



Declaration

- Views are mine
- SVDK kits supplied by Seqirus

OVERVIEW

- General Introduction including history of snake bite and management.
- SVDK
- Looking at Redback bite and management
- Open forum/discussion
- Questions

And...... I have a spider named after me...

Orsolobidae Hickmanolobus nimorakiotakisi new species



WHAT IS TOXINOLOGY?

Toxinology:

the study of poisons, with particular emphasis on relatively unstable proteinaceous substances

What do we study?

- Snakes
- Spiders (redback spider, funnel-web spider, other spiders)
- Arthropods (ticks, bees, wasps, ants, scorpions)
- Venomous marine creatures (jellyfish, stinging fish, blue ringed octopus, cone snails)
- Marine fauna (sponges, coral)
- Ingestions of toxins (ciguatera)
- Other venomous creatures

Definition Venomous

Ven•om•ous ('vɛn ə məs)

adj.

- 1. (of an animal) having a gland or glands for secreting venom; able to inflict a poisonous bite or sting.
- 2. full of or containing venom; poisonous.
- 3. spiteful; malignant.

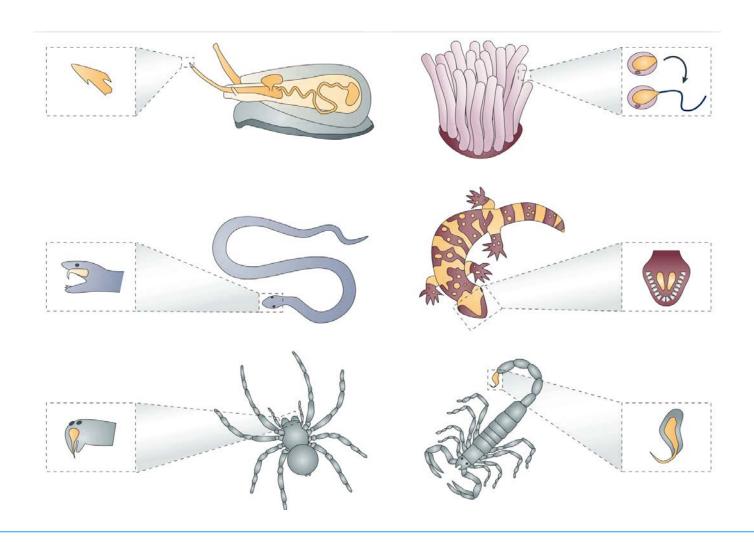
[1250-1300; Middle English < Anglo-French, Old French]

ven'om•ous•ly, adv.

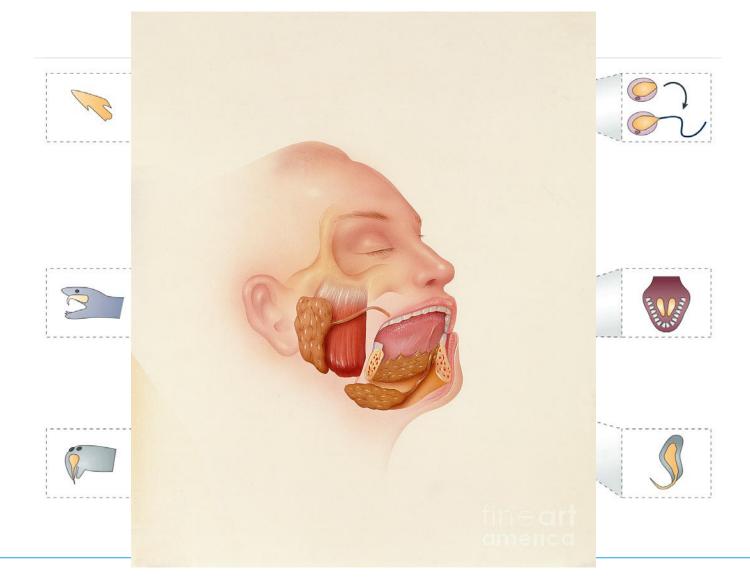
ven'om•ous•ness, n.

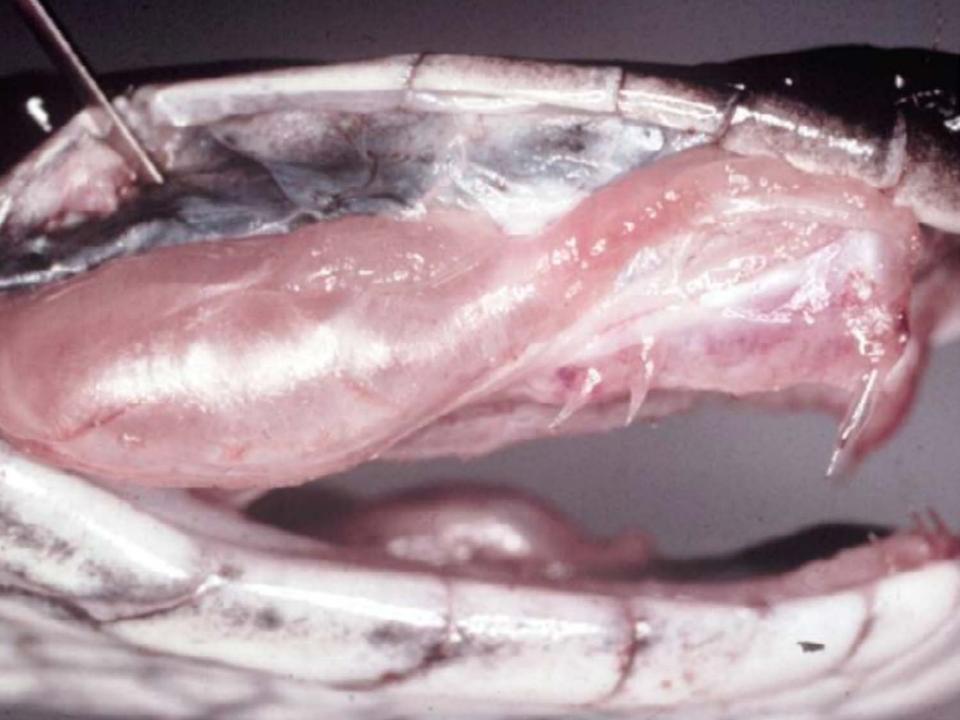
"CITE" C Random House Kernerman Webster's College Dictionary, © 2010 K Dictionaries Ltd. Copyright 2005, 1997, 1991 by Random House, Inc. All rights reserved.

How animals deliver the venom



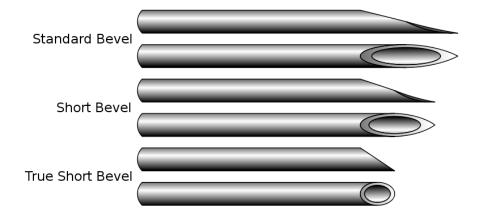
How animals deliver the venom





Fang of a Tiger snake





EXOTIC SNAKE



Brief Overview of the History



Medical symbol: Staff or rod of Asklepios with a snake curled around





Asklepios "Ασκληπιός" Ancient Greek god of medicine and healing



In honour of Asclepius, snakes were often used in healing rituals

Early Snake Bite Treatments

- Setting fire to gunpowder heaped on the area
- Amputation of the bitten area with an axe
- Ingestion of mercury or Stychnine (two types of toxins were unlikely to co-exist)
- Ingestion of alcohol to overcome fear



The Illusion of Complete Knowledge...

"The story is complete and there is **no longer** any room for the astonishing differences of opinion that have characterised some of the communications on the subject in the pages of this journal."

Editorial, Med J Aust, June 15, 1929

Dr Jack Barnes: Wisdom of the Elders

"...and we're back to the stage where Flecker started. We know something and we know almost nothing. We've solved two or three problems and it appears [we have] at least another four to go."

Dr Jack Barnes in: Kinsey, B. More Barnes on Box Jellyfish, James Cook University Press, 1988

AUS Snakebite









Hospitalisation Data

	2002–03	2003–04	2004–05	Total 2002-05
X20 Contact with venomous snakes & lizards	628	613	510	1,751
X21 Contact with spiders	1,321	1,320	1,246	3,887
X22 Contact with scorpions	*	11	*	24
X23 Contact with hornets, wasps & bees	1,195	1,162	1,200	3,557
X24 Contact with centipedes & venomous millipedes	8	15	8	31
X25 Contact with other specified arthropods	329	351	447	1,127
X26 Contact with venomous marine animals & plants	337	346	358	1,041
X27 Contact with other specified venomous animals	*	6	*	14
X28 Other specified venomous plants	8	8	7	23
X29 Contact with unspecified venomous animal or plant	57	50	40	147
Total X20–X29	3,896	3,882	3,824	11,602

Summary of Hospitalisation Data

Spiders and bees cause most venomous bite and sting hospitalisations

Over 11,000 people in Australia were hospitalised because of a venomous bite or sting between 2002 and 2005, according to a report released today by the Australian Institute of Health and Welfare (AIHW).

Spider bites accounted for a third of those hospitalisations, and the vast majority of spider bite cases were attributed to red-backs (59%).

A much smaller proportion of cases were attributed to white-tailed spiders (7%) and funnel web spiders (3%).

Clare Bradley of the AIHW's National Injury Surveillance Unit, said that 3 in 10 bite and sting hospitalisations were because of wasp and bee stings.

'Bee stings alone accounted for almost 25% of all bite and sting hospitalisations,' she said.

Bites from snakes accounted for just 15% of bite and sting hospitalisations.

'Just over half of those snake bite cases were attributed to brown snakes (54%). Black snake (15%) and tiger snake (11%) bites were also common,' Ms Bradley said.

Other venomous bites and stings requiring hospitalisation in 2002-05 were attributed to venomous arthropods, such as ants, centipedes, and millipedes (10% of cases) and venomous marine animals, such as jellyfish and stingrays (9%).

The report, *Venomous bites and stings in Australia to 2005*, also revealed strong correlations between the rate of venomous bites and stings and place of residence.

Not surprisingly, residents of major cities had the lowest rate while residents of the very remote regions of Australia had the highest.

OVERVIEW: SNAKE BITE in AUSTRALIA

MORBIDITY

- 500-600 bites/annum
- occasional long-term neurological deficit
- Mean length of stay 1.2 days

MORTALITY

- 2-3 per annum (58 period 1979-2000)
- Brown Snakes 54%, Black Snake 15%, Tiger Snakes 11%
- Early cardiorespiratory collapse 29%
- Most deaths occurred in rural areas
- First Aid not applied in majority of cases

No.	Snake	Origin
	Inland Taipan (Oxyuranus microlepidotus)	OZ
)	Common Brown Snake (Pseudonaja textilis)	OZ
3	Taipan (Oxyuranus scutellatus)	OZ
1	Tiger Snake (Notechis scutatus)	OZ
5	Reevesby Island Tiger Snake (Notechis ater niger)	OZ
3	Beaked Sea Snake (Enhydrina schistosa)	OZ
7	W.A. Tiger Snake (Notechis ater occidentalis)	OZ
3	Chappell Island Tiger Snake (Notechis ater serventyi)	OZ
)	Death Adder (Acanthophis antaraticus)	OZ
0	Western Brown (Pseudonaja nuchalis)	OZ
1	Copperhead (Austrelaps superbus)	OZ
2	Indian Cobra (<i>Naja naja</i>)	Asia
3	Dugite (Pseudonaja affinis)	OZ
1	Papuan Black Snake (Pseudechis papuanus)	OZ
5	Stephens Banded Snake (Hoplocephalus stephensii)	OZ
6	Rough Scaled Snake (Tropedechis carlnatus)	OZ
7	King Cobra (Ophiaphagus hannah)	Asia
8	Blue Bellied Black Snake (Pseudechis guttatus)	OZ
9	Collett's Snake (Pseudechis colletti)	OZ
0	Mulga Snake (Pseudechis australis)	OZ
1	Red Bellied Black Snake (Pseudechis porphyriacus)	OZ
2	Small-eyed Snake (Cryptophis nigrescens)	OZ
23	Eastern Diamond Back Rattlesnake (Crotalus adamanteus)	USA

'But I'm lucky to be here'

By MARIA BILLIAS

A Darwin man told yesterday how his left arm was amputated after being bitten nine times by a deadly snake.

Gordon Lyons said he almost died after his heart stopped three times on the operating table at Royal Darwin Hospital.

He spent seven weeks in a coma and was kept alive with a dialysis machine and ventilator after a king brown bit his left arm two months ago.

Mr Lyons, who has still not regained movement in his legs, said doctors revived him three times on the operating table.

He said: "I'm lucky to be here right now."

Continued Page 2



Gordon Lyons ... lucky to be alive after being bitten by a potentially deadly king brown snake

@ From Page 1

"But I still can't believe my arm's been chopped off just for one snake. I still have my life and I guess that's the most important thing."

Mr Lyons said he was bitten by the snake, considered to be one of the most venomous, after he picked it up from the side of the road near Litchfield.

Mr Lyons, who admitted he was drunk at the time, said he and a mate had been driving from Mandorah to Darwin when they saw it.

He said: "I remembered the guys at the Mandorah Pub wanted something to put in their huge fish tank.

"But I made the stupid mistake of grabbing it with my left hand because I was holding a beer in my right one. I had its head in my hand but it got loose and grabbed the web of my left hand ... its fangs were that big it ripped my hand open.

"I tore it off me and put it in a plastic bag and threw it in the back of the car.

Stupid

"For some stupid reason, I stuck my hand back in the bag, and it must have smelled blood, and it bit me another eight times."

Mr Lyons said he began vomiting and suffering diarrhoea "about three seconds later".

He said: "My mate was trying to keep me awake by whacking me in the head and pouring beer on me."

Mr Lyons said his last memory was passing out, covered in blood, at the Noonamah Hotel moments before being taken by ambulance to the Royal Darwin Hospital.

RDH specialist physician Bart Currie said the venom had caused severe damage to Mr Lyons' muscles, which led to his left arm turning black and becoming "dead".

Mr Currie said: "Of all the snake bites in Australia I'm aware of, this man is the sickest to have ever survived.



Mulga (King Brown Snake)



Missing person

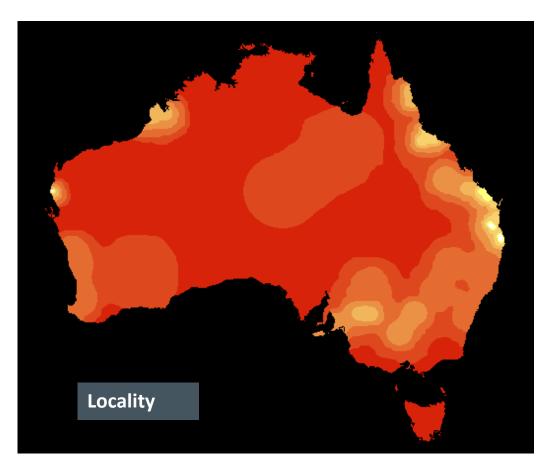
 A piece of cardboard with the words "I have been bitten by a snake" was found in the South Australian outback, near where his body and ute were located

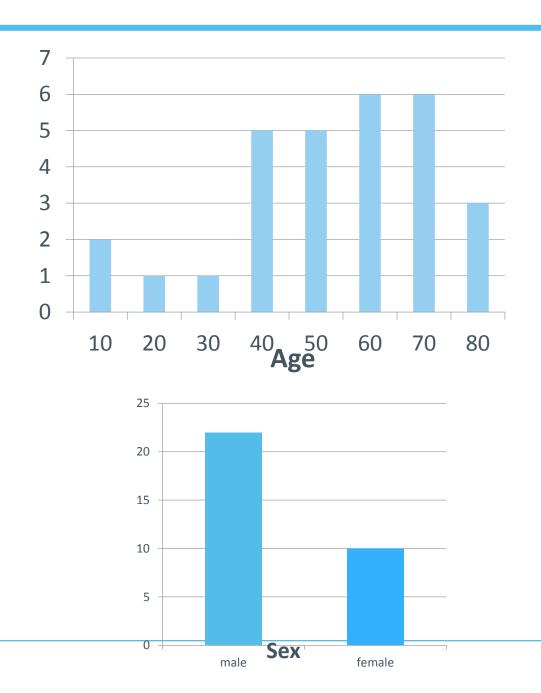


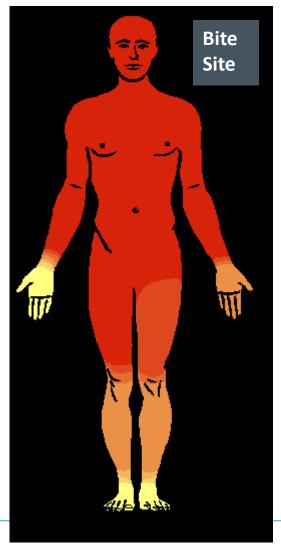


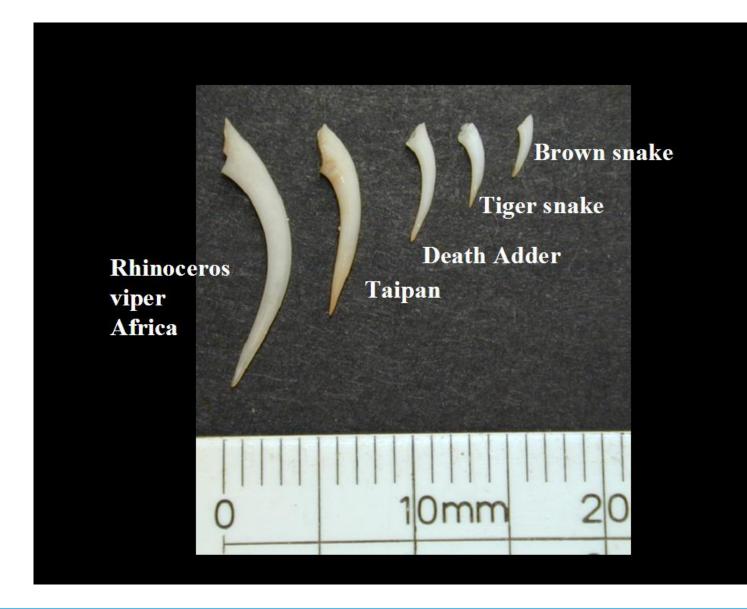


Australian snakebite-related fatalities from 1 January 1979 - 31 December 2012: Total 32 (approx 1 per/year)









ANNUAL WORLD SNAKE BITE MORTALITY

(Chippaux, Bulletin WHO 1998; 76; 515-24)

IOIAL (Underestimated)	125,500
• Asia	100,000
Africa	20,000
 Central & South America 	5000
Oceania	200
 Middle East 	100
• Europe	30
USA & Canada	15
AUSTRALIA	1-5

WHAT IS NOT DOCUMENTED!!!!

WHAT IS THE MORBIDITY?

VIETNAM



























BITE SITE



Can look like anything!





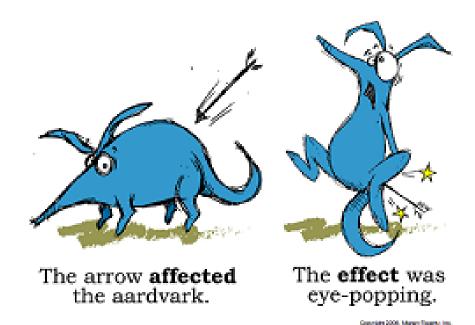








What are the effects of snake venom?



What do snakes eat?





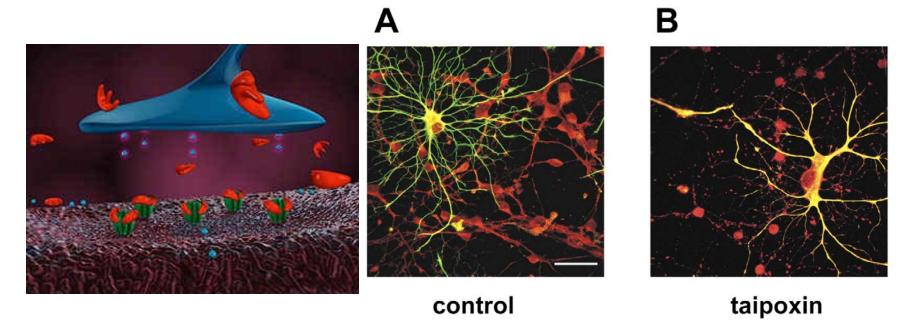
Stop that rat:



Neurotoxicity

POST SYNAPTIC

PRE SYNAPTIC



Snake presynaptic neurotoxins with phospholipase A2 activity induce punctate swellings of neurites and exocytosis of synaptic vesicles

Neurotoxicity

- Snakes such as
 - Tiger
 - Taipan
 - Death Adder

Easy to digest:

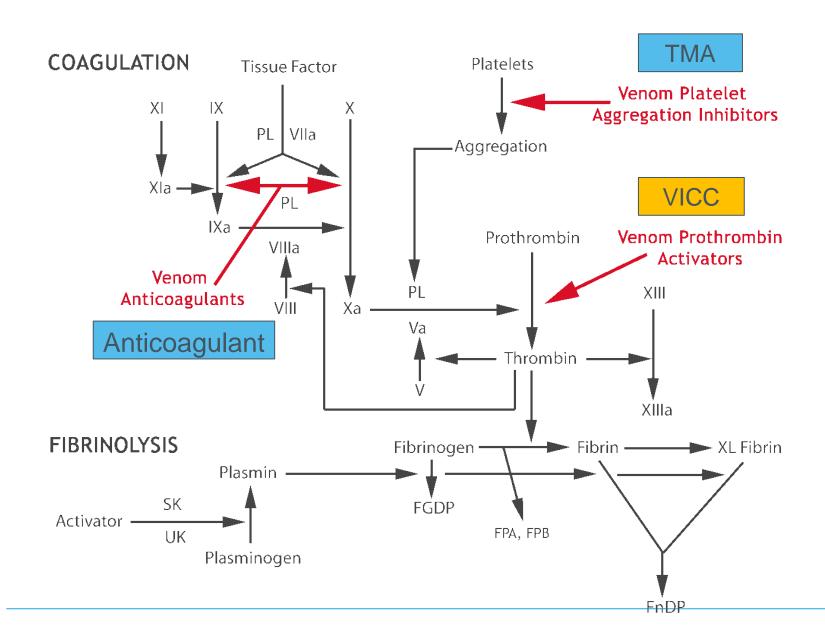


Snakes that effect the Coagulation Pathway

- Brown
- Tiger
- Taipan
- Rough Scaled Snakes

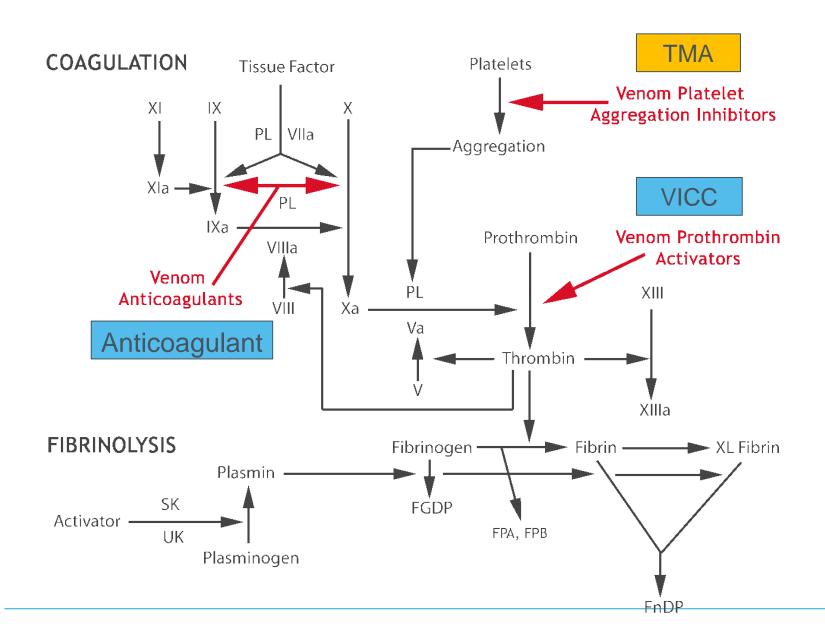
PROCOAGULANT EFFECT (VICC)

- Venom induced Consumptive Coagulopathy (VICC).....like DIC
- MOST COMMONLY SEEN



THROMBOTIC MICROANGIOPATHY (TMA): characterized by thrombocytopenia, microangiopathic haemolytic anaemia (MAHA) and acute renal failure (ARF).

- Usually seen >48hrs post bite
- Can take over a week to resolve
- Characterised by:
 - severe thrombocytopenia (<20 x 10(9)/L)
 - Anaemia with fragmented RBC on blood film
 - Acute "anuric" renal failure



Tenderise the meat:



MYOTOXICITY

- Tiger Snake,
- Rough Scaled,
- Mulga Snakes
- Red-bellied
- black snake bite
- Can be seen >24hrs post bite

SYMPTOMS & SIGNS of SNAKE ENVENOMATION

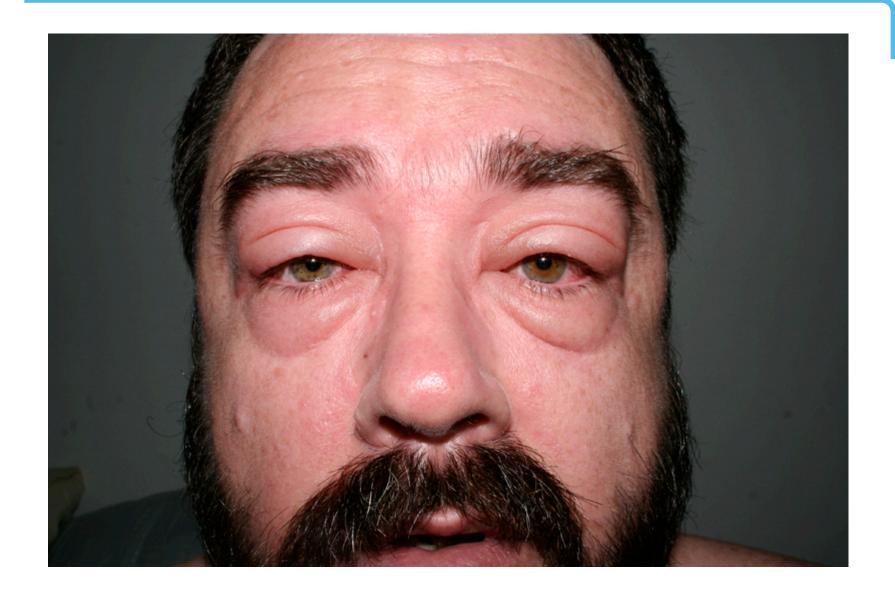
- EARLY (within 30 minutes)
 - allergy
 - headache, nausea/vomiting, abdominal pain
 - coagulopathy
- LATE (within several hours)
 - cranial nerve palsies (ptosis, ext' ophthalmoplegia, dysarthria, dysphonia, dysphagia)
 - limb & truncal weakness
 - respiratory failure
 - haemorrhage
- VERY LATE (delayed presentation, wrong/inadequate treatment)
 - prolonged paralysis
 - renal failure
 - uncontrollable haemorrhage

In general symptoms and signs are SPECIES SPECIFIC:

Clinical Syndromes

Snake	Coags	Neurotoxicity	Myotoxicity	NSS	TMA	CVS effects	AV
Brown Snake	VICC	Rare/mild	-	<50%	10%	Collapse (33%)	Brown
						Cardiac arrest	
						(5%)	
Tiger snake	VICC	Uncommon	Uncommon	Common	5%	Rare	Tiger
Rough-scale	VICC	Uncommon	Uncommon	Common	<5%	Rare	Tiger
Hoplocephalus	VICC	-	-	< 50%	-	-	Tiger/
							Brown
Mulga snake	AC	-	Common	Common	-	-	Black
RBBS	AC	-		Common	-	-	Tiger
Death Adder	-	Common	-	Common	-	-	DAAV
Taipan	VICC	Common	Rare	Common	5%	Uncommon	Taipan













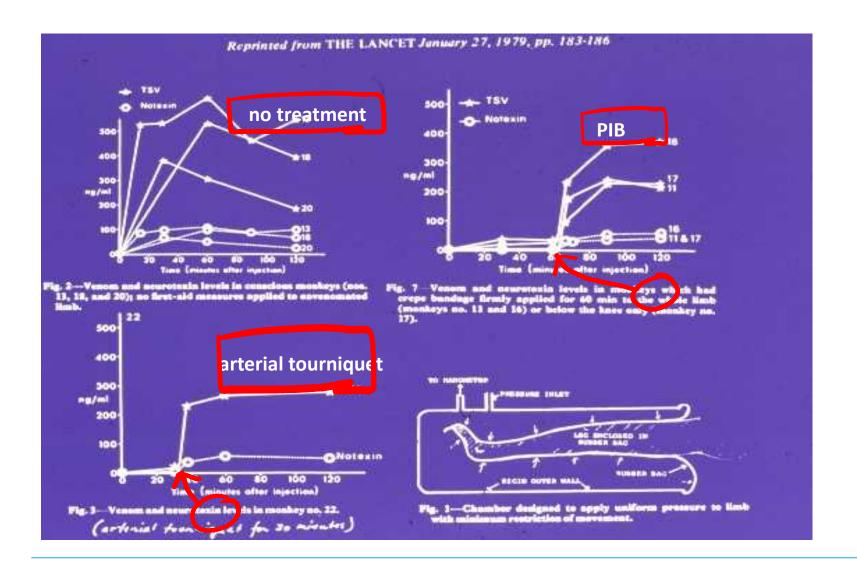




TWO PARTS

- Immobilisation
- Compression bandage

Development of Pressure-immobilisation first-aid technique



How do you put it on?



PIB









Tourniquet

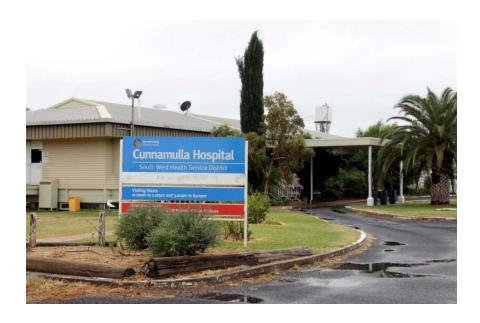


Tourniquet





HOSPITAL MANAGEMENT



History is vital!



- Very important!
- Ask about the circumstance surrounding the bite
- What "specific" symptoms does the patient have to make you suspect snake bite

Lab tests

- Point of care INR is unreliable
- Formal Bloods-
 - FBE
 - EUC
 - INR
 - APTT
 - Fibrinogin
 - CK



Patients bloods come back:

DATE	25/03
INR	>9
APTT	>200
FIB	<0.6
D-Dimer	High
СК	215

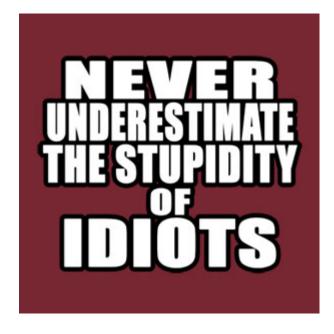
SOMEONE BRINGS IN THE SNAKE



SNAKE IDENTIFICATION

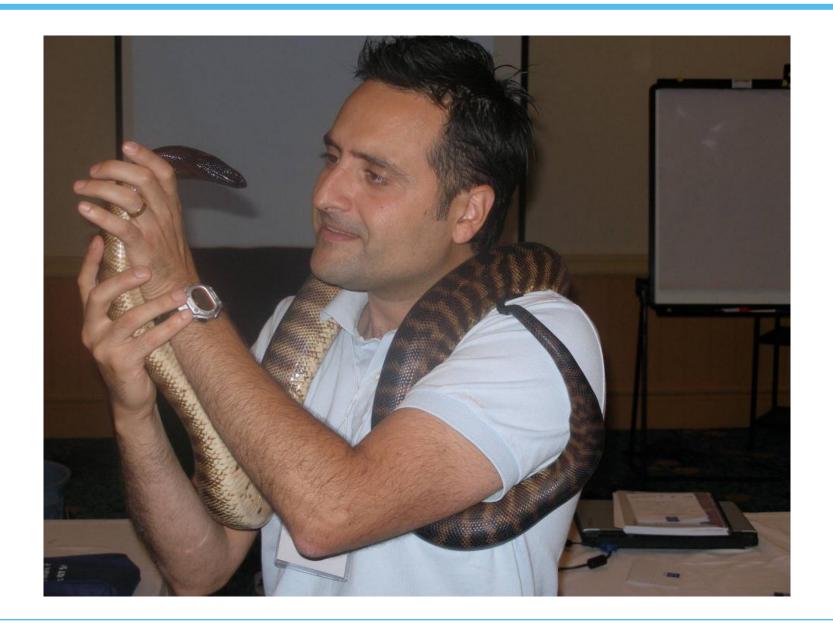


DO NOT DO THIS!









Key to the Identification of Australian Snakes

It is Difficult to Identify Australian Snakes!

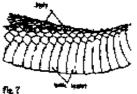
I. In the tail fluidened from side to side, forming a goddle (Fig. 11) Yes . . . go to 3 Dio . . . go to 3



Fly J.

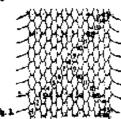
- The apprimen is a sea stocke belonging to one of two elevatly whited Facality, which together include approximately thirty-cut Assurblen species.
- Am the beily scales obvious trang of basis neveral stops, wider then there on the back and sides (Fig. 2)?

មីព...ព្រះសង់ ២...ព្រះសំ



 Are there more than thirty mass of scales searchding the based belly scales around the middle of the body counted diagonally (Fig. 3)?

Yes...gow6 No...gow7



 Are the scales smooth and abiny, while the eyes are just black spots visible under the surface of the scales on the head (Fig. 4)?

Yes...go 10 8 No...po to 9



Fig. 1.

Do not attempt snake identification unless you are an expert

Never guess!







SVDK?







Facts about SVDK

DOES NOT

- tell the clinician snake has bitten the patient
- If you need to give antivenom
- How much antivenom to give
- If negative the patient is Not envenomed

DOES

• Aid the clinician as to which is the most appropriate monovalent to give

Controversies

The Australian Snakebite Project, 2005–2015 (ASP-20)

Christopher I Johnston, Nicole M Ryan, Colin B Page, Nicholas A Buckley, Simon GA Brown, Margaret A O'Leary and Geoffrey K Isbister Med J Aust 2017; 207 (3): 119-125. Il doi: 10.5694/mja17.00094

Results: 1548 patients with suspected snakebites were enrolled, including 835 envenomed patients (median, 87 per year), for 718 of which the snake type was definitively established, most frequently brown snakes (41%), tiger snakes (17%) and red-bellied black snakes (16%). Clinical effects included venom-induced consumption coagulopathy (73%), myotoxicity (17%), and acute kidney injury (12%); severe complications included cardiac arrest (25 cases; 2.9%) and major haemorrhage (13 cases; 1.6%). There were 23 deaths (median, two per year), attributed to brown (17), tiger (four) and unknown (two) snakes; ten followed out-of-hospital cardiac arrests and six followed intracranial haemorrhages. Of 597 SVDK test results for envenomed patients with confirmed snake type, 29 (4.9%) were incorrect; 133 of 364 SVDK test results for non-envenomed patients (36%) were false positives. 755 patients received antivenom, including 49 non-envenomed patients; 178 (24%), including ten non-envenomed patients, had systemic hypersensitivity reactions, of which 45 (6%) were severe (hypotension, hypoxaemia). Median total antivenom dose declined from four vials to one, but median time to first antivenom was unchanged (4.3 hours; IQR, 2.7-6.3 hours).

Conclusions: Snake envenoming is uncommon in Australia, but is often severe. SVDKs were unreliable for determining snake type. The median antivenom dose has declined without harming patients. Improved early diagnostic strategies are needed to reduce the frequently long delays before antivenom administration.



Contents lists available at ScienceDirect

Toxicon





Prospective assessment of the false positive rate of the Australian snake venom detection kit in healthy human samples



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ABSTRACT

The Snake Venom Detection Kit (SVDK; bioCSL Pty Ltd, Australia) distinguishes venom from the five most medically significant snake immunotypes found in Australia. This study assesses the rate of false positives that, by definition, refers to a positive assay finding in a sample from someone who has not been bitten by a venomous snake. Control unbroken skin swabs, simulated bite swabs and urine specimens were collected from 61 healthy adult volunteers [33 males and 28 females] for assessment. In all controls, simulated bite site and urine samples [a total of 183 tests], the positive control well reacted strongly within one minute and no test wells reacted during the ten minute incubation period. However, in two urine tests, the negative control well gave a positive reaction (indicating an uninterpretable test). A 95% confidence interval for the false positive rate, on a per-patient rate, derived from the findings of this study, would extend from 0% to 6% and, on a per-test basis, it would be 0-2%. It appears to be a very low incidence (0-6%) of intrinsic true false positives for the SVDK. The clinical impresssion of a high SVDK false positive rate may be mostly related to operator error.

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Patients bloods come back:

DATE	25/03
INR	>9
APTT	>200
FIB	<0.6
D-Dimer	High
СК	215

You decide to give ANITIVENOM



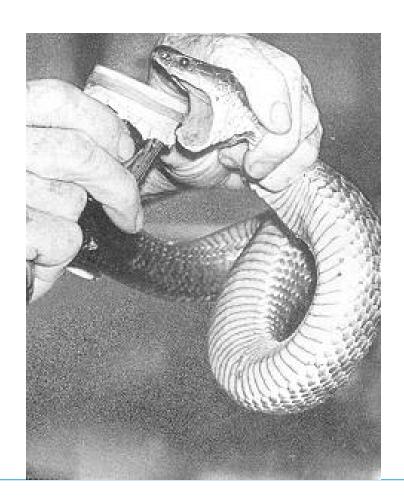
Seqirus Range of Antivenoms

- Equine Antivenoms (Horse-derived), Large Scale Process: 250 litres plasma
 - Brown Snake
 - Black Snake
 - Tiger Snake
 - Taipan
 - Death Adder
 - Polyvalent Snake (includes all of the above)
 - Sea Snake
 - Redback Spider
 - Stonefish

- Box Jellyfish Antivenom (Sheep-derived): 5 litres starting plasma
 - Small Scale Process static dialysis (7 days), centrifugation
- Funnel Web Spider Antivenom (Rabbit-derived): 1 litre starting plasma
 - Small Scale Process Chromatography, machine dialysis
 - Funnel Web Spider AV is the only freeze dried AV- all others liquid

ANTIVENOMS HISTORY

FIRST
Tiger Snake AV in 1930



PRODUCTION



Collecting and Defibrinating Horse Blood in the 1930s



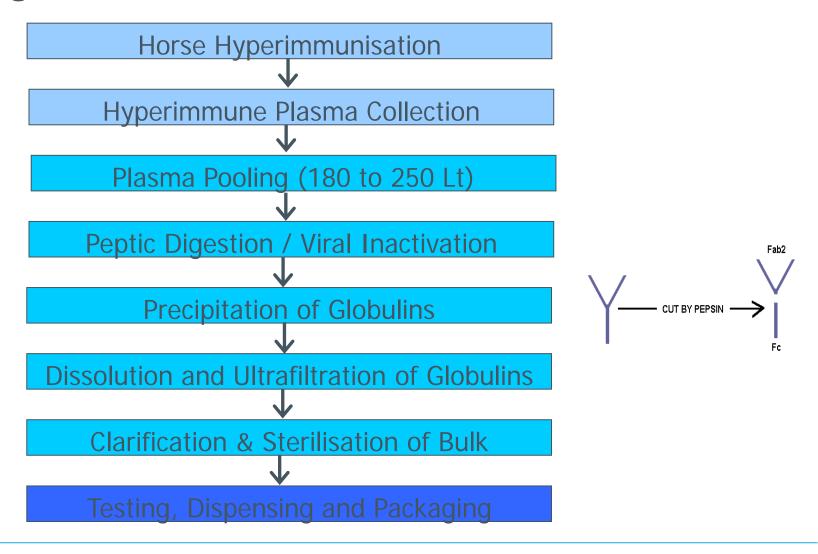
Woodend field station







Large Scale Antivenom Production Overview



Typical Fill Volumes for Seqirus Antivenoms

- Polyvalent Snake, Black Snake, Taipan, Death Adder, Sea Snake AVs:
 25 to 50 mL
- Tiger Snake AV: 6 to 20 mL
- Brown Snake AV: 2.5 to 8 mL
- Box Jellyfish AV: 1.5 to 6 mL
- Stonefish AV: 1 to 3 mL
- Redback Spider AV: 1 to 1.5 mL
- Funnel Web Spider AV:

Freeze dried powder plug, reconstitute with 10 mL sterile water



Are they all "polyvalent"?

- Technically "YES"
- BUT!

So IF YES why can't I give them to everyone no matter what they have been bitten by?

- NO
- The product only guarantees neutralisation for an average bite from for that immunotype
- Unsure about neutralisation for others

• NOTE: TIGER SNAKE ANTIVENOM is also active against the venom of the copperhead snakes (Austrelaps spp), the black snakes (Pseudechis spp), Collett's snake (Pseudechis colletti) and the rough scaled snake (Tropidechis carinatus).

How much do we give?

- Controversial
- History is important as 1 vial might be sufficient for and average bite.....but what is an average bite????





What people are saying......

Copy from other toxinologists talk

You can sleep now...

Snake envenoming

usually managed in an ED observation unit

Distribution:

Tigers south; Browns north, east and west

VDK:

Adds little to clinical care - expensive

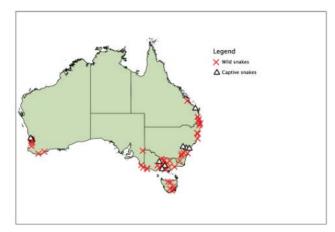
Antivenom:

Early

1 vial and no re-dosing

Suspected snake-bite

Most of the work!

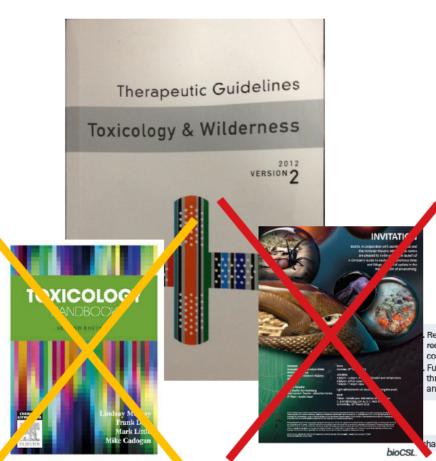




Brown Snake 1 vial
Tiger Snake/Rough Scale 1 vial
Black Snakes:Mulga Snake 1 vial
Red-bellied Black Snake 1 vial tiger/black
Taipan 1 vial
Death Adder 1 vial

Resources

Therapeutic Guidelines Toxicology and Wilderness



If presenting to a health care facility that does not have critical care and on-site pathology facilities with antivenom, maintain basic life support, apply PBI and arrange urgent transfer.

History of snake bite

Poison Centre

131126

ASP

1800 676 844

Toxicology Service

- Give antivenom; monovalent antivenom based on geography, clinical effects and VDK
- 2. Be prepared for anaphylaxis
- Release PBI after antivenom

Repeat bloods at 6, 12 and 24 hours [NB4] to check for recovery of coagulopathy and development of complications such as kidney impairment Further treatment of neurotoxicity, myotoxicity or thrombotic microangiopathy may require intensive care and clinical toxicology advice

harge in daylight hours with advice on serum sickness [NB5]

ods [NB3]
1 hour after removing
PBI and 6 and 12
hours after bite

logical on and

Laboratory or clinical evidence of enveroming

No J

Discharge in daylight hours

Antivenom

- How do you give it?
 - Intravenous diluted with N/Saline



Do I give FFP or other blood products to reverse the coagulopathy?

FFP	No FFP	P value	
34 (14 to 230)	39 (14 to 321)	0.44	
1	0	-	
1	0	-	
3 (7%)	4 (17%)	0.41	
1 (2%)	1 (4%)	1.0	
16.5 (4 to 58) n=33	31 (12 to 69) n=16	0.0051	
	34 (14 to 230) 1 1 3 (7%) 1 (2%)	34 (14 to 230) 39 (14 to 321) 1 0 1 0 4 (17%) 1 (2%) 1 (4%)	

- Dr...patient is still coagulopathic 3hrs post antivenom...do I give them more antivenom?
 - NO
 - WHY?

Antivenom

- Do we need to "pre-medicate" patients with adrenaline and Phenergan?
 - NO



Antivenom

- How do I know if I have given enough?
 - Mmmmmmm difficult to know



General recommendation in repeating blood tests:

- On arrival
- 1 hr post removal of PIB
- 6hr post antivenom
- 12hrs post antivenom
- Or until bloods return to normal

- Can I manage them in my hospital?
- When do I take PIB down?



What advice would you give to patients on discharge?



IN SUMMARY

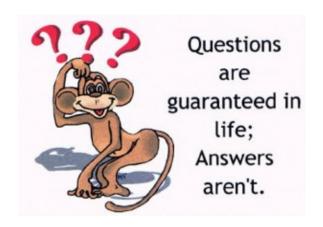
IF NOT UNWELL

- If First Aid ON...Keep it ON
- If NO first aid and NO signs/symptoms of envenomation no need to apply pressure bandage BUT still immobilise
- Resuscitation area of department
- IV lines and bloods sent
- If all bloods are normal (in particular clotting)
 - If first aid on take off and monitor patient clinically for signs/symptoms of envenomation
 - if patient develops signs and symptoms reapply and repeat bloods if patient is stable o
 - If no first aid on keep off
- I generally observe patient for 8-12hrs (repeat bloods at 6 hours)

IF UNWELL

- In no first aid apply it
- Resuscitation area of department and resuscitate patient as required.
- IV access...send bloods
- Give one vial of Polyvalent antivenom in every state except Victoria (Brown/Tiger) and Tasmania (Tiger)
- If patients are stable no reason why the can't be admitted to a short stay unit.





"I seem to be sweating a lot and I have a lot of pain"







Management

- ADT
- Local Measures
- Antivenom
 - Controversies
 - Do you give it IMI or IV
 - Do you give it at all?

Controversies:

Redback antivenom has gone in and out of favour over the years between initial thoughts that it
was effective then IM was ineffective. Recently a trial (RAVE II) would suggest that there is no
benefit to IV antivenom administration over simple analgesia. However, many toxicologists have
seen examples of patients with severe laterdectism respond to antivenom and it will be virtually
impossible to create a trial based on these extreme cases.

