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Australia is the lucky country when it comes to snakes

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Abstract

Despite the common perception worldwide that Australia is a dangerous and deadly place when it comes to snakes, Dr Zdenek begs to differ. Here are seven facts as to why: first, Australian snakes bolt away from humans; second, Australia has very few snakebite deaths; third, Australia has great access to excellent antivenom; fourth, Australia has the world's only snake venom detector kits; fifth, if you do get bitten, you're very unlikely to lose a limb; sixth, snakebite treatment in Australia is covered by Medicare; and, seventh, snake venom can save lives.

Introduction[1]

Australia has a global reputation as a land full of danger, where seemingly everything can kill you. Crocodiles lurk in tropical waters, large spiders creep in our bathrooms, we have venomous plants, and we share our suburbs with some of the most venomous snakes on the planet.

Snakes hold a particular fascination for many people in many cultures, often accompanied with fear (Polak et al. 2016). The bite of an Australian eastern brown snake (*Pseudonaja* spp.) can kill a human in under an hour (Allen et al. 2012). That's just one of more than 150 species of venomous snakes inhabiting the island continent across land and sea. Australian snakes are well and truly overrepresented out of the world's top 25 most venomous snakes (as measured on mice) (Broad et al. 1979).

Counterintuitively, Australia is relatively very lucky when it comes to snakes. Here are seven facts why.

Australian snakes bolt away from humans

The best way to survive a snakebite is of course not to be bitten (Zdenek 2021). Keeping your distance is the easiest way to avoid a bite.

But what if you're walking through the bush and don't see the snake? Luckily, most Australian snakes will rapidly slither away from us or are at least physically capable of doing so (Whitaker and Shine 1999) because their morphology permits it. With most Australian snakes being active foragers that pursue their prey, this renders them physically capable of rapidly escaping danger too, such as a human (predator) unknowingly walking toward them. In Australia, by staying still, you stay safe.

In contrast, sit-and-wait ambush predators such as rattlesnakes and vipers (e.g. in Mexico and Indonesia) are physically incapable of rapidly escaping danger. Instead, they have to hold their ground, relying on crypsis (avoiding detection by remaining still) to escape danger, and therefore can be

1 Earlier versions of this paper appeared in *The Conversation* of 7 February 2022, and on the ABC's Radio National, Occam's Razor, 3 April 2022.

easily trodden on. They're physically incapable of rapidly bolting away due to their ambushing foraging mode and stout, short body morphology. Furthermore, these venomous snakes sense body heat via infra-red sensing pit organs on their face. In Australia, the only snakes with such heat-sensing ability are non-venomous pythons.

Australia has very few snakebite deaths

Compared to other snake-inhabiting countries, Australia has orders of magnitude fewer snakebites and related deaths (Gutiérrez et al. 2017). For example, South Africa, which has just 2.2 times the population of Australia, has 159 times the snakebite deaths (476) on average every year (Halilu et al. 2019). Every year in India, they average around 58,000 snake bite deaths (Laxme et al., 2021). By contrast, Australia has two or three snake bite deaths per year on average (Welton et al. 2016). Furthermore, this low death count is not merely due to the population size of countries, as is illustrated when controlling for population size by calculating the annual number of snakebite deaths per 100,000 inhabitants. India has up to 6.7 deaths per 100,000, whereas Australia has 0.13 snake bite deaths. This is because Australia has great access to high-quality care and treatment.

Australia has great access to excellent antivenom

Antivenom is the only specific treatment for snakebites (Williams et al. 2018). If you're unlucky enough to be bitten by a highly venomous snake, getting the antivenom as quickly as possible is vital. Luckily, antivenoms work quickly, and Australia's are of high quality. Australia actually pioneered the development of this life-saving medicine in the early 1900s (Winkel et al. 2006).

Antivenom is often produced from purified horse antibodies, after the horse has been dosed with a small amount of venom. It's well known that antivenom can sometimes cause anaphylaxis, which occurs around 10% of the time in Australia (Ibister et al. 2008). These reactions are much less common in modern antivenoms produced using Good Manufacturing Practices (Bush et al., 2015) and can be quickly reversed by adrenaline administered in a hospital.

By contrast, some other countries have alarmingly ineffective antivenoms, as well as triggering anaphylaxis over 50% of the time (Variawa et al. 2021; Williams et al. 2007). Moreover, many antivenoms in foreign countries fail to actually improve patient outcomes. Very few have actually undergone clinical trials, or even preclinical testing (Alirol et al., 2015). Australian antivenoms are regularly tested for quality control during manufacture by the pharmaceutical company Seqirus (part of CSL, Commonwealth Serum Laboratory) (Verity et al. 2021). Further illustrating the quality of Australian antivenoms, even compared to other rich nations, is the small average dose required (4 vials median dose, interquartile range 2–5 vials) (Isbister et al., 2008), compared to extremely high doses (dozens of vials) often required in the USA (Bush et al., 2012).

When available, specific (monovalent) antivenoms are superior to polyvalents because there are higher titre levels of specific antibodies against toxins from the offending species, thereby increasing effectiveness. Higher specific titre levels also reduces the foreign protein load (injection dose), thereby decreasing the chance for

serum sickness (Williams et al. 2018). In many parts of the world (e.g. USA, Indonesia, and India), only polyvalents are available.

We're lucky in Australia to have five types of monovalent snake antivenoms for treating bites from our most dangerous groups of land-based snakes (Tiger Snake, Black Snake, Brown Snake, Taipan, and Death Adder) and one polyvalent, which is a mixture of the other five, used when antivenom choice is unclear. A sixth specific antivenom exists for sea snakes.

Antivenom is available at most (~750) major hospitals in Australia. For more remote regions, snakebite victims benefit from proven pressure-immobilisation snakebite first-aid (Sutherland et al. 1979), which should be applied before the Royal Flying Doctor comes to the rescue.

Some less lucky countries such as the USA do not have this snakebite first-aid option, due to the extensive cytotoxicity and necrosis of rattlesnake bites, which cause significant local tissue damage. Thus, patients may be worse off when arriving at hospital compared to Australian snakebite patients, due to the lack of a suitable first-aid measure being available.

Australia has the world's only snake venom detection kits

Using the wrong antivenom can lead to ineffective treatment, and the victim's snake identification is unreliable (Wolfe et al. 2020).

In 1979, Australia became the first country in the world to have a commercial snake venom detection kit to make quick antivenom choice more accurate (Knudsen et al. 2021). Even now, Australia is the only country with this option. This is probably because the kits are expensive to develop, and the people most in need of them are the ones least able to afford it. So, it's a small market.

Other countries must rely on more dangerous options. Either the victim brings the snake to hospital for a professional ID, or doctors have to rely on the patient's symptoms and the location where the patient was

Eastern Brown Snake, by the Author

bitten to take an educated guess as to which antivenom might work (Blaylock 2005).

This is a challenge because there can be extensive overlap of symptoms caused by venom from totally unrelated species (Feola et al. 2020). Plus, snakebite envenoming is very complicated, making years of experience treating snakebite often a prerequisite in correctly identifying the species responsible.

If you do get bitten, you're very unlikely to lose a limb

Snakebites in Australia are often painless. This is in part due to the short fangs of the most offending group of snake in Australia, our brown snakes (*Pseudonaja* spp.), which are responsible for most bites in Australia (Ibister et al. 2009), but mainly because most Australian snakes have venom which has little to no local effect at the bite site (White 1991). As such, snakebites in Australia very rarely result in amputations.

By contrast, across sub-Saharan Africa, amputation is unfortunately common (Chippaux 2011), with nearly 2400 amputations per year reported in Africa's most populous country, Nigeria (Halilu et al. 2019). Unfortunately, the people most at risk of snakebite, and losing a limb as a result, are the ones least able to afford the high treatment costs (Harrison et al. 2009).

Snakebite treatment in Australia is covered by Medicare

Antivenom can be prohibitively expensive (Zdenek et al. 2019), costing thousands of dollars per dose, making it out of reach for many people in poorer countries. But our snakebite treatment is covered by Medicare.

Our nearest neighbour, Papua New Guinea, is a snakebite hotspot. Yet many people simply do not have the money to pay for the antivenom, which can cost up to 60% of their annual income. As a result, in some areas in PNG, taipans kill more people than malaria, owing to high treatment costs and and distant clinics. This leads to there being 120 deaths per 1000 snakebites in PNG, whereas in Australia it's 1 in 1000. This massive disparity in survivability exists despite both countries sharing multiple very closely related venomous snake species, illustrating how fortunate we are in Australia.

In the USA, where, similar to Australia, relatively good healthcare is available, snakebite patients can be left with medical bills over $140,000. These exorbitant bills result from costly antivenom (over $3,000/vial), the high dose (dozens) of antivenom used on average to correct symptoms, and high daily cost in intensive care units.

Despite Australian snakes being much more venomous (drop-for-drop on lab mice) than American snakes (Broad et al., 1979), in Australia, treatment for a bite without medical evacuation may cost around $6,000 — antivenom costs $347–$2,320 per vial (Johnston et al. 2017), plus care — but this cost is covered by Medicare for permanent residents and citizens. For countries less fortunate, cheaper snakebite treatments are desperately needed (Gutierrez et al., 2011; Laustsen et al., 2017). In the venom lab[2] I manage, we are working to make snakebite treatment more affordable by testing next-generation snakebite treatments (Chowdhury et al. 2021). One compound (Varespladib (LY333013)) performed exceptionally well in our extensive pre-clinical

2 The Venom Evolution Lab at The University of Queensland.

tests (e.g. Chowdhury et al., 2021b; Zdenek et al., 2020), thereby assisting the orally-administered drug to recently (15 Aug. 2021) progress to Phase 2 human clinical trials.

Snake venom can save lives

Snake venoms save hundreds of thousands of lives every year. There are six therapeutic drugs on the global market designed from snake venom toxins, with another three at least in clinical trials.

One excellent example is Captopril, a drug that was modelled off a toxin from a snake venom in South America (the Brazilian pit viper, the jararaca, *Bothrops jararaca*). Captopril lowers high blood pressure that otherwise can result in heart disease, the world's biggest killer[3] (Opie & Kowolik, 1995). Since its development, it has led to an entirely new class of drugs (ACE inhibitors) being developed to treat heart disease.

Australian venomous snakes may also contribute to the therapeutic drug market. A toxin from the venom of eastern brown snakes (*Pseudonaja textilis*) is currently being tested as a drug to reverse life-threatening bleeding complications in patients on Direct Oral Anticoagulants (DOACs) for the prevention of stroke and deep vein thrombosis (Verhoef et al. 2017). What's more, this same venom has recently been used in a gauze delivery scaffold called Snake Venom Hydrogels (Yegappan et al. 2022) as a novel rapid wound sealant. Australia's many venomous snake species hold in their venom glands a "mini drug library" for scientists to trawl through for new life-saving drugs.

Conclusion

The Australian and global perspective on Australian snakes and snakebite is largely negative and undeserving.

Australian snakes pose little risk to humans: they flee from approaching humans, their bites can usually be treated quickly, and, counterintuitively, their venom holds therapeutic promise. Furthermore, snakes play a vital role in controlling populations of introduced rats and mice — vermin that can have devastating financial impacts on crops and communities (Brown & Singleton, 2000). Ticks and fleas live on those vermin can also increase incidence of disease and pet death (Fearn et al. 2002).

Perspective and attitudes alter human behaviour (Eiksund 2009). Persecution of snakes by humans is a relatively common practice in Australia, which stems from fear. This fear, which is not evidence-based and fails to consider the points made herein, increases one's risk to snakebite and also reduces populations of an otherwise important taxon that serves as predators and prey in ecosystems.

Rather than harming snakes, we are better off appreciating and respecting Australia's wealth of venomous snakes.

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3 In the late 1960s John Vane of England and Sérgio Henrique Ferreira of Brazil found that one of the viper's venom's peptides selectively inhibited the action of angiotensin-converting enzyme (ACE), which was thought to function in blood pressure regulation; the snake venom functions by severely depressing blood pressure. Captopril, an analogue of the snake venom's ACE-inhibiting peptide, was first synthesized in 1975. In 1982 Vane was awarded a Nobel Prize. [Ed.]

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