



BRILL

JOURNAL OF APPLIED ANIMAL  
ETHICS RESEARCH (2024) 1–22

JOURNAL OF  
APPLIED  
ANIMAL ETHICS  
RESEARCH

brill.com/jaae

# Neglected Tropical Diseases and Long-Term Captive Animals: Ethical Considerations with Venom Lab Snakes

*Derek Halm* | ORCID: 0000-0001-8174-8448

Institute for Practical Ethics, University of California San Diego,  
San Diego, CA 92117, USA  
*dhalm@ucsd.edu*

Received 23 August 2023 | Accepted 15 April 2024 |

Published online 24 April 2024

## Abstract

Venomous snakebite is a neglected tropical disease and disease of poverty, affecting hundreds of thousands of people annually. The only effective medical intervention for snakebite is antivenom, produced primarily using captive venomous snakes as a source of venom. This paper analyzes snakes' welfare at venom labs within this global health context. I recommend significant changes to improve the welfare of captive snakes, particularly in light of recent ethological research and attention on snakes. These recommendations are broadly consequentialist, aiming to improve the lives of the snakes and ensure that people have increased access to affordable antivenom.

## Keywords

animal welfare – global snakebite – neglected tropical disease – snakes

## 1 Introduction

Captive animals are kept in many contexts. Some are pets. Some are at zoos. Some are raised for human consumption. Others are held in research labs. Regardless of the circumstances, this heterogeneity raises unique ethical dimensions. What welfare considerations or rights are afforded or recognized

with these animals plausibly varies depending on the context and circumstances of their confinement. Here, I highlight one often overlooked captive context: snakes kept in venom extraction facilities used to produce antivenom.

To spotlight this, I first outline the how and why of these animals' long-term captivity. To do that, I introduce snake envenomation as a neglected tropical disease, venom variation, and the global manufacturing of antivenom. This foregrounds ethical obligations to captive snakes and a growing body of scientific evidence. In sum, I recommend expanded institutional and ethical obligations for these animals while affirming broadly consequentialist and welfare-based reasons why continued captivity is justified but must be improved.

## 2      **Venom and Global Envenomation**

Venom is a secretion produced in specialized cells or organs in one animal and then delivered, often injected, into another animal. This secretion, used for defense, feeding, or other specialized behavior, disrupts biochemical processes in the receiving organism (Mackessy 2010; Fry 2015). Snakes are well-recognized venomous organisms, partly because of some species' capacity to dangerously affect humans with their venom.

Venomous snakebite ("snakebite") is a neglected tropical disease primarily affecting rural, poor individuals in India, sub-Saharan Africa, Central and South America, and Southeast Asia (Gutiérrez et al. 2017). This international problem is characterized as a "disease of poverty," which is a disease far more prevalent in low-income people and populations; with snakebite, the people bitten or at risk of being bitten primarily live in poor rural communities without sufficient economic opportunities or infrastructure (Harrison et al. 2009). Exact figures are difficult to determine, but somewhere between 50 and 100 thousand people die from venomous snake bites yearly (GBD 2022). The number of non-fatally bitten people ranges much higher, perhaps as high as five hundred thousand (Kasturiratne 2008). Long-term complications from snake bites, such as disfigurement, kidney failure, mental illness, or permanent injury, are understudied and underreported aspects of an already neglected problem (Jayawardana et al. 2018; Waidyanatha et al. 2019).

The World Health Organization (WHO) suggests that 137 million US\$ is necessary to halve global snakebite by 2030 (WHO 2019), primarily by decreasing the price of antivenom and making it more accessible. Antivenom is often prohibitively expensive due to a limited number of local and international manufacturers, influencing the supply. In West Africa, for example, vials of antivenom may cost over three hundred dollars, which is in stark contrast

to WHO recommendations for antivenom to cost around three dollars a vial (Habib et al. 2020). Other regions, such as India, are similarly unaffordable (WHO 2019, 5).

The supply and availability of antivenom is paramount because it is the only effective medical treatment for snake envenomation (WHO 2019). Antivenom is primarily developed by extracting venom from a snake and injecting it into another animal (often called a “donor animal”), such as a sheep or horse, triggering an immune response. Over time, increasing amounts of venom are injected into the donor animal, further increasing the number of antibodies the donor animal produces, which effectively inoculates the animal against that venom. The donor animal then has its blood drawn, and the hyperimmune serum can be used as a source of antivenom. This allows the previously developed antibodies to bind to the venom proteins injected into a human or other animal via snake bite. In brief, donor animals are used to develop antibodies in response to specific venom proteins, which are used to produce antivenom (Laloo & Theakston 2003; Mackessy 2010; León et al. 2018).<sup>1</sup>

Antivenom, however, often must be sensitive to specific genera or individual species. A range of proteins constitutes snake venom, and antivenom’s effectiveness is often gauged in terms of targeting these proteins. Protein structure and composition variations may render an antivenom less effective or ineffective against some envenomations. For example, venom from rattlesnakes (genus *Crotalus*) often has a high number of cytotoxins, which cause cell death; contrast this with many cobras (genus *Naja*), which typically have a higher number of neurotoxins in their venom, which affect breathing and motor control.<sup>2</sup> Antivenom developed for one genus (or species) is unlikely to be as effective with another: rattlesnake antivenom will not be as effective against cobra envenomation as opposed to rattlesnake envenomation, and vice versa. Polyvalent/polyspecific antivenoms, composed of venoms across regions and species, are manufactured to simplify administering antivenom after a bite but do not entirely dissolve the concern of antivenom efficacy.

The concern of venom variation is further compounded because of variation between and within species. Phenotypic, ontogenetic, or geographic variation in snake venom is well documented in medically significant taxa: *Daboia* (Pla et al. 2019; Lingam et al. 2020), *Bothrops* (Rodrigues et al. 1998; da Silva Aguiar et al. 2019; Del-Rei et al. 2019; Hatakeyama et al. 2021), *Bitis* (Youngman et al. 2019), *Naja* (Wong et al. 2018; Shashidharamurthy et al. 2020), *Ophiophagus*

---

1 There are ethical dimensions to keeping and using donor animals, such as horses and sheep, in antivenom production. However, I do not discuss them in this paper.

2 This example is meant to be illustrative of broad generalities, not exact.

(Tan et al. 2020), *Echis* (Hashmi et al. 2020), and *Crotalus* (Boldrini-França et al. 2010; Sunagar et al. 2014; Dowell et al. 2018; Zancolli et al. 2019).

There is variation across the range of an organism (Smith et al. 2023), which complicates research, manufacturing, and delivery of antivenom (Fry et al. 2003a). Variation in non-medically significant to human snakes (i.e., *Diadophis*) is not as well studied (Fry et al. 2003b; Mackessy 2010; Mackessy & Saviola 2016).

The effectiveness of antivenom may also vary based on the source animals (e.g., their health and quantity of venom), the quality of antivenom production, and its manufacturing and distribution. These concerns compound an already underappreciated medical and economic burden (Habib & Brown 2018). Furthermore, there are too few venom labs and snakes in captivity to meet global demand, which affects the price and availability of effective treatment.

To summarize: venom is a secretion many snakes use for feeding and defense. Its composition varies from species to species, even if genera often have broad similarities. Since antivenom is the only effective treatment for snake bite, and snake bite is a widespread problem for hundreds of thousands of people, many snakes are kept in captivity to harvest their venom for eventual injection into donor animals and antivenom production. With this background information in mind, I turn next to the captive animals in venom extraction facilities.

### 3 Care

Since there are compelling reasons to manufacture antivenom, specialized facilities house snakes and extract venom (“venom labs”). Snakes are often housed at one facility for venom extraction. The venom is then shipped to separate facilities for injection into donor animals and antivenom manufacturing. I focus on the housing of the snakes and extraction of their venom.

Baseline information on the number and operations of venom labs is not clear (Powell et al. 2006).<sup>3</sup> Furthermore, these institutions may keep the snakes for a variety of reasons. Some labs solely keep snakes for antivenom production. Others have different purposes, such as research using venom to develop cancer treatments. While I focus on the lab-to-antivenom process, my recommendations apply to any institutions that house snakes for venom extraction.

Snakes have their venom extracted in various ways depending on the species; however, regardless of species, working with venomous reptiles requires

---

<sup>3</sup> Venom facilities have changed considerably over time (Winkel et al. 2006; Grego et al. 2021).

safe handling (Lock 2008). In general, snakes are moved outside their enclosure using either snake hooks or tongs; sometimes, they are chemically immobilized or lightly anesthetized beforehand (Wiley & Harrison 2021). Once outside the enclosure, snakes may be placed in a tube, manually held, or restrained to limit their movement before extraction. A venom receptacle, such as a beaker with a paraffin cover or a pipette for smaller snakes (e.g., genus *Micrurus*), is used. A snake is either encouraged to bite the receptacle or has the receptacle placed over its fangs. The snake may then bite, such as in the case of the paraffin, which then allows venom to flow into the receptacle for collection. If the snake does not do this on its own, or there is relatively minor flow, manual manipulation of the venom glands may be used to collect additional venom. After this, the snake is returned to its enclosure. Venom collection rates per individual animal vary, but collecting from an animal every two to four weeks is typical.

No agreed-upon standard exists for how reptiles, particularly venomous reptiles, ought to be kept and housed in captivity. The World Health Organization (WHO), in its 2016 guidelines for the production of snake antivenom, claims that it is “imperative” that venom producers that use animals “adhere to the highest ethical standards” (13). The WHO refers to the International Guiding Principles for Biomedical Research Involving Animals (2012), which outlines principles that ought to govern animal use in research. These include the well-known 3Rs (*Replacement, Reduction, and Refinement*), that there are moral obligations to using animals for research, and that “measures should be taken to ensure that the animals’ environment and management are appropriate for the species and contribute to the animals’ well-being” (3) along with “health and welfare should be continuously monitored and assessed with measures to ensure that indicators of potential suffering are promptly detected and managed” (*ibid*). Finally, the document claims that “there is a moral imperative to prevent or minimize stress, distress, discomfort, and pain in animals, consistent with sound scientific or veterinary medical practice” (4). There are no direct recommendations for the housing and maintenance of snakes (e.g., no minimum size of enclosure requirements). Specific recommendations for housing (32–34) suggest the inclusion of hide boxes, adequately sized enclosures, access to water, and other items that are in line with “local and international standards” (32) without making clear what they are directly referring to.

Other recommendations are also suggestive but not entirely clear. Two recent articles (Wiley & Harrison 2016; Wiley & Harrison 2021) state strong ethical obligations towards captive snakes. The animals should not be considered a “disposable resource” (Wiley & Harrison 2021, 625), snakes should be sourced

from captive populations so long as this does not affect antivenom potency (625–626), and natural history should be incorporated into housing to ensure long-lived and well-maintained animals (627–628). For example, the authors suggest that many snake species “do well” in snake racks (628), compact enclosures analogous to drawers or cabinets for housing snakes commonly used to house and maintain captive snakes. Regardless of the enclosure, they suggest that snakes should be kept so that wary species have places to hide, larger species should have more space, and arboreal species can climb.

All documents stress human safety. Safely housing, handling, and restraining venomous snakes are often venom labs’ most serious concerns (cf. Lock 2008). Venomous snakes are significantly different from other animals because of the potential harm to humans they pose. Seemingly minor considerations like enclosure ventilation are complicated with venomous snakes.

I want to take a step back by first returning to the 3Rs. First, the 3Rs have fair criticisms. These include omitting or understating salient moral dimensions, such as the social benefits of research, or not offering practical guidance in the contexts animals are placed in for research, such as transporting the animals (DeGrazia & Beauchamp 2019; Strech & Dirnagl 2019). Other criticisms of the 3Rs (Eggel & Würbel 2021) may not have much bearing on venom labs concerning producing antivenom. So, I want to set aside some of these criticisms because, as I hope to show, existing concerns about animal welfare, like the 3Rs, may accommodate ethical changes for venom labs. Furthermore, concerns about social or scientific license, at least with antivenom production, are met; there are good reasons that antivenom is produced and should continue to be produced, at least for the time being.

#### 4 Captivity

There are different views on animal captivity. Some philosophers emphasize that the animal should have a worthwhile life, be respected, have its basic needs met, and have no unnecessary harm (DeGrazia 2011). Others suggest that focusing on pleasure and pain, which is often the case in animal ethics, overshadows other considerations like natural foraging behaviors or social interactions that are part of the animal’s life or goals (Rollin 2012). Others foreground the animal’s subjective experience rather than humans’ feelings about confinement (Browning & Veit 2021).

There are philosophical disagreements on these points, but I suggest that they are pointing in a similar direction: animals are living beings with subjective preferences or experiences, and ensuring or improving welfare means

that these preferences, such as normal behavior, should be largely met.<sup>4</sup> Importantly, this means there must be some way to validly measure welfare. If improving animal welfare is important, there should be a way to measure or understand those animals' welfare. This is difficult when there is limited understanding of the species, such as with most snakes. Valid indicators might be possible, but they depend on scientists or researchers devising an appropriate indicator (Browning 2022).

In the case of snakes, there is speculative and interesting research, but it is impoverished compared to other taxa. That said, there are good reasons to assume that non-avian reptiles, including snakes, are sentient (Birch 2017), which in this context means the organisms have subjective experiences with attractive or aversive qualities (3). One may attribute sentience to snakes even though there are long-standing biases against making these attributions; for example, there is less investigation of reptiles concerning sentience and less attribution of behavioral language like "play" (Schuett et al. 2016; Lambert et al. 2019; Learmonth 2022).

There are some common welfare metrics in the literature. Fecal sampling shows long-term stress for some snakes after enclosure cleaning or handling (Spain et al. 2020; Augustine et al. 2022); though there are concerns with baseline measurements and what a "normal" stress level is, these measurements may still be a helpful tool for welfare insofar as they provide a measure for comparison (Doody 2023). Other studies point toward preferences for larger enclosures that allow for more movement, which likely affects other behaviors, such as searching or movement (Warwick et al. 2018; Spain et al. 2020; Hoehfurtner et al. 2021). Together, these studies suggest snakes generally prefer limited handling, minimal enclosure disruption, and larger enclosures, pushing against how they are often kept in labs: snakes are handled and restrained with regularity, and their enclosures are typically small snake racks that may only have a water dish, a hide box, and perhaps an additional feature depending on the species (i.e., an arboreal species may have silk or plastic plants to climb on).

However, there is another salient ethical dimension for consideration. There is burgeoning research suggesting that, at least in some snake species, there are underappreciated social dimensions that may have a bearing on captivity (Doody et al. 2021).

Social behaviors, such as parental care and defending neonates or eggs, are widespread, though understudied, in *Crotalinae* (pit vipers, including

---

4 There are caveats, but one salient one for working with venomous snakes, in particular, is human safety, which may place some limits on welfare. I discuss this more later in the paper.

rattlesnakes) (Greene et al. 2002). For example, cottonmouths (*Agkistrodon piscivorus*) change their antipredator behavior in the presence of young (Hoss & Clark 2014). Observations of rattlesnakes show non-random associations, with what appears to be snakes selecting which con-specifics they interact with (Amarello et al. 2012), perhaps indicating social preferences. Timber rattlesnakes (*Crotalus horridus*) have preferential aggregations during certain conditions, suggesting cryptic sociality (Clark et al. 2012), and may utilize public information from conspecific ambush sites in their foraging (Clark 2007). Other social behaviors, such as the defense of females and neonates (Hewlett & Schuett 2019), males guarding a particular location (Howey and Maisch 2017), or rattlesnakes social buffering (Martin et al. 2023), suggest complexity and individual relationships. Furthermore, field observations of maternal care, such as the protection of neonates by males and females and social interactions with neonates, may have welfare implications (Amarello et al. 2011).

This research plausibly raises some ethical concerns. These social behaviors present difficulties for the captive welfare of reptiles since there are normal behaviors (e.g., social behaviors) the animal cannot express (Doody et al. 2023; Gillingham & Clark 2023). This is particularly salient with snakes, as standard husbandry practices emphasize keeping animals solitary in snake racks in venom labs. Some venom lab scientists suggest that newly born rattlesnakes should stay with their mothers for the first two weeks (Wiley & Harrison 2016, 2021), but this is unlikely to be a common practice. For example, the WHO (2016) recommends removing neonates from their mothers as “soon as possible” (239).

There are two main points here. First, snakes in venom labs are often kept alone in small snake racks and minimally furnished enclosures for safety and medical reasons. This contributes to a life of stress, as the snakes would otherwise prefer not to be handled and would likely select alternative living quarters if given a choice. Second, research shows that some snakes, particularly vipers, are more social than often thought.

## 5 Suggestions

Venom lab snakes are a relatively unique case. The animals are kept for as long as possible and not euthanized after an experiment or set period. Some of these snakes live their entire lives in captivity and spend little time outside their enclosure, whether it is a small snake rack or otherwise. A lifetime of captivity raises unique ethical dimensions, particularly when many snakes can live over twenty years. This unusual context informs my recommendations.



Before I list those, let me return to the three R's: replacement, reduction, and refinement. Unlike in other cases involving animals in laboratory settings, there is no adequate *replacement* for captive venomous snakes at the moment (cf. Post et al. 2020). Even if there may be potential technologies, such as using cultures of venom gland cells to create venom without an animal (León et al. 2018; Ukken et al. 2022), there is no currently available option to replace captive snakes in antivenom production.

Furthermore, due to an understanding of venom variation, there may even be a general imperative to bring more wild snakes into captive arrangements if it may improve human health; from a global ethical perspective, investing in more snakes in captivity may be the correct ethical choice, which runs strongly counter to *reduction* (Habib & Brown 2018).<sup>5</sup> Animals may be bred in captivity for venom production, even increasing individual snake venom yields, but it is unknown what the long-term effects of captivity have on snake venom composition, which may change over generations, further incentivizing an increase in snakes (Modahl et al. 2010).

A natural direction is one towards *refinement*.<sup>6</sup> The welfare refinements balance several ethical considerations outlined in this paper: global health concerns are tied to lab design and practices. Alongside this pressing global need, there is a growing body of scientific literature that is suggestive, though not definitive, of welfare considerations largely ignored in venom lab design. My recommendations address these concerns while foregrounding global human health (see Table 1 for a summary).

First, there should be more financial investment and support for venom lab facilities. This means supporting the WHO's funding goals, but it goes beyond that. Specifically, this means that there should be more facilities, more animals at these facilities, more trained staff and research members, and these facilities should be located in regions where antivenom is needed in larger quantities. These recommendations aim to bring more antivenom into the market, which should reduce costs, particularly for economically stratified individuals in rural communities worldwide. Furthermore, more international investment

---

5 Polyvalent/polyspecific antivenoms, which are antivenoms used to medically address a range of species in a region, require sampling across the range of a species and must include common toxins present in various species to be effective. These require increasing the number of animals, at least in the short term. Furthermore, those kinds of antivenoms may be more expensive. However, see Laustsen et al. (2017) and Jenkins and Lausten (2020) on the price specifically of recombinant antivenoms, which has some bearing on this point. I am grateful to a reviewer for raising this point.

6 This is not to say this is the only direction available. Other possibilities, such as animal liberation, are not considered in-depth since that is outside the bounds of this applied project.

TABLE 1 Summary of recommendations

Enclosures	Enclosures should be designed to, at minimum, be as long as the snake in width and length and half as tall as the length of the snake (i.e., a four-foot snake has a $4 \times 4 \times 2$ enclosure at minimum). Enclosures should ensure snakes have a photoperiod that closely matches natural light. Snakes should have at least two hide boxes to coil, a water dish, and sufficient furnishing for skin sloughing. Venom lab workers should use chemical cues for animal enrichment.
Social housing	For those species where social housing improves welfare, venom labs should provide opportunities for snakes to interact socially with one another. This includes mothers interacting with their young, but it might also involve having animals be able to freely interact with one another through interlocking enclosures with gates or partitions. This must be done in such a way as to ensure that animals are easily accounted for to maintain safety.
Number of snakes	The number of snakes in captivity in venom labs should increase. This should be specific to the needs of a particular facility, the snakes it houses, and the antivenom produced. This aims to increase the number of snakes to minimize the stress on individual animals through venom extraction and assist in antivenom production. A sufficient increase in animals would mean that no snake should have its venom extracted more than once every month while producing sufficient antivenom at a reasonable cost and rate. This will vary considerably from place to place and the demands on particular taxa.
Staff	Facilities should have more knowledgeable and well-trained staff to ensure animals are appropriately interacted with and safety is maintained. Recommendations for more snakes and social housing hinge on appropriate staff levels and training.

and attention ideally increases the quality of available antivenoms, which can vary substantially regarding regional quality (WHO 2019).

Manufacturing, distribution, and accessibility of antivenom is an international effort tied to social, economic, and political factors that must be sensitive to particular, often local, contexts (Gutiérrez 2012). This also means that future labs should be built not just in the global North. Furthermore, regional

and local people should ideally staff and be significant partners in these facilities to avoid colonial concerns.<sup>7</sup>

Since global snake bite is a disease of poverty, merely increasing the supply of antivenom is not sufficient to solve the problem. Significant changes are necessary, whether on a country-wide scale or precipitated by local communities. More robust infrastructure, stable governments, and other social and economic changes are necessary to address the root causes. However, the availability of antivenom is a necessary component of long-term changes to solve this problem, even if social dimensions and factors are critical for long-term solutions.

Second, and following this increased financial investment, the way snakes are kept in captivity should dramatically change. Enclosures should be much larger, allowing animals significant space to move, hide, and display normal behaviors; this follows from ethological research and basic philosophical principles for animal welfare. I follow recommendations from Warwick et al. (2019) that the length and width of an enclosure be, at minimum, the same size as the snake (e.g., a three-foot snake requires a three-foot by three-foot enclosure), and the height should be half the size of the snake. This is increased from other standards that emphasize the perimeter. I also suggest hiding boxes in at least two locations where the animal may entirely coil, photo changes to emulate a day and night cycle, and using chemical cues for enrichment to stimulate seeking behavior (Krishnan et al. 2022). Considering many, if not most, snakes in venom labs are kept in racks, these are far-reaching suggestions.

These changes must be balanced against staff safety, which requires considering ethology alongside safety. One way to accommodate these considerations is to increase research on snake welfare metrics, such as those discussed previously on snake preferences and movements in captivity. There are good reasons to believe that snakes will utilize space provided for them and that limiting space is ethically insufficient to meet their welfare needs. More research should help refine the basic needs of snakes in venom labs and captivity in general.

Along with this, ongoing ethological research on social behaviors in snakes should become part of venom lab design. Some snakes seem to prefer social behavior and seek out one another throughout the year. This seems primarily associated with sexual reproduction, but not always (Martin et al. 2023). Keeping these species in captivity means that normal behaviors, such as interacting with conspecifics, should be allowed. Depending on the species,

---

<sup>7</sup> I am grateful to a commentator at APPE 2024 for recommending that I emphasize this point.

mothers should be housed with their babies until after ecdysis, and animals should have possibilities for social interactions, such as co-housing or movement between enclosures.<sup>8</sup>

How this will play out requires ethological involvement with husbandry. For example, housing animals together or allowing animals to interact with one another for at least some time will likely increase the welfare of some species or individuals. Venom labs already ensure their animals' health but do not adequately ensure that their affective states and ability to lead reasonably natural lives are considered (Fraser 2009). This is why my recommendations primarily focus on the natural lives ("normal behaviors") of captive snakes; the lab animals are free of disease but live socially impoverished lives with few opportunities for many normal behaviors, such as searching, sociality, or hunting. This is why I recommend increasing enclosure size, more hiding places, and possibilities for social interactions within species, particularly for vipers.

Before turning to objections, I want to make one point clear. On-the-ground difficulties, such as securing sufficient diversity of snakes, ensuring standards for antivenom are maintained across countries and facilities, and that facilities are transparent about production is no easy feat, particularly as what I recommend would necessitate international cooperation (Gutiérrez et al. 2007; Whitaker & Whitaker 2012; Ortiz-Prado et al. 2021). Additional funding and attention are necessary but insufficient to solve the social, economic, and political problems associated with adequately distributing and supplying antivenom. These concerns go well beyond the scope of this paper, but I am hopeful that increased international attention and investment in this neglected tropical disease can improve the lives of thousands of people, even if it will likely take longer than desired to address it fully.

## 6 Objections

Several objections could be raised against these suggestions. I will respond to several potential criticisms here, but I hope my responses might be generalized to other criticisms aimed at this applied ethical project.

First, some might suggest that these changes, particularly with social housing, may make workers' jobs more dangerous, thus placing an undue burden

---

<sup>8</sup> Snakes cannibalize non-viable offspring or ova and may, occasionally, consume healthy neonates (Mociño-Deloya et al. 2009). This is a risk of keeping young with the mothers, but the rate of cannibalism seems low based on available evidence. Therefore, given the potential benefits versus the harms, it seems better to prioritize ways for co-housing. I am grateful to a reviewer raising this point.

and risk on these workers. It may also increase the stress of some animals, particularly when little understanding of social behavior in these animals is available.

My recommendations may increase safety concerns for people working in some labs. However, safety for lab workers is a function of institutional design and culture, with some labs never having bites (Powell et al. 2006). While some social housing might increase safety concerns, it is more likely that better training and more employees at labs should offset these concerns, which is what I mean by “more investment.” At the very least, it is not obvious that changing the housing situations of some snakes under some circumstances will increase risk. Larger enclosures and places to hide can be constructed to ensure ease of accessibility for staff, such as using locking hide or squeeze boxes.

To the latter point, social housing may increase some animals’ stress, and we may be ill-equipped to judge this on a case-by-case basis. However, this speaks more to the paucity of snake welfare metrics. An increased understanding of their needs would make my recommendations more fine-tuned. It could be possible that social behavior is primarily, if not exclusively, aligned with female snakes during birth, making some existing recommendations for keeping neonates with their mothers sufficient (Wiley & Harrison 2021). The point is that more investigation is necessary. My suggestions to improve welfare are informed by ongoing research. Because of the context of lifelong captives, venom labs are in a unique situation for responding to and implementing these welfare improvements.

Second, some animal ethicists might object to my suggestion for more snakes in captivity. The snakes lead lives filled with stress; there is no reason to believe snakes that have their venom extracted enjoy that process. Therefore, bringing more animals into these facilities is unacceptable.

There are several reasons why this objection is not decisive. First, from a broadly consequentialist reading, there are at least some venom facilities where the snakes lead reasonably good lives on some welfare metric, such as longer lifespan or freedom from predation (Fraser 2009). The long-term benefits for people from having these animals in captivity cannot currently be met any other way. Therefore, refinement is a reasonable strategy to maintain and increase antivenom access. That said, venom facilities that do not provide larger enclosures, social housing, or more hide locations may be inappropriate and should be changed. Furthermore, with more snakes in captivity, the burden on an individual snake is reduced, improving their individual lives.

Unless one is an absolutist about not having animals in captivity, the real-world benefits may provide sufficient justification. An absolutist about animals in captivity or research (cf. (Korsgaard 2018 for the latter) would also need a compelling answer to how to develop antivenom or currently mitigate the

problem of global snakebite. Regarding ethical tradeoffs, improving the lives of captive animals seems more straightforward.

Third, it may be objected that the research I have discussed about snakes, either some forms of social behavior or stress, is too marginal to take seriously. There are no reasons to change welfare considerations for this minimal evidence.

Available evidence is minimal compared to other species, but this owes much to historical biases. Being open-minded is important as more evidence is gathered. I stake no claim on where the evidence may end up falling. However, dismissing the evidence out of hand would be unwise. Regardless of whether social behavior remains a compelling reason on its own, there are still good reasons to increase the number of animals in captivity and make their individual lives better. Even if the strongest version of my thesis cannot stand, a moderated version is sufficient for many of the welfare changes I have in mind.

Another concern is that I focus too much on a medical solution to snakebite rather than the social dimensions. Snakebite is a disease of poverty, so one might argue interventions to address it should be more social than medical. If this is correct, focusing on the medical production of snake venom is wrong-headed, a waste of resources, and worsens animal lives.

No doubt, social intervention on a large scale is necessary to address the scourge of global snakebites. However, no as-of-yet scenario exists where antivenom production should be entirely stopped. Even in countries where the problem is not widespread, such as Australia and the United States, antivenom is still produced, which means animals are kept in captivity. So even if social dimensions of health researchers are correct, that is still an insufficient reason not to improve the lives of captive animals and maintain some in captivity.

## 7 Conclusion

This argument should resemble those made by effective altruists (Berkey 2021). I do not endorse all aspects of the movement, but I believe it is a valuable lens to think about the intersection of global snake bite, poverty (Gabriel & McElwee 2019), and the welfare of captive animals. Investing in venom labs will improve the lives of hundreds of thousands of people, which in part makes it the right choice morally. This paper supports this but adds a provision: the captive animals should have their welfare taken more seriously by these facilities.

Snake venom labs are complex ethical cases because of their location within a global supply chain addressing a neglected tropical disease. Snakebite negatively affects people's lives worldwide and must be addressed through

concerted international efforts, working with local communities, and substantial investment in medical and social changes. This is why I recommend increasing the number of venom labs and the number of snakes at them. However, I also believe there are better ways to address this problem while ethically addressing the many concerns of keeping animals in captivity for their entire lives. Larger enclosures, more staff, better worker support, and social accommodations for captive animals are all components of this.

Both ethical dimensions – snakebite as a disease of poverty and practical concerns with animal welfare – should be addressed simultaneously. More financial investment in venom labs and incorporating more ethological research into their design is one step in that direction. The WHO is correct in trying to help people respond to the scourge of snake bites in the tropics. Along with that investment, I hope to have shown that additional welfare considerations for venom labs are justified and should be part of the long-term solution until some as-of-yet-unknown medical advancement bears fruit.<sup>9</sup>

Investing in improved venom production will help stabilize communities, improve people's lives and the lives of future people, and benefit overlooked captive animals. In conjunction, these provide compelling ethical reasons to make the suggested changes and bring long-term attention to help alleviate the burdens of neglected tropical diseases and diseases of poverty.

### Acknowledgements

I thank Drew Ruble, Drew Dittmer, and Bill Heyborne for helpful comments on an earlier draft. I am also grateful to Joseph Ehrenberger and Nick Brandehoff for their time and conversation on topics related to this manuscript. I am also grateful to the audience at APPE 2024 for their questions and comments. Finally, I thank two anonymous reviewers for helpful feedback.

### References

Aguiar, W.D.S., Galizio, N.D.C., Serino-Silva, C., Sant'Anna, S.S., Grego, K.F., Tashima, A.K., Nishiduka, E.S., de Moraes-Zani, K., & Tanaka-Azevedo, A.M. (2019). Comparative compositional and functional analyses of *Bothrops moojeni* specimens reveal several individual variations. *PLOS ONE*, 14 (9), e0222206. <https://doi.org/10.1371/journal.pone.0222206>.

---

9 One possibility is synthetic development of neutralizing antibodies (Khalek et al. 2024).

- Amarello, M. (2012). Social Snakes? Non-random association patterns detected in a population of Arizona black rattlesnakes (*Crotalus cerberus*) Melissa Amarello. PhD thesis. Arizona State University.
- Amarello, M., Amarello, M., Smith, J., & Slone, J. (2011). Family values: Maternal care in rattlesnakes is more than mere attendance. *Nature Precedings*. <https://doi.org/10.1038/npre.2011.6671.1>.
- Augustine, L., Baskir, E., Kozlowski, C.P., Hammack, S., Elden, J., Wanner, M.D., Franklin, A.D., & Powell, D.M. (2022). Investigating welfare metrics for snakes at the Saint Louis zoo. *Animals*, 12 (3), 373. <https://doi.org/10.3390/ani12030373>.
- Berkey, B. (2021). The philosophical core of effective altruism. *Journal of Social Philosophy*, 52 (1), 92–113. <https://doi.org/10.1111/josp.12347>.
- Birch, J. (2017). Animal sentience and the precautionary principle. *Animal Sentience*, 2 (16). <https://doi.org/10.51291/2377-7478.1200>.
- Boldrini-França, J., Corrêa-Netto, C., Silva, M.M., Rodrigues, R.S., De La Torre, P., Pérez, A., Soares, A.M., Zingali, R.B., Nogueira, R.A., Rodrigues, V.M., Sanz, L., & Calvete, J.J. (2010). Snake venomomics and antivenomics of *Crotalus durissus* subspecies from Brazil: assessment of geographic variation and its implication on snakebite management. *Journal of Proteomics*, 73 (9), 1758–1776.
- Browning, H. (2022). Assessing measures of animal welfare. *Biology & Philosophy*, 37 (4), 36. <https://doi.org/10.1007/s10539-022-09862-1>.
- Browning, H., & Veit, W. (2021). Freedom and animal welfare. *Animals*, 11 (4), 1148. <https://doi.org/10.3390/ani11041148>.
- Clark, R.W. (2007). Public information for solitary foragers: timber rattlesnakes use conspecific chemical cues to select ambush sites. *Behavioral Ecology*, 18 (2), 487–490. <https://doi.org/10.1093/beheco/arm002>.
- Clark, R.W., Brown, W.S., Stechert, R., & Greene, H.W. (2012). Cryptic sociality in rattlesnakes (*Crotalus horridus*) detected by kinship analysis. *Biology Letters*, 8 (4), 523–525. <https://doi.org/10.1098/rsbl.2011.1217>.
- Degrazia, D. (2011). *The ethics of confining animals: From farms to zoos to human homes*. In T.L. Beauchamp & R.G. Frey (Eds.), *The Oxford Handbook of Animal Ethics*. Oxford: Oxford University Press.
- DeGrazia, D., & Beauchamp, T.L. (2021). Beyond the 3 Rs to a more comprehensive framework of principles for Animal Research Ethics. *ILAR Journal*, 60 (3), 308–317. <https://doi.org/10.1093/ilar/ilz011>.
- Del-Rei, T.H.M., Sousa, L.F., Rocha, M.M., Freitas-de-Sousa, L.A., Travaglia-Cardoso, S.R., Grego, K., Sant'Anna, S.S., Chalkidis, H.M., & Moura-da-Silva, A.M. (2019). Functional variability of *Bothrops atrox* venoms from three distinct areas across the Brazilian Amazon and consequences for human envenomings. *Toxicon*, 164, 61–70.
- Doody, J.S. (2023). Social behaviour as a challenge for welfare. In C. Warwick, P.C. Arena, & G.M. Burghardt (Eds.) *Health and Welfare of Captive Reptiles*, (pp. 189–209). Springer, Cham, Switzerland. [https://doi.org/10.1007/978-3-030-86012-7\\_6](https://doi.org/10.1007/978-3-030-86012-7_6).



- Doody, J.S., Dinets, V., & Burghardt, G.M. (2021). *The Secret Social Lives of Reptiles*. Baltimore: Johns Hopkins University Press. <https://doi.org/10.1353/book.84105>.
- Dowell, N.L., Giorgianni, M.W., Griffin, S., Kassner, V.A., Selegue, J.E., Sanchez, E.E., & Carroll, S.B. (2018). Extremely divergent haplotypes in two toxin gene complexes encode alternative venom types within rattlesnake species. *Current Biology*, 28 (7), 1016–1026. <https://doi.org/10.1016/j.cub.2018.02.031>.
- Eggel, M., & Würbel, H. (2021). Internal consistency and compatibility of the 3Rs and 3Vs principles for project evaluation of animal research. *Laboratory Animals*, 55 (3), 233–243. <https://doi.org/10.1177/0023677220968583>.
- Fraser, D. (2009). Assessing animal welfare: different philosophies, different scientific approaches. *Zoo Biology*, 28 (6), 507–518. <https://doi.org/10.1002/zoo.20253>.
- Fry, B.G., Winkel, K.D., Wickramaratna, J.C., Hodgson, W.C., & Wüster, W. (2003). Effectiveness of snake antivenom: Species and regional venom variation and its clinical impact. *Journal of Toxicology: Toxin Reviews*, 22 (1), 23–34. <https://doi.org/10.1081/txr-120019018>.
- Fry, B.G., Wüster, W., Ryan Ramjan, S.F., Jackson, T., Martelli, P., & Kini, R.M. (2003). Analysis of Colubroidea snake venoms by liquid chromatography with mass spectrometry: Evolutionary and toxicological implications. *Rapid Communications in Mass Spectrometry*, 17 (18), 2047–2062. <https://doi.org/10.1002/rcm.1148>.
- Fry, B. (2015). *Venomous Reptiles and Their Txins: Evolution, Pathophysiology and Biodiscovery*. Oxford: Oxford University Press.
- Gabriel, I., & McElwee, B. (2019). Effective altruism, global poverty, and systemic change. In H. Greaves, & T. Pummer (Eds.), *Effective Altruism: Philosophical Issues*, (pp. 99–114). <https://doi.org/10.1093/os0/9780198841364.003.0007>.
- GBD 2019 Snakebite Envenomation Collaborators. (2022). Global mortality of snakebite envenoming between 1990 and 2019. *Nature Communications*, 13 (1), 6160. <https://doi.org/10.1038/s41467-022-33627-9>.
- Gillingham, J.C., & Clark, D.L. (2023). Normal behaviour. In C. Warwick, P.C. Arena, & G.M. Burghardt (Eds.), *Health and Welfare of Captive Reptiles*, (pp. 143–188). Springer, Cham, Switzerland. [https://doi.org/10.1007/978-3-030-86012-7\\_5](https://doi.org/10.1007/978-3-030-86012-7_5).
- Greene, H.W., Peter, G., May, D.L., Sr, J.M., & Scituro, T.M. (2002). Parental behavior by vipers. In *Biology of the Vipers*, (pp. 179–205).
- Grego, K.F., Vieira, S.E.M., Vidueiros, J.P., Serapicos, E. de O., Barbarini, C.C., da Silveira, G.P.M., Rodrigues, F. De S., Alves, L. de C.F., Stuginski, D.R., Rameh-de-Albuquerque, L.C., Furtadom M. de F.D., Tanaka-Azevedo, A.M., de Moraes-Zani, K., Teixeira da Rocha, M.M., Wilson Fernandes, W., & Sant'Anna, S.S. (2021). Maintenance of venomous snakes in captivity for venom production at Butantan Institute from 1908 to the present: a scoping history. *The Journal of Venomous Animals and Toxins Including Tropical Diseases*, 27, e20200068. <https://doi.org/10.1590/1678-9199-JVATITD-2020-0068>.

- Gutiérrez, J.M. (2012). Improving antivenom availability and accessibility: science, technology, and beyond. *Toxicon*, 60 (4), 676–687. <https://doi.org/10.1016/j.toxicon.2012.02.008>.
- Gutiérrez, J.M., Higashi, H.G., Wen, F.H., & Burnouf, T. (2007). Strengthening antivenom production in Central and South American public laboratories: report of a workshop. *Toxicon*, 49 (1), 30–35. <https://doi.org/10.1016/j.toxicon.2006.09.005>.
- Guile, L., Lee, A., & Gutiérrez, J.M. (2023). Factors associated with mortality after snakebite envenoming in children: a scoping review. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, 117 (9), 617–627. <https://doi.org/10.1093/trstmh/trad031>.
- Habib, A.G., & Brown, N.I. (2018). The snakebite problem and antivenom crisis from a health-economic perspective. *Toxicon*, 150, 115–123. <https://doi.org/10.1016/j.toxicon.2018.05.009>.
- Habib, A.G., Musa, B.M., Ilyasu, G., Hamza, M., Kuznik, A., & Chippaux, J.-P. (2020). Challenges and prospects of snake antivenom supply in sub-Saharan Africa. *PLOS Neglected Tropical Diseases*, 14 (8), e0008374. <https://doi.org/10.1371/journal.pntd.0008374>.
- Harrison, R.A., Hargreaves, A., Wagstaff, S.C., Faragher, B., & Lalloo, D.G. (2009). Snake envenoming: a disease of poverty. *PLOS Neglected Tropical Diseases*, 3 (12), e569. <https://doi.org/10.1371/journal.pntd.0000569>.
- Hashmi, S.U., Alvi, A., Munir, I., Perveen, M., Fazal, A., Jackson, T.N.W., & Ali, S.A. (2020). Functional venomomics of the Big-4 snakes of Pakistan. *Toxicon*, 179, 60–71. <https://doi.org/10.1016/j.toxicon.2020.03.001>.
- Hatakeyama, D.M., Jorge Tasima, L., da Costa Galizio, N., Serino-Silva, C., Fabri Bittencourt Rodrigues, C., Rodrigues Stuginski, D., Sant'Anna, S.S., Grego, K.F., Tashima, A.K., Nishiduka, E.S., de Moraes-Zani, K., & Tanaka-Azevedo, A.M. (2021). From birth to adulthood: An analysis of the Brazilian lancehead (*Bothrops moojeni*) venom at different life stages. *PLOS ONE*, 16 (6), e0253050. <https://doi.org/10.1371/journal.pone.0253050>.
- Hewlett, J.B., & Gordon, W. (2019). *Crotalus horridus* (timber rattlesnake). Male defense of mother and offspring. *Herpetological Review*, 50 (2), 389–390.
- Hoehfurtner, T., Wilkinson, A., Walker, M., & Burman, O.H.P. (2021). Does enclosure size influence the behaviour & welfare of captive snakes (*Pantherophis guttatus*)? *Applied Animal Behaviour Science*, 243, 105435. <https://doi.org/10.1016/j.applanim.2021.105435>.
- Hoss, S.K., & Clark, R.W. (2014). Mother cottonmouths (*Agkistrodon piscivorus*) alter their antipredator behavior in the presence of neonates. *Ethology*, 120 (9), 933–941.
- Howey, C.A.F., & Maisch, Z. (2017). Defense of a female hotspot by a male timber rattlesnake. *Herpetological Review*, 48 (1), 16–19.
- International guiding principles for biomedical research involving animals. (2012). Retrieved from [https://olaw.nih.gov/sites/default/files/Guiding\\_Principles\\_2012.pdf](https://olaw.nih.gov/sites/default/files/Guiding_Principles_2012.pdf).

- Jayawardana, S., Arambepola, C., Chang, T., & Gnanathanan, A. (2018). Long-term health complications following snake envenoming. *Journal of Multidisciplinary Healthcare*, 11, 279–285. <https://doi.org/10.2147/JMDH.S126648>.
- Jenkins, T.P., & Laustsen, A.H. (2020). Cost of manufacturing for recombinant snakebite antivenoms. *Frontiers in Bioengineering and Biotechnology*, 8, 703.
- Kasturiratne, A., Wickremasinghe, A.R., de Silva, N., Gunawardena, N.K., Pathmeswaran, A., Premaratna, R., Savioli, L., Lalloo, D.G., & de Silva, H.J. (2008). The global burden of snakebite: a literature analysis and modelling based on regional estimates of envenoming and deaths. *PLOS Medicine*, 5 (11), e218. <https://doi.org/10.1371/journal.pmed.0050218>.
- Khalek, I.S., Senji Laxme, R.R., Nguyen, Y.T.K., Khochare, S., Patel, R.N., Woehl, J., Smith, J.M., Saye-Francisco, K., Kim, Y., Misson Mindrebo, L., Tran, Q., Kędzior, M., Boré, E., Limbo, O., Verma, M., Stanfield, R.L., Menzies, S.K., Ainsworth, S., Harrison, R.A., Burton, D.R., Sok, D., Wilson, I.A., Casewell, N.R., Sunagar, K., & Jardine, J.G. (2024). Synthetic development of a broadly neutralizing antibody against snake venom long-chain  $\alpha$ -neurotoxins. *Science Translational Medicine*, 16 (735), eadk1867. <https://doi.org/10.1126/scitranslmed.adk1867>.
- Krishnan, S., Klahake, E., Rao, S., & Sadar, M.J. (2022). The effect of varied enrichment types on snake behavior. *Journal of Zoo and Wildlife Medicine*, 53 (2), 266–274. <https://doi.org/10.1638/2020-0031>.
- Korsgaard, C.M. (2018). *Fellow Creatures: Our Obligations to the Other Animals*. Oxford: Oxford University Press.
- Lalloo, D.G., & David, R.G. (2003). Snake antivenoms: antivenoms. *Journal of Toxicology: Clinical Toxicology*, 41 (3), 277–290.
- Lambert, H., Carder, G., & D'Cruze, N. (2019). Given the cold shoulder: A review of the scientific literature for evidence of reptile sentience. *Animals*, 9 (10), 821. <https://doi.org/10.3390/ani9100821>.
- Laustsen, A.H., Johansen, K.H., Engmark, M., & Andersen, M.R. (2017). Recombinant snakebite antivenoms: A cost-competitive solution to a neglected tropical disease? *PLOS Neglected Tropical Diseases*, 11 (2), e0005361.
- Learmonth, M.J. (2020). The matter of non-avian reptile sentience, and why it 'matters' to them: A conceptual, ethical and scientific review. *Animals*, 10 (5), 901. <https://doi.org/10.3390/ani10050901>.
- León, G., Vargas, M., Segura, Á., Herrera, M., Villalta, M., Sánchez, A., Solano, G., Gómez, A., Melvin Sánchez, Estrada, R., & Gutiérrez, J.M. (2018). Current technology for the industrial manufacture of snake antivenoms. *Toxicon*, 151, 63–73. <https://doi.org/10.1016/j.toxicon.2018.06.084>.
- Lingam, T.M.C., Tan, K.Y., & Tan, C.H. (2020). Proteomics and antivenom immunoprofiling of Russell's viper (*Daboia siamensis*) venoms from Thailand and Indonesia. *The Journal of Venomous Animals and Toxins Including Tropical Diseases*, 26, e20190048. <https://doi.org/10.1590/1678-9199-JVATITD-2019-0048>.

- Lock, B. (2008). Venomous snake restraint and handling. *Journal of Exotic Pet Medicine*, 17 (4), 273–284. <https://doi.org/10.1053/j.jepm.2008.07.012>.
- Mackessy, S.P. (2010). *Handbook of Venoms and Toxins of Reptiles*. Boca Raton: CRC Press. <https://doi.org/10.1201/9780429054204>.
- Mackessy, S.P., & Saviola, A.J. (2016). Venoms from 'non-venomous' snakes: Rear-fanged snake venoms as sources of novel compounds. In Y.N. Utkin, & A.V. Krivoshein (Eds.), *Snake Venoms and Envenomation: Modern Trends and Future Prospects*, (pp. 23–51). New York: Nova Science Publishers.
- Martin, C.E., Gerad, A., Fox, B.J., & Putman, W.K. (2023). Social Security: Can rattlesnakes reduce acute stress through social buffering? *Frontiers in Ethology*, 2. <https://doi.org/10.3389/fetho.2023.1181774>.
- Mociño-Deloya, E., Setser, K., Pleguezuelos, J.M., Kardon, A., & Lazcano, D. (2009). Cannibalism of nonviable offspring by postparturient Mexican lance-headed rattlesnakes, *Crotalus polystictus*. *Animal Behaviour*, 77 (1), 145–150.
- Modahl, C.M., Doley, R., & Kini, R.M. (2010). Venom analysis of long-term captive Pakistan cobra (*Naja naja*) populations. *Toxicon*, 55 (2–3), 612–618. <https://doi.org/10.1016/j.toxicon.2009.10.01>.
- Ortiz-Prado, E., Yeager, J., Andrade, F., Schiavi-Guzman, C., Abedrabbo-Figueroa, P., Terán, E., Gómez-Barreno, L., Simbaña-Rivera, K., & Izquierdo-Condoy, J.S. (2021). Snake antivenom production in Ecuador: Poor implementation, and an unplanned cessation leads to a call for a renaissance. *Toxicon*, 202, 90–97. <https://doi.org/10.1016/j.toxicon.2021.09.014>.
- Pla, D., Sanz, L., Quesada-Bernat, S., Villalta, M., Baal, J., Chowdhury, M.A.W., León, G., Gutiérrez, J.M., Kuch, U., & Calvete, J.J. (2019). Phylovenomics of *Daboia russelii* across the Indian subcontinent. Bioactivities and comparative in vivo neutralization and in vitro third-generation antivenomics of antivenoms against venoms from India, Bangladesh and Sri Lanka. *Journal of Proteomics*, 207, 103443. <https://doi.org/10.1016/j.jprot.2019.103443>.
- Post, Y., Puschhof, J., Beumer, J., Kerckamp, H.M., Merijn, A.G., & De Bakker, J. (2020). Buys de Barbanson et al. "Snake venom gland organoids". *Cell*, 180 (2), 233–247.
- Rodrigues, V.M., Soares, A.M., Mancin, A.C., Fontes, M.R., Homsí-Brandeburgo, M.I., & Giglio, J.R. (1998). Geographic variations in the composition of myotoxins from *Bothrops neuwiedi* snake venoms: biochemical characterization and biological activity. *Comparative Biochemistry and Physiology. Part A, Molecular & Integrative Physiology*, 121 (3), 215–222. [https://doi.org/10.1016/S1095-6433\(98\)10136-8](https://doi.org/10.1016/S1095-6433(98)10136-8).
- Rollin, B.E. (2011). Telos. In C. Wathes, S. Corr, S. May, S. McCulloch, & M. Whiting (Eds.), *Veterinary & Animal Ethics: Proceedings of the First International Conference on Veterinary and Animal Ethics, September 2011*, (pp. 75–83). Oxford: Blackwell Publishing Ltd.

- Sánchez, E., Pérez, J., & Powell, R. (2006). Farming for venom: Survey of snake venom extraction facilities worldwide. *Applied Herpetology*, 3 (1), 1–10. <https://doi.org/10.1163/157075406775247067>.
- Schuett, G.W., Rulon, W., Clark, R.A., Repp, M., Amarello, C.F., & Smith, H.W. (2016). Social behavior of rattlesnakes: a shifting paradigm. *Rattlesnakes of Arizona*, 2, 161–244.
- Shashidharamurthy, R., Jagadeesha, D.K., Girish, K.S., & Kemparaju, K. (2002). Variations in biochemical and pharmacological properties of Indian cobra (*Naja naja naja*) venom due to geographical distribution. *Molecular and Cellular Biochemistry*, 229 (1–2), 93–101. <https://doi.org/10.1023/a:1017972511272>.
- Smith, C.F., Nikolakis, Z.L., Ivey, K., Perry, B.W., Schield, D.R., Balchan, N.R., Parker, J., Hansen, K.C., Saviola, A.J., Castoe, T.A., & Mackessy, S.P. (2023). Snakes on a plain: biotic and abiotic factors determine venom compositional variation in a wide-ranging generalist rattlesnake. *BMC Biology*, 21 (1), 136. <https://doi.org/10.1186/s12915-023-01626-x>.
- Spain, M., Fuller, G., & Allard, S. (2020). Effects of habitat modifications on behavioral indicators of welfare for Madagascar giant hognose snakes (*Leioheterodon madagascariensis*). *Animal Behavior and Cognition*, 7 (1), 70–81. <https://doi.org/10.26451/abc.07.01.06.2020>.
- Strech, D., & Dirnagl, U. (2019). 3Rs missing: animal research without scientific value is unethical. *BMJ Open Science*, 3 (1), bmjos-2018-000048. <https://doi.org/10.1136/bmjos-2018-000048>.
- Sunagar, K., Undheim, E.A.B., Scheib, H., Gren, E.C.K., Cochran, C., Person, C.E., Koludarov, I., Kelln, W., Hayes, W.K., King, G.F., & Agosthino Antunes Fry, B.G. (2014). Intraspecific venom variation in the medically significant Southern Pacific Rattlesnake (*Crotalus oreganus helleri*): Biodiscovery, clinical and evolutionary implications. *Journal of Proteomics*, 99, 68–83. <https://doi.org/10.1016/j.jprot.2014.01.013>.
- Tan, K.Y., Ng, T.S., Bourges, A., Ismail, A.K., Maharani, T., Khomvilai, S., Sitprija, V., Tan, N.H., & Tan, C.H. (2020). Geographical variations in king cobra (*Ophiophagus hannah*) venom from Thailand, Malaysia, Indonesia and China: On venom lethality, antivenom immunoreactivity and in vivo neutralization. *Acta Tropica*, 203, 105311. <https://doi.org/10.1016/j.actatropica.2019.105311>.
- Ukken, F.P., Dowell, N.L., Hajra, M., & Carroll, S.B. (2022). A novel broad spectrum venom metalloproteinase autoinhibitor in the rattlesnake *Crotalus atrox* evolved via a shift in paralog function. *Proceedings of the National Academy of Sciences of the United States of America*, 119 (51), e2214880119. <https://doi.org/10.1073/pnas.2214880119>.
- Waidyanatha, S., Silva, A., Siribaddana, S., & Isbister, G.K. (2019). Long-term effects of snake envenoming. *Toxins*, 11 (4), 193. <https://doi.org/10.3390/toxins11040193>.

- Warwick, C., Arena, P., & Steedman, C. (2019). Spatial considerations for captive snakes. *Journal of Veterinary Behavior: Clinical Applications and Research*, 30, 37–48. <https://doi.org/10.1016/j.jveb.2018.12.006>.
- Whitaker, R., & Whitaker, S. (2012). Venom, antivenom production and the medically important snakes of India. *Current Science*, 103 (6), 635–643.
- Wiley, K.L., & Harrison, J.R. (2016). Venom production in the 21st century. In Utkin, Y.N., & Krivoshein, A.V. (Eds.), *Snake Venoms and Envenomation: Modern Trends and Future Prospects* (pp. 53–66). New York: Nova Science Publishers.
- Wiley, K.L., & Harrison, J.R. (n.d.). Large-scale snake colonies for venom production: Considerations and challenges. In S.P. Mackessy (Ed.), *Handbook of Venoms and Toxins of Reptiles*. Boca Raton: CRC Press.
- Winkel, K.D., Mirtschin, P., & Pearn, J. (2006). Twentieth century toxinology and antivenom development in Australia. *Toxicon*, 48 (7), 738–754. <https://doi.org/10.1016/j.toxicon.2006.08.001>.
- Wong, K.Y., Tan, C.H., Tan, K.Y., Quraishi, N.H., & Tan, N.H. (2018). Elucidating the biogeographical variation of the venom of *Naja naja* (spectacled cobra) from Pakistan through a venom-decomplexing proteomic study. *Journal of Proteomics*, 175, 156–173. <https://doi.org/10.1016/j.jpro.2017.12.012>.
- World Health Organization (2016). WHO guidelines for the production, control and regulation of snake antivenom immunoglobulins. Retrieved from <https://www.who.int/publications/m/item/snake-antivenom-immunoglobulins-annex-5-trs-n0-1004>.
- World Health Organization. (2019) Snakebite envenoming – a strategy for prevention and control. Retrieved from <https://www.who.int/publications/i/item/9789241515641>.
- Youngman, N.J., Debono, J., Dobson, J.S., Zdenek, C.N., Harris, R., Op den Brouw, B., Coimbra, F.C.P., Naude, A., Coster, K., Sundman, E., Braun, R., Hendriks, I., & Fry, B.G. (2019). Venomous landmines: Clinical implications of extreme coagulotoxic diversification and differential neutralization by antivenom of venoms within the viperid snake genus *Bitis*. *Toxins*, 11 (7), 422. <https://doi.org/10.3390/toxins11070422>.
- Zancolli, G., Calvete, J.J., Cardwell, M.D., Greene, H.W., Hayes, W.K., Hegarty, M.J., Herrmann, H.-W., Holycross, A.T., Lannutti, D.I., Mulley, J.F., Sanz, L., Travis, Z.D., Whorley, J.R., Wüster, C.E., & Wüster, W. (2019). When one phenotype is not enough: divergent evolutionary trajectories govern venom variation in a widespread rattlesnake species. *Proceedings of the Royal Society B*, 286 (1898), 20182735.