4: Zootoxins (toxins of animals) [Biological-origin toxins]

Distinction should be made between **poisonous animals** – those with toxins in their skin or other organs and which are toxic on ingestion – and **venomous animals** – those with specialised structures for production and delivery of toxins (venoms) to prey species or adversaries.

Halstead (1988) published a monumental review of poisonous and venomous marine animals. A world list of snake venoms and other animal toxins including bee venoms, sawfly toxins, amphibian and fish toxins has been compiled by Theakston & Kamiguti (2002).

Animals acquire toxins by one of three methods (Mebs 2001):

- expression of genes coding for the toxin structures
- metabolic synthesis (production of secondary metabolites)
- uptake, storage and sequestration of toxins produced by other organisms (microbes, plants, or other animals)

References:

Halstead BW (1988) *Poisonous and Venomous Marine Animals of the World.* 2nd revised edition. The Darwin Press Inc., Princeton, New Jersey.

Mebs D (2001) Toxicity in animals. Trends in evolution? *Toxicon* **39**:87-96.

Theakston RDG , Kamiguti AS (2002) A list of animal toxins and some other natural products with biological activity. *Toxicon* **40**:579-651.

PROTOZOA (PROTISTA) - DINOFLAGELLATES

See Marine Microalgal (Dinoflagellate & Diatom) Toxins

ARTHROPODS - INSECTS

☑ *Sawfly larval peptides*

Core data

Common sources:

- *Lophyrotoma interrupta* (Australian cattle-poisoning sawfly larvae)
- *Arge pullata* (European birch sawfly larvae)
- *Perreyia flavipes* & *P. lepida* (South American sawfly larvae)

Animals affected: cattle, sheep, pigs
Mode of action: uncharacterised
Poisoning circumstances: consumption of larvae (dead & alive) at base of trees or on pasture
Main effects: acute liver necrosis
Diagnosis: pathology + evidence of larval presence
Therapy: nil
Prevention: deny access

Syndrome names: sawfly larval poisoning, sawfly poisoning
Chemical structure:

Lophyrotomin [L] is a linear octapeptide (Oelrichs *et al.* 1999)
Pergidin [P] is a linear heptapeptide (Oelrichs *et al.* 1999)

Sources:

Hymenopteran **insect larvae** of the Family Pergidae (sawflies)
Lophyrotoma interrupta [=*Pterygophorus analis* Costa] (Australian cattle-poisoning sawfly larvae) [L > P] (Tryon 1921, Callow 1955, Oelrichs *et al.* 1977, Dadswell *et al.* 1985, McKenzie *et al.* 1985a,b)
Lophyrotoma zonalis (*Melaleuca quinquenervia* sawfly larvae) [P > L]; no association with toxicity incidents on record; insect introduced to Florida USA as biological control agent for weed-pest populations of the Australian native tree *Melaleuca quinquenervia* (paper-barked tea tree) in wetlands (P.B. Oelrichs, personal communication 2 Feb 2000)

Arge pullata (European birch sawfly larvae) [L > P] (Brummerstedt *et al.* 1987, Thamsborg SM *et al.* 1987, Kannan *et al.* 1988, Olaechea *et al.* 1991, Thamsborg *et a.* 1996)

Perreyia flavipes (South American sawfly larvae) [P + some L] (Dutra *et al.* 1997, Riet-Correa *et al.* 1998, Oelrichs *et al.* 1998, Soares *et al.* 2001)

Perreyia lepida (mata porco [= pig killer]) Toxin(s) uncharacterised (Rodrigues Camargo 1955)

Toxicity:

Animals affected are cattle (Australia), sheep (Europe) and cattle and pigs (South America)

Dried *Lophyrotoma interrupta* larval masses retain toxicity

Mode of action: Undescribed. The toxins may have similar activity to amatoxins from *Amanita* spp. mushrooms.

Conditions of poisoning:

Lophyrotoma interrupta:

Poisoning occurs in a restricted area of southern inland Queensland centred on the town of Injune where the host tree of the insect, *Eucalyptus melanophloia* (silver-leaved ironbark), occurs in extensive dense stands. In winter-spring, dead and dying larvae accumulate in mounds at the base of host trees in seasons when the population density of the larvae outstrips its food supply (silver-leaved ironbark leaves). Hungry larvae fall from the crowns of the defoliated trees, attempt to climb other trees to feed, fall again, weaken and die. Cattle avidly seek out and eat the larval masses and are poisoned usually during the period July-September. Occasionally, dried-out larval masses are rehydrated by summer storms and poisoning of cattle has been recorded from these in December-February.

Area of occurrence of sawfly larval toxicity in cattle in Australia

Distribution of the host tree *Eucalyptus melanophloia* (silver-leaved ironbark)

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

Pathology :

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

Lophyrotoma interrupta: (McKenzie *et al.* 1985b)

In many cases, the extent of hepatocyte necrosis is total (panacinar coagulation necrosis).

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

Therapy:

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

Lophyrotoma interrupta:

Treatment regimens similar to those used in humans against amatoxins from *Amanita* spp. mushrooms have been suggested, but by the time clinical signs are apparent, massive liver necrosis is well established and the prognosis is hopeless. Also, such intervention in extensively-grazing cattle could not be justified economically.

Prevention & control:

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

Lophyrotoma interrupta (Dadswell *et al.* 1985):

- Remove cattle from areas with heavily-infested trees before mass die-off of larvae occurs (June-July)
- If possible, provide *E. melanophloia*-free refuge areas on the affected property to receive cattle in high-risk years, having regard to the risks to soil stability from deforestation which are prohibitive in many at-risk areas
- Do not return cattle to infested areas before the end of October, removing any remaining dried larval masses (if possible).

- Some graziers claim that providing phosphorus-based dietary supplements prevents consumption of larvae by cattle, but this has not been scientifically established.
- Insufficient data are available to predict seasons in which dangerous increases in the population density of sawflies may occur.
- Long-term improvement in profitability of an affected property may mitigate against the effects of periodic sawfly larval poisoning of cattle, but the region in which poisoning occurs is mostly marginal grazing land and such improvements are difficult.
- Development of an immunogen against the toxin has been suggested, but such a product is judged unlikely to be protective given the massive rapid influx of toxin into the body and uneconomic to manufacture commercially because of the very limited market.

References:

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Brummerstedt E, Kristensen A, Nielsen R, Bille-Hansen V (1987) [Death in puppies following uptake of sawfly larvae *Arge pullata*] *Dansk Veterinaertidsskrift* **70**:758-760.

Callow LL (1955) Sawfly poisoning in cattle. *Qd. Agric. J.* **81**:155-161.

da Costa Lima A (1941) Bichos "mata porcos". *Chacaras e quintais* **63**:43. cited by Soares *et al.* 2000

Dadswell LP, Abbott WD, McKenzie RA (1985) The occurrence, cost and control of sawfly larval (*Lophyrotoma interrupta*) poisoning of cattle in Queensland 1972-81. *Aust. Vet. J.* **62**:94-97.

Dutra F, Riet-Correa F, Mendez M, Paiva N (1997) Poisoning of cattle and sheep in Uruguay by sawfly (*Perreyia flavipes*) larvae. *Vet. Hum. Toxicol.* **39**:281-286.

Kannan R, Oelrichs PB, Thamsborg ST, Williams DH (1988) Identification of the octapeptide lophyrotomin in the European birch sawfly (*Arge pullata*). *Toxicon* **26**:224-226.

Leonard GJ (1972) The isolation of a toxic factor from sawfly (*Lophyrotoma interrupta* Klug) larvae. *Toxicon* **10**:597-603.

McKenzie RA Rogers RJ, Oelrichs PB (1985a) Sawfly larval poisoning of cattle in Queensland. In *Plant Toxicology*. Seawright AA, Hegarty MP, James LF, Keeler RF (eds), Queensland Poisonous Plants Committee, Brisbane. pp.524-532.

McKenzie RA, Dunster PJ, Twist JO, Dimmock CK, Oelrichs PB, Rogers RJ, Reichmann KG (1985b) The toxicity of sawfly larvae (*Lophyrotoma interrupta*) to cattle. Queensland Department of Primary Industries Bulletin QB85001. 48 pp.

Oelrichs PB, Vallely JV, Macleod JK, Cable J, Kiely DE, Summons RE (1977) Lophyrotomin, a new toxic octapeptide from the larvae of the sawfly *Lophyrotoma interrupta*. *Lloydia* **40**:209-214.

Oelrichs PB, MacLeod JK, Williams DH (1983) Lophyrotomin, a new hepatotoxic octapeptide from sawfly larvae *Lophyrotoma interrupta. Toxicon* Suppl. 3, pp.321-323.

Oelrichs PB, MacLeod JK, Seawright AA, Ng JC, Dutra F, Riet-Correa F, Mendez MC (1998) The purification and isolation of two hepatotoxic compounds from the Uruguay sawfly *Perreyia flavipes*. Chapter 101 in *Toxic Plants and Other Natural Toxicants*. eds Garland T, Barr AC. CAB International, Wallingford. pp. 517-521.

Oelrichs PB, MacLeod JK, Seawright AA, Moore MR, Ng JC, Dutra F, Riet-Correa F, Mendez MC, Thamsborg SM (1999) Unique toxic peptides isolated from sawfly larvae in three continents. *Toxicon* **37**:537-544.

Olaechea FV, Thamsborg SM, Christensen NO, Nansen P, Robles A (1991) Interference with sawfly (*Arge pullata*) poisoning in *Fasciola hepatica*-infected lambs. *J. Comp. Path.* **104**:419-433.

Riet-Correa F, Dutra F, Soares MP, Mendez MC (1998) Sawfly (*Perreyia flavipes*) larval poisoning of cattle, sheep and swine. Chapter 58 in *Toxic Plants and Other Natural Toxicants*. eds Garland T, Barr AC. CAB International, Wallingford. pp.291-296.

Roberts FSH (1932) The cattle-poisoning sawfly (*Pterygophorus analis* Costa). *Qd. Agric. J.* **37**:41-52.

Rodrigues Camargo O (1955) Contribuicao ao estudo do Tenthredinideo "mata porcos", *Paraperreyia dorsuaria* (Konow 1899), no Rio Grande do Sul. Thesis, Escola de Agronomia e Veterinaria de Universidade do Rio Grande do Sul, Brazil cited by Riet-Correa *et al*.(1998)

Soares MP, Riet-Correa F, Smith DR, Periera Soares M, Mendez MC, Brandolt AL (2001) Experimental intoxication by larvae of *Perreyia flavipes* Konow 1899 (Hymenoptera: Pergidae) in pigs and some aspects of its biology. *Toxicon* **39**: 669-678.

Thamsborg SM, Jorgensen RJ, Brummerstedt E (1987) Sawfly poisoning in sheep and goats. *Vet. Rec.* **121**:253-255.

Thamsborg SM, Jorgensen RJ, Brummerstedt E, Bjerregard J (1996) Putative effect of silymarin on sawfly (*Arge pullata*)-induced hepatotoxicosis in sheep. *Vet. Human Toxicol.* **38**:89-91.

Tryon H (1921) Special cattle fatality in the Maranoa district, and its relation to the larvae of *Pterygophorus analis* Costa. *Qd. Agric. J.* **16**:208-216.

Williams DH, Santikarn S, Oelrichs PB, De Angelis F, MacLeod JK, Smith RJ (1982) The structure of a toxic octapeptide, containing 4 D-amino acids, from the larvae of a sawfly, *Lophyrotoma interrupta*. *J. Chem. Soc., Chem. Commun.* pp.1394-1396.

Williams DH, Bojensen G, Santikarn S, De Angelis F, Oelrichs PB, MacLeod J (1983) Study of a toxic octapeptide from the larvae of sawfly by fast atom bombardment mass spectrometry. *Int. J. Mass Spectrometry Ion Phys.* **46**:427-430.

Bee venom peptides

Immune-mediated haemolytic anaemia secondary to bee stings reported in dogs
Multiple stings

Haemolysing components of bee venom in descending order of importance are the peptides (proteins) melittin, phospholipase A_2 and apamin (Schmidt 1995). Mouse IV LD_{50} of honeybee venom is 2.8-3.1 mg/kg, with strikingly similar toxicity for all 6 *Apis* species and varieties tested (Schmidt 1995).
Clinical signs: lethargy, haematuria
References:

Cowell AK, Cowell RL, Tyler RD, Nieves MA (1991) Severe systemic reactions to *Hymenoptera* stings in three dogs. *J. Am. Vet. Med. Assoc.* **198**:1014-1016. [1 fatal case of severe bee envenomation; haemolysis, DIC]

Noble SJ, Armstrong PJ (1999) Bee sting envenomation resulting in secondary immune-mediated hemolytic anemia in two dogs. *J. Am. Vet. Med. Assoc.* **214**:1026-1027.

Schmidt JO (1995) Toxinology of venoms from the honeybee genus *Apis*. *Toxicon* **33**:917-927.

Wysoke JM, van den Berg PB, Marshall C (1990) Bee sting-induced haemolysis, spherocytosis and neural dysfunction in three dogs. *J. S. Afr. Vet. Assoc.* **61**:29-32.

Lucibufagins (firefly toxins) – Australian lizards & frogs captive in North America

Chemical structure:

lucibufagins = steroidal pyrones structurally related to bufadienolide cardiac glycosides

Sources:

- North American fireflies of genus ***Photinus*** ; an individual insect contains about 90 µg lucibufagins
- fireflies of genus *Photuris* (females feed on *Photinus* spp. and take in lucibufagins)
- fireflies are beetles in the Order Coleoptera, Family Lampyridae; uncommon in Australia and confined mostly to rainforest and mangroves of eastern Australia, mostly north Queensland (Lawrence & Britton 1991)

Toxicity:

- lucibufagins are known to protect fireflies against spider and bird predation
- no quantitative toxicity data available for reptiles/amphibia
- toxic dose: 1-6 insects fed to each reptile/amphibian

Mode of action: undetermined in reptiles/amphibians, but experimentally in dogs cause ventricular arrhythmia IV @ 0.06 mg/kg (*Pogona* spp. weigh about 100 g)

Conditions of poisoning:

- captive pet reptiles or amphibians exotic to North America fed North American fireflies
  - 2 cases in pet Australian lizards (*Pogona vitticeps* – a bearded dragon)
  - 1 case in pet African chameleons (*Chamaeleo pardalis*)
  - 1 case in pet *Lacerta derjugini* (lizard native of Caucasus)
  - 2 cases in pet Australian frogs (*Litoria caerulea* – green or White's tree frog)
- Australian reptiles and amphibians of the above genera/species may not have evolved effective chemical defenses against lucibufagins or a sensitivity to the feeding deterrent effects of these compounds because they have seldom or never encountered them in their natural habitats.

Clinical signs:

- onset 30-90 min after ingestion
- violent head shaking followed by pronounced frequent oral gaping
- regurgitation of the ingested insect was not seen in *Pogona* spp., but was noted in *Lacerta derjugini*
- severe dyspnoea
- skin colour change in *Pogona* sp., brown → black
- death within 15 min - 1 hr of onset

Pathology:

- *Photinus* sp. body parts in stomach contents
- no gross lesions in viscera

Diagnosis: access + syndrome

Therapy: none recorded

Prevention & control: screen fireflies from diets of captive exotic reptiles and amphibians

References:

Knight M, Glor R, Smedley SR, Gonzales A, Adler K, Eisner T (1999) Firefly toxicosis in lizards. *J. Chem. Ecol.* **25**:1981.

Lawrence JF, Britton EB (1991) Coleoptera (beetles). Chapter 35 in Division of Entomology, CSIRO, *The Insects of Australia.* 2nd edition, Melbourne University Press, Melbourne. Volume 2, pp.543-683 [Lampyridae p. 640.]

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

Syndrome names: Fire ant sting

Chemical structure:

Fire ant venom contains several components comprising

- **Solenopsins** which are 2-alkyl or alkenyl 6-methyl **piperidine alkaloids** (Brand *et al.* 1972, 1973; Leclercq *et al.* 1994, 1996; MacConnell *et al.* 1971, 1976)
- **peptide allergens** of which 4 are known (Hoffman 1993)

Sources:

Australia:

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 (DPI, unpublished data 2001, Cas Vanderwoude, personal communication 13 July 2002). A single nest has been detected in Auckland, New Zealand.

Solenopsis geminata [Fabricius] (tropical fire ant), native to North America, but now with a pan-tropical world distribution, and has been present in and around Darwin in the Northern Territory of Australia for some decades (Chin 1998; Hoffman & Andersen 1999; Cas Vanderwoude, personal communication 13 July 2002).

In addition, Australia has at least 6 native *Solenopsis* species (Cas Vanderwoude, personal communication 13 July 2002). A key to Australian *Solenopsis* to aid local identification of the exotic species has been constructed by Marlene Elson-Harris & Cas Vanderwoude.

Americas:

Several species of *Solenopsis* are present, either endemic or introduced.

Organ systems affected: Skin, Respiratory-cardiovascular

Toxicity:

The amount of venom delivered by a single fire ant sting is < 1 μg (King 1996).

Solenopsis invicta

Despite the widespread and dense populations of *S. invicta* in the southern United States, published evidence of negative effects on domestic animals in infested areas is very sparse.

Newborn calves – corneal ulcers (Joyce 1983)

Dogs – allergies have been documented, but severe hypersensitivity/anaphylactic reactions are apparently undocumented at this time, although they are believed to be possible (Willis *et al.* 1996, Bevier 1999)

Ferret - dermatitis (King *et al.* 1996)

Aquacultured rainbow trout died after eating alate fire ants (that is, winged forms produced by colonies for dispersal events) landing on the water surface in 2 consecutive years (Contreras & Labay 1999).

Humans – dermatitis and (rarely) anaphylaxis (Rhoades 1977, Stafford 1996). One case of anaphylaxis is reported from Brisbane, Queensland (Solley *et al.* 2002; McCubbin & Weiner 2002)

Ecological effects: Wildlife have been affected in southern USA (Allen *et al.* 1998). Recent literature includes reference to effects on white-tailed deer (Allen *et al.* 1997a), bobwhite quails (Giuliano *et al.* 1996, Mueller *et al.* 1999), least terns (Lockley 1995), crested caracara (Dickinson 1995), lizards (Chalcraft & Andrews 1999) and alligators (Allen *et al.* 1997b). A preliminary study of ecological effects in Brisbane has been published (Nattrass & Vanderwoude 2001)

Mode of action:

Allergy/anaphylaxis: Following exposure, susceptible individuals may develop sustained concentrations of venom-specific IgE and IgG antibodies. IgE antibodies are bound to mast cells and basophils. Cross-linking of cell-bound IgE antibodies by multivalent antigens or allergens causes release of chemical mediators that trigger allergic responses. (King 1996)

Conditions of envenomation:

Defensive stinging

Disturbance of a nest will provoke an aggressive response from worker ants. The individual ants grasp the victim with their jaws and then inflict single or multiple stings with their abdominal stinger. Venom may act as a pheromone, summoning other ants to attack. Adult and mobile animal victims are unlikely to suffer severe effects if they can distance themselves rapidly from ant colonies.

Offensive stinging

Small neonates such as chickens and nestling birds may be deliberately predated, overwhelmed and die of stings. Large neonates such as calves may suffer severe damage to eyes or other soft body parts before they can escape. Immobile geriatric humans have been overwhelmed and suffered fatal multiple stings.

Clinical signs:

Stung animals jump or shy away from the locality. Dogs may yelp.

Local effects at the sting site

An immediate sharp pain occurs at the site, with an urticarial weal forming within minutes, and transforming to a vesicle and then to a pustule within 24 hr. The pustule may persist for 3-8 days in humans before rupture and crusting.

Systemic effects (very rare)

Multiple stings may provoke shock, convulsions, apnoea and rapid death. Animals including humans that become sensitised to the venom allergens may suffer severe anaphylaxis and die if untreated. Anaphylaxis has not been recorded in non-human animals (Fowler 1993).

Signs of systemic hypersensitivity reactions in dogs and cats to insect stings in general (Bevier 1999) are (alone or in combination, with rapid progression):

Pruritis around the head or sting site
Facial urticaria and angio-oedema
Salivation & lacrimation
Vomiting, abdominal pain signs, diarrhoea
Hepatosplenomegaly in dogs
Dyspnoea & cyanosis in cats
Shock
Incoordination, collapse, convulsions, death

Pathology: Pustules at sting sites

Diagnosis: Access to ant colonies + syndrome

Therapy:

Local experience with stings in humans indicates that cold running water provides the best short-term symptomatic relief and that creams containing lignocaine may also be helpful [Cas Vanderwoude (Manager, Scientific Services, Fire Ant Control Centre), personal communication 13 July 2002]

Emergency therapy for anaphylaxis in dogs and cats (Bevier 1999):

Animals in shock:

- If in respiratory distress, establish a patent airway and give oxygen
- Insert an intravenous cannula
- Immediately give IV 0.2-1.0 ml adrenaline HCl (1:10,000 ratio). If IV dosage not possible, give 0.2-2.0 ml SC.
- Give shock doses of IV fluids, such as 5%dextrose-water solution or lactated Ringer's solution, @ 50-100 ml/kg/hr for 1-2 hr
- Give fast-acting corticosteroids such as dexamethasone IV @ 2-4 mg/kg
- Give diphenhydramine (Benadryl) IM or slow IV @ 2 mg/kg
- Inject 0.2-0.5 ml adrenaline HCl (1:10,000 ratio) at the sting site
- Apply cold to the sting site
- After 20-30 min, if signs continue or worsen, repeat adrenalin injection

Animals with less severe signs:

- Give 0.2-2.0 ml adrenalin HCl (1:10,000 ratio) SC

- ❖ Give diphenhydramine (Benadryl) SC @ 2 mg/kg
- ❖ If stridor or dyspnoea exists, monitor closely for airway patency and correct if required
- ❖ Inject 0.2-0.5 ml adrenaline HCl (1:10,000 ratio) at the sting site
- ❖ Apply cold to the sting site
- ❖ If shock develops, initiate therapy as above

Prevention & control:

Carefully-targeted insecticide and biological control methods for the ants are used in USA. The specific name of *Solenopsis invicta* reflects the lack of success to date in controlling these ants in the southern United States. An eradication program under the control of the Queensland Department of Primary Industries is under way in Brisbane. For publicly-available details, see the website http://www.dpi.qld.gov.au/fireants/

Historically, Rachel Carson in *Silent Spring* (1962) highlighted some of the serious negative effects on livestock and wildlife of the early failed broad-acre control programs using the chlorinated hydrocarbon insecticides (*q.v.*) dieldrin and heptachlor distributed by aircraft in the southern United States. These methods have been abandoned and the chemicals used withdrawn from sale.

References:

Review Literature

Blum MS (1984) Poisonous ants and their venoms. In Tu AT (ed) *Hand book of Natural Toxins. Volume 2. Insect Poisons, Allergens and Other Invertebrate Toxins.* Marcel Dekker, New York. p. 225.

Fowler ME (1993) *Veterinary Zootoxicology.* CRC Press, Boca Raton. pp .41-46.

Harwood RF, James MT (eds.) (1979) *Entomology in Human and Animal Health.* 7th edition. Macmillan, New York.

Hayashi AM (1999) Attack of the fire ants. *Scientific American* **280** (2):14

Rhoades RB (1977) *Medical Aspects of the Imported Fire Ant.* The University Presses of Florida, Florida.

Taber SW (2000) *Fire Ants.* Texas A&M University Press, College Station, Texas.

General Literature

Allen CR, Demarais S, Lutz RS (1997a) Effects of red imported fire ants on recruitment of white-tailed deed fawns. *J. Wildl. Mgmt.* **61**:911-916.

Allen CR, Rice KG, Wojcik DP, Percival HF (1997b) Effect of red imported fire ant envenomization on neonatal American alligators. *J. Herpetology* **31**:318-321.

Allen CR, Lutz RS, Demarais S, Wadsworth KG (1998) Ecological effects of the invasive nonindigenous ant, *Solenopsis invicta*, on native vertebrates: the wheels on the bus. *Trans. 63rd N. Am. Wildl. Nat. Resources Conf., Orlando, Florida, 20-24 March 1998.* Wildlife Management Institute, Washington DC. pp. 56-65.

Attygalle AB, Morgan ED (1984) Chemicals from the glands of ants. *Chem. Soc. Rev.* **13**:245-278.

Bevier DE (1999) Insect and arachnid hypersensitivity. *Vet. Clinics N. Am., Small Anim. Pract.* **29** (6):1385-1405.

Brand JM, Blum MS, Fales HM, MacConnell JG (1972) Fire ant venoms: comparative analyses of alkaloidal components. *Toxicon* **10**:259-271.

Brand JM, Blum MS, Barlin MR (1973) Fire ant venoms: intraspecific and interspecific variation among castes and individuals. *Toxicon* **11**:325-331.

Carson R (1962) *Silent Spring.* Houghton Mifflin Co., New York. [Folio Society edition 2000, pp. 164-173.

Chalcraft DR, Andrews RM (1999) Predation on lizard eggs by ants: species interactions in a variable physical environment. *Oecologia* **119**:285-292.

Chin D (1998) Ants in the household and backyard. *Agnote-Darwin* No. 546, pp.1-5 [Describes common pest ant species of Darwin]

Contreras C, Labay A (1999) Rainbow trout kills induced by fire ant ingestion. *Texas J. Sci.* **51**:199-200.

Deslippe RJ, Guo Y-J (2000) Venom alkaloids of fire ants in relation to worker size and age. *Toxicon* **38**:223-232.

Dickinson VM (1995) Red imported fire ant predation on crested caracara nestlings in south Texas. *Wilson Bull.* **107**:761-762.

Guiliano WM, Allen CR, Lutz RS, Demarais S (1996) Effects of red imported fire ants on northern bobwhite chicks. *J. Wildl. Mgmt.* **60**;309-313.

Hoffman BD, Andersen AN (1999) Impact of an introduced ant on native rainforest invertebrates: *Pheidole megacephala* in monsoonal Australia. *Oecologia* **120** (4):595-604. [*Solenopsis geminata* included among 9 introduced ant species studied]

Hoffman DR (1993) Allergens in Hymenoptera venom XXIV: the amino acid sequences of imported fire ant venom allergens Sol I II, Sol I III, and Sol I IV. *J. Allergy Clin. Immunol.* **91**:71-78.

Hoffman DR (1997) Reactions to less common species of fire ants. *J. Allergy Clin. Immunol.* **100**:679-683.

Joyce JR (1983) Multifocal ulcerative keratoconjunctivitis as a result of stings by imported fire ants. *Vet. Med.* **78**:1109.

King TP (1996) Immunochemical studies of stinging insect venom allergies. *Toxicon* **34**:1455-1458.

King WW, Lemarie SL, Veazey RS, Hodgin EC (1996) Superficial spreading pyoderma and ulcerative dermatitis in a ferret. *Vet. Dermatology* **7**:43-47.

Leclercq S, Thirionet I, Broeders F, Daloze D, Vander Meer RK, Braekman JC (1994) Absolute configuration of the solenopsins, venom alkaloids of the fire ants. *Tetrahedron* **50**:8465-8478.

Leclercq S, Braekman JC, Daloze D, Pasteels JM, Vander Meer RK (1996) Biosynthesis of the solenopsins, venom alkaloids of the fire ants. *Naturwissenschaften* **83**:222-225.

Lockley TC (1995) Effect of imported fire ant predation on a population of the least tern – an endangered species. *Southwestern Entomologist* **20**:517-519.
Lofgren CS, Vander Meer RK (eds.) (1986) *Fire Ants and Leaf-cutting Ants: Biology and Management.* Westview Press, Boulder, Colorado.
MacConnell JG, Blum MS, Fales HM (1971) The chemistry of fire ant venom. *Tetrahedron* **26**:1129-1139.
MacConnell JG, Blum MS, Buren WF, Williams RN, Fales HM (1976) Fire ant venoms: chemotaxonomic correlations with alkaloidal compositions. *Toxicon* **14**:69-78.
McCubbin KI, Weiner JM (2002)Fire ants in Australia: a new medical and ecological hazard. *Med. J. Aust.* **176**:518-519.
Mueller JM, Dabbert CB, Demarais S, Forbes AR (1999) Northern bobwhite chick mortality caused by red imported fire ants. *J. Wildl. Mgmt.* **63**:1291-1298.
Nattrass R, Vanderwoude C (2001) A preliminary investigation of the ecological effects of red imported fire ants (*Solenopsis invicta*) in Brisbane. *Ecological Management & Restoration* **2**:220-223.
Solley GO, Vanderwoude C, Knight GK (2002) Anaphylaxis due to red imported fire ant sting. *Med. J. Aust.* **176**:521-523.
Stafford CT (1996) Hypersensitivity to fire ant venom. *Ann. Allergy Asthma Immunol.* **77**:87-95.
Willis EL, Kunkle GA, Esch RE, Grier TJ, Kubilis PS (1996) Intradermal reactivity to various insect and arachnid allergens among dogs from the south-eastern United States. *J. Am. Vet. Med. Assoc.* **209**:1431-1434.

Identification of fire ants

Cook JL (2001) in preparation
Hung A, Barlin MR, Vinson SB (1977) *Texas Agricultural Experiment Station Bulletin* No. 1185.
O'Keefe ST, Cook JL, Vinson SB (2001) Texas fire ant identification: an illustrated key. http://fireant.tamu.edu/material/factssheets/fapfs0~13.htm
Trager JC (1991) [Technical key to identification of fire ants of North and South America] *J. N. Y. Entomol. Soc.* **99** (2):141-198.

Cantharidin (blister beetles, Spanish fly)

Core data

Syndrome names: blister beetle poisoning
Common sources: several *Epicauta* spp. beetles
Animals affected: horses
Mode of action: direct irritation of alimentary tract and urinary tract
Poisoning circumstances: ingestion of contaminated fodder hay, usually *Medicago sativa* (lucerne, alfalfa)
Main effects: gastroenteritis, cystitis and urethritis, cardiomyopathy
Diagnosis: syndrome + assay for cantharidin
Therapy: activated charcoal + saline cathartic, rehydration, electrolytes, antibiotics
Prevention: inspection of suspect hay, careful harvesting technique

Syndrome names:

blister beetle poisoning

Chemical structure:

Cantharidin = hexahydro-3a,7a-dimethyl-4,7-epoxyisobenzofuran-1,3-dione

Cantharidin is a defense chemical for the beetle species which synthesise it, deterring other insects from feeding on them (Carrel & Eisner 1974). Male beetles synthesise cantharidin and pass it to females during copulation (Arnold 1976).

Sources:

Insects

Beetles in the genus *Epicauta* of Family Meloidae endemic to North America, more common in the southern and south-eastern United States. The adults feed on nectar and pollen of flowers and to a much lesser extent on leaves. Eggs are laid in soil and the larvae feed on the eggs of grasshoppers and solitary bees (Hutchison *et al.* 1990). Some 200 species occur in the United States, but while only a few have been associated with natural cases of poisoning (Fowler 1993; see below), others are potentially toxic (Capinera *et al.* 1985).

Species associated with toxicity include the following, the first two being the most commonly involved (Fowler 1993):

Epicauta occidentalis
Epicauta lemniscata
Epicauta vittata
Epicauta pardalis
Epicauta pennsylvanica

Epicauta temexa
Epicauta albida
Epicauta attrivittata

Cantharidin content of dried *Epicauta* spp. varies between 1 and 5% by weight (Ray *et al.* 1989).

Mylabris phalerata (Chinese blister beetle) (VM9:1708)

Pyrota insulata (Os437)

Lytta vesicatoria [= *Cantharis vesciatoria*] (Spanish fly, blistering fly, blistering beetle, blister bug) occurs in southern and central Europe, mainly on plants in the families Oleaceae and Caprifoliaceae (Windholz 1983).

Commercial / Therapeutic substances

Cantharides. Highly toxic and historically used therapeutically as a vesicant, rubefacient and counter irritant, and notoriously as an aphrodisiac (Windholz 1983).

Toxicity:

horses: as little as 4 g of dried *Epicauta* sp. beetles may be lethal

cantharidin oral lethal doses (Ray *et al.* 1979):

experimental: dogs & cats 1.0-1.5 mg/kg; rabbits 20 mg/kg

estimated: horses about 0.5 mg/kg; humans < 1.0 mg/kg

Organ systems affected: alimentary tract, urinary system

Mode of action:

Cantharidin causes intense direct irritation of skin and mucous membranes on contact. Excretion through the kidneys leads to irritation of the urinary tract.

Conditions of poisoning:

Horses eating fodder hay containing dead *Epicauta* sp. beetles :

usually *Medicago sativa* (lucerne, alfalfa) hay

rarely, other types of hay may be involved if they are contaminated with flowering weeds which provide food for the beetles

Epicauta spp. that swarm in groups and move about in hay fields feeding on flowers are most likely to be involved in poisoning. Hay harvesting methods introduced since the mid-1960s that cut, crimp and swathe plants in one operation to speed drying may trap, crush and incorporate beetle swarms into the finished product. Older harvesting methods that mowed the plants and left them to dry without crimping, allowed the beetles to escape (Arnold 1976). Trapped and crushed groups of beetles may be concentrated in only a small portion of hay, and thus only one or a few of a group of animals may be poisoned by a batch of hay.

Clinical signs:

Horse

Large doses may cause shock and death within 4 hr (MacKay & Wollenman 1981, Schoeb & Panciera 1979). Smaller doses cause gastroenteritis, nephrosis, cystitis and urethritis, and may cause myocarditis. The course of lethal intoxication may be up to 5 days. The case fatality ratio is 50% with horses surviving over a week having a favourable prognosis.

Signs include:

anorexia
faeces soft or mucoid to bloody; diarrhoea may occur in horses surviving a few days
intestinal atony
colic
dysuria – frequent painful urination or oliguria to anuria
haematuria
hyperthermia to 41^{o}C
dehydration
weakness
muscle rigidity
collapse
sweating
dyspnoea (tachypnoea) with rales on auscultation (from pulmonary oedema)
tachycardia
congested mucous membranes, slow capillary refill time

synchronous diaphragmatic flutter
buccal ulceration

Pathology:

Horses (clinical pathology):

hypocalcaemia
hypomagnesaemia
azotaemia
neutrophilia
low urine specific gravity
haematuria
dehydration (haemoconcentration)

Horses (necropsy & histopathology):

No lesions may be found in many cases. Vesication (acantholysis) or ulceration of the squamous epithelium of the mouth, oesophagus and pars oesophagaea of the stomach may occur. Congestion and haemorrhage may occur in the urinary tract mucosa and oedema in the lungs. Nephrosis and myocarditis are seen. Hepatomegaly and splenomegaly may occur.

Diagnosis:

Syndrome + detection of beetles in remaining hay or cantharidin in samples
Assay (HPLC, GC/MS) for cantharidin in urine, alimentary tract contents and kidney is available in some laboratories (Ray *et al.* 1989).

Therapy:

General decontamination should be applied early - activated charcoal + saline cathartic PO
Attention must be given to rehydration and correcting electrolyte imbalances and to control of secondary infection through alimentary tract lesions by antibiotics, avoiding those that may be nephrotoxic (aminoglycosides).

Prevention & control:

careful inspection of hay before feeding to horses
reduction in grasshopper numbers to reduce prey numbers for blister beetle larvae
hay harvesting should take account of the behaviour of blister beetles

heavily blooming *Medicago sativa* is the most attractive stage for beetles
harvester operators need to be alert for the presence of groups of swarming beetles to avoid incorporating them into hay by stopping to allow them to disperse or by moving to an area of the crop free of beetles

References:

Review literature

Os437; VM8:1610; VM9:1708
Fowler ME (1993) *Veterinary Zootoxicology*. CRC Press, Boca Raton, Florida. pp. 61-67.
Helman RG, Edwards WC (1997) Clinical features of blister beetle poisoning in equids: 70 cases (1983-1996). *J. Am. Vet. Med. Assoc.* **211**:1018
Schmitz DG (1989) Cantharidin toxicosis in horses. *J. Vet. Intern. Med.* **3**:208-215.

General literature

Arnold DC (1976) *Blister beetles of Oklahoma.* Technical Bulletin T-145, Agricultural Experiment Station, Oklahoma State University, Stillwater, Oklahoma. [cited by Fowler 1993]
Capinera JL, Gardner DR, Stermitz FR (1985) Cantharidin levels in blister beetles, (*Coleoptera:* Meloidae) associated with alfalfa in Colorado. *J. Economic Entomol.* **78**:1052
Carrel JE, Eisner T (1974) Cantharidin: potent feeding deterrent to insects. *Science* **183**:755
Edwards WC *et al.* (1989) *Vet. Human Toxicol.* **31**:442
Hutchison WD, Murphy MJ, Tufte GN (1990) *Blister Beetles in Alfalfa. Management Options to Minimise Poisoning in Horses.* AG-FO 5510-D, Minnesota Agricultural Extension Service, University of Minnesota, St.Paul, Minnesota. [cited by Fowler 1993]
MacKay RJ, Wollenman P (1981) An outbreak of blister beetle poisoning in horses in Florida. *Florida Vet. J.* **10**:11
Ray AC, Tamulinas SH, Reagor JC (1979) High pressure liquid chromatographic determination of cantharidin, using a derivatization method in specimens from animals acutely poisoned by ingestion of blister beetles, *Epicauta lemniscata. Am. J. Vet. Res.* **40**:498
Ray AC, Kyle ALG, Murphy MJ, Reagor JC (1989) Etiologic agents, incidence, and improved diagnostic methods of cantharidin toxicosis in horses. *Am. J. Vet. res.* **50**:187
Schoeb TR, Panciera RJ (1979) Pathology of blister beetle *Epicauta* poisoning in horses. *Vet. Pathol.* **16**:18
Shawley RV, Rolf LL (1984) Experimental cantharidiasis in the horse. *Am. J. Vet. Res.* **45**:2261
Windholz M (ed.) (1983) *The Merck Index* 10th ed., Merck & Co. Inc., Rahway New Jersey. pp.241-242.

ARTHROPODS – ARACHNIDS (SPIDERS, SCORPIONS, TICKS)

Spider envenomations

Latrodectus hasselti (red-back spider) venom

Sutherland (1983) citing Brown (1980) speculates that bitten domestic animals would be distressed and probably chew at the bitten area and that systemic signs would include vomiting, sweating (where possible), tachycardia and muscle spasm and possibly abdominal rigidity and diarrhoea. Cats are more likely to salivate excessively and be hyperexcitable.

References:

Brown RA (1980) Red-back spider envenomation in dogs. *Control & Therapy Series, Post Grad Foundation in Vet. Sci., Uni. Sydney* No.989

Sutherland SK (1983) *Australian Animal Toxins. The creatures, their toxins and care of the poisoned patient.* Oxford University Press, Melbourne. pp. 253-254.

Necrotising arachnidism

Lampona cylindrata Koch (white-tailed spider) bites are suspected to cause ulceration spreading from the bite site in humans (Sutherland & Sutherland 1999). A suspected case is on record in a female greyhound (McOrist & Dorling 1981).

References:

McOrist S, Dorling J (1981) Case 18:4 in Sutherland SK (1983) *Australian Animal Toxins. The creatures, their toxins and care of the poisoned patient.* Oxford University Press, Melbourne. p. 231.

Sutherland SK, Sutherland J (1999) *Venomous Creatures of Australia. A Field Guide with Notes on First Aid.* 5th edition. Oxford University Press, Melbourne. p. 63.

Atrax spp. (funnel-web spiders) venom

Mammals other than humans are believed **not** to be susceptible to funnel-web spider bites under natural conditions. Male Sydney funnel-web spiders (*Atrax robustus*) are more toxic than those of females (Wiener 1957) and there is geographic variation in toxicity, with spiders from Sydney's north shore being twice as venomous as those from Gosford (Sutherland 1979). Human fatalities from the Sydney funnel-web spider occur after bites by males within a radius of 160 km of Sydney (Sutherland 1983). Classically, untreated signs and symptoms are intense local pain at the bite site, numbness around the mouth, spasms of the tongue, nausea and vomiting, abdominal pain, profuse sweating, brisk salivation, lachrymation, severe dyspnoea from non-cardiogenic pulmonary oedema, local and general muscle fasciculation, hypertension and deterioration of mental state from confusion to irrationality to coma, probably from raised intra-cranial pressure; death occurs in 15 to 90 minutes in children and 30 hrs or later in adults (Sutherland 1983). An effective antivenom is available.

Experimental fatal envenomation with large venom doses has been produced in guinea pigs, mice and rabbits. Transient mild envenomation has been produced experimentally with large doses of venom in dogs, cats, horses and sheep. Transient hypotension lasting 1 hr was produced by IV injection of 55 μg male venom/kg in dogs and 70 μg male venom/kg in cats (Duncan *et al.* 1980). A cat injected IV with 10 mg female venom/kg suffered mild transient hypotension and brief apnoea, but recovered completely (Sutherland SK, unpublished data 1972, cited by Sutherland 1983 p.261). A horse injected SC with 60 mg female venom was anorexic for 24 hr and some mild twitching was noted at the site of injection (Wiener 1963). Venom yields obtained by milking spiders are recorded as 0.28 mg for females and 0.175 for males and yields obtained from dissection of whole venom glands were 2.05 and 0.81 mg respectively (Wiener 1957).

References:

Duncan AW, Tibballs J, Sutherland SK (1980) Effects of Sydney funnel-web spider envenomation in monkeys and their clinical implications. *Med. J. Aust.* **2**:429-435.

Sutherland SK (1983) *Australian Animal Toxins. The creatures, their toxins and care of the poisoned patient.* Oxford University Press, Melbourne. pp. 253-254.

Sutherland SK (1979) Clinical and experimental aspects of arachnid poisoning in Australia. In Chubb IW, Geffen LB (eds.) *Neurotoxins, Fundamental and Clinical Advances.* Adelaide University Union Press, Adelaide.

Wiener S (1957) The Sydney funnel-web spider (*Atrax robustus*) I. Collection of venom and its toxicity in animals. *Med. J. Aust.* **2**:377-382.

Wiener S (1963) Antigenic and electrophoretic properties of funnel-web spider (*Atrax robustus*) venom. In Keegan HL, MacFarlane WV (eds.) *Venomous and Poisonous Animals and Noxious Plants of the Pacific Region.* Pergamon Press, London.

Scorpion venoms

Serious human envenomation by some species of scorpion is described from Asia, Africa & the Americas (Ishmail 1995):

- Cardiovascular effects: stimulation of the autonomic nervous system (predominantly sympathetic) leading to myocardial damage, heart failure, blood pressure changes (hypotension, hypertension), arrhythmias, pulmonary oedema, respiratory failure
- CNS effects: hyperirritability, seizures, hemiplegia, hyperthermia, hypothermia
- Pancreatitis

Not all scorpion species are dangerously venomous. Australian scorpions very rarely cause serious illness in humans and only two fatal cases (both in infants) are recorded (Sutherland 1983). Stings normally cause local pain and swelling.
Australian scorpions belong to 6 genera and 29 species (Koch 1977, 1981): *Cercophonius, Isometroides, Isometrus, Liocheles, Lychas* and *Urodacus*. The most likely to cause serious envenomation are *Lychas marmoreus* and the larger species of *Urodacus* (Southcott 1976).

No cases have been reported in domestic animals in Australia.

References:

Allen C (1992) Arachnid envenomation. *Emerg. Med. Clin. N. Am.* **10**:269-298.

Ismail M (1995) The scorpion envenoming syndrome. *Toxicon* **33**:825-858.

Koch LE (1977) The taxonomy, geographic distribution and evolutionary radiation of Australo-Papuan scorpions. *Rec. West. Aust. Mus.* **5**:83-367.

Koch LE (1981) The scorpions of Australia: aspects of their ecology and zoogeography. In Keast A (ed.) *Ecological Biogeography of Australia.* Monographiae Biologicae (ed. Illies-Schlitz J), The Hague-Boston-London **41**:873-884

Possani LD (1984) Structure of scorpion toxins. In Tu E (ed.) *Handbook of Natural Toxins. Vol. 2. Insect Poisons, Allergens and Other Invertebrate Venoms.* Marcel Dekker, New York. pp. 607-637.

Russel FE (1991) Venomous arthropods. *Vet. Human Toxicol.* **33**:505-508.

Southcott RV (1976) Arachnidism and allied syndromes in the Australian region. *Rec. Adelaide Child. Hosp.* **1**:97-186.

Sutherland SK (1983) *Australian Animal Toxins. The creatures, their toxins and care of the poisoned patient.* Oxford University Press, Melbourne. pp. 327-329.

Ixodes holocyclus *venom*

[N.B. This section is incomplete]

References:

Allen GS, Pursell RT (1971) Pulmonary involvement and other sequelae of tick poisoning. *Aust. Vet. Practit.* **1**:39

Arundel JH, Sutherland AK (1988) *Animal Health in Australia. Volume 10. Ectoparasitic Diseases of Sheep, Cattle, Goats and Horses.* Australian Government Publishing Service, Canberra. pp.142-145.

Askenase PW, Bagnall BG, Worms MJ (1982) Cutaneous basophil-associated resistance to ectoparasites (Ticks) I. Transfer with immune serum or immune cells. *Immunity* **45**:501

Atwell RB, Fitzgerald M (1994) Unsolved issues in tick paralysis. *Aust. Vet. Practit.* **24**:155

Atwell RB, Campbell FE, Court E (2000) The attachment sites of the paralysis tick (*Ixodes holocyclus*) on dogs. *Aust. Vet. Practit.* **30**:68, 70-72. [practitioner survey of dogs presented with tick paralysis; identity of the ticks studied were not independently confirmed]

Atwell RB (2000) Tick paralysis and choking in dogs. *Aust. Vet. Practit.* **30**:72.

Atwell RB, Campbell FE (2001) Reactions to tick antitoxin serum and the role of atropine in treatment of dogs and cats with tick paralysis caused by *Ixodes holocyclus*: a pilot survey. *Aust. Vet. J.* **79**:394-397.

Atwell RB, Campbell FE, Evans EA (2001) Prospective survey of tick paralysis in dogs. *Aust. Vet. J.* **79**:412-418.

Bancroft J (1884) Queensland ticks and tick blindness. *Aust. Med. Gaz.* **4**:37.

Campbell FE, Atwell RB (2001) Megaoesophagus in dogs with tick paralysis (*Ixodes holocyclus*). *Aust. Vet. Practit.* **31**:75-79.

Cooper BJ (1975) Studies in the pathogenesis of tick paralysis. Ph.D. Thesis, University of Sydney.

Cooper BJ, Cooper HL, Ilkew JE, Kelly JD (1976) Tick paralysis. Proceedings No. 30, Post-Graduate Committee in Veterinary Science, University of Sydney. pp. 57-61.

Davey MW, Ratcliffe R, Titchen DA (1989) Aspects of the symptomatology and intoxication produced by *Ixodes holocyclus.* In *Adverse Reactions to Arthropods in Australia.* Proceedings of the Sydney Allergen Group, North Ryde NSW. Volume 6 p. 49

Dodd S (1921) Tick paralysis. *J. Comp. Path. Therap.* **34**:309

Doube BM (1975) Cattle and the paralysis tick *Ixodes holocyclus*. *Aust. Vet. J.* **51**:511-515.

Doube BM, Kemp DH (1975) Paralysis of cattle by *Ixodes holocyclus* Neumann. *Aust. J. Agric. Res.* **26**:635-640.

Doube BM, Kemp DH, Bird PE (1977) Paralysis of calves by the tick, *Ixodes holocyclus*. *Aust. Vet. J.* **53**:39-43.

Fearnley A (2002) Possible reasons for variation in *Ixodes holocyclus* toxicity. *Aust. Vet. Practit.* **32**:76-77.
Fitzgerald M (1998) *Ixodes holocyclus* poisoning. In *Clinical Toxicology*. Proceedings318. Post-Graduate Foundation in Veterinary Science, University of Sydney. pp. 203-220.
Furneaux RW (1969) Tick (*Ixodes holocyclus*) paralysis. Report No. 31, Post-Graduate Committee in Veterinary Science, University of Sydney.
Goodrich BS, Murray MD (1978) Factors influencing the toxicity of salivary gland extracts of *Ixodes holocyclus* Neumann. *Int. J. Parasitol.* **8**:313
Goodrich BS, Murray MD, Holmes PR (1978) The establishment of a laboratory colony of *Ixodes holocyclus*. *Aust, Vet. J.* **54**:490-493.
Gratton-Smith PJ, Morris JG, Johnston HM, Yiannikas C, Malik R, Russell R, Ouvrier RA (1997) Clinical and neurophysiological features of tick paralysis. *Brain* **120**:1975
Ilkiw JE (1979) A study of the effects in the dog of *Ixodes holocyclus*. PhD Thesis, University of Sydney.
Ilkiw JE, Turner DM (1988) Infestation in the dog by the paralysis tick, *Ixodes holocyclus*. 5. Treatment. *Aust. Vet. J.* **65**:236-238.
Jackson J, Chiltern NB, Beveridge I, Morris M, Andrews RH (1998) An electrophoretic comparison of the Australian paralysis tick, *Ixodes holocyclus* Neumann, 1899, and *I. cornuatus* Roberts, 1960 (Acari:Ixodidae). *Aust. J. Zool.* **46**:109
Jackson J, Chiltern NB, Beveridge I, Morris M, Andrews RH (2000) Genetic variation within the ticks *Ixodes holocyclus* and *Ixodes cornuatus* from south-eastern Australia. *Int. J. Parasitol.* **30**:1159
Knott SG (1961) Scrub tick paralysis. *Qd. Agric. J.* **87**:41
Legg J (1923) Townsville Stock Experiment Station. A Year's Review. *Qd. Agric. J.* **19**:172-177. [Paralysis in dogs due to the bite of scrub ticks. p.177]
Malik R, Farrow BRH (1991) Tick paralysis in North America and Australia. *Vet. Clinics N. Am.: Sm. Anim. Pract.* **21**:157
Malik R, King J, Allan GS (1988) Megaoesophagus associated with tick paralysis in three dogs. *Aust. Vet. Practit.* **18**:156
Malik R (1998) Tick paralysis in the cat. In *Clinical Toxicology*. Proceedings318. Post-Graduate Foundation in Veterinary Science, University of Sydney. pp. 147-148.
Mason RW, Kemp DH, King SJ (1974) *Ixodes cornuatus* and tick paralysis. *Aust. Vet. J.* **50**:580.
McKay WJS (1928) Observations on the anatomy and poison of the dog tick (*Ixodes holocyclus*). *Syd. Uni. Med. J.* **21**:93
Moorehouse DE (1966) Observations on copulation in *Ixodes holocyclus* (Neumann) and the feeding of the male. *J. Med. Entomol.* **3**:168.
Oxer DT, Ricardo CL (1942) Notes on the biology, toxicity and breeding of *Ixodes holocyclus* (Neumann). *Aust. Vet. J.* **18**:194-199.
Roberts FSH (1960) A systemic study of the Australian species of the genus *Ixodes*. *Aust. J. Zool.* **8**:392
Roberts FSH (1970) *Australian Ticks*. CSIRO, Melbourne
Ross IC (1924) The bionomics of *Ixodes holocyclus* (Neumann), with a redescription of the adult and nymphal stages and a description of the larvae. *Parasitology* **16**:365.
Ross IC (1926) An experimental study of tick paralysis in Australia. *Parasitology* **18**:410-429.
Ross IC (1934) Tick paralysis in the dog: period elapsing between attachment of tick and the onset of symptoms. *Aust. Vet. J.* **10**:182-183.
Ross IC (1935) Tick paralysis: a fatal disease of dogs and other animals in eastern Australia. *J. Council for Scientific and Industrial Research of Australia* **8**:8-13.
Seddon HR, Albiston HE (1968) *Diseases of Domestic Animals in Australia. Part 3. Arthropod Infestations (Ticks and Mites).* 2nd edition, Service Publication (Veterinary Hygiene) No. 7, Commonwealth Department of Health, Canberra. pp.68-80.
Stone BF (1988) Tick paralysis, particularly involving *Ixodes holocyclus* and other *Ixodes* species. In Harris KF (ed.) *Advances in Disease Vector Research.* Springer-Verlag, New York. Volume 5 pp. 61-85.
Stone BF, Doube BM, Binnington KC, Goodger BV (1979) Toxins of the Australian paralysis tick *Ixodes holocyclus*. In Rodriguez JG (ed.) *Recent Advances in Acarology* **1**
Stone BF, Aylward JH (1987) Tick toxicosis and the causal toxins: tick paralysis. In Gopalakhrishnekone P, Tan CK (eds.) *Progress in Venom and Toxin Research.* National University of Singapore Press, Singapore. pp. 594-682.
Stone BF, Wright IG (1981) Tick toxins and protective immunity. In Whitehead GB, Gibson JD (eds.) *Tick Biology and Control.* Tick Research Unit, Rhodes University, South Africa. pp. 1-5.
Stone BF, Neish AL, Wright IR (1983) Tick (*Ixodes holocyclus*) paralysis in the dog – quantitative studies on immunity following artificial infestation with the tick. *Aust. Vet. J.* **60**:65
Strakosch MR (2000) Lufenuron and tick paralysis. *Aust. Vet. J.* **78**:98.
Sutherland SK (1983) *Australian Animal Toxins. The creatures, their toxins and care of the poisoned patient.* Oxford University Press, Melbourne. pp. 314-315.

Ixodes cornuatus *venom*

Ixodes cornuatus is widespread in Victoria and Tasmania (Roberts 1960). A case of fatal infestation with a single female in an adult cat has been recorded from Tasmania (Mason *et al.* 1974).
References:

Mason RW, Kemp DH, King SJ (1974) *Ixodes cornuatus* and tick paralysis. *Aust. Vet. J.* **50**:580.
Roberts FSH (1960) A systemic study of the Australian species of the genus *Ixodes* (Acarina: Ixodidae). *Aust. J. Zool.* **8**:392-485.

ARTHROPODS - CRUSTACEANS

Toxic coral reef crabs

No cases of domestic animal or human poisoning from eating coral reef crabs are on record from Australia, but human fatalities have occurred in Japan, south-eastern Asia, the Philippines, Timor and the Pacific Islands. Toxins involved include **saxitoxin** and other **paralytic shellfish poisons** (*q.v.* - see also the section on neurotoxic cyanobacteria), **tetrodotoxin** (*q.v.*) and **palytoxin** (*q.v.*). Crabs prepared as human food by boiling may have the water-soluble toxins leached from their bodies, making the broth highly toxic (Llewellyn & Davie 1987).

Potentially-toxic (toxins isolated) species known from Australian waters in 1987 (Llewellyn & Davie 1987) included:

Family Xanthidae (xanthid crabs)

- *Zosimus aeneus* Linné 1758 - Heron Island
- *Atergatis floridus* Linné 1767 (shawl crab)- Moreton Bay
- *Eriphia sebana* Shaw & Nodder 1803 (red-eyed reef crab) - Heron Island
- *Etisus splendidus* Rathburn 1906 (splendid reef crab) - Wilson Island off Gladstone
- *Lophozozymus pictor* Fabricius 1798 (red and white reef crab) - Moreton Bay
- *Carpilius convexus* Forskål 1775
- *Phymodius ungulatus* H. Milne Edwards 1834
- *Pilodius areolatus* H. Milne Edwards 1834

Family Portunidae (portunids or swimmer crabs)

- *Thalamita stimpsoni* A. Milne Edwards 1861

Family Grapsidae

- *Grapsus albolineatus* Lamark 1818

Family Parthenopidae

- *Daldorfia horrida* Linné 1758

Neither mud crabs (*Scylla serrata*) nor sand crabs (*Portunus pelagicus*) are known to contain toxins, but humans may develop allergic reactions to them.

References:

Review literature

Llewellyn LE, Davie P (1987) Crabs and other crustaceans. In Covacevich J, Davie P, Pearn J (eds.) *Toxic Plants and Animals: A Guide for Australia.* Queensland Museum, Brisbane. pp. 126-135.

General literature

Llewellyn LE, Endean R (1988) Toxic coral reef crabs from Australian waters. *Toxicon* **26**:1085-1088.

Llewellyn LE, Endean R (1989a) Toxins extracted from Australian specimens of the crab *Eriphia sebana* (Xanthidae). *Toxicon* **27**:579-586.

Llewellyn LE, Endean R (1989b) Toxicity and paralytic shellfish toxin profiles of the xanthid crabs *Lophozozymus pictor* and *Zosimus aeneus* collected from some Australian coral reefs. *Toxicon* **27**:596-600.

Tsai YH, Hwang DF, Chai TJ, Jeng SS (1995) Occurrence of tetrodotoxin and paralytic shellfish poison in the Taiwanese crab *Lophozozymus pictor. Toxicon* **33**:1669-1673.

MOLLUSCS

Human envenomations and intoxications by molluscs under Australian conditions are reviewed by Williamson & Rifkin (1996).

Reference:

Williamson JA, Rifkin JF (1996) Phylum Mollusca. Chapter 13 in Williamson JA, Fenner PJ, Burnett JW, Rifkin JF (eds.) *Venomous and Poisonous Marine Animals: A Medical and Biological Handbook.* University of New South Wales Press, Sydney. pp.327-339.

GASTROPOD MOLLUSCS (Snails)

Marine gastropods contain a variety of venoms and poisons. See West *et al.* (1996) for a short review. West *et al.* (1996) list the following toxins and venoms with their source gastropods.

Toxin or venom	Gastropod species	Source organ	References
Acrylylcholine	*Buccinum undatum*	Hypobrachial glands	Whittaker 1958
Conotoxins	*Conus* spp.	Venom glands	West *et al.* 1996
Dihydromurexine	*Thais haemastoma*	Hypobrachial glands	Roseghini 1971
N-methylmurexine	*Nucella emarginata*	Hypobrachial glands	Bender *et al.* 1974
Senecioylcholine	*Thais floridana*	Hypobrachial glands	Keyl *et al.* 1957
Serotonin (5-HT)	*Nucella lapillus*	Venom glands	West *et al.* 1994
Surugatoxin	*Babylonia japonica*	Mid-gut gland	Kosuge *et al.* 1972
Tetramine	*Neptunia antiqua*	Salivary gland	Anthoni *et al.* 1989
	Neptunia arthritica	Salivary gland	Asano & Itoh 1960
	Neptunia lyrata	Salivary gland	Shiomi *et al.* 1994
	Buccinum leucostoma	Salivary gland	Asano & Itoh 1960
	Fusitriton oregonense	Salivary gland	Asano & Itoh 1960
Tetrodotoxin (TTX)	*Niotha clathrata*	Digestive glands	Hwang *et al.* 1991a
	Natica alapapollonis	Digestive glands	Hwang *et al.* 1991b
	Natica lineata	Digestive glands	Hwang *et al.* 1991b
	Natica vitellus	Digestive glands	Hwang *et al.* 1991b
	Rapana rapiformis	Digestive glands	Hwang *et al.* 1991c
	Rapana venosa	Digestive glands	Hwang *et al.* 1991c
	Polinices didyma	Digestive glands	Hwang *et al.* 1991b
	Zeuxis castus-like	Digestive glands	Hwang *et al.* 1991c
	Zeuxis scalaris	Digestive glands	Hwang *et al.* 1991c
	Tutufa lissostoma	Digestive glands	Noguchi *et al.* 1984
Anhydro-TTX	*Natica vitellus*	Digestive glands	Hwang *et al.* 1991b
	Polinices didyma	Digestive glands	Hwang *et al.* 1991b
Urocanylcholine	*Acanthina spirata*	Hypobrachial glands	Bender *et al.* 1974
	Murex brandaris	Hypobrachial glands	Whittaker 1960
	Murex fulvescens	Hypobrachial glands	Keyl *et al.* 1957
	Murex trunculus	Hypobrachial glands	Erspamer & Benati 1953
	Nucella lapillus	Hypobrachial glands	Keyl *et al.* 1957
	Tritonlia erinacea	Hypobrachial glands	Whittaker 1960
	Urosalpinx cinereus	Hypobrachial glands	Keyl *et al.* 1957
Unidentified	*Cymatium muricinum*	Salivary gland	Houbrick & Fetter 1969
	Cymatium nicobaricum	Salivary gland	Houbrick & Fetter 1969
	Cymatium pileare	Salivary gland	Houbrick & Fetter 1969
	Cymatium intermedia	Salivary gland	West *et al.* unpublished
	Monoplex echo	Salivary gland	Shiomi *et al.* 1994
	Buccinum undatum	Salivary gland	Welsh 1956
	Cassis tuberosa	Salivary gland	Corman 1963
	Thais haemastoma	Salivary gland	Hwang & Mir 1972
	Neptunea antiqua	Salivary gland	West *et al.* unpublished
	Nucella lapillus	Venom glands	West *et al*. 1996
	Acanthina spirata	Unknown	Hemingway 1978

References:

Anthoni U, Bohlin L, Larsen C, Neilsen P, Nielsen NH, Christophersen C (1989) The toxin tetramine from the "edible" whelk *Neptunea antiqua. Toxicon* **27**:717-723.
Asano M, Itoh M (1960) Salivary poison of a marine gastropod, *Neptunea arthritica* Bernadi, and the seasonal variation of its toxicity. *Ann. N. Y. Acad. Sci.* **90**:675-688.
Bender JA, DeRiemer K, Roberts TE, Rushton R, Boothe P, Mosher HS, Fuhrman FA (1974) Choline esters in the marine gastropods *Nucella emarginata* and *Acanthina spirata*: a new choline ester, tentatively identified as *N*-methylmurexine. *Comp. Gen. Pharmac.* **5**:191-198.
Corman I (1963) Toxic properties of the saliva of *Cassis. Nature* **200**:88-89.
Erspamer V, Benati O (1953) Identification of murexine as β-[Imidazolyl-(4)]-Acryl-Choline. *Science* **117**:161-162.
Hemingway GT (1978) Evidence for a paralytic venom in the intertidal snail *Acanthina spirata* (Neogastropoda: Thaisidae). *Comp. Biochem. Physiol.* **60C**:79-81.
Houbrick JR, Fetter V (1969) Some aspects of the functional anatomy and biology of *Cymatium* and *Bursa. Proc. Malac. Soc. London* **38**:415-429.
Huang CL, Mir GN (1972) Pharmacological investigation of salivary gland of *Thais haemastoma* (Clench). *Toxicon* **10**:111-117.
Hwang DF, Lin LC, Jeng SS (1991a) Occurrence of some tetrodotoxin-related toxins in the gastropod mollusc *Niotha clathrata* from Taiwan. *Nippon Suisan Gakkaishi* **58**:63-67.
Hwang DF, Tai KP, Chueh CH, Lin LC, Jeng SS (1991b) Tetrodotoxin and derivatives in several species of the gastropod Naticidae. *Toxicon* **29**:1019-1024.
Hwang DF, Lu SC, Jeng SS (1991c) Occurrence of tetrodotoxin in the gastropods *Rapana rapiformis* and *R. venosa venosa. Mar. Biol.* **111**:65-69.
Keyl MJ, Michaelson IA, Wittaker VP (1957) Physiologically-active choline esters in certain marine gastropods and other invertebrates. *J. Physiol.* **139**:434-454.
Kosuge T, Zenda H, Ochiai A (1972) Isolation and structure determination of a new marine toxin, surugatoxin, from the Japanese ivory shell, *Babylonia japonica. Tetrahedron Lett.* **25**:2545-2548.
Noguchi T, Maruyama J, Narita H, Hashimoto K (1984) Occurrence of tetrodotoxin in the gastropod mollusc *Tutufa lissostoma* (frog shell). *Toxicon* **22**:219-226.
Roseghini M (1971) Occurrence of dihydromurexine (imidazolepropionylcholine) in the hypobrachial gland of *Thais (purpura) haemastoma. Experientia* **27**:1008-1009.
Shiomi K, Mizukami M, Shimakura K, Nagashima Y (1994) Toxins in the salivary gland of some marine gastropods. *Comp Biochem. Physiol.* **107B**:427-432.
Welsh JH (1956) Neurohormones of invertebrates I: cardioregulators of *Cyprina* and *Buccinum. J. Mar. Biol. Assoc. U.K.* **35**:193-201.
West DJ, Andrews EB, McVean AR, Osborne DJ, Thorndyke MC (1994) Isolation of serotonin from the accessory salivary glands of the marine snail *Nucella lapillus. Toxicon* **32**:1261-1264.
West DJ, Andrews EB, Bowman D, McVean AR, Thorndyke MC (1996) Toxins from some poisonous and venomous marine snails. *Comp. Biochem. Physiol.* **113C**:1-10.
Whittaker VP (1958) Acrylylcholine: a new naturally occurring pharmacologically active choline ester from *Buccinum undatum. Biochem. Pharmac.* **1**:342-346.
Whittaker VP (1960) Pharmacologically active choline esters in marine gastropods. *Ann. N. Y. Acad. Sci.* **90**:695-705.

Conotoxins

Conotoxins (conopeptides) are small disulphide-rich peptides in the venom glands of **cone shells** which are piscivorous marine gastropod molluscs (snails). There are about 50,000 different conotoxins, each *Conus* species having a suite of peptides (Olivera & Cruz 2001). Individual conotoxins receive a code designating its source and physiological activity. The venom paralyses fish very rapidly through interference with neuromuscular transmission. Researchers have identified so-called *toxin cabals,* groups of toxins working synergistically, that produce prey immobilisation. For example, in *Conus purpurascens* which harpoons fish, cabals include a "lightning-strike cabal" which causes an immediate tetanic immobilisation of prey fish through inhibition of inactivation of voltage-gated sodium channels and inhibition of voltage-gated potassium channels producing massive depolarisation of axonal fibres near the venom injection site, and a "motor cabal" which then abolishes neuromuscular transmission throughout the body. In contrast, *Conus geographicus* which engulfs small prey with a highly distensible mouth before injecting venom, there is no "lightning-strike cabal", but a "nirvana cabal" which damps down neural activity

No cases of envenomation of domestic animals are on record. Fatal human envenomation is recorded. The conotoxins have activities as potent nicotinic antagonists and sodium channel blockers in mammals and these effects probably account for their natural toxicity in mammals. Basic research on a series of peptides has revealed a diversity of sites of activity in the CNS, leading to several candidate pharmaceutical products for analgesia and epilepsy (Olivera & Cruz 2001).

References:

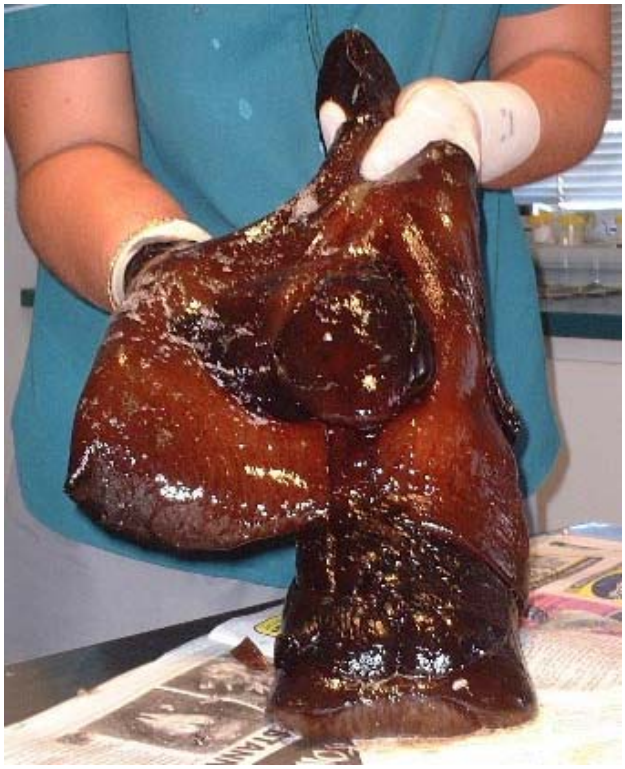
Olivera BM, Cruz LJ (2001) Conotoxins, in retrospect. *Toxicon* **39**:7-14.

*Tetrodotoxin (*q.v.*)*

Sea hares (Subclass Opisthobranchia, Order Tectibranchia) - dogs

Sea hares, so-called from their large erect grooved rhinophores resembling the ears of hares, are members of the Family Aplysiidae within the Subclass Opisthobranchia (sea slugs) of which some of the most colourful are called nudibranchs from their exposed gill arrays. About 20 species of sea hares are known from tropical and warm temperate Australian waters, of which three-quarters belong to the genus *Aplysia* (Eales 1960, Bebbington 1977, Carefoot 1987, Beesley *et al.* 1998). Sea hares live no more than one year and grow rapidly by bulk consumption of red or green algae (Beesley *et al.* 1998). Toxins are known in skin, opaline gland fluid, purple 'ink' and digestive gland (Carefoot 1987, Nolan *et al.* 1995).

Aplysia gigantea (specimens identified by the WA Museum; Wells 1986) was washed ashore in large numbers at Geraldton on the Western Australian coast in February 2002. Dogs eating or licking them developed a syndrome of tetanic convulsions, hyperthermia and respiratory failure similar to that of strychnine toxicity (*q.v.*). For treatment, affected dogs were anaesthetised to effect and the hyperthermia treated with ice packs. Mortality was 50% in 10 recorded cases. (P. Taylor, personal communication 27 February 2002). *A. gigantea* are a uniform dark brown or black, measure up to 60 cm long, are endemic to Western Australia, range from Bluff Point north of Geraldton to Duke of Orleans Bay east of Esperence and have been collected from the intertidal zone to a depth of 180 m (Wells 1986). They appear to come into shallow water in summer and early autumn to spawn, and hundreds of animals can be found stranded on beaches during this time, prompting public enquiries about "livers" on the beaches (Wells 1986).



Aplysia gigantea associated with dog toxicity, Geraldton, summer 2002 [Peter Taylor photo]

At the same time as the dog-*A. gigantea* interaction, other sea hares, *Dolabella auricularia*, were being washed ashore around Perth. No intoxications of dogs or other animals were reported from them. *D. auricularia* is reported as being eaten by humans in some Pacific countries (Beesley *et al.* 1998). This animal is reported to often consume the cyanobacterium *Symploca hydnoides* which produces the microtubule toxin dolastatin that has similar activity to phomopsins (*q.v.*). Extracts of the alimentary tract and digestive gland of *D. auricularia* from near Perth produced no effect during the 24 hr after being injected IP into mice (J.G.Allen, personal communication 1 March 2002).

Halstead (1988) cites a study by Flury (1915) with *Aplysia depilans* from the Atlantic Ocean and Mediterranean Sea in which frogs injected with 0.1 ml of "opaline secretion" harvested directly from the skin of the animal "developed hyperactive reflexes and pronounced muscular paralysis within … 25 minutes. Death usually occurred within 2 to 4 hours." This could be interpreted as tetanic seizures, but this is uncertain. R.A. McKenzie speculated that the tetanic spasms seen in affected dogs may have resulted from the indole alkaloid lyngbyatoxins if the *A. gigantea* had been browsing on the marine filamentous cyanobacterium *Lyngbya majuscula* (*q.v.*) known to bloom under certain conditions and had accumulated these toxins. In southern Queensland, the sea hare *Stylocheilus longicorda* is known to selectively graze blooms of this cyanobacterium, undergoing a population explosion and then mass mortality when the cyanobacterium is exhausted with numerous individuals washing ashore, but is not known to induce poisoning in predators or scavengers despite evidence that it can accumulate the ichthyotoxic lipopeptide malyngamide in its tissues (Angela Caper, personal communication 1 March 2002).

Halstead (1988) reports no confirmed human cases of intoxication by sea hares despite the creatures having a poisonous reputation originating in antiquity - emperors (Roman?) were held to kill political enemies with sea hare extracts and even contact with the animals was said to be fatal. Modern research has isolated toxins, but has not confirmed human susceptibility. One case of acute liver damage (apoptosis and mitosis in hepatocytes) with vomiting and pyrexia is reported in a 40-year-old Japanese man who had eaten a specimen of *Aplysia kurodai*in 1995 (Akamoto *et al.* 1998).

References

Akamota Y, Nakajima T, Misawa S, Ishikawa H, Itoh Y, Nakashima T, Okanoue T, Kashima K, Tsuji T (1998) Acute liver damage with characteristic apoptotic hepatocytes by ingestion of *Aplysia kurodai*, a sea hare. *Internal Medicine (Tokyo)* **37**:927-929.

Bebbington A (1977) Aplysiid species from eastern Australia with notes on the Pacific Ocean Aplysiomorpha (Gastropoda: Opisthobranchia). *Trans. Zool. Soc. London* **34**: 87-147.

Beesley PL, Ross GJB, Wells A (eds.) (1998) *Mollusca: The Southern Synthesis. Fauna of Australia. Volume 5.* CSIRO Publishing, Melbourne. Family Aplysiidae pp.975-977.

Carefoot TH (1987) *Aplysia*: its biology and ecology. *Oceanography and Marine Biology, Annual Review* **25**:167-284.

Eales NB (1960) Revision of the world species of *Aplysia* (Gastropoda: Opisthobranchia). *Bull. Brit. Mus. (Natural History) (Zoology)* **5**:267-404. [cited by Beesley *et al.* 1998]

Halstead BW (1988) *Poisonous and Venomous Marine Animals of the World.* 2nd revised edition. The Darwin Press Inc., Princeton, New Jersey. pp. 278-284.

Nolen TG, Johnson PM, Kicklighter CE, Capo T (1995) Ink secretion by the marine snail *Aplysia californica* enhances its ability to escape from a natural predator. *J. Comp. Physiol. (A)* **176**:239-254.

Wells FE (1986) A redescription of the sea hare *Aplysia gigantea* Sowerby 1869. *J. Malacological Soc. Aust.* **7**:173-178.

CEPHALOPOD MOLLUSCS (Octopus & squid)

*Tetrodotoxin (*q.v.*)*

Family Octopodidae: *Hapalochlaena* spp. (blue-ringed octopuses)

BIVALVE MOLLUSCS (Mussels, scallops, clams & oysters)

*Human shellfish poisoning syndromes related to marine dinoflagellates and diatoms (*q.v.*)*

FISH

☑ Ciguatoxins (& maitotoxin)

Core data

Syndrome name: ciguatera poisoning
Common sources: dinoflagellate *Gambierdiscus toxicus*
Animals affected: cat, dog, human
Mode of action: opens voltage-gated Na channels in cell membranes → Na influx (opposite to tetrodotoxin)
Poisoning circumstances: consumption of viscera or flesh of carnivorous reef fish
Main effects: partial posterior + anterior paresis/paralysis
Diagnosis: fish consumption history + syndrome
Therapy:

- emetic (if required) + activated charcoal, atropine, supportive including IV fluids
- future immunotherapy

Prevention: future rapid screening tests for fish

Syndrome names:

- **Ciguatera.** The human syndrome was first recognised in the Caribbean region in the 16th century, with the name being coined for toxicity from ingestion of the marine turban snail, *Turbo pica*, (called cigua), and later extended to the syndrome from ingestion of toxic fish in the region (Pottier *et al.* 2001).
- **Tropical fish poisoning**

Chemical structure:

The chemical structure of ciguatoxins differs between examples in the Pacific (Murata *et al.* 1989, 1990) and those in the Caribbean (Lewis *et al.* 1998), the molecules being identical in their middle regions, but differing at both ends.

Sources:

tropical Pacific regions & Caribbean
benthic dinoflagellate *Gambierdiscus toxicus* eaten by herbivorous fishes
→ fat-soluble toxin **bioaccumulation** & slight modification up the food web; *G. toxicus*
→ gambiertoxin (precursor of ciguatoxin) which is biotransformed to ciguatoxin by acid-catalysed spiroisomerisation in the stomach of herbivorous fish → more easily excreted (ciguatoxin more polar than gambiertoxin)
→ toxin concentrated in viscera (some in muscle) of **large carnivorous & reef fishes**, e.g. Spanish mackerel, coral trout, snapper, barracuda, grouper, Chinaman fish, moray eel; some fish produce a protein that binds ciguatoxin, possibly protecting them from its effects and allowing larger toxin loads in their tissues; fish are susceptible to ciguatoxin → locomotory disorders, possibly making them more susceptible to predation and thus promoting bioaccumulation
→ sporadic mammalian toxicity
possible sources in other dinoflagellates & their associated bacteria
G. toxicus is an epiphyte of various species of filamentous marine algae that inhabit **detritus associated with surface of dead coral**
habitat disturbance (damage to tropical reefs e.g. harbour construction, cyclones) may → ↑populations of toxin-producing dinoflagellates

Even in areas known to produce toxic fish, fewer than 1 in 1000 fish may actually contain sufficient ciguatoxin to cause human poisoning. Most of the known toxic species are caught in commercial quantities and eaten without ill effect. (Gillespie 1987)

Fish species associated with ciguatera in Australia [Gillespie 1987, Lewis & King 1996, Grant 1999, Sutherland & Tibballs 2001]

☠ = major risks: species reported by Gillespie (1987)

N.B. This is not an exclusive list. Other species may also be toxic.

- Sea -perch, red emperor, chinaman-fish
  - ☠ ***Lutjanus bohar*** **(Forskal) (red bass)** [Grant p.736-738] - distributed in reefs in Qld, NT
  - ☠ ***Lutjanus gibbus*** **(Forskal) (paddletail)** [Grant p.734-735] - distributed from southern Qld to Gulf of Carpentaria
  - ☠ ***Lutjanus sebae*** **(Cuvier) (red emperor, government bream)** [Grant p.352-354]
  - *Lutjanus malabaricus* (Bloch & Schneider) (large-mouthed sea-perch, large-mouthed nannygai, red jew) [Grant p. 355-356] - large specimens are routinely marketed as "red emperor"
  - ☠ ***Symphorus nematophorus*** **(Bleeker)** (**chinaman-fish**; one of the sea-perches) [Grant p.730-733] - reef-dweller distributed in northern Australia (Qld, NT, WA)
- Cod [Grant p.220-261]
  - *Anyperodon* spp.
  - *Cephalopholis* spp.
    - *Cephalopholis miniatus* (Forskal) (coral cod, round-tailed trout [Lucas *et al.* 1997]
  - *Cromileptes* spp.
  - ☠ ***Epinephalus*** **spp.**
    - *Epinephalus fuscoguttatus* (flowery cod)
    - *Epinephalus lanceolatus* (groper)
    - *Epinephalus tauvina* (spotted cod)
- Coral & Coronation trout [Grant p.208-219]
  - ☠ ***Plectropomus maculatus*** **(Bloch) (coral trout)** [classification in dispute]
  - *Variola louti* (Forskal) (coronation trout, lunar-tailed cod, fairy cod) [Pearn *et al.* 1982]
- **Mackerel** ☠ [Grant p.652-660]
  - ☠ ***Scomberomorus*** **spp.** (Gillespie 1987)
    - ☠ *Scomberomorus commersoni* (narrow-barred Spanish mackerel)
    - ☠ ***Scomberomorus queenslandicus*** **(Queensland school mackerel)**
    - *Scomberomorus munroi* (spotted mackerel)
    - *Scomberomorus semifasciatus* (grey mackerel)
  - *Scomberoides* spp. [Grant p.343-344]
    - ☠ ***Scomberoides commersonianus*** **(giant dart, giant leatherskin)**
    - *Scomberoides lysan* (Forskal) (queenfish)
- Dart (*Trachinotus* spp.) [Grant p.338-342]
  - *Trachinotus bailloni* (Lacepede) (northern swallowtail)
  - *Trachinotus blochi* (Lacepede) (snub-nosed dart, snub-nosed swallowtail, oyster-eater)
  - *Trachinotus coppingeri* (Gunther) (southern dart, southern swallowtail, surf trevally)
- Southern fusilier (*Paracaesio pedleyi* McCulloch & Waite = *Caesio xanthurus*?) [Grant p.378]
- Yellow sweetlip *Lethrinus nebulosus* (Forskal) [Grant p.413]
- Yellowtail kingfish *Seriola lalandi* Cuvier & Valenciennes [Grant p.297]
- Barramundi (*Lates calcarifer* (Bloch)) [Grant p.202]
- Javelin-fish or grunters [Grant p.406-409]
  - *Pomadasys maculatus* (blotched javelin-fish) [Holmes *et al.* 1994 cited by Lewis & King 1996]
- Barracudas (sea-pike) [Grant p.548-551]
  - *Sphyraena barracuda* (Walbaum) (great barracuda, great sea-pike) [= *S. microps* Marshall and *S. akerstromi* Whitley]

- ☠ ***Sphyraena jello*** **Cubier (pickhandle barracuda)**
- Reef-eels (morays, moray eels) [Grant p.108-115]
  - *Gymnothorax aurostus* (Abbot) (white-speckled moray)
  - *Gymnothorax cribroris* Whitley (brown-flecked moray)
  - *Gymnothorax favagineus* Bloch & Schneider (black-blotched reef-eel, giraffe moray)
  - *Gymnothorax nudivomer* (Playfair & Gunther) (yellow-mouth moray)
  - *Gymnothorax pictus* (Ahl) (black-speckled reef-eel)
  - *Gymnothorax prasineus* (Richardson) (green moray)
  - *Gymnothorax pseudothyrsoideus* Bleeker (highfin moray)
  - *Gymnothorax undulatus* (Lacepede) (leopard moray)
  - *Thyrsoidea macrura* (Bleeker) (long-tailed eel)
- Unicornfish [Grant p.642-643]
  - *Naso* spp., particularly *Naso lituratus* (Bloch & Schneider) (black-finned or smooth-headed unicorn fish)
- Tangs & surgeonfish (Acanthuridae) [Grant p.634-641]
  - *Acanthurus* spp.
  - *Paracanthurus hepatus*
- Parrotfish (Scaridae) [Grant p.599-607]
  - *Scarus* spp.

Toxicity:

humans, cats > dogs

cat lethal dose < 100 ng ciguatoxin/kg; toxic fish flesh contains approx. 2 ng/g → toxic dose for 4kg cat = 400 ng ciguatoxin = 200 g fish flesh

mouse IP LD_{50} = 0.45 μg/kg

human mean dose for 50% illness = 2 ng/kg (dose for standard human 70kg = 70g fish flesh); minimum lethal dose = 20 ng/kg

ciguatoxins

can be cumulative

heat stable at normal cooking temperatures

fat-soluble; penetrate blood-brain barrier

maitotoxin

polyether structure resembling ciguatoxin

water soluble; concentrated in intestines of herbivorous fish

believed to cause the gastrointestinal signs of ciguatera poisoning in cats

named after "maito", the Tahitian name for the coral reef fish *Ctenochaetus straiatus* frequently involved in ciguatera poisoning (Igarashi *et al.* 1999)

no abnormal taste or appearance to toxic fish flesh

Mode of action:

ciguatoxin

opens the voltage-gated Na channels of cell membranes of neurones and sarcolemma (neuromuscular junction, myocardium) → ↑ permeability to Na ions

opposite action to tetrodotoxin (*q.v.*)

nerve conduction eventually blocked after initial period of stimulation (depolarising effects of Na influx); no initial stimulation in motor nerves

cardiac muscle function disrupted after initial strengthening of contraction

maitotoxin

very potent elevator of intracellular Ca^{2+} concentration through an influx of extracellular Ca^{2+} (a Ca^{2+} channel activator)

haemolytic activity through similar mechanism (Igarashi *et al.* 1999)

exact mechanism of action unknown (Igarashi *et al.* 1999)

Conditions of poisoning:

consumption of **viscera/flesh of large reef fish** (sporadically toxic in endemic areas)

- cats fed table or kitchen scraps including fish flesh/viscera (see also thiaminase)
- cats scavenging

Clinical signs:

Cat (Clark & Whitwell 1968, Cave 1996)

onset within 6 hr of consumption

mild cases → staggering (walk with rolling motion), dragging hind legs, recover completely within 48 hr

more severe cases → anorexia, excessive salivation, excessive lacrimation, moaning (puppies)/howling (cats) → **partial posterior + anterior paralysis / paresis**, recovery may take 14 days

very severe cases (viscera consumption) → dyspnoea, vomiting, diarrhoea, cardiac arrhythmias (bradycardia, tachycardia, heart block), coma, death in 24 hr

Human

A range of gastrointestinal & neurological signs (Pottier et al. 2001)

Most common in Queensland: loss of energy, myalgia, paradoxical diasthaesia, arthralgia, diarrhoea

Other signs/symptoms include a metallic taste in the mouth (said to be a hallmark of the intoxication), decrease in mental acuity, nausea, vomiting

Paradoxical diasthaesia (reversal of temperature perception, making cold objects feel hot and visa versa) – pathognomonic in humans

Chronic cases are difficult to diagnose and can be confused with chronic fatigue syndrome.

Evaluation of visual contrast sensitivity (VCS – tests the ability to discriminate between white black and grey) reveals a unique deficit, greatest at 6 cycles per degree of visual arc, also seen in patients intoxicated by *Pfiesteria piscicidia* and morphologically-related dinoflagellate organisms (Shoemaker 2000).

Pathology: necropsy → no gross lesions

Diagnosis:

fish-consumption history (fish species); clinical syndrome

differentiate from *Ixodes holocyclus* envenomation (ciguatera → forelimb involvement, no loss of voice or alertness, GI tract signs [Clark & Whitwell 1968]), tetrodotoxin, botulism, polyether ionophore antibiotic toxicity

rapid quantitative toxin assay methods are under development locally for screening fish flesh (currently expensive, but feasible using 2.5 g of flesh for a result in under 12 hr); a rapid colorimetric immunoassay ('stick test') is reported as simple, cheap and rapid (15 min)

Therapy:

induce vomiting (if this has not occurred already), dose with activated charcoal

atropine (1 mg/kg IV) to alleviate GI signs, bradycardia, hypotension

lidocaine (400 μg/kg/min IV) can abolish all cardiovascular effects in cats

propranolol successful in treating tachycardia

calcium gluconate (200 μg/kg/min IV) reduces toxin effects (↑ plasma Ca)

supportive therapy (IV fluids) until recovery (animals unable to feed themselves)

immunotherapy (antibodies against ciguatoxin) may be a future development as a specific treatment

humans: cholestyramine (ion exchange resin) PO at rates used to treat hypercholesterolaemia has been effective in chronic cases, resulting in a maximum time to recovery of 12 weeks (Shoemaker 2000)

humans: mannitol IV infusion (useful in humans [Palafox *et al.* 1988], but not in all cases (Sutherland & Tibballs 2001) and **not in cats**)

References:

Review literature:

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Bagnis R (1993) Ciguatera fish poisoning. Chapter 6 in Falconer IR (ed.) *Algal Toxins in Seafood and Drinking Water.* Academic Press, London. pp.105-115.

Gillespie N (1987) Ciguatera poisoning. In Covacevich J, Davie P, Pearn J (editors) *Toxic Plants and Animals. A Guide for Australia.* Queensland Museum, Brisbane. pp.161-169.

Lehane L (1999) *Ciguatera Fish Poisoning. A review in a risk-assessment framework.* National Office of Animal & Plant Health, Canberra. pp. iv + 82.

Lewis RJ (2001) The changing face of ciguatera. *Toxicon* **39**:97-106.

Lewis RJ, King GK (1996) Ciguatera (fish poisoning). Chapter 15 in Williamson JA, Fenner PJ, Burnett JW, Rifkin JF (eds.) *Venomous and Poisonous Marine Animals: A Medical and Biological Handbook.* University of New South Wales Press, Sydney & Surf Lifesaving, Queensland, Inc., Fortitude Valley, Queensland. ISBN 0 86840 279 6 pp.346-353.

Lucas RE, Lewis RJ, Taylor JM (1997) Pacific ciguatoxin-1 associated with a large common-source outbreak of ciguatera in east Arnhem Land, Australia. *Nat. Toxins* **5**:136-140.
McPherson C (1998) Ciguatoxin and tetrodotoxin poisoning in the cat: their diagnosis, treatment and management. *Aust. Vet. Practit.* **28**:26-34.
Pottier I, Vernoux J-P, Lewis RJ (2001) Ciguatera fish poisoning in the Caribbean Islands and western Atlantic. *Rev. Environ. Contam. Toxicol.* **168**:99-141.
Sutherland SK, Tibballs J (2001) *Australian Animal Toxins. The creatures, their toxins and care of the poisoned patient.* 2nd edition, Oxford University Press, Melbourne. Ciguatoxin pp.741-754, Maitotoxin pp. 754-757.

General Literature:

Cave J (1996) Clinical signs of ciguatera poisoning. *Control & Therapy Series, Post Grad Foundation in Vet. Sci., Uni. Sydney* No.3822, Mailing190, p.865. [report based on cases in cats and dogs in the Cook Islands]
Clark L, Whitwell GB (1968) Ciguatera poisoning in cats in Brisbane. *Aust. Vet. J.* **44**:81.
Grant EM (1999) *Grant's Guide to Fishes.* 8th ed. E.M. Grant Pty. Ltd., Redcliffe.
Holmes MJ, Lewis RJ, Sellin M, Street R (1994) The origin of ciguatera in Platypus Bay, Australia. *Memoirs of the Queensland Museum* **34**:505-512.
Igarashi T, Aritake S, Yasumoto T (1999) Mechanisms underlying the hemolytic and ichthyotoxic activities of maitotoxin. *Nat. Toxins* **7**:71-79.
Lewis RJ, Vernoux J-P, Brereton IM (1998) Structure of Caribbean ciguatoxin isolated from *Caranx latus*. *J. Am. Chem. Soc.* **120**(24): 5914-5920.
Murata M, Legrand AM, Ishibashi Y, Yasumota T (1989) Structures of ciguatoxin and its congener. *J. Am. Chem. Soc.* **111**:8929-8931.
Murata M, Legrand AM, Ishibashi Y, Fukui M, Yasumota T (1990) Structures and configurations of ciguatoxin from the moray eel *Gymnothorax javanicus* and its likely precursor from the dinoflagellate *Gamberodiscus toxicus*. *J. Am. Chem. Soc.* **112**:4380-4386.
Palafox NA, Jain LG, Pinano AZ, Gulick TM, Williams RK, Schatz IJ (1988) Successful treatment of ciguatera fish poisoning with intravenous mannitol. *J. Am. Med. Assn.* **259** (18):
Pearn JH, Harvey P, De Ambrosis W, Lewis R, McKay R (1982) Ciguatera and pregnancy. *Med. J. Aust.* **1**:57-58.
Shoemaker RC (2000) A new approach to the diagnosis and treatment of chronic ciguatera. *Abstract. Annual Meeting of the American Society of Tropical Medicine & Hygiene.* 26 October 2000. Press release at www.astmh.org/ciguatera.html

Tetrodotoxin

Core data

Common sources: toad fish (puffer fish)
Animals affected: cats, dogs
Mode of action: blocks voltage-gated Na channels in nerves, muscles → ↓↓ force of muscle contraction, ↓↓nerve conduction
Poisoning circumstances: consumption of viscera of toad fish
Main effects:

- flaccid paralysis
- mydriasis
- respiratory paralysis

Diagnosis: access + syndrome
Therapy:

- intubation and respiratory support
- gastric lavage + activated charcoal

Prevention: deny access

Chemical structure:

tetrodotoxin = a guanidinium alkaloid named after the fish family that contains it

Sources:

Tetrodotoxin is ultimately of bacterial origin (*Vibrio alginolyticus, V. parahaemolyticus, Pseudomonas, Aeromonas, Streptococcus*) and bioaccumulated up the food web. (Furlow 2001)

Known vehicles of the toxin are:

FISH

Order Tetraodontiformes. **toad fish** (puffer fish, blow-fish), **tobies** (sharp-nosed puffers), **porcupine fish**: About 30 species in Australia. Typically smooth-skinned without scales and with the teeth in both jaws fused into plates divided by a midline cleft (forming a "beak" - tetra- = four & odonti- = teeth)

- species most commonly encountered (Australia): common small toad fish, golden or silver toad fish, other toad fish in genus *Tetraodon*
- habitats: estuaries and inshore coastal waters
- when threatened, these fish massively inflate their bodies by taking in water or air. The porcipine fish have spines embedded in their skin which are erected by the inflation

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Toadfish, puffers or blow-fishes & Tobies or sharp-nosed puffers in the Australian fauna [Grant 1999]

- *Arothron* spp.
  - *Arothron aerostaticus* (Jenyns) (diagonal-banded toadfish) [Grant p. 748 & 750] - distributed in northern Australia (Qld, NT, WA)
  - *Arothron hispidus* L. (stars-and-stripes toadfish) [Grant p. 743-745] - distributed in northern Australia (Qld, NT, WA)
  - *Arothron manilensis* (de Proce) (narrow-lined toadfish) [Grant p. 749 & 755] - distributed in Qld & NSW
  - *Arothron mappa* (Lesson) (map toadfish) [Grant p.740] - distributed in northern Australia (Qld, NT, WA) in reef environments
  - *Arothron nigropunctatus* (Bloch & Schneider) (black-spotted toadfish) [Grant p. 750] - distributed along the Great Barrier Reef, Qld
- *Canthigaster* spp.
  - *Canthigaster bennetti* (Bleeker) (black spot toby) [Grant p. 752,753, 755]- distributed in the northern Great Barrier Reef region
  - *Canthigaster coronatus* (Vaillant & Sauvage) (four-barred toby) [Grant p. 755] - distributed along the Great Barrier Reef & replaces the black-saddled toby in water over 4 fathoms deep
  - *Canthigaster solandri* (Richardson) (netted toby) [Grant p. 755-756] - distributed along the Great Barrier Reef (Qld)
  - *Canthigaster valentini* (Bleeker) (black-saddled toby) [Grant p. 754-755] - distributed in northern Australia (Qld, NT, WA) & northern NSW
- *Contusus richei* (Freminville) (barred toadfish) [Grant p. 750-751] - distributed around southern Australia [? = *Amblyrhynchotes richei* associated with Case 31:2 in Sutherland & Tibballs (2001)]
- *Lagocephalus* spp.
  - *Lagocephalus lunaris* (Bloch & Schneider) [=*Gastrophysus lunaris*] (golden toadfish, silver toadfish) [Grant p. 742 & 750] - distributed in northern Australia (southern Qld, NT, WA)
  - *Lagocephalus sceleratus* (Gmelin) (giant toadfish) [Grant p.739 & 745] - distributed in northern Australia (Qld, NT, WA); the species has a history of attacking waders or swimmers in the Indo-Pacific region, biting or amputating toes (depending on the relative sizes of the victim and the fish) and is reputed to be the identity of "Thomas the Terrible Toadfish which severed toes of waders in the Whitsunday region (Grant 1999). It is reputed to be the species which poisoned Captain James Cook in 1774 (Southcott 1975 cited by Sutherland & Tibballs 2001)
- *Marilyna pleurosticta* (Gunther) (banded toadfish) [Grant p. 745-746] - distributed in Qld & NSW
- *Tetractenos* spp.
  - *Tetractenos hamiltoni* (Gray & Richardson) [=*Sphaeroides hamiltoni*] (common toadfish) [Grant p. 740-741] - distributed in tidal shallows of Qld & NSW
  - *Tetractenos glaber* (Freminville) [Grant p.740-741] - distributed from southern NSW, Vic, Tas, SA, southern WA [? = *Spheroides liosomus*

associated with Case 31:1 in Sutherland & Tibballs (2001)] - Associated with Case 31:3 in Sutherland & Tibballs (2001) - Tibballs (1988), Toncich (1987)

- *Torquigener pleurogramma* (Regan) (weeping toadfish) [Grant p.747 & 750] - distributed from southern Qld, NSW, Vic, Sa, southern WA

Porcupinefish, burrfish or globefish in the Australian fauna [Grant 1999]

- *Dicotylichthys punctulatus* Kaup (three-bar porcupinefish) [Grant p.757 &759] - distributed mainly in NT, Qld & NSW with some in Vic & Tas
- *Diodon* spp.
  - *Diodon liturosus* Shaw (brown-backed porcupinefish) [Grant p. 758-759] - distributed in Great Barrier Reef region (Qld)
  - *Diodon nichthemerus* Cuvier (southern globefish) [Grant p.759-760] - distributed in southern Australia (NSW, Vic, Tas, SA, WA)

CEPHALOPOD MOLLUSCS

Salivary (venom) glands of **blue-ringed octopuses** in Australia (and beyond). At least 6 species are known from Australia. The biology of octopuses is described in Beesley *et al.* (1998) and Norman & Reid (2000); that of blue-ringed octopus is described by Tranter & Augustine (1978). An account of the Australian members of the Cephalopoda is given in Lu (2001).

Three species have been associated with human fatalities (Sutherland & Tibballs 2001), namely

- *Hapalochlaena maculosa* Hoyle (lesser or southern blue-ringed octopus) – frequent in shallow waters, mud flats and rock pools along the temperate coasts of Australia (Sutherland & Lane 1969)
- *Hapalochlaena fasciata* (blue-lined octopus) [previously included in *H. maculosa* - not distinguished in Lu (2001)] - southern NSW to Moreton Bay (Qld)
- *Hapalochlaena lunulata* Quoy & Gaimard (tropical, greater or northern blue-ringed octopus) – from sub-tropical Australian waters to the equator

GASTROPOD MOLLUSCS

gastropod mollusc *Niotha clathrata* (→ human shellfish poisoning, Taiwan)

MARINE ARTHROPOD - HORSESHOE CRAB (Class Merostomata)

Horseshoe crab *Carcinoscorpius rotundicauda* ingestion induced human poisoning in Thailand (Kanchanapongkul & Krittayapoositpot 1995).

AMPHIBIANS

skin/skin glands of **amphibians** (Daly *et al.* 1993) e.g.

- South American frogs of the genera *Atelopus*, *Colostethus*
- newts/salamanders of the genera *Taricha* (California), *Cynops*, *Triturus*, *Notophthalamus*, *Paramesotriton*, *Ambystoma*

Toxicity:

- **cats**, dogs, birds
  - Cats: Cases in cats in Australia are recorded by Duncan (1951) (*Spheroides liosomus* [? = *Tetractenos glaber*]); in association with a fatal human case) and Atwell & Stutchbury (1978)
  - Dog: a non-fatal case was reported in a Jack Russell terrier after eating a porcupine fish at Beaumaris Beach, Victoria in April 1985. The dog remained normal for 24 hr, then developed ataxia followed by paralysis until only its head would move by the third day. Supportive veterinary treatment was followed by slow recovery over 6 weeks (Sutherland & Tibballs 2001)
  - Birds: Duncan (1951) recorded paralysis and death in poultry that ate the vomitus from poisoned cats. A fatal case in a bird (unspecified crow or magpie) was associated with a human poisoning near Nowra, NSW (Torda *et al.* 1973).
- cat oral LD_{50} = 0.2 mg/kg
- humans

- Japanese culinary delicacy "fugu" (flesh of puffer fish) → affected 3000 people 1955-75, killing 51%; lethal dose 15-30 μg/kg; death from 1-2 mg tetrodotoxin (=1-10 g fish eggs or liver)
- Captain James Cook is reputed to have almost died of tetrodotoxin poisoning in New Caledonia in 1774 after sampling a little of the roe and liver of a toad fish (Kao 1966)

- tetrodotoxin **concentrated in liver and gonads** of fish, in **salivary glands** of blue-ringed octopuses
- tetrodotoxin **heat-stable** at normal cooking temperatures
- toxic to all vertebrates except those that contain it naturally

Octopus kill their prey using the secretion produced by the posterior salivary glands which appears to penetrate crabs without physical damage being done to their carapace (Ghiretti 1959, 1960). Toxin produced by blue-ringed octopus has been reported by Flecker & Cotton (1955), Croft & Howden (1972), Savage & Howden (1977)

Mode of action:

- blocks the voltage-gated Na channels in cell membranes → inhibits/abolishes membrane action potential in electrically-excitable tissues (nerves, muscles) → ↓↓ force of muscle contraction, ↓↓ nerve conduction.
- reduces permeability of cell membrane to Na → prevents depolarisation, acting in a similar manner to local anaesthetics
- effect on vasomotor nerves → hypotension
- effect on neuromuscular junctions → flaccid paralysis (hind limbs & diaphragm most susceptible)
- cardiac muscle less sensitive than nerve or skeletal muscle, but severe intoxication can → first degree heart block, bradycardia, asystole
- effects are at the same site but opposite to those of ciguatoxin

Conditions of poisoning in Australia:

- cats/dogs fed (or scavenged) toad fish
- bite of a blue-ringed octopuses when out of water and provoked (Note: human victims commonly do not report feeling the bite)

Clinical signs:

Cats

- drooling saliva (failure to swallow)
- vomiting, diarrhoea → **muscular weakness**, ataxia → **flaccid paralysis**
- hypothermia
- marked **mydriasis**
- shallow respiration → respiratory paralysis
- terminal convulsions (hypoxia?)

Pathology: necropsy → no lesions

Diagnosis:

- fish consumption history (fish species) + clinical syndrome
- differential diagnoses include
  - ciguatera
  - *Ixodes holocyclus* envenomation
  - brown snake (*Psuedonaja textilis*) envenomation
  - botulism
  - polyether ionophore antibiotic toxicity
- no routine laboratory diagnostic tests; toxin detectable in tissue by GC-MS

Therapy:

- tracheal intubation → respiratory support if required
- gastric lavage + activated charcoal
- recovery should occur if respiration, cardiovascular and renal function can be maintained
  - hypotension treated best with IV fluids + peripheral vasoconstricting agent (dopamine, noradrenaline)
  - cardiovascular & respiratory stimulant etamiphylline (cat: 210mg IM)
- possible future immunotherapy developed for human intoxication

- promising experimental data suggest that the potassium channel blocker 4-aminopyridine is an effective adjunct to treatment (Benton *et al.* 1996, Chang *et al.* 1996)

Prevention & control: deny consumption of toadfish (see Pratchett *et al.* 1999)

References:

Se343

Atwell RB, Stutchbury GB (1978) Toadfish poisoning (tetrodotoxin) in the cat. *Aust. Vet. J.* **54**:308-310.

Beesley PL, Ross GJB, Wells A (eds.) (1998) *Mollusca: The Southern Synthesis. Fauna of Australia. Volume 5.* CSIRO Publishing, Melbourne. Family Octopodidae pp.548-550.

Benton BJ, Spriggs DL, Capacio BR, Chang F-CT (1996) 4-aminopyridine antagonises the lethal effects of saxitoxin (STX) and tetrodotoxin (TTX). *Toxicon* **34**:335.

Chang F-CT, Bauer RM, Benton BJ, Keller SA, Capacio BR (1996) 4-aminopyridine antagonizes saxitoxin- and tetrodotoxin-induced cardiorespiratory depression. *Toxicon* **34**:671-690.

Croft JA, Howden MEH (1972)Chemistry of maculotoxin: a potent neurotoxin isolated from *Hapalochlaena maculosa. Toxicon* **10**:645-651.

Daly *et al.* (1993) *The Alkaloids* **43**:185

Duncan C (1951) A case of toadfish poisoning. *Med. J. Aust.* **2**:673-674.

Flecker H, Cotton BC (1955) Fatal bite from octopus. *Med. J. Aust.* **2**:329-331.

Furlow B (2001) The freelance poisoner. *New Scientist* **169** (2274): 30-33.

Ghiretti F (1959) Cephalotoxin: the crab-paralysing agent of the posterior salivary glands of cephalopods. *Nature (London)* **183**:1192-1193.

Ghiretti F (1960) Toxicity of octopus saliva against Crustacea. *Ann. N. Y. Acad. Sci.* **90**:726-741.

Grant EM (1999) *Grant's Guide to Fishes.* 8th ed. E.M.Grant Pty. Ltd. , Redcliffe. pp. 739-760.

Kanchanapongkul J, Krittayapoositpot P (1995) An epidemic of tetrodotoxin poisoning following ingestion of the horseshoe crab *Carcinoscorpius rotundicauda. Southeast Asian J. Trop. Med. Public Health* **26**:364-367.

Kao CY (1966) Tetrodotoxin, saxitoxin and their significance in the study of the excitation phenomenon. *Pharmacol. Rev.* **18**:997-1049.

Lu CC (2001) Cephalopoda. In Wells A, Houston WWK (eds.) *Zoological Catalogue of Australia.* Vol. 17.2. Mollusca: Aplacophora, Polyplachophora, Scaphopoda, Cephalopoda. CSIRO Publishing, Melbourne. pp. 129-308.

McPherson C (1998) Ciguatoxin and tetrodotoxin poisoning in the cat: their diagnosis, treatment and management. *Aust. Vet. Practit.* **28**:26-34

Norman M, Reid A (2000) *A Guide to Squid, Cuttlefish and Octopuses of Australasia.* Gould League of Australia & CSIRO Publishing, Melbourne.

Pratchett T, Briggs S, Hannan T, Kidby P (1999) Deep-sea Blowfish (The Easy Version – not requiring years of training). In *Nanny Ogg's Cookbook.* Doubleday, London. p.27-28.

Savage IVE, Howden MEH (1977) Hapalotoxin, a second lethal toxin from the octopus *Hapalochlaena maculosa. Toxicon* **15**:463-466.

Southcott RV (1975) *Australian Venomous and Poisonous Fishes.* R.V. Southcott, Mitcham, South Australia.

Sutherland SK, Lane WR (1969) Toxins and mode of envenomation of the common ringed or blue-banded octopus. *Med. J. Aust.* **1**:893-898.

Sutherland SK, Tibballs J (2001) *Australian Animal Toxins. The creatures, their toxins and care of the poisoned patient.* 2nd edition, Oxford University Press, Melbourne. pp. 726-741.

Tibballs J (1988) Severe tetrodotoxic fish poisoning. *Anaesthesia and Intensive Care* **16**:215-217.

Toncich G (1987) Two 'fishy' tales. *Australian Family Physician* **16**:1038.

Torda TA, Sinclair E, Ulyatt DB (1973) Puffer fish (tetrodotoxin) poisoning. Clinical record and suggested management. *Med. J. Aust.* **1**:599-602.

Tranter JH, Augustine O (1978) Observations on the life history of the blue-ringed octopus *Hapalochlaena maculosa. Mar. Biol.* **18**:115-128.

Histamine fish poisoning (HFP) - humans

Histamine fish poisoning is not reported in domestic animals in Australia, but human cases are on record. The syndrome has been reviewed from a risk-assessment perspective for Australia by Lehane & Olley (1999).

Syndrome names:

Histamine fish poisoning

Scombroid fish poisoning (note that fish other than members of the Family Scombridae are involved)

Chemical structure:

Toxins are biogenic amines, principally histamine but possibly including cadaverine and putrescine

Sources:

- scombroid fish (family Scombridae) associated with HFP include
  - mackerel (*Scomber* spp.)
  - tuna (*Thunnus* spp.)
  - saury (*Cololabis saira*)
  - bonito (*Sarda* spp.)

- non-scombroid fish associated with HFP include
    - mahi-mahi or dolphin fish (*Coryphaena* spp.)
    - sardines (*Sardinella* spp.)
    - pilchards (*Sardina pilchardus*)
    - anchovies (*Engraulis* spp.)
    - herring (*Clupea* spp.)
    - marlin (*Makaira* spp.)
    - tailor or bluefish (*Pomatomus* spp.)
    - Western Australian salmon (*Arripis truttaceus*)
    - sockeye salmon (*Oncorhynchus nerka*)
    - cape yellowtail (*Seriola lalandii*)

Toxin production:

- HFP is not simply histamine poisoning; other toxins may be involved.
- biogenic amines are produced from amino acids by the action of bacteria (mainly of the family Enterobacteriaceae) through bacterial histidine decarboxylases (HD) under certain environmental conditions
    - histidine → histamine
    - ornithine → putrescine
    - lysine → cadaverine
- fish of the family Scombridae, mainly tuna and mackerel, contain abundant histidine and are most often implicated
- histidine decarboxylating bacteria (HDB) include *Morganella morganii*, *Klebsiella pneumoniae, Hafnia alvei*, *Vibrio* spp., *Photobacterium* spp.; uncertain if significant HDB are normal microflora of fish or post-harvest contaminants; once a large bacterial population is established, enzyme activity continues despite cessation of bacterial growth under refrigeration; some bacteria (including the latter 2 above) can grow at 0-5^{o}C

Distribution:

- most reports of human poisoning since 1970 from Japan, USA, UK
- less frequently in other countries including Australia, New Zealand
- only 3 reports in the literature from Australia; tailor (a WHO Report 1985), Western Australian salmon caught in South Australia caused 2 incidents affecting a total of 7 people (Smart 1992); 2 people were affected by eating tuna in a Brisbane restaurant (Brown 1993)

Mode of action:

- pathogenesis of HFP is obscure; toxins other than histamine may be involved
- histamine consumed in spoiled fish is more toxic than an equal quantity consumed as an aqueous solution; hypotheses attempting to explain this include
    - other biogenic amines in spoiled fish may potentiate the action of histamine by inhibiting diamine oxidase (DAO or histaminase) and histamine methyl transferase (HMT) in the intestines.
    - "barrier disruption " hypothesis: other biogenic amines may interfere with intestinal mucin which normally binds histamine
    - toxins in spoiled fish may cause release of endogenous histamine from mast cells, adding to the effects of ingested histamine; Lehane & Olley (1999) suggest that the evidence for this is good and propose urocanic acid, a known degranulator of mast cells, as a major agent; histidine also → urocanic acid through L-histidine ammonia lyase (HAL or histidase) in bacteria or fish muscle itself
- histamine interacts with histamine receptors (H_1, H_2 and H_3) on cell membranes

Conditions of poisoning:

- improper handling or storage of fish
- consumption of spoiled or bacterially-contaminated fish; fish species associated with HFP are harmless when caught; they may still appear and smell normal after they become toxic
- spoiled "fresh" fish, frozen or smoked fish & canned fish products may all be toxic
- toxicity associated with histamine concentrations ≥ 50 mg/100g in spoiled fish
- histamine largely heat stable (cooking temperatures)
- persons taking medications such as isoniazid are predisposed (inhibit intestinal histamine-degrading enzymes)

Clinical syndrome:

- usually mild disease of rapid onset (several minutes to hours) and short duration (typically about 8 hr but may extend to several days)
- cardiovascular effects most common – flushing of face & neck, urticaria, hypotension, headache
- gastrointestinal effects – abdominal cramps, diarrhoea, vomiting
- neurological effects – pain & itching associated with urticaria
- in severe cases bronchospasm and dyspnoea

Diagnosis:

- differential diagnoses include food allergy
- numerous tests available to detect histidine decarboxylating bacteria and histamine; HPLC, capillary electrophoresis commonly used, ELISA test kits available
- diagnostic problems:
  - non-uniform distribution of histamine in toxic fish; more close to gills and intestines
  - histamine not the sole factor involved

Therapy:

- antihistamines are effective (but may not always be necessary)
  - H_1 antagonists – diphenhydramine, chlorpheniramine
  - H_2 antagonists - cimetidine

Prevention and control:

- effective prompt refrigeration (< 10^oC) of fish after catching, particularly hazardous fish species
- heat processing can destroy bacterial contamination and even HD, but has little or no effect on histamine concentrations
- Australian Food Standard Code stipulates no more than 100 mg histamine/kg in fish; a small proportion of imported fish products exceed this concentration
- Hazard analysis and critical control point (HACCP) principles and quality control methods have reduced the incidence of HFP from processed fish in recent times; those now most at risk are amateur (including recreational) fishers in tropical regions

References:

Brown C (1993) Scombroid poisoning (Letter). *Med. J. Aust.* **158**(6):435-436.

Lehane L, Olley J (1999) *Histamine (Scombroid) Fish Poisoning. A review in a risk-assessment framework*. National Office of Animal & Plant Health, Canberra. pp. iv + 80.

Smart DR (1992) Scombroid poisoning. A report of seven cases involving the Western Australian salmon, *Arripid truttaceus. Med. J. Aust.* **157**(11-12):748-751.

Poisonous fish [additional to ciguatera & tetrodotoxin]

Grant EM (1999) *Grant's Guide to Fishes.* 8th ed., E.M.Grant Pty. Ltd., Redcliffe.

Ostracitoxin - Boxfish

Ostracion spp. (boxfish) - northern Australia (Great Barrier Reef, NT, northern WA); ostracitoxin discharged into the water is toxic to other fish; flesh is poisonous to humans [Grant pp722-725]

Ostracion cubicus L. (blue-spotted box fish) [Grant p. 722-724]

Ostracion meleagris Lacepede [= *O. lentiginosum* Bloch] (ornate boxfish) [Grant p. 723 & 725]

Strophiurichthys robustus Fraser-Brunner (freckled boxfish) [Grant p.726] as for other boxfish above; distributed in southern Qld & NSW

Anoplocapros lenticularis (Richardson) [Grant p.726& 729] as for other boxfish above; distributed from southern NSW to southern WA, also seen in southern Qld

Undescribed (?) toxin(s) - Ocean sunfish

Mola mola L. - closely associated with the Toadfishes [no further information offered]; distributed in ocean waters

Undescribed (?) toxin(s) - Cowfish

[Grant p.727-728]

Aracana ornata (Gray) (ornate cowfish) - distributed Vic, Tas, SA southern WA; flesh toxic to humans

Lactoria cornuta L. (long-horned cowfish - distributed northern Australia (Qld, NT, WA); flesh toxic to humans

Undescribed (?) toxin(s) - Turret-fish

Tetrosomus reipublicae (Ogilby) (turret-fish) [Grant p.728] - northern Australia (Qld, NT, WA); flesh toxic to humans

Venomous (or physically injurious) fish

Grant EM (1999) *Grant's Guide to Fishes.* 8th ed., E.M.Grant Pty. Ltd., Redcliffe.

Numbfish or Electric ray

Hypnos monopterygium (Shaw & Nodder) [Grant p.70-72] - distributed from central & southern sectors of the Great Barrier Reef through NSW, SA and southern WA; paired electric organs lying behind the eyes along the dorsum of the body are capable of delivering 50 shocks in 10 minutes ranging in power from a maximum of 200 volts

Rays

Dasyatis fluviorum (Ogilby) (brown stingray) [Grant p.77 & 79] - distributed in estuaries of southern Qld & NSW

Dasyatis kuhlii (Muller & Henle) [Grant p.79-80] - distributed in northern Australia (northern NSW, Qld, NT, WA)

Dasyatis thetidis Waite (black stingray) [Grant p.75] - distributed in southern Australia (Qld, NSW, Vic, Tas, SA, WA)

Himantura granulata (Macleay) (mangrove ray) [Grant p.79-80] - distributed in Great Barrier Reef region (Qld)

Himantura uarnak (Forskal) (long-tailed ray, coachwhip ray) [Grant p.74-75] - distributed in northern Australia (NSW, Qld, NT, WA)

Myliobatus australis Macleay (bull-ray) [Grant p.87] - distributed in southern Australia (Qld, NSW, Vic, Tas, SA, southern WA)

Pastinachus sephen (Forskal) (cowtail ray, banana-tailed ray) [Grant p.75-76] - probably responsible for more ray stings in Australia than any other species; distributed in northern Australia (NSW, Qld, NT, WA)

Taeniura lymna (Forskal) (lagoon ray) [Grant p.82-83] - distributed in northern Australia (Qld, NT, WA)

Trygonoptera testacea (Muller & Henle) (stingaree) [Grant p.73] -distributed in southern Australia (Qld-WA)

Urolophus bucculentus Macleay (sandy-back stingaree) [Grant p.73] - distributed Qld, NSW, Vic, Tas

Urolophus cruciatus (Lacepede) (crossback stingaree) [Grant p.73 & 78] - distributed Vic, Tas, SA, southern WA

Stonefish [Grant p. 762-764]

Synanceia horrida (L.) (estuarine stonefish) - muddy mainland foreshores

Synanceia verrucosa Bloch & Schneider (reef stonefish) - reef flats

Scorpionfish [Grant p. 765-783]

Marine fish with venom glands are set at the bases of the dorsal fin that deliver venom through the fin's spines.

Apistops caloundra (De Vis) (short-spined waspfish) - northern Australia (Qld, NT)

Centropogon marmoratus (Gunther) (fortescue, fortie, bullrout) - southern Qld estuaries & canal systems to NSW

Dendrochirus zebra (Cuvier) (dwarf lionfish, dwarf firefish) - northern Australia (Qld, NT, WA)

Erosa erosa (Cuvier & Valenciennes) (Pacific monkeyfish) - northern Australia (Qld, NT, WA)

Gymnapistes marmoratus (Cuvier & Valenciennes) (soldierfish, South Australian cobbler) - southern Australia (NSW, Vic, Tas, SA, southern WA)

Helicolenus papillosus (Bloch & Schneider) (red gurnard perch, kuriaki [NSW], ocean perch [NZ]) - southern Australia (southern Qld, NSW, Vic, Tas, ?SA, ?WA), New Zealand

Inimicus caledonicus (Sauvage) (demon stinger, bearded ghoul) - southern Qld - Torres Strait - New Caledonia
Minous versicolor Ogilby (plum-striped waspfish) - northern Australia (Qld, NT, WA)
Neosebastes incisipinnis Ogilby (red stinger, black-spot stingfish) - southern Great Barrier Reef to NSW
Neosebastes scorpaenoides Guichernot (common gurnard perch, spotted gurnard perch) - southern Australia (Tas, Vic, SA)
Parascorpaena picta (Cuvier) (painted stingfish) - northern Australia (Qld, NT, WA)
Peristrominous dolosus (Whitley) (brown carpetfish) - Qld
Pterois volitans (L.) (red firefish, butterfly-cod, lionfish, zebrafish) - northern Australia (northern NSW, Qld, NT, WA)
Rhinopias aphanes Eschmeyer (weedy scorpionfish) - Greta Barrier Reef - New Guinea - Japan
Scorpaena cardinalis Richardson (red scorpion-cod, red rock-cod, poor man's lobster) - southern Qld & northern NSW
Scorpaena ergastulorum Richardson (southern red rock-cod) - NSW, Vic, Tas, SA
Scorpaena sumptuosa Castelnau (western scorpion-cod) - WA
Scorpaenodes guamensis (Quoy & Gaimard) (Guam scorpionfish) - northern Australia (Qld, NT, WA)
Scorpaenopsis diabolus (Cuvier) (false stonefish) - northern Australia (Qld, NT, WA)
Sebastapistes bynoensis (Richardson) (coral scorpionfish, marbled scorpionfish) [? = *Scorpaena picta* (Cuvier)] - Great Barrier Reef (Qld)

Freshwater bullrout [Grant p. 811]

Notesthes robusta (Gunther) (freshwater bullrout, freshwater stonefish) - coastal streams Cape York (Qld) to Bateman's Bay (NSW)

AMPHIBIANS

Granular or serous glands of the skin (multicellular exocrine glands derived from the epidermis) are the source of most toxins in amphibians, being distributed to optimise their role in defense of the animal (Toledo & Jared 1995). All types of amphibian – gymnophiona (apoda), urodela (newts & salamanders) and anura (frogs & toads) – contain toxins.

Toxins produced include

- ❖ cardioactive steroids
- ❖ biogenic amines
- ❖ alkaloids
- ❖ peptides
- ❖ haemolytic proteins
- ❖ guanidine derivatives - tetrodotoxin

References:

Toledo RC, Jared C (1995) Cutaneous granular glands and amphibian venoms. *Comp. Biochem. Physiol.* **111A**:1-29.

Cardioactive steroids of Bufo *spp. toads - dogs (cats)*

Core data

Common source: Bufo marinus (cane toad, marine toad) parotid glands + skin generally
Principal toxins: bufadienolide cardioactive steroids [= aglycones of cardiac glycosides]
Animals affected: dog (cat)
Poisoning circumstances:

- attacking & mouthing toad
- warmer months

Main effects:

- sialorrhoea (ptyalism)
- cardiac arrhythmia
- seizures

Diagnosis: exposure history; clinical syndrome
Therapy:

- flush mouth with water
- monitor ECG in severe cases
- atropine for bradycardias < 50 beats/min
- esmolol or propranolol for tachycardias
- diazepam or anaesthesia for seizures
- severe cases: decontaminate with activated charcoal PO + diuretics

Toxins:

- The main toxins in toad venom are **cardioactive steroids**, structurally analogous to the **aglycones of cardiac glycosides** (*q.v.*) such as occur in plants. These are bufadienolides or bufagenins and their conjugates with suberylarginine substituents (bufotoxins) (Meyer & Linde 1971)
  - bufadienolides present include arenobufagin, argentinogenin, bufalin, bufotalidin, gamma-bufotalin, hellebrigenol, marinobufagin, resibufogenin, telocinobufagin
  - bufotoxins present include marinobufotoxin, jamaicobufagin
- also present in small quantities:
  - catecholamines (adrenalin, noradrenalin, dopamine, epinine (a dopamine derivative))
  - tryptamine alkaloids (bufotenine, serotonin [= 5- hydroxytryptamine])

Sources:

Toads in the genus *Bufo* (Family Bufonidae) bearing granular glands, usually in the dorsal body skin.

Bufo marinus (giant toad, marine toad, cane toad [Australia])

Bufo marinus is native to the Americas. It was introduced to Hawaii from Puerto Rico in 1932 and from thence to Queensland sugar cane farms near Cairns in 1935-6 for cane beetle control [vs. larvae of the greyback beetle (*Dermolepida albohirtum*) and Frenchi beetle (*Lepidiota frenchi*)]. It has

become naturalised and is spreading in tropical & subtropical coastal areas of Q, NSW, NT (Cogger 2000) reaching Kakadu National Park in 2001. Toxic venom is present in skin glands all over the body, and particularly in the **parotid glands**. Ovaries, eggs and blood are also known to be toxic (Covacevich & Archer 1975, Tyler 1975).

Bufo alvarius (Colorado river toad)

Bufo vulgaris [= *B. bufo*] (common European toad) reported causing toxicity in dogs and cats in England (Bedford 1974). Parotid glands are the main source of venom. Poisoning is uncommon and seldom fatal.

Bufo regularis reported causing commonly-fatal poisoning of dogs and cats in Addis Ababa, Ethiopia (Perry & Bracegirdle 1973).

Bufo bufo gargarizans (Chinese toad). Medicinal preparations of toad skin have been and are used for various purposes, often in traditional oriental medicine (dried toad venom is used in Chan Su and Kyushin). They are mainly used for their cardiotonic or diuretic properties. Other uses are for putative aphrodisiac or psychodelic properties (Brubacher *et al.* 1999).

Toxicity:

Bufo marinus

Mammals, birds and reptiles are susceptible to toad toxins. One early record of poisoning is in dogs in Fiji (Turbet 1938).

- death can follow 1 exposure
- fatal dose of crude venom in dogs = 1 mg/kg (Tyler 1987); 0.1 g/dog or the contents of both parotid glands (Palumbo *et al.* 1975)
- Why isn't the toad affected by the toxins in its secretions? Suggested that a high K concentration in body fluids protects against the cardiac glycoside effects on heart muscle. See discussion in McFarland (1999).
- What is the function of the toxin mix? It has been suggested that the antibiotic effect of secretions is the most important function, allowing the animal to survive a high microbe load in its environment (Tyler 1987). Despite opinion to the contrary, the concentration of toxin-secreting glands in the parotid region and the dorsal skin strongly suggests a defensive function against predation by vertebrates as well.

Conditions of poisoning:

Bufo marinus

- dogs (rarely cats) attacking and mouthing toads. Individual dogs will attack toads and become intoxicated on more than one occasion (Roberts *et al.* 2000). The smaller the dog, the greater the likelihood that it will require hospitalisation for therapy (Roberts *et al.* 2000).
- usually in warmer months (Sep-Apr) in southern Q & NSW; all year in northern Q

Clinical signs:

Bufo marinus

Rapid onset after contact

Buccal irritation

- immediate **profuse salivation** (ptyalism) with head shaking and pawing at the mouth
- **hyperaemia of buccal mucosa**

Systemic signs

- vomiting
- ataxia (weakness), prostration
- **cardiac arrhythmia:** sinus arrhythmia and sinus tachycardia are the most common rhythms on ECGs, some dogs have bradycardia (Roberts *et al.* 2000).
- polypnoea
- diarrhoea (frequently haemorrhagic)
- **convulsive seizures** (severe cases) precede death (often within 15 min of onset)

In a series of 94 cases reported from Florida USA (Roberts *et al.* 2000), clinical signs in descending order of frequency of occurrence were neurological abnormalities (54%), hyperaemic mucus membranes (51%), ptyalism (42%), recumbency or collapse (18%), tachypnoea (16%), and vomiting (12%). Neurological abnormalities were seizures (23%), stupor (18%), ataxia

(18%), nystagmus (17%), extensor rigidity (5%), and opisthotonus (4%). 9% were in status epilepticus on presentation.

Pathology: no significant lesions

Diagnosis:

history of exposure, clinical signs

There should be a high index of suspicion of toad toxicity for dogs with acute onset of neurological abnormalities in *Bufo marinus*-endemic areas (Roberts *et al.* 2000).

Therapy:

Bufo marinus

Timely oral cavity lavage with tap water and treatment of neurological signs with sedatives and anticonvulsants form the basis of successful therapy (Roberts 2000). Mild cases have a good prognosis with early intervention. Dogs with convulsions have a guarded to poor prognosis.

Suggested therapeutic regimen:

- **Oral cavity lavage** to remove any remaining venom from the mouth: Advise the owner to immediately flush the mouth with running water. Apply the water jet from a garden hose, *carefully directed towards the front of the mouth to avoid aspiration of water*, for 5 minutes before prompt presentation at the clinic, ***unless the dog is seizuring or unconscious*** when immediate transport to the clinic is recommended.
- **ECG**s are indicated for dogs with bradycardia, tachycardia, auscultable cardiac abnormalities, neurological signs or signs of shock and the ECG should be monitored continuously in these dogs (Roberts *et al.* 2000).
- **Atropine** treatment of **bradycardia** should be reserved for dogs with heart rates ≤ 50 beats/min. Atropine treatment of ptyalism and bronchoconstriction in dogs with normal heart rates or tachycardia may result in more severe dysrhythmias. (Roberts *et al.* 2000)
- Treat **prolonged sinus tachycardia** with IV esmolol (Brevibloc®, Boots Healthcare Australia) @ 0.1 mg/kg or IV propranolol @ 2 to 5 mg/kg. (Palumbo *et al.* 1975, Roberts *et al.* 2000)
- Treat **seizures** with IV diazepam or anaesthetise & intubate; barbiturate anaesthesia has been effective in dogs (Turbet 1938, Palumbo *et al.* 1975).
- In severe cases (collapse, stupor or coma), continue decontamination with **diuretics** to promote urinary excretion of the toxins and PO **activated charcoal** to prevent further absorption and intercept the enterohepatic circulation of toxins. Diuretics suggested include IV furosemide @ 1 to 2 mg/kg or IV mannitol @ 250 to 1000 mg/kg. (Roberts *et al*. 2000)

Digoxin-specific Fab fragments have been used successfully to treat humans intoxicated by toad venoms (Brubacher *et al.* 1996, 1999).

Prevention & control:

Biological control of *Bufo marinus* has been investigated to some extent (Speare 1990), but no useful biocontrol organism has been released into the Australian population to date.

References: Os443, Se315

Bedford PGC (1974) Toad venom toxicity and its clinical occurrence in small animals in the United Kingdom. *Vet. Rec.* **94**:613-614.

Brubacher JR, Ravikumar PR, Bania T, Heller MB, Hoffman RS (1996) Treatment of toad venom poisoning with digoxin-specific Fab fragments. *Chest* **110**:1282-1288.

Brubacher JR, Lachmanen D, Ravikumar PR, Hoffman RS (1999) Efficacy of digoxin specific Fab fragments (Digibind®) in the treatment of toad venom poisoning. *Toxicon* **37**:931-942.

Cogger HG (2000) *Reptiles and Amphibians of Australia*. 6th edition, Reed Books, Sydney. p.169.

Covacevich J, Archer M (1975) The distribution of the cane toad, *Bufo marinus*, in Australia and its effects on indigenous vertebrates. *Mem. Qld. Mus.* **17**:305-310.

Daly JW, Myers CW, Whittaker N (1987) Further classification of skin alkaloids from neotropical poison frogs (Dendrobatidae), with a general survey of toxic/noxious substances in the amphibia. *Toxicon* **25**:1023-1095.

Fitzgerald MP (1998) Toxic amphibians, In Galey FD, Raisbeck MF *et al.* (1998) *Clinical Toxicology.* Proceedings 318, Post-Graduate Foundation in Veterinary Science, University of Sydney. pp.195-200.

Freeland WJ (1984) Cane toads: A review of their biology and impact on Australia. Conservation Commission of the Northern Territory, Technical Report No. 19. pp. v + 67.

Macdonald B (1990) Terrier toad toxicity syndrome. *Aust. Vet. Practit.* **20**:118

McFarland PJ (1999) Toad toxicity. *Aust. Vet. Practit.* **29**:98-103.

Meyer K, Linde H (1971) Collection of toad venoms and chemistry of the toad venom steroids. Chapter 40 in Bucherl W, Buckley EE (eds.) *Venomous Animals and Their Venoms. Volume 2. Venomous Vertebrates.* Academic Press, New York. pp.521-556.
Otani A, Palumbo N, Read G (1969) Pharmacodynamics and treatment of mammals poisoned by *Bufo marinus* toxin. *Am. J. Vet. Res.* **30**:1865-1872.
Palumbo NE, Perri S, Read G (1975) Experimental induction and treatment of toad poisoning in the dog. *J. Am. Vet. Med. Assoc.* **167**:1000-1005.
Roberts BK, Aronsohn MG, Moses BL, Burk RL, Toll J, Weeren FR (2000) *Bufo marinus* intoxication in dogs: 94 cases (1997-1998). *J. Am. Vet. Med. Assoc.* **216**:1941-1944.
Speare R (1990) A review of the diseases of the cane toad, *Bufo marinus*, with comments on biological control. *Aust. Wildl. Res.* **17**:387-410.
Turbet CR (1938) Poisoning of dogs by the giant toad, *Bufo marinus*: its treatment with nembutal. *Aust. Vet. J.* **14**:152-153.
Tyler MJ (1975) *The Cane Toad (*Bufo marinus*). An historical account and modern assessment.* Vermin and Noxious Weeds Destruction Board, Victoria and the Agriculture Protection Board, Western Australia.
Tyler MJ (1987) Frog and cane toad skin secretions. In Covacevich J, Davie P, Pearn J (eds.) *Toxic Plants and Animals. A Guide for Australia.* Queensland Museum, Brisbane. pp.329-339.

Alkaloids of frogs and salamandas

There are nearly 300 alkaloids known from the skin of amphibians where they are believed to act as chemical defense against predators or microbes (Daly *et al.* 1993). Most are known from the skin of frogs in the Family Dendrobatidae and have been referred to as dendrobatid alkaloids (Daly *et al.* 1993). A classification of amphibian alkaloids is given by Daly *et al.* (1987, 1993) and listed below. Those regarded as **clinically significant toxins** are indicated by the symbol ✋.

Steroidal alkaloids

✋ **Batrachotoxins** (batrachotoxin, homobatrachotoxin) from the skin of the brightly-coloured neotropical (South American) poison dart frogs in the genera *Phyllobates, Dendrobates* and *Epipedobates* (Family Dendrobatidae) are the basis of the poison used on blow-pipe darts by indigenous peoples of Colombia. *Phyllobates terribilis* contains *ca.* 2000 μg batrachotoxins/g skin. It is believed that these are not endogenous compounds, but are acquired by the frogs through their diet (Daly *et al.* 1994) before being sequestered in granular skin glands where they are presumed to serve as chemical defense against predators. Some of the alkaloid classes are known from such animals as ants, beetles and millipedes. Others have not been detected beyond frog skin. These neurotoxins interact with the voltage-dependent sodium channels in nerve and muscle membranes to stabilise them in an open position, leading to massive sodium influx and depolarisation. Tetrodotoxin (*q.v.*) blocks this effect. The voltage-dependant sodium channels of these frogs themselves are insensitive to the batrachotoxins.

✋ **Samandarines** occur in the parotid skin glands of the European fire salamander (*Salamandra salamandra*) and alpine salamanda (*Salamandra atra*). These are endogenous compounds with a neurotoxic effect (parenteral mouse lethal dose *ca.* 70 μg; convulsions, respiratory failure, cardiac arrhythmias and partial paralysis precede death).

Bicyclic alkaloids

Histrionicotoxins (azaspiro[5.5]undecanols) of various types (with 15, 17 or 19 carbon molecules) occur only in dendrobatid frogs (named after *Dendrobates histrionicus*) and are of relatively low toxicity (1000μg SC in a mouse produces ataxia and recumbency) and are non-competitive blockers of neuromuscular conduction through interference with 3 types of channels – receptor-regulated, voltage-dependent sodium and voltage-dependent potassium channels. Similar hydroxy-azaspiro-undecane compounds (sibirine, nitramine, isonitramine) occur in plants of the genus *Nitraria* (McCloskey & Schultz 1970).

Decahydroquinolines occur in the skins of dendrobatid frogs (genera *Dendrobates, Epipedobates, Phyllobates*) and bufonid toads (genus *Melanophryniscus*). They are relatively non-toxic (*ca.* 100μg SC in mice causes ataxia, posterior paralysis, salivation, piloerection; minimum lethal dose is *ca.* 400 μg).

Pumiliotoxin-A class (pumiliotoxins A and B, allopumiliotoxins, homopumiliotoxins), indolizidine alkaloids, have been isolated from the neotropical dendrobatid frogs (major toxins in *Dendrobates pumilio* from Panama and Costa Rica; also major toxins in *Epipedobates, Minyobates*), the Australian frogs of genus *Pseudophryne* (*q.v.*), Madagascan ranid frogs of genus *Mantella* , and bufonid toads of South American species in the genus *Melanophryniscus*. These are neurotoxins (mouse SC lethal doses *ca.* 20-50 μg) interacting with voltage-dependent sodium channels and possibly interfering with calcium mobilisation in nerves and muscles. Effects are reported on cardiac muscle.

Pyrrolizidines (*q.v.*) are minor or trace constituents of skin extracts of dendrobatid and ranid frogs and bufonid toads. All appear to be 3,5-disubstituted pyrrolizidines except the tricyclic pyrrolozidine oximes described below. Biological activity is unstudied.

Indolizidines (*q.v.*) in addition to the pumiliotoxins are the 3,5-disubstituted and the 5,8-disubstituted indolizidines from dendrobatid and ranid frogs and bufonid toads. They are neurotoxins blocking nicotinic receptor channels (mouse SC 80 μg indolizidine 223AB causes prolonged ataxia and recumbency). The 3,5-disubstituted indolizidine alkaloids also occur in certain ants (genera *Monomorium* and *Solenopsis*).

Quinolizidines (*q.v.*) of the 1,4-disubstituted class occur in dendrobatid and ranid frogs and bufonid toads. Their biological activity is unstudied, but they probably have similar activity to the indolizidines (above).

Tricyclic alkaloids

Gephyrotoxins occur only in certain populations of *Dendrobates histrionicus* from Colombia and are relatively non-toxic (mouse SC 80 μg causes reduced spontaneous activity only). They are weak muscarinic antagonists and non-competitive nicotine receptor channel blockers.

Coccinellines were first detected in beetles of Family Coccinellidae and in Australian soldier beetles (Moore & Brown 1978) where they may serve as defense chemicals, then from dendrobatid frogs and bufonid toads.

Cyclopenta[*b*]quinolizidines have been detected only from the Colombian poison frog *Minyobates bombetes*. Biological activity is unstudied.

Pyrrolizidine oximes (spiropentano-pyrrolizidine oximes) have been isolated from certain populations of *Dendrobates pumilio* and from the Argentinean toad *Melanophryniscus stelzneri*. Their origin may be from defense chemicals of a millipede. Biological activity is unknown.

Monocyclic alkaloids

These compounds appear to originate in the venoms of ants, serving in a defensive repellent function.

Pyrrolidines have been detected in only certain populations of *Dendrobates* spp. and are non-competitive blockers of nicotinic receptor channels.

Piperidines have only been found in dendrobatids and are potent non-competitive blockers of nicotinic receptor channels.

Pyridine alkaloids

Epibatidines occur in trace amounts in dendrobatid frogs of the genus *Epipedobates* (first from *E. tricolor* from Ecuador) and have analgesic properties.

Norananbasamine occurs in 3 western Colombian species of *Phyllobates* frogs, and appears to originate from myrmicine ant venoms. Its biological activity has not been assessed.

Indole alkaloids

Pseudophrynamines have been isolated from the Australian myobatrachid frogs in the genus *Pseudophryne.* The biological activity of these compounds is unknown, but their structure resembles physostigmine, a potent cholinesterase inhibitor. See below for chemical structures. **Related alkaloids**, chimonanthine (*q.v.*) and calycanthine (*q.v.*) (the optical enantiomers of which occur in plants) have been isolated from the dendrobatid frog *Phyllobates terribilis*.

Indole amines. Many frogs and toads contain large amounts of N- and O-methylated amines derived from serotonin and tryptamine (indolic biogenic amines) as well as other amines including tyramines and catecholamines.

Dehydrobufotenine occurs in large amounts in the parotid gland secretions of *Bufo marinus* (*q.v.*). This compound is moderately toxic (mouse SC lethal dose *ca.* 120 μg; causes clonic convulsions). The *O*-sulphate (bufothionine) also occurs in *Bufo marinus*.

Trypargine, isolated from African hyperolid frogs in the genus *Kassina*, is moderately toxic (mouse IV lethal dose 200 μg; causes paralysis and respiratory failure).

Imidazole alkaloids

Many frogs have large amounts of *N*-methylhistamine and *N,N*-dimethylhistamine in their skin. Spinceamine and 6-methylspinceamine occur in leptodactylid frogs (genus *Leptodacytlus*) and hylid frogs (genera *Litoria and Nictimystes*). Spinceamine has bacteriostatic activity.

Morphine

Morphine, well known from plants, has been detected in trace amounts in skin of *Bufo marinus*, and may have originated in plants and been concentrated in toad skin through ingestion of insects feeding on such plants.

Guanidinium alkaloids

Tetrodotoxin (*q.v.*) has been identified in several amphibians, including newt & salamanders (Order Caudata) and frogs (Order Anura). In the amphibians of the Order Caudata, tetrodotoxin has been identified in the Family Salamandridae in species of the genera *Taricha, Cynops, Notophthalamus, Triturus, Paramesotriton* and in the Family Ambystomatidae in *Ambystoma tigrinum*. In amphibians of the Order Anura, tetrodotoxin has been identified in several species of the neotropical bufonid genus *Atelopus* and in the dendrobatid frog *Colostethus inguinalis*. It is highly toxic (mouse IP LD_{50} is *ca.* 0.2 μg), blocking voltage-dependent sodium channels.

Chiriquitoxin, a congener of tetrodotoxin, occurs in the bufonid frog *Atelopus chiriquiensis* in combination with tetrodotoxin, is nearly as toxic as tetrodotoxin (mouse IP LD_{50} is *ca.* 0.3 μg) and also acts by blockage of voltage-dependent sodium channels.

Zetekitoxin (formerly atelopidtoxin) occurs in the Panamanian golden frog *Atelopus zeteki*, is as toxic as tetrodotoxin and affects heart function. Its structure has not been elucidated.

Other alkaloids

Nearly 70 unclassified alkaloids are known, most in trace amounts.

References:

Daly JW, Myers CW, Whittaker N (1987) Further classification of skin alkaloids from neotropical poison frogs (Dendrobatidae), with a general survey of toxic/noxious substances in the amphibia. *Toxicon* **25**:1023-1095.

Daly JW, Garraffo HM, Spande TF (1993) Amphibian alkaloids. Chapter 3 in Cordell GA (ed.) *The Alkaloids* **43**:185-288.

Daly JW, Garraffo HM, Spande TF, Jaramillo C, Rand AS (1994) Dietary source for skin alkaloids of poison frogs (Dendrobatidae). *J. Chem. Ecol.* **20**:943-955.

McCloskey PJ, Schultz AG (1970) *Heterocycles* **25**:437 [cited by Daley *et al.* 1993]

Moore BP, Brown WV (1978) *Insect Biochem.* **8**:393. [cited by Daley *et al.* 1993]

Peptides of frogs

Four groups of peptides have been identified from frog skin (Erspamer & Melchiorri 1973).

Physalaemin-like peptides

Physalaemin, phyllomedusin, uperolein: intense action on vascular and extravascular smooth muscle and on lachrymal and salivary glands. Physalaemin is a very potent hypotensive agent.

Bradykinin-like peptides

Bradykinin, phyllokinin, Val^{1}-Thr^{5}-bradykinin: effect the calibre and permeability of capillaries

Caerulein-like peptides

Caerulein, phyllocaerulein: mimic the effects of cholecystokinin-pancreozymin and gastrin

Bombesin-like peptides

Bombesin, alytesin, ranatensin: act on vascular and extravascular smooth muscle, gastric acid secretion and kidney function; activate renin-angiotensin system and stimulate erythropoietin release

References:

Erspamer V, Melchiorri P (1973) Active polypeptides of the amphibian skin and their synthetic analogue. *Pure Appl. Chem.* **35**:463-494.

Toxic Australian frogs

Heleioporus (burrowing frogs)

***Heleioporus* Gray** is a genus of moderate-to-large sized indigenous burrowing frogs in the Family Myobatrachidae (previously in Leptodactylidae) (Lee 1967, Cogger 2000). Species distributed in south-western Australia are

Heleioporus eyrei (moaning frog) [-]
Heleioporus inornatus [-]
Heleioporus albopunctatus
Heleioporus psammophilus [-]
Heleioporus barycragus

One species, *Heleioporus australasicus* (giant burrowing frog, eastern owl frog), is known from coastal eastern Australia (Gosford NSW to Victoria).

Softly (1974) noted sporadic reports from Western Australia of poisoning of **dogs** and **cats**, sometimes fatal, after mouthing frogs. Two **human** cases allowed frogs of the genus *Heleioporus* to be positively identified as associated with poisoning (Softly & Nairn 1975). Clinical signs in humans included intense irritation of the eye after contact from fingers contaminated with frog skin secretions from a recently-dead frog and dryness of the mouth, difficulty breathing and bradycardia for about half an hour after ingestion of an antacid tablet accidentally contaminated by frog skin secretions on the fingers. Softly & Nairn (1975) reported dorsolateral subcutaneous glands containing large amounts of thick, gelatinous creamy material and with openings to the skin surface in *H. eyrei, H. inornatus* and *H. albopunctatus*. They determined a mouse SC LD_{50} of 0.5 ml of filtered gland secretion with mice having local dermal irritation at the injection site followed in 2 hrs by posterior paralysis and dying some 20 hrs later of ascending paralysis. Toxicity of the frogs was greater in summer-autumn than in winter-spring.
Lemckert (2001) reported sticky white secretions produced by *Heleioporus australiacus* from their skin glands as presumably toxic, but that no specific tests for toxicity have been done.
Daly *et al.* (1990) detected no alkaloids in skins of the species indicated by the symbol [-] above.

Pseudophryne (toadlets)

***Pseudophryne* Fitzinger** is a genus of small (maximum length 30 mm) terrestrial indigenous frogs in the Family Myobatrachidae (previously in Leptodactylidae) distributed in various locations throughout

Australia, mostly in the south-east and south-west (Barker & Grigg 1977, Cogger 2000). Species and ranges are

Pseudophryne nichollsi (Nicholl's toadlet) – karri (*Eucalyptus diversicolor*) forests of southern WA
Pseudophryne bibroni (brown toadlet) [+] – south-eastern Q to south-eastern SA
Pseudophryne dendyi (southern toadlet) –south-eastern Q to south-eastern SA
Pseudophryne semimarmorata (southern toadlet) [+] – south-eastern Q to south-eastern SA + Tasmania
Pseudophryne major – Burnett River valley, south-eastern Q
Pseudophryne corroboree (coroboree frog) [+] – sphagnum bogs in the Southern Alps above 1500 m.
Pseudophryne australis (red-crowned toadlet) [+] – Hawksbury sandstone region of central NSW
Pseudophryne coriacea (red-backed or Keferstein's toadlet) [+] – south-eastern Q & north-eastern NSW
Pseudophryne guentheri (Guenther's toadlet) [+] – south-western WA
Pseudophryne douglasi – Pilbara coast of WA
Pseudophryne occidentalis (orange-crowned toadlet) [+] – arid inland areas of WA and SA
Pseudophryne covacevichae (magnificent broodfrog) [previously the northern population of *P. major*] – Ravenshoe region, north Q
Pseudophryne pengilleyi (northern corroboree frog) – Brindabella and associated mountain ranges NSW, ACT
Pseudophryne raveni (copper-backed broodfrog) – coast and hinterland south-eastern Queensland to Mackay region

Daly *et al.* (1990) detected alkaloids of two types (pumiliotoxin A and B class and pseudophrynamine class) from the skins of the 7 species indicated by the symbol [+] above. The other 4 species were not examined. Pseudophrynamines are indole alkaloids. There are no records of clinical cases of toxicity from these frogs in the literature.

Litoria caerulea (green tree frog)

Chemical structure:

The toxin responsible for toxicity of *Litoria caerulea* is **caerulein**, a decapeptide produced by skin glands. Caerulein-like peptides including the nonapeptide, phyllocaerulein, have been isolated from other frogs.

Sources (Erspamer & Melchiorri 1973):

Australian frogs(Family Hylidae)

Litoria caerulea (green tree frog) is very common throughout northern and eastern Australia (WA, NT, SA, Q, NSW) and well-known around human habitation (Cogger 2000). Caerulein content of a single *L. caerulea* skin is about 1 mg. Caerulein concentration in fresh *L. caerulea* skin is 100-1000 μg/g with dorsal skin containing 8-10 times more than ventral skin (Erspamer & Melchiorri 1973).

Dried skins of *Litoria infrafrenata* (giant or white-lipped tree frog) of coastal northern Queensland and *Litoria moorei* (western green & golden bell frog) from coastal south-western Australia contain 2500-3000 μg caerulein /g (Erspamer & Melchiorri 1973).

New Guinean frog

Nictymystes disrupta : contains caerulein-like peptides

South-east Asia (New Guinea, Borneo, Philippines)

Rana erythraea : contains caerulein-like peptides

South American frogs

Leptodactylus pentadactylus labyrinthicus – caerulein present
Leptodactylus laticeps : up to 1300 μg caerulein /g fresh skin
Phyllomedusa sauvagei : 200-650 μg phyllocaerulein /g fresh skin
Phyllomedusa bicolor : about 500 μg phyllocaerulein /g fresh skin

South African frogs

Xanopus laevis : 300-800 μg caerulein /g in fresh skin
Xenopus gilli : up to 100 to 1500 μg caerulein /g fresh skin
Hylanbates maculatus : contains caerulein-like peptides

Organ systems affected: Gastrointestinal tract, Pancreas

Toxicity:

Three clinical cases of dogs intoxicated by mouthing green tree frogs were reported by Fitzgerald (1998) from the Alstonville area of New South Wales.

Acute toxicity of caerulein appears to be low: mouse IV LD_{50} = 1030 mg caerulein/kg

Mode of action:

Caerulein has close structural affinities with cholecystokinin and gastrin II, but is 16 times as potent as the former and 170 times as potent as the latter (Erspamer & Melchiorri 1973).

Experimental administration of caerulein to dogs causes direct stimulation of

- gastrointestinal, gall bladder and bile duct smooth muscle causing vomiting and bowel evacuation
- gastric, bile and exocrine pancreas secretions
- vascular muscle tone causing hypotension

Conditions of poisoning: Dogs encountering green tree frogs on summer nights

Clinical signs:

Severe and protracted **vomiting** lasting 30-45 minutes was seen and resolved without treatment in 60 minutes.

Pathology: None recorded in natural cases

Diagnosis: history of exposure (dog outside on summer night) + acute onset of vomiting

Therapy:

Therapy does not appear to be mandatory, but fluid and electrolyte replacement may be indicated if vomiting is particularly severe. Atropine will abolish some of the effects (Erspamer & Melchiorri 1973).

Contra-indications:

- Centrally-acting anti-emetics are probably ineffective
- α-adrenergic blocking agents enhance hypotension induced by caerulein

References:

Barker J, Grigg GC (1977) *A Field Guide to Australian Frogs.* Rigby Ltd., Adelaide.

Cogger HG (2000) *Reptiles and Amphibians of Australia.* 6th edition. Reed New Holland, Sydney.

Daly JW, Highet RJ, Myers CW (1984) Occurrence of skin alkaloids in non-dendrobatid frogs from Brazil (Bufonidae), Australia (Myobatratchidae) and Madagascar (Mantellinae). *Toxicon* **22**:905-919.

Daly JW, Garaffo HM, Pannell LK, Spande TF (1990) Alkaloids from Australian frogs (Myobatrachidae): pseudophrynamines and pumiliotoxins. *J. Nat. Prod.* **53**:407-421.

Daly JW, Garraffo HM, Spande TF (1993) Amphibian alkaloids. Chapter 3 in Cordell GA (ed.) *The Alkaloids* **43**:185-288.

Erspamer V, Melchiorri P (1973) Active polypeptides of the amphibian skin and their synthetic analogue. *Pure Appl. Chem.* **35**:463-494.

Fitzgerald MP (1998) Toxic amphibians, In Galey FD, Raisbeck MF *et al.* (1998) *Clinical Toxicology.* Proceedings 318, Post-Graduate Foundation in Veterinary Science, University of Sydney. pp.195-200.

Lee AK (1967) Studies in Australian amphibia. Part I: Taxonomy, ecology and evolution of the genus *Heleioporus* Gray (Anura: Leptodactylidae). *Aust. J. Zool.* **15**:367-439.

Lemckert F (2001) Digging up the dirt on giant burrowing frogs. *Nature Australia* **27** (2):26-33.

Softly A (1974) The unsuspected poison potential of an indigenous frog. *Herpetofauna* **7** (1):18-20.

Softly A, Nairn ME (1975) A newly reported toxic Australian frog (Genus *Heleioporus*). *Med. J. Aust.* **1**:560-561.

REPTILES

Snake envenomation folklore

Lay treatment of snake bite in Australian dogs: Anecdotes

Peter Darvall, long-time veterinary practitioner of Chinchilla in southern inland Queensland, relates the application of a couple of methods (Darvall 2001):
Case 1 - The "Hypoxia" Method: From the hospital record sheet - "Rainbow, blue heeler female, 3 yrs. Admit with snake bite (no identification of snake species) and pneumonia. Owners tried to treat snake bite by holding the dog in a muddy dam – bloody-near drowned her; ? inhalation pneumonia." The dog recovered after intensive treatment.
Case 2 – The "Slash & Relax" Method: Owner of a snake-bitten pig-dog phoning from 120 km away: "We're on our way to you; the dog's been bitten by a black snake; we cut his ears." Quite some hours later, the party arrived *via* a prolonged sojourn at the Condamine pub, dumped a large handsome pig-dog on my table where it promptly expired – from blood loss. Its ears had been totally amputated.

The rational basis of the "cut its ears and sling it in the dam" method of treating snake bites in dogs is inapparent, but may in part originate from the discontinued practice of the therapeutic bleeding (phlebotomy) of sick humans. Medical phlebotomy has an antipyretic effect (Root-Bernstein & Root-Bernstein 1997)

References:

Darvall P (2001) Snake bite "remedies". *Post-Grad. Committee in Vet Science, University of Sydney: Control & Therapy Series*. Mailing 218, No.4311.

Root-Bernstein R, Root-Bernstein M (1997) *Honey, Mud, Maggots, and Other Medical Marvels. The Science Behind Folk Remedies and Old Wive's Tales.* Macmillan, London. pp.72-86.

Australian venomous snakes

✷ and ✷✷ = species indicated by Cogger (2000) as dangerous to humans.
This list is compiled from data presented by Sutherland (1983) and Cogger (2000).

Venomous snakes
The **colubrids** are the dominant family of snakes in all parts of the world, except Australia (Cogger 2000). Venomous species of this family in Australia are rear-fanged and not considered significant threats to conventional domestic animal or human health.
Australia's venomous **elapid** snakes are proteroglyphous – possessing fixed (immovable) fangs at the front of the maxillae (upper jaws). This description of "fixed" is relative to the maxillae. The maxillae themselves are movable, allowing the fangs to swing forwards through about 90^{o} into a position at right-angles with the whole jaw when the mouth opens to strike prey or in defense.
There are six major groups of proteroglyphs in the world

- mambas
- American coral snakes
- viviparous sea snakes
- cobras, kraits and related Afro-Asian snakes
- Australian 'elapids'
- oviparous 'sea kraits'

Family Colubridae

Boiga irregularis Merrem 1802 (brown tree snake)
Cercerus rynchops Schneider 1799 (bockadam)
Enhydris polylepis Fischer 1886 (Macleay's water snake)

Family Elapidae (Australian elapids)

✷✷ *Acanthophis antarcticus* Shaw & Nodder 1802 (common death adder)
✷✷ *Acanthophis praelongus* Ramsay 1877 (northern death adder)
✷✷ *Acanthophis pyrrhus* Boulenger 1898 (desert death adder)

✸✸ *Austrelaps labialis* Jan 1859 (dwarf, pigmy or Adelaide Hills copperhead)
✸✸ *Austrelaps ramsayi* Krefft 1864 (highland copperhead)
✸✸ *Austrelaps superbus* Günther 1858 (copperhead)
Cacophis churchilli Wells & Wellington 1985
Cacophis harriettae Krefft 1869 (white-crowned snake)
Cacophis krefftii Günther 1863 (dwarf crowned snake)
Cacophis squamulosus Duméril, Bibron & Duméril 1854 (golden crowned snake)
✸ *Demansia atra* Macleay 1884 (black whip snake)
✸ *Demansia olivacea* Gray 1842
Demansia papuensis Macleay 1877
✸ *Demansia psammophis* Schlegel 1837
Dermansia reticulata Gray 1842
Demansia simplex Storr 1978
Demansia torquata Günther 1862 (collared whip snake)
✸ *Denisonia devisi* Waite & Longman 1920 (De Vis' banded snake or De Vis' snake)
✸ *Denisonia maculata* Steindachner 1867 (ornamental snake)
Drysdalia coronata Schlegel 1837 (crowned snake)
Drysdalia coronoides Günther 1858 (white-lipped snake)
Drysdalia mastersii Krefft 1866 (Masters' snake)
Drysdalia rhodogaster Jan & Sordelli 1873
Echiopsis atriceps Storr 1980
✸✸ *Echiopsis curta* Schlegel 1837 (bardick)
Elapognathus minor Günther 1863 (little brown snake)
Furina barnardi Kinghorn 1939 (yellow-naped snake)
Furina diadema Schlegel 1837 (red-naped snake)
Furina dunmalli Worrell 1955 (Dunmall's snake)
Furina ornata Gray 1842 (orange-naped snake)
Furina tristis Günther 1858 (brown-headed snake)
✸ *Hemiaspis damelii* Günther 1876 (grey snake)
Hemiaspis signata Jan 1859 (black-bellied swamp snake, marsh snake)
✸ *Hoplocephalus bitorquatus* Jan 1859 (pale-headed snake)
✸ *Hoplocephalus bungaroides* Schlegel 1837 (broad-headed snake)
✸ *Hoplocephalus stephensii* Krefft 1869 (Stephens' banded snake)
✸✸ *Notechis ater* Krefft 1866 (black or island tiger snake)
✸✸ *Notechis scutatus* Peters 1861 (eastern or mainland tiger snake)
✸✸ *Oxyuranus microlepidotus* McCoy 1879 (fierce or small-scaled snake, western taipan)
✸✸ *Oxyuranus scutellatus* Peters 1867 (taipan)
✸✸ *Pseudechis australis* Gray 1842 (mulga snake, king brown snake)
✸✸ *Pseudechis butleri* Smith 1982
✸✸ *Pseudechis colletti* Boulenger 1902 (Collett's snake)
✸✸ *Pseudechis guttatus* De Vis 1905 (spotted or blue-bellied black snake)
✸✸ *Pseudechis papuanus* Peters & Doria 1878 (Papuan black snake)
✸✸ *Pseudechis porphyriacus* Shaw 1794 (red-bellied or common black snake)
✸✸ *Pseudonaja affinis* Günther 1872 (dugite) [includes *Pseudonaja tanneri* Worrell (Tanner's brown snake)]
✸ *Pseudonaja guttata* Parker 1926 (speckled brown snake [or Downs tiger snake – Barkley Tableland])
✸✸ *Pseudonaja inframacula* Waite 1925 (Peninsula brown snake)
✸✸ *Pseudonaja ingrami* Boulenger 1908 (Ingram's brown snake)
✸ *Pseudonaja modesta* Günther 1872 (ringed or collared brown snake)
✸✸ *Pseudonaja nuchalis* Günther 1858 (western brown snake or gwardar)
✸✸ *Pseudonaja textilis* Duméril, Bibron & Duméril 1854 (common or eastern brown snake)
Rhinoplocephalus bicolor Müller 1885
Rhinoplocephalus boschmai Brongersma & Knaap-van Meeuwen 1964 (Carpentaria whip snake)
✸✸ *Rhinoplocephala nigrescens* Günther 1862 (eastern small-eyed snake) [= *Crytophis nigricans* Worrell]
Rhinoplocephalus nigrostriatus Krefft 1864 (black-striped snake)
Rhinoplocephalus pallidiceps Günther 1858 (northern small-eyed snake)
Rhinoplocephalus incredibilis Wells & Wellington 1985 (pink snake)
Simoselaps anomalus Sternfeld 1919

Simoselaps approximans Glauert 1954
Simoselaps australis Krefft 1864 (coral snake)
Simoselaps bertholdi Jan 1859 (desert banded snake)
Simoselaps bimaculatus Duméril, Bibron & Duméril 1854 (western black-naped snake)
Simoselaps calonotus Duméril, Bibron & Duméril 1854 (western black-striped snake)
Simoselaps fasciolatus Günther 1872 (narrow-banded snake)
Simoselaps incinctus Storr 1968
Simoselaps littoralis Storr 1968
Simoselaps minimus Worrell 1960
Simoselaps morrisi Horner 1998
Simoselaps semifasciatus Günther 1863 (half-girdled snake)
Simoselaps warro De Vis 1884
Suta fasciata Rosén 1905 (Rosen's snake)
Suta flagellum McCoy 1878 (little whip snake)
Suta gouldii Gray 1841 (black-headed snake)
Suta monachus Storr 1964 (hooded snake)
Suta nigriceps Günther 1863
Suta ordensis Storr 1984
Suta punctata Boulenger 1896 (little spotted snake)
Suta spectabilis Krefft 1869
✸✸ *Suta suta* Peters 1863 (myall snake, curl snake)
✸✸ *Tropidechis carinatus* Krefft 1863 (rough-scaled or Clarence River snake)
✸ *Vermicella annulata* Gray 1841 (bandy-bandy)
✸ *Vermicella multifasciata* Longman 1915 (northern bandy-bandy)

Family Hydrophiidae (sea snakes)

Acalyptophis peronii Duméril 1853
Aipysurus apraefrontalis Smith 1926
✸✸ *Aipysurus duboisii* Bavay 1869
✸✸ *Aipysurus eydouxii* Gray 1849 (spine-tailed sea snake)
Aipysurus foliosquama Smith 1926
Aipysurus fuscus Tschudi 1837
✸✸ *Aipysurus laevis* Lacépède 1804 (olive-brown sea snake)
✸✸ *Aipysurus tenuis* Lönnberg & Andersson 1913
✸✸ *Astrotia stokesii* Gray 1846 (Stoke's sea snake)
✸✸ *Disteira kingii* Boulenger 1896 (King's sea snake) [= *Hydrophis kingii*]
✸✸ *Disteira major* Shaw 1802 [= *Hydrophis major*]
Emydocephalus annulatus Krefft 1869 (ringed sea snake) – listed in Sutherland (1983), but stated by Cogger (2000) to be non-venomous through atrophy of teeth and venom structures
✸✸ *Enhydrina schistosa* Daudin 1803 (beaked sea snake)
Ephalophis greyae Smith 1931
Hydrelaps darwiniensis Boulenger 1896 (Port Darwin sea snake)
✸✸ *Hydrophis atriceps* Günther 1864
✸✸ *Hydrophis belcheri* Gray 1849
✸✸ *Hydrophis caerulescens* Shaw 1802
✸✸ *Hydrophis coggeri* Kharin 1984
✸✸ *Hydrophis czeblukovi* Kharin 1984
✸✸ *Hydrophis elegans* Gray 1842
✸✸ *Hydrophis gracilis* Shaw 1802
✸✸ *Hydrophis inornatus* Gray 1849
✸✸ *Hydrophis macdowelli* Kharin 1983
✸✸ *Hydrophis melanosoma* Günther 1864
✸✸ *Hydrophis ornatus* Gray 1842 (reef sea snake)
✸✸ *Hydrophis pacificus* Boulenger 1896
✸✸ *Hydrophis vorisi* Kharin 1984
✸✸ *Lapemis hardwickii* Gray 1835 (Hardwick's sea snake)
Parahydrophis mertoni Roux 1910 [= *Ephalophis mertoni*]
✸✸ *Pelamis platurus* Linnaeus 1766 (yellow-bellied sea snake, pelagic sea snake)
✸✸ *Laticauda colubrina* Schneider 1799 (banded sea snake or yellow-lipped sea krait)
✸✸ *Laticauda laticaudata* Linnaeus 1758 (black-banded sea snake)

Snake envenomation of humans – review literature

References:

Acott CJ, Williamson JA (1996) Sea snakes. Chapter 17 in Williamson JA, Fenner PJ, Burnett JW, Rifkin JF (eds.) *Venomous and Poisonous Marine Animals: A Medical and Biological Handbook.* University of New South Wales Press, Sydney & Surf Lifesaving, Queensland, Inc., Fortitude Valley, Queensland.

Covacevich J, Davie P, Pearn J (editors) (1987) *Toxic Plants and Animals. A Guide for Australia.* Queensland Museum, Brisbane.

Sutherland SK (1983) *Australian Animal Toxins. The creatures, their toxins and care of the poisoned patient.* Oxford University Press, Melbourne.

Sutherland SK, Sutherland J (1999) *Venomous Creatures of Australia. A Field Guide with Notes on First Aid.* 5th edition. Oxford University Press, Melbourne.

Sutherland SK, Tibballs J (2001) *Australian Animal Toxins. The creatures, their toxins and care of the poisoned patient.* 2nd edition, Oxford University Press, Melbourne.

Snake envenomation of domestic animals in Australia – some literature

[N.B. This section is incomplete]

References:

Crawford RD (1979?) Case 7:5 [Report of canine envenomation by *Pseudonaja textilis*] in Sutherland (1983) p.77

Fairley NH (1929a) The present position of snake bite and the snake bitten in Australia. *Med. J. Aust.* **1**:65-77. [includes data on susceptibility of sheep]

Fairley NH (1929b) Criteria for determining the efficacy of ligature in snake bite (the subcutaneous-intravenous index). *Med. J. Aust.* **1**:377-394. [includes data on goat envenomation]

Fitzgerald WE (1975) Snakebite in the horse. *Aust. Vet. J.* **51**:37-39.

Flashman AF (1955) Suspected snakebite in a dog. *Aust. Vet. J.* **31**:41.

Foote HG (1979?) Case 8:2 [Report of canine envenomation by *Austrelaps superbus*] in Sutherland (1983) p.90.

Gilam MW, Williams OJ (1984) The curl snake *Denisonia suta* (Peters) a dangerous elapid in the Northern Territory. *Northern Territory Naturalist* **7**:12-17. [= *Suta suta*; cited by Sutherland (1983) p.150 as in press; fatal case in a cat]

Girdlestone TM (1876) Report of the special committee on the subject of snake poisoning. *Aust. Med. J.* **21**:104-132. [cited by Sutherland 1983 p.2; experiments included envenomation of dogs]

Gordon RN (1958) The symptoms [*sic*], diagnosis and treatment of snake-bite in the dog. *Aust. Vet. J.* **34**:216-221.

Hill FWG (1979) Snake bite in dogs. *Aust. Vet. J.* **55**:82-85.

Hill FWG, Campbell T (1978) Snake bite in cats. *Aust. Vet. J.* **54**:437-439.

Keep JM (1957) Antivenene in a case of snake bite in the dog. *Aust. Vet. J.* **33**:95-96.

Kellaway CH (1929a) The venom of *Notechis scutatus*. *Med J. Aust.* **1**:348-358. [includes data on toxicity to cats and horses]

Kellaway CH (1929b) A preliminary note on the venom of the Australian copperhead (*Denisonia superba*): its toxic effects in the common laboratory animals. *Med J. Aust.* **1**:358-365. [includes data on toxicity to horses]

Kellaway CH (1931) Observations on the certainly lethal dose of the venom of the common brown snake (*Demansia textilis*) for the common laboratory animals. *Med. J. Aust.* **2**:747-751. [includes data on toxicity to cats and horses]

Lewis PF (1978) Snakebite in animals in Australia. *Proceedings No. 36. Post-Grad. Committee in Vet. Sci., Uni. Sydney* pp. 287-309.

Lynch PJ (1979?) Case 15:3 [Report of canine envenomation by *Hemiaspis damelii*] in Sutherland (1983) p.156.

Maaten F (1981?) Case 13:2 [Report of canine envenomation by *Rhinoplocephala nigrescens*] in Sutherland (1983) p.138.

Mirtschin PJ, Masci P, Paton DC, Kuchel T (1998) Snake bites recorded by veterinary practices in Australia. *Aust. Vet. J.* **76**:195-198.

Munday BL (1959) Antivenene in a suspected case of snake bite in the cat. *Aust. Vet. J.* **35**:44. [*Notechis ater*]

Pascoe RR (1975) Brown snake bite in horses in south-eastern Queensland. *J. S. Afr. Vet. Assoc.* **46**:129-131.

Pollitt CC (1981) Studies on the venom and blood of the eastern small-eyed snake *Cryptophis nigrescens* (Günther). In Banks CB, Martin AA (eds) *Proceedings of the Melbourne Herpetological Symposium*. Zoological Board of Victoria, Melbourne. pp. 44-54.

Seddon HD (1974) Snakebite in a cat by a five-ringed snake (*Demansia modesta*). *Aust. Vet. J.* **50**:326-327. [*Pseudonaja modesta*]

Sutherland SK (1983) *Australian Animal Toxins. The creatures, their toxins and care of the poisoned patient.* Oxford University Press, Melbourne. Veterinary data are included: Case 6:8 *Notechis ater,* cat - from Munday (1959); Case 6:9 *Notechis ater*, dog (Anon.); Case 7:5 *Pseudonaja textilis*, dog (RD Crawford); Case 8:2 *Austrelaps superbus,* dog (HG Foote); Case 10:1 *Acanthopis antarcticus*, dog (Anon.); Case 12:6 *Tropidechis carinatus,* dog - from Trinca *et al.* (1971); Case 12:7 *Tropidechis carinatus*, fowl - from Trinca *et al.* (1971); Case 13:2 *Rhinoplocephala nigrescens*, dog (F Maarten); Case 15:3 *Hemiaspis damelii,* dog (PJ Lynch); section on snake bite in domestic animals pp. 214-221.

Sutherland SK, Tibballs J (2001) *Australian Animal Toxins. The creatures, their toxins and care of the poisoned patient.* 2nd edition, Oxford University Press, Melbourne. Veterinary data included are identical to those in the first edition.

Shea GM (1999) The distribution and identification of dangerously venomous Australian terrestrial snakes. *Aust. Vet. J.* **77**:791-798.

Trinca GF (1959) Snake bite as a veterinary problem. *Aust. Vet. Assoc. (Vic. Division) Proceedings* pp. 81-99.

Trinca JC, Graydon JJ, Covacevich J, Limpus C (1971) The rough-scaled snake (*Tropidechus carinatus*) a dangerously venomous Australian snake. *Med. J. Aust.* **2**:801-809. [includes case histories of dog and fowl envenomations]

Winter H, Pollitt CC (1978) On the pathology of small-eyed snake (*Cryptophis nigrescens*) poisoning. *Aust. Adv. Vet. Sci. (Proc. 55th Ann. Conf. Aust. Vet. Assoc., Sydney)* p.98.

BIRDS

Batrachotoxins in Pitohui *and* Ifrita *birds of New Guinea*

These birds contain batrachotoxins, the neurotoxic steroidal alkaloids first recognised in neotropical frogs (*q.v.*) and are the only known poisonous birds.

The batrachotoxins were recently discovered in the skin and feathers of birds from two genera in New Guinea – *Pitohui* (Dumbacher *et al.* 1992, 2000) and *Ifrita kowaldi* (blue-capped ifrita) (Dumbacher *et al.* 2000) known to cause sneezing and upper respiratory irritation when handled and to be bitter-tasting and burning to the mouth if eaten. There are 6 species of *Pitohui*, the most consistently poisonous of which are *Pitohui dichrous* (hooded pitohui) and *Pitohui kirhocephalus* (variable pitohui), but there is wide variation in toxin content (Dumbacher *et al.* 2000). No toxins have been detected in *Pitohui incertus* (white-bellied pitohui) or *Pitohui ferrugineus* (rusty pitohui), and small amounts in *Pitohui cristatus* (crested pitohui) and *Pitohui nigrescens* (black pitohui) (Dumbacher *et al.* 2000). Greatest concentrations of batrachotoxins are found in the contour feathers of belly, breast or legs, with lesser amounts in head, back tail and wing feathers (Dumbacher *et al.* 2000). Similarly to the poison-dart frogs, it is thought that these birds obtain these toxins from an unidentified exogenous (dietary) source (Dumbacher *et al.* 2000).

References:

Dumbacher JP, Beehler BM, Spande TF, Garraffo HM, Daly JW (1992) Homobatrachotoxin in the genus *Pitohui*: chemical defense in birds? *Science* **258**:799-801.

Dumbacher JP, Spande TF, Daly JW (2000) Batrachotoxin alkaloids from passerine birds: a second toxic bird genus (*Ifrita kowaldi*) from New Guinea. *Proc. Nat. Acad. Sci.* **97**:12970-12975.

Roder JD, Stair EL (1999) Homobatrachotoxin poisoning from pitohui. *Vet. Human Toxicol.* **41**:117. [short review]

MAMMALS

☑ *Vitamin A (hypervitaminosis A)*

Core data

Common sources: sheep liver
Animals affected: cat
Mode of action: inhibits osteoblasts and chondrocytes
Poisoning circumstances: cat fed exclusively on raw sheep liver for prolonged period
Main effects: deforming cervical spondylosis
Diagnosis: syndrome + feeding history
Therapy: remove source of excess intake
Prevention: feed balanced diet

Syndrome name: hypervitaminosis A
Chemical structure:

Vitamin A (retinol), a primary alcohol, is a fat-soluble vitamin unable to be synthesised by vertebrates and obtained from the diet. Green plants contain precursors including carotenes and these are converted to vitamin A in the intestinal mucosa and liver.

Sources:

- sheep liver (commonly > 1000 μg/g) >> cattle, pig, horse liver
- synthetic vitamin A ester concentrates for adding to compounded feeds
- carrots (*Daucus carota*) – rich in provitamin A (beta carotene), not retinol

Toxicity:

- **cats**
  - normal dietary requirement for kittens = 0.6 μg/g bodyweight/day
  - experimentally, young cats fed 15-35 μg/g bodyweight/day for 6-12 months; naturally-occurring cases usually take longer → onset in young adulthood
  - excess vitamin A stored in reticuloendothelial system (may → amyloidosis in long-standing cases)
- pigs
  - single oral doses > 200,000 μg vitamin A at 3-7 days old are toxic (Dobson 1969)
  - 330, 600 μg vitamin A/kg feed given to weaner pigs for 14 days or more is toxic; normal diets contain *ca.* 3600 μg vitamin A/kg feed (Pryor *et al.* 1969)
- ?cattle – "hyena disease" (Woodard *et al.* 1997)
- human Arctic/Antarctic travellers have been poisoned after ingesting livers of huskie (dog) (Southcott *et al.* 1971; 1376 ± 669 μg total vitamin A/g in dogs - Raila *et al.* 2000), seal (Southcott *et al.* 1971; arctic: bearded seal 1780 IU/g, ringed seal 2450 IU/g – Lewis & Lentfer 1967) or polar bear (15,000-30,000 IU/g - Lewis & Lentfer 1967).
- rabbit are uniquely capable, with rats and poultry, of converting 100% of dietary beta carotene into retinol. Diets containing 70,000 IU vitamin A/kg have produced reproductive failure and poor growth rates. (Frater 2001)

Mode of action:

- excess vitamin A → inhibits osteoblasts & chondrocytes → premature closure of epiphyseal plates → permanent shortening of long bones & joint deformities
- coat-cleaning activity in cats may account for cervical site of lesions by → repeated stimulus/trauma to vertebral periosteum

Conditions of poisoning:

Cats

- **cats fed mainly or exclusively on raw sheep liver for long periods**

Pigs

- pigs fed diets containing excess vitamin A concentrate (feed formulation error)
- deliberate overdose with oral vitamin A preparation (attempt to boost production) (Dobson 1969)
- pigs fed fish silage (Coates *et al.* 1998)

Rabbit

- 4.5 year-old rabbit fed a life-time diet comprised almost totally of carrots (3 kg/week), subsequently calculated to provide about 120,000 IU vitamin A/kg diet (10 times the suggested requirement for rabbits) (Frater 2001)

Clinical signs:

Cats

- irritable, apprehensive, depressed, resent handling about the head & neck
- forelimb hyperaesthesia
- ± lameness
- ± loss of incisor & molar teeth + gingivitis

Pigs

- lameness; abnormal stance with feet together and back arched (suggestive of painful feet)
- preference for sitting rather than standing
- decreased growth rate
- shortening of long bones

Rabbit

- lameness; painful, swollen joints (Frater 2001)
- reproductive failure, stillbirths, hydrocephalus and high post-natal mortality
- poor growth rates in young rabbits

Pathology:

Cats

- **deforming cervical spondylosis** (fusion of vertebrae + exostoses) beginning with vertebrae C3 + 4 and extending distally, lateroventrally, proximally
- severe & very chronic cases → all cervical vertebrae involved + deformity & exostoses of sternum, elbow, iliosacral joint, hind limb bones
- fatty liver & kidneys
- single & multinucleated macrophages with foamy cytoplasm in hepatic sinusoids

Pigs

- abnormally-short long bones
- premature closure of epiphyses of long bones
- flaring of ends of long bones
- disappearance of epiphyseal cartilages

Rabbit

- hyperostotic polyarthropathy (radiographic changes) (Frater 2001)

Diagnosis:

- cats: dietary history, clinical signs, lesions

Therapy:

- no specific therapy
- removal of excessive intake → normal demeanour in days + lesion regression, but not full return to normal bone structure where lesions are extensive
- note that an established food preference for liver in cats may frustrate attempts to change the patient's diet

References:

Se345

Clark L (1971) Hypervitaminosis A: a review. *Aust. Vet. J.* **47**:568-571.

Coates JW, Holbek NE, Beames RM, Puls R, O'Brien WP (1998) Gastric ulceration and suspected vitamin A toxicosis in grower pigs fed fish silage. *Can. Vet. J.* **39**:167-170.

Dobson KJ (1969) Osteodystrophy associated with hypervitaminosis A in growing pigs. *Aust. Vet. J.* **45**:570-573.

English PB, Seawright AA (1964) Deforming cervical spondylosis of the cat. *Aust. Vet. J.* **40**:376-381.

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.

Lewis RW, Lentfer JW (1967) The vitamin A content of polar bear liver: range and variability. *Comp. Biochem. Physiol.* **22**:923-926.

Pryor WJ, Seawright A, McCosker PJ (1969) Hypervitaminosis A in the pig. *Aust. Vet. J.* **45**:563-569.

Raila J, Bucholz I, Aupperle H, Raila G, Schoon H-A, Schweigert FJ (2000) The distribution of vitamin A and retinol-binding protein in the blood plasma, urine, liver and kidneys of carnivores. *Vet. Res.* **31**:541-551.

Seawright AA, English PB (1964) *J. Path. Bact.* **88**:503.

Seawright AA, English PB, Gartner RJW (1965) *Nature* **206**:1171.

Seawright AA, English PB, Gartner RJW (1967) *J. Comp. Path.* **77**:29.

Seawright AA, Steele DP, Clark L (1968) Hypervitaminosis A of cats in Brisbane. *Aust. Vet. J.* **44**:203-206.

Seawright AA, Hrdlicka J (1974) Pathogenetic factors in tooth loss in young cats on a high daily oral intake of vitamin A. *Aust. Vet. J.* **50**:133-141.

Seawright AA, Hrdlicka J (1974) Severe retardation of growth with retention and displacement of incisors in young cats fed a diet of raw sheep liver high in vitamin A. *Aust. Vet. J.* **50**:306-315.
Southcott RV, Chesterfield NJ, Lugg DJ (1971) Vitamin A content of the livers of huskies and some seals from antarctic and subantarctic regions. *Med. J. Aust.* **1**:311-313.
Watson ADJ (1998) An old, lame cat with reduced food intake and stiff neck. (Diagnosis & Therapy Article) *Aust. Vet. J.* **76**:792, 800-801.
Woodard JC, Donovan AG, Eckhoff C (1997) Vitamin (A and D)-induced premature physeal closure (hyena disease) in calves. *J. Comp. Path.* **116**:353-366.

Platypus venom

Syndrome names: Platypus "sting"

Chemical structure:

The components of the venom responsible for clinical signs are not entirely clear. The venom contained hyaluronidase and proteolytic activities (de Plater *et al.* 1995). A 39-residue C-type natriuretic peptide, ovCNP-39, appears to be at least partly responsible for oedema and pain at envenomation sites (de Plater *et al.* 1998).

Sources:

The platypus (*Ornithorhynchus anatinus* Shaw 1799) occurs in many unpolluted fresh water streams of the eastern coast of Australia from Cooktown to Tasmania and the far south-east of South Australia. Platypus **males** have a single kidney-shaped venom or crural gland under the muscles of the dorsal aspect of each hind limb, connected through a venom duct to a movable hollow curved conical **spur** measuring about 15 mm long on the medial aspect of the leg at the tarsal region. The venom glands vary in size, being largest (about 40 x 20 x 15 mm) during the breeding season in July-August in northern Australia and October in the south. Envenomation is effected by erection of the spurs at 90^{o} to the legs, and squeezing the victim between the legs, driving in the spurs.

Toxicity:

Most envenomations are reported in **humans** handling a male platypus caught on a fishing line or in a net. Hunting **dogs** are reported to have been envenomated (Burrell 1927). Other platypuses have been fatally envenomated (Fleay 1980).

Fatal IV venom dose in mice is 75-90 mg/kg; an adult male is considered capable of injecting between 0.2 and 4.0 ml of venom (Temple-Smith 1973).

Organ systems affected: Nervous, Vascular

Mode of action:

ovCNP-39 causes rapid mast cell degranulation releasing histamine and promoting oedema (de Plater *et al.* 1998)

Conditions of poisoning: Handling of, or attack on, a male platypus

Clinical signs:

Dogs (Burrell 1927):

Gross swelling at the site of envenomation
Prostration
Death in some cases

Humans (Sutherland 1983; Fenner *et al.* 1992)

Intense persistent pain, hyperaesthesia and swelling at the site of envenomation. Generalised hyperaesthesia and pain may occur after some time. The swelling may persist for weeks to months and relapses occur after exercise of the affected limb. Loss of muscle mass may occur in the envenomated limb.
No fatalities have been recorded.

Pathology: None reported.

Diagnosis: access + syndrome

Therapy (Sutherland 1983, Fenner & Williamson 1996):

No antivenom is available. No restriction should be placed on the movement of venom, as this may increase local pain. Hospitalisation is essential for adequate pain management. Strong analgesics, opiates or a regional nerve block may be required to relieve pain. Short-term systemic steroids are useful. NSAIDs provide little benefit.

The spur wounds should be assumed to be contaminated and prophylactic antibiotics used. Tetanus prophylaxis should be established.

References:

Review literature

Calaby JH (1968) The platypus (*Ornithorhynchus anatinus*) and its venomous characteristics. In Bücherl W, Buckley EE, Deulofeu V (eds.) *Venomous Animals and their Venoms.* Vol. 1. Academic Press, New York.

Sutherland SK (1983) *Australian Animal Toxins. The creatures, their toxins and care of the poisoned patient.* Oxford University Press, Melbourne. pp.338-343.
Fenner PJ, Williamson JA (1996) Platypus envenomation. Chapter 25 in Williamson JA, Fenner PJ, Burnett JW, Rifkin JF (eds.) *Venomous and Poisonous Marine Animals: A Medical and Biological Handbook.* University of New South Wales Press, Sydney. pp. 436-440.

General literature

Burrell H (1927) *The Platypus.* Angus & Robertson, Sydney. [cited by Sutherland 1983]
de Plater GM, Martin RL, Milburn PJ (1995) A pharmacological and biochemical investigation of the venom from the platypus (*Ornithorhynchus anatinus*). *Toxicon* **33**:157-169.
de Plater GM, Martin RL, Milburn PJ (1998a) The natriuretic peptide (ovCNP-39) from platypus (*Ornithorhynchus anatinus*) venom relaxes the isolated rat uterus and promotes oedema and mast cell histamine release. *Toxicon* **36**:847-857.
de Plater GM, Martin RL, Milburn PJ (1998b) A C-type natriuretic peptide from the venom of the platypus (*Ornithorhynchus anatinus*): structure and pharmacology. *Comp. Biochem. Physiol. C Pharmacol. Toxicol. Endocrinol.* **120**:99-110.
Fenner PJ, Williamson JA, Meyers D (1992) Platypus envenomation: a painful learning experience. *Med. J. Aust.* **157**:829-832.
Fleay DH (1980) *Paradoxical platypus.* Jacaranda Press, Brisbane. [cited by Sutherland 1983]
Kellaway CH, Le Messurier DH (1935) The venom of the platypus (*Ornithorhynchus anatinus*). *Aust J. Exp. Biol. Med. Sci.* **13**:205-221.
Kourie JI (1999a) Calcium dependence of C-type natriuretic peptide-formed fast K(+) channel. *Am. J. Physiol.* **277**:C43-50.
Kourie JI (1999b) Characterisation of a C-type natriuretic peptide (CNP-39)-formed cation-selective channel from platypus (*Ornithorhynchus anatinus*) venom. *J. Physiol. (London)* **518**:359-369.
Martin CJ, Tidswell F (1894) Observations on the femoral gland of *Ornithorhynchus* and its secretions; together with an experimental enquiry concerning its supposed toxic action. *Proc. Linn. Soc. NSW* **9** (2):471-500.
Temple-Smith PD (1973) Seasonal breeding biology of the platypus, *Ornithorhynchus anatinus* (Shaw 1799), with special reference to the male. Ph.D. Thesis, Department of Zoology, Australian National University, Canberra. [cited by Sutherland 1983]
Torres AM, Wang X, Fletcher JI, Alewood D, Alewood PF, Smith R, Simpson RJ, Nicholson GM, Sutherland SK, Gallagher CH, King GF, Kuchel PW (1999) Solution structure of a defensin-like peptide from platypus venom. *Biochem J.* **341**:785-794.