed) Family Mimosaceae [DM82]
  - in North America:
    - obligate indicator plants (require Se for growth)
      - *Artemisia canescens* (4-wing saltbush)
      - *Astragalus* spp. (some locoweeds)
      - *Oonopsis* spp. (goldenweed)
      - *Stanleya pinnata* (prince's plume)
      - *Xylorrhiza* spp. (woody aster)
    - facultative indicator plants (absorb and tolerate large amounts of Se, but do not require it for growth
      - *Atriplex* spp. (saltbrush)
- **feed formulation error** in pig feed (Helie *et al.* 1998)
- normal pasture on localised soils with high Se content (Crinion & O'Connor 1978)

Toxicity:

- **horses** mainly affected in Australia
  - Se accumulated in *M. reticulata* and *N. amplexicaulis* as the non-protein seleno-amino acid, selenocystathionine
  - *M. reticulata* - commonly > 200 mg Se/kg (1.5-1141.0 mg/kg)
  - *N. amplexicaulis* - mean 3000 mg Se/kg (can contain > 4000 mg/kg)
  - seleno-amino acids more readily absorbed than other forms of Se (including elemental Se)
- pigs rarely
  - cases in growers when feed Se concentration in the range 5-8 mg/kg (Helie *et al.* 1998)
  - newborn piglets affected with claw lesions when sows fed 6.2 mg Se/kg feed in second half of gestation (premix 2000 mg Se/kg) (Mensink *et al*. 1990)
- cattle: experimental dietary exposure for 4 months to 0.28 and 0.8 mg Se/kg in the form of selenomethionine and to 0.8 mg Se/kg in the form of sodium selenite reproduces in some cattle mild (subclinical) to severe (clinical) forms of disease (O'Tool & Raisbeck 1995)

Mode of action:

- Se replaces S in amino acids → interference with keratinisation

Conditions of poisoning:

Horses (Australia)

- *M. reticulata*
  - on Cape York peninsula
  - abundant, palatable young regrowth in burnt pasture after spring storms

- most Se in young leaf
- *N. amplexicaulis*
  - confined to Richmond-Hughenden area, north Q
  - abundant in areas of soil disturbance

Horses (Ireland)
- drought periods promote higher-than-normal intake of Se from localised areas of high-Se soils (Crinion & O'Connor 1978)

Pigs
- affected through feed formulation error (excess Se in pre-mix)
- newborn piglets affected when sows fed high Se feed in second half of gestation (Mensink *et al*. 1990)

Copper deficient animals are more susceptible to the effects of Se excess

Clinical signs:

Horses
- **loss of hair from mane and tail**
- **lameness** from hoof lesions
- cracking of hooves (horizontal, vertical)
- ± hoof shedding

Pigs
- growers (Helie *et al.* 1998)
  - onset within 1 week of access to toxic feed
  - decreased weight gains
  - hoof separation at the coronary band
  - ± partial or total alopecia
- newborn piglets (Mensink *et al.* 1990)
  - defective formation of claw wall and sole, haemorrhage, secondary infection
  - no alopecia
  - lameness → starvation through lack of access to sow

Pathology:

Horses
- laminitis (but see histological description of cattle lesions below)

Pigs
- necrosis of coronary band with separation of hoof wall

Cattle (O'Tool & Raisbeck 1995)
- 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
- horse hair, hoof Se > 5 mg/kg; assays are unreliable because of problems with ridding samples of contamination from soil and with interpretation because of temporal variation in deposition of Se within hoof / hair
- pig normal liver Se 0.7 – 1.8 mg/kg; kidney Se 5.0 – 11.5 mg/kg

Therapy:
- no therapy available

Prevention & control:
- horses: supplementary feeding during hazardous periods
- pigs: correct feed formulation error
- in Australia the Maximum Permissible Concentration of selenium in edible offal is 2 mg/kg and in meat 1 mg/kg, wet weight.

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Sulphur

See notes on sulphur under industrial toxins. See also thiaminase.

Syndrome name: `Rape blindness'

Sources:

Plants in the Family Brassicaceae

Brassica spp. (rape, kale etc.)

Rapistrum rugosum (turnip weed)

Toxicity:

Cattle

Toxin uncertain, but **probably associated with high sulphur content** (see S-associated polioencephalomalacia).

Clinical signs:

Sudden onset of blindness ± mania, head pressing

References: Se38