

Supplement to Venom immunization IgG/IgE titers, safety, risk, methods of the VIPRBITEM cohort

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1. Lethal dose data for snake venoms presented in this study

Cohort lethal dose (LD) values in Table 1 show wet venom, assuming 75% water, because that is how it is reported. Wet venom dose is multiplied by 82 kg for scaling. The minimum lethal dose (MLD) is the lowest dose within a set of studies, not a conventional MLD within one study.

Table 1 – **Minimum and median lethal dose data (wet/dry venom)** values for MLD and LD50 wet and dry values translated to the amount for an 82 kg human are provided with the number of studies used to derive it. On the right, this table makes use of probability distribution and associated equations for estimating range and midpoint LD ^[1].

			Alpha	Body mass kg:	82	82			
			0.1	Wet dilution:	0.75	0.75			
						82 kg			
				Dry	82 kg	Wet		Dry	Estimated
				median	Wet	median		range ×	Dry 50%
				MLD	LD50	MLD	LD50	Dry	Dry 50%
				mg/kg	mg/kg	mg	mg	range	midpoint
Elapids	<i>n</i>	1 tail <i>t</i>						mg/kg	mg/kg
Naja haje	19	1.73	0.025	0.75	2.7	82.0		5.98	10.36
Naja kaouthia	4	2.35	0.114	0.229	12.5	25.0		0.39	0.91
Naja nivea	19	1.73	0.00014	0.334	0.015	36.5		4.00	6.94
Naja annulata	2	6.31	0.0835	0.143	9.1	15.6		0.02	0.15
Naja annulifera	3	2.92	1.75	1.98	191.3	216.5		2.75	8.03
Ophiophagus hannah	5	2.13	0.355	1.5	38.8	164.0		1.56	3.32
Dendroaspis angusticeps	8	1.89	0.381	1.04	41.7	113.7		2.94	5.57
Dendroaspis viridis	5	2.13	0.33	0.71	36.1	77.6		0.47	1.00
Dendroaspis jamesoni	5	2.13	0.26	0.84	28.4	91.8		0.76	1.62
Dendroaspis polylepis	5	2.13	0.26	0.32	28.4	35.0		0.42	0.90
Oxyuranus scutellatus	8	1.89	0.009	0.057	1.0	6.2		0.15	0.28

Viperids									
Crotalus scutulatus	14	1.77	0.02	0.195	2.2	21.3	0.68	1.20	0.196
Crotalus atrox	17	1.75	0.143	1.9	15.6	207.7	19.11	33.36	5.019
Crotalus pyrrhus	4	2.35	1.143	2.7	125.0	295.2	8.46	19.90	4.052
Crotalus ruber	16	1.75	0.857	4	93.7	437.3	20.39	35.75	6.082
Crotalus horridus	16	1.75	0.006	2.44	0.7	266.8	24.89	43.64	6.385
Agkistrodon contortrix	14	1.77	0.024	0.927	2.6	101.4	20.98	37.15	5.453
Agkistrodon c. laticinctus	14	1.77	0.024	0.927	2.6	101.4	20.98	37.15	5.453
Agkistrodon c. mokasen	14	1.77	0.024	0.927	2.6	101.4	20.98	37.15	5.453
Agkistrodon c. pictigastor	14	1.77	0.024	0.927	2.6	101.4	20.98	37.15	5.453
Agkistrodon piscivorus	13	1.78	0.18	5	19.7	546.7	14.82	26.41	4.041
Agkistrodon h. blomhoffi	4	2.35	1.32	6.35	1443	694.3	16.97	39.94	7.157
Atheris squamigera	1	NA	0.611	0.611	66.8	66.8	NA	NA	0.611

The right side of Table 1 uses the range distribution equations 1-3 to estimate the mass midpoint of the distribution, as shown in figure 1. For these equations, it is at 14.6% ^[1].

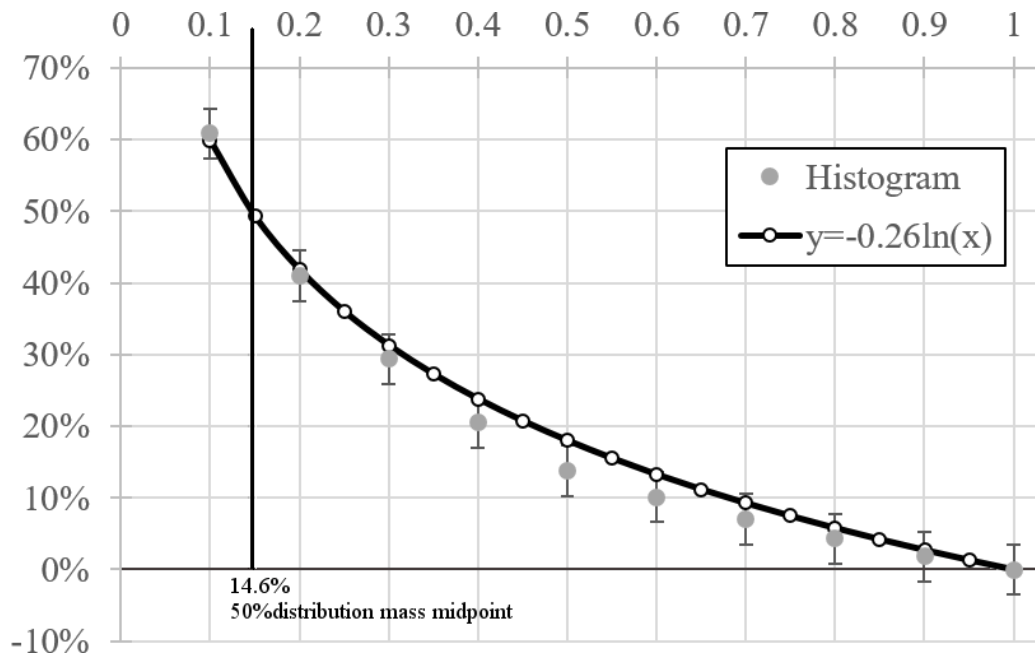


Figure 1 – Range distribution: $y = -0.26\ln(x)$. Standard error bars show simplified equation adequately represents this distribution. Approximately 40% of LD distribution is in the first 10%.

$$y = -0.26 \cdot \ln(x) \quad (\text{eq. 1}) \quad x = e^{-3.84615y} \quad (\text{eq. 2}) \quad L_D = x \cdot K + m \quad (\text{eq. 3})$$

Where: K = LD range; x = fraction of K , $0.1 < x < 1$; y = distribution mass fraction from x to 1;

L_D = lethal dose at a point x ; m = MLD for the species

The starting degree of dilution (typically 1:1000) and dose of 1 ml of such a dilution appears to be sufficient. Similar to treatment of snakebite based on symptoms, we recommend that doses start low and advance or backtrack based on symptoms. Generally speaking, the more individual venoms within a venomous species are mixed, the closer the lethal dose of that mixture should get to the 50% midpoint in the distribution of figure 1. The lethal dose data in the figure captions is intended for safety, and readers can refer back to table 1 for the mass midpoint.

2. Cohort immunization detail

Doses shown in figures below are translated to **median wet dose LD50 (mdLD50)** for an 82 kg man, with dry median dose in mg/kg in parens. Example: *C. atrox* mdLD50 207.7 mg (dry 1.9 mg/kg).

2.1. V0001 immunization

These V0001 data are shown in figures 2-5.

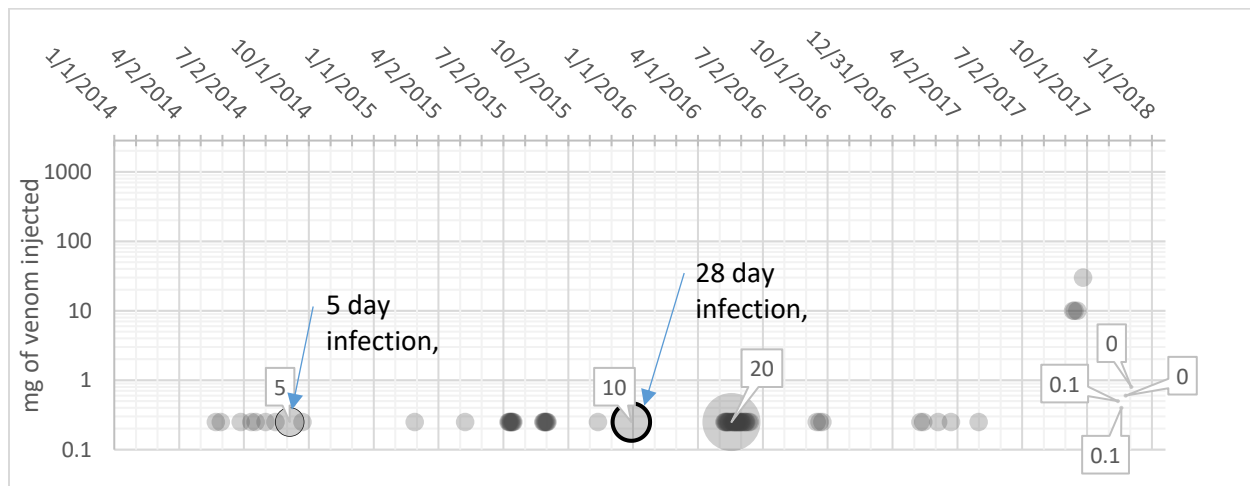


Figure 2 – Mixture of *Crotalus atrox* (Western diamondback), *Crotalus horridus* (Timber rattlesnake) immunization. *C. atrox* mdLD50 207.7 mg (dry 1.9 mg/kg). *C. horridus* mdLD50 266.8 mg (dry 2.44 mg/kg) Black outline indicates abscess. Total of 75 injections.

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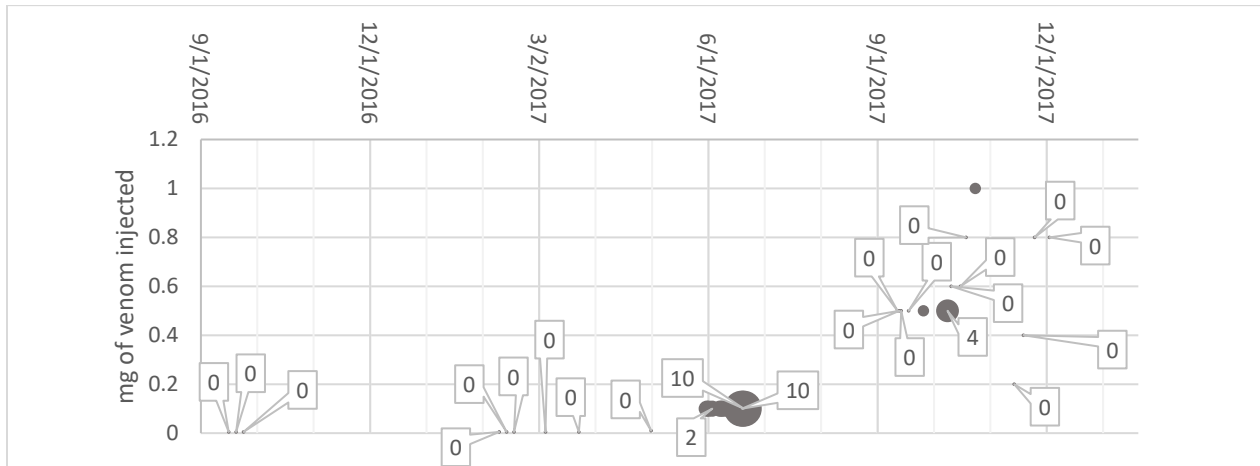


Figure 3 – *Naja kaouthia* (Monocled cobra) immunization. *N. kaouthia* mdLD50 25.0 mg (dry 0.229 mg/kg). Size of bubble shows swelling in square inches. Total of 38 injections.

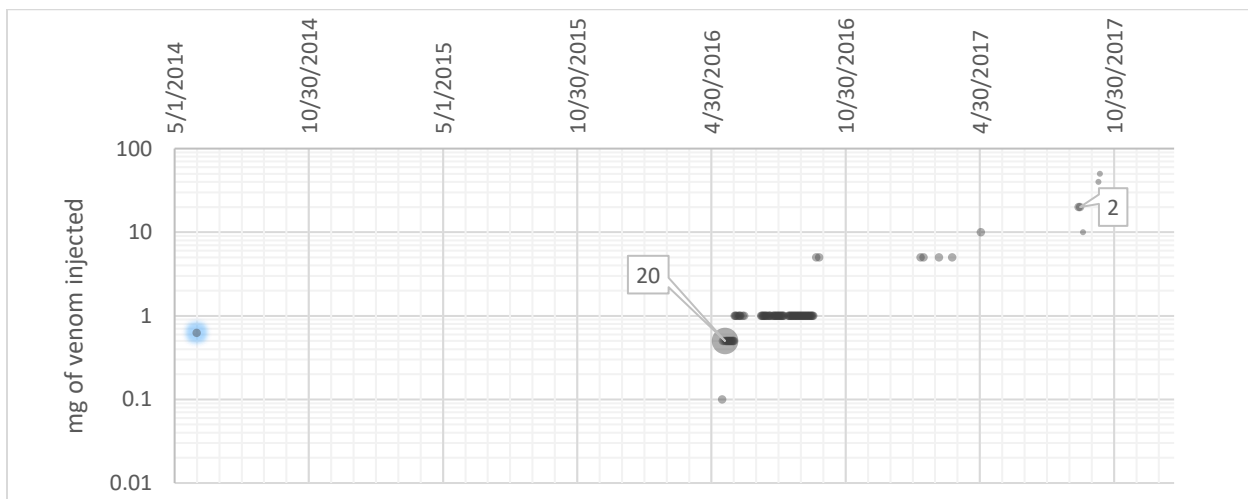


Figure 4 – *Agkistrodon contortrix contortrix* (Common copperhead), *A. c. laticinctus* (broad-banded copperhead), *A. c. mokasen* (northern copperhead), *A. c. pictigaster* (western copperhead) immunization mixture, log scale. *A. contortrix* spp mdLD50 101.4 mg (dry 0.927 mg/kg). Size of bubble indicates swelling. Blue glow indicates significant venom poisoning for 1st injection. Total of 103 injections.

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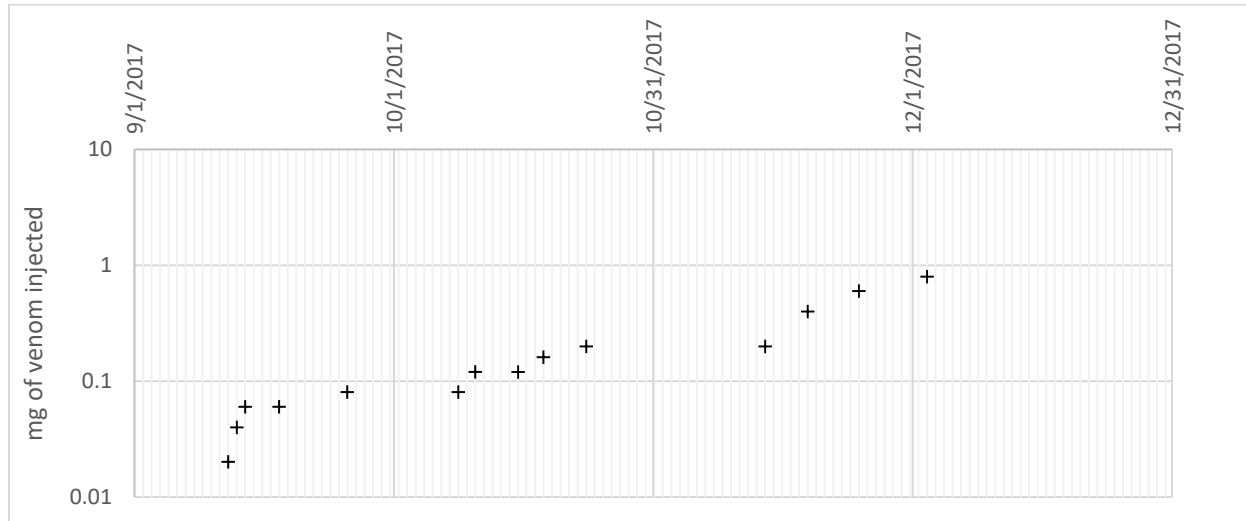


Figure 5 – *Agkistrodon piscivorus* (water moccasin) immunization. *A. piscivorus* $mdLD_{50}$ 546.7 mg (dry 5 mg/kg) No swelling reported for these injections. 14 injections.

2.2. V0002 immunization

This participant estimates hundreds of injections from 2014-2017 using a mix composed of: *Crotalus tigris* (Tiger rattlesnake), *Crotalus viridis* (Western rattlesnake), *Crotalus vergrandis* (Uracoan rattlesnake), *Crotalus mitchellii* (Mitchell's rattlesnake), *Crotalus abyssus* (Grand Canyon rattlesnake), *Crotalus lutosus* (Great Basin rattlesnake), *Crotalus cerastes lateropens* (Colorado Desert sidewinder), *Crotalus cerastes cerastes* (Mohave Desert Sidewinder), *Crotalus Cerberus* (Arizona black rattlesnake), *Crotalus molossus* (Black-tailed rattlesnake), *Crotalus helleri* (Southern Pacific rattlesnake), *Sistrurus miliarus* (Pygmy rattlesnake), *Crotalus atrox* (Western diamondback rattlesnake), and *Crotalus horridus horridus* (Timber rattlesnake). The starting dilution of this mix was a unit at 1:1000. Aside from definition of the mix and general record of injections, records are incomplete. Thus, no data is shown graphically.

2.3. V0003 immunization

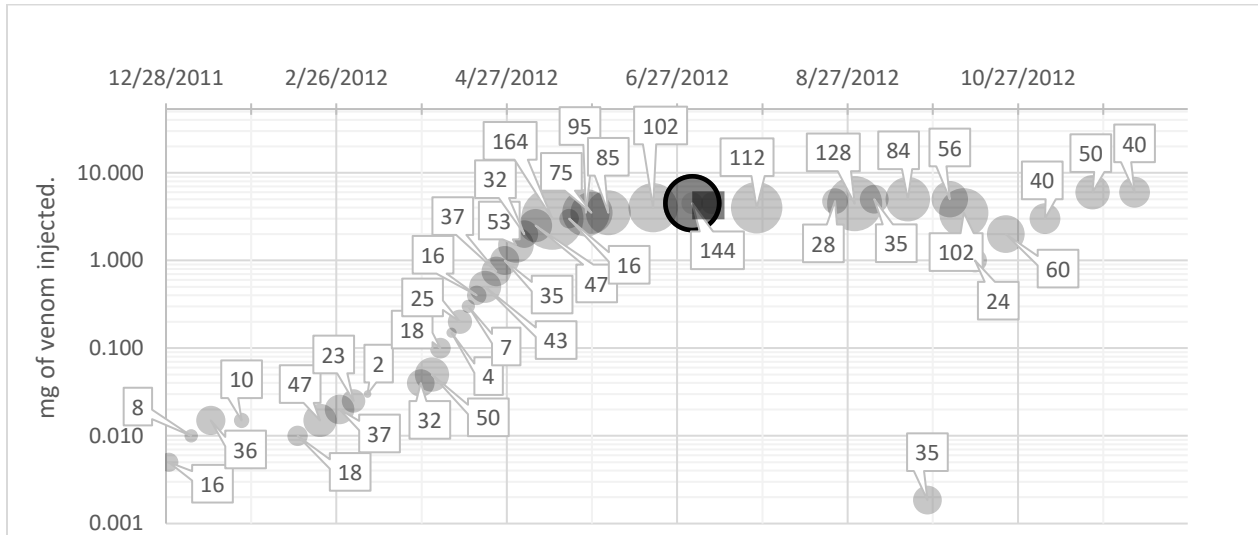


Figure 6 – *Agkistrodon halys blomhoffii* (Japanese Mamushi) immunization, log scale. *A. h. blomhoffii* mdLD50 694.3 mg (dry 6.35 mg/kg). Bubble size callout is peak swelling in square inches. Dark gray fill indicates infection & black border indicates abscess. Recovery from infection took 7 days with daily IV antibiotics as shown by dark gray bar. This infection was judged to be due to contamination of dilution buffer. Total of 42 injections.

2.4. V0004 immunization

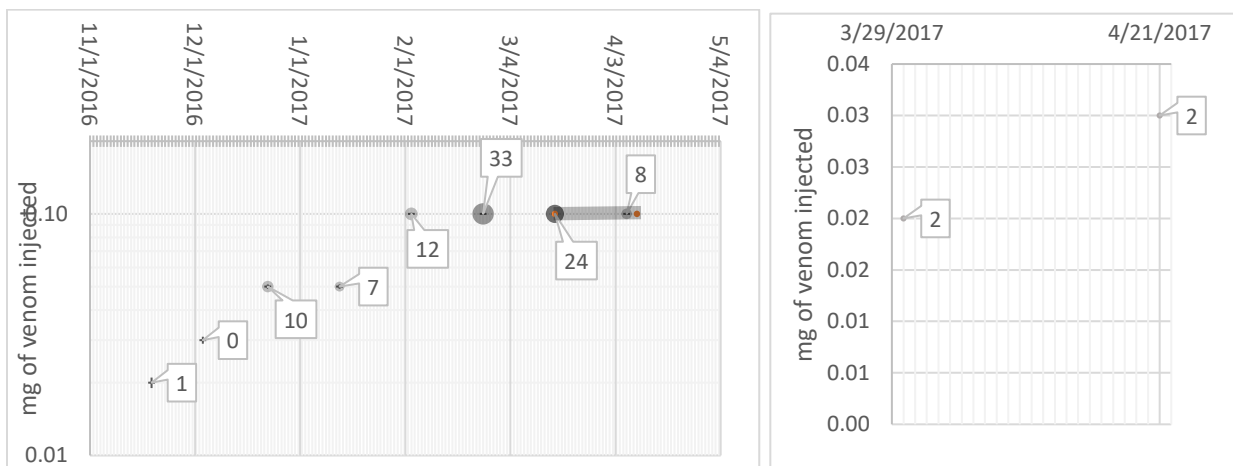


Figure 7 – **Left:** *Crotalus atrox* (Western diamondback rattlesnake) immunization. *C. atrox* mdLD50 207.7 mg (dry 1.9 mg/kg). Lymphangitis began 2 days after 3/17/2017 injection (dark bubble). Recovery at home without medical care took 24 days, while still going to work. Total of

8 injections. **Right: *Agkistrodon contortrix mokasen* (Osage copperhead) immunization.** *A. contortrix* spp mdLD50 101.4 mg (dry 0.927 mg/kg). Total of 2 injections. Bubble size callouts are peak swelling in square inches.

V0004 had an invasive infection after an injection with diluted venom as shown in figures 7-8. This received a diagnosis of lymphangitis after the fact since medical care was not sought until it was healed. Probable scarring of a biceps tendon occurred diagnosed by a “guitar string” sign. The injection was subcutaneous to the upper forearm near the elbow. After several days, an infection appears to have followed the connective tissue around the elbow joint, along the inner biceps tendon, and involved the lymph duct in that area. In a photo, a line of redness following the duct is seen. Recovery occurred without antibiotics.

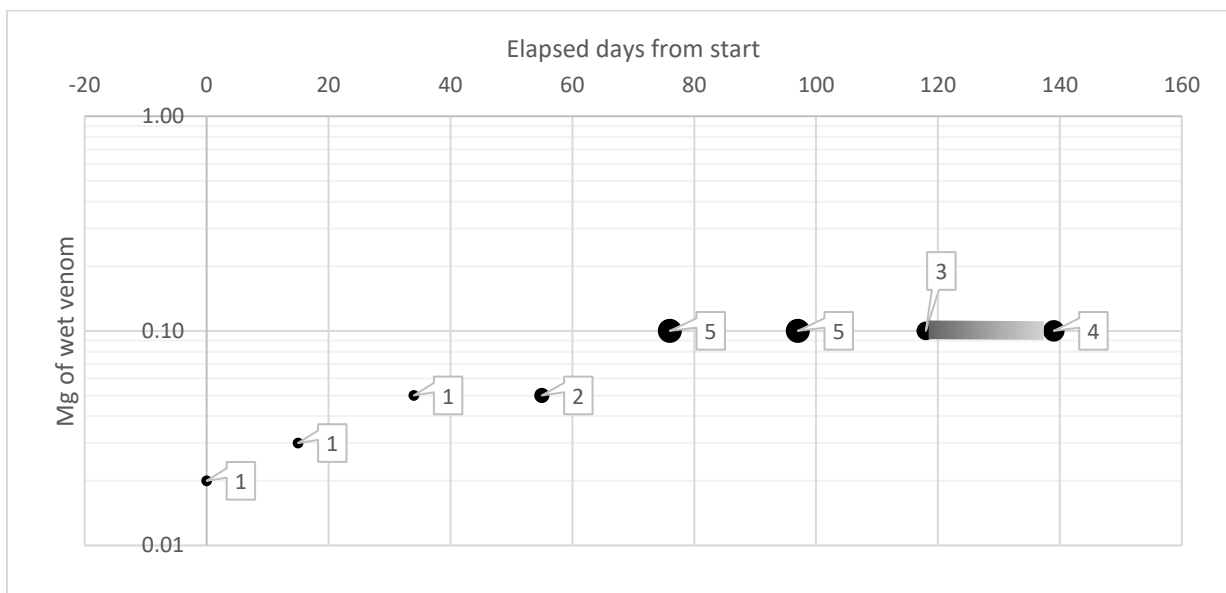


Figure 8 – **Pain.** Corresponds to Figure 6 left. *Crotalus atrox* (Western diamondback) pain. Bubble size indicates pain level. Gradient line following injection on day 118 indicates approximate pain level during recovery from infection. 8 injections.

2.5. V0005 immunization

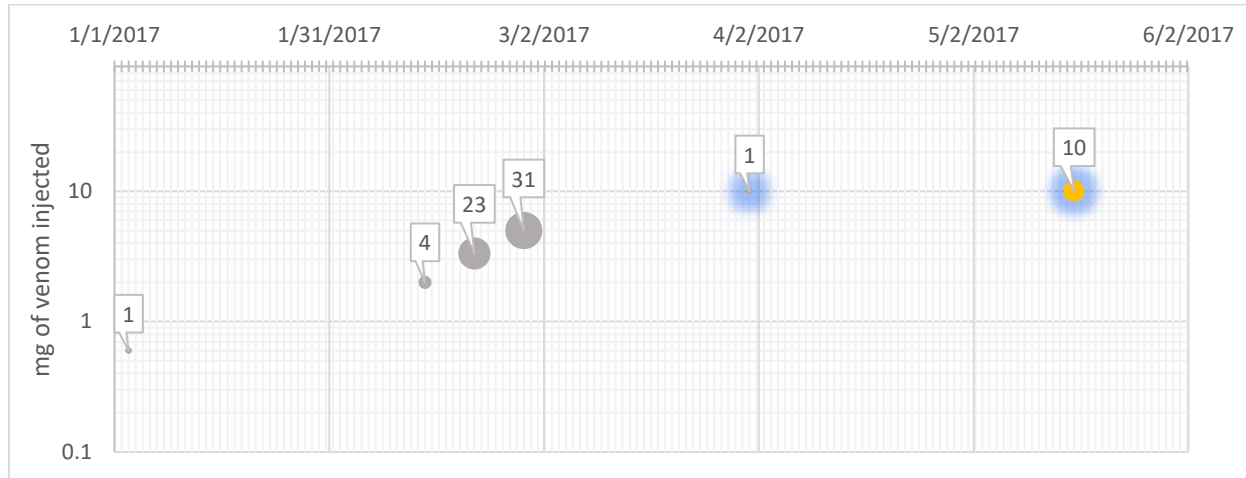


Figure 9 – *Ophiophagus hannah* (King cobra) immunization. *O. Hannah* mdLD50 164.0 mg (dry 1.5 mg/kg). Bubble size callout is peak swelling in square inches. Blue glow is experience of venom effect. Orange is atopy/anaphylaxis. Total of 6 injections. An available epinephrine injector was not used.

The anaphylactic type symptoms of figure 9 included some tightening of the throat, hives, hanging eyelids, swollen lips, vomiting, and intense itching. Self-treated with Atarax antihistamine. Epinephrine injector was on-hand but not used. Symptoms subsided in roughly 30 minutes followed by a 30 minute hot shower for the itching. Itching subsided in 3 hours. Venom effect was a half hour of drowsiness that required sitting down. The totality of V0005's data is presented in figures 9-11.

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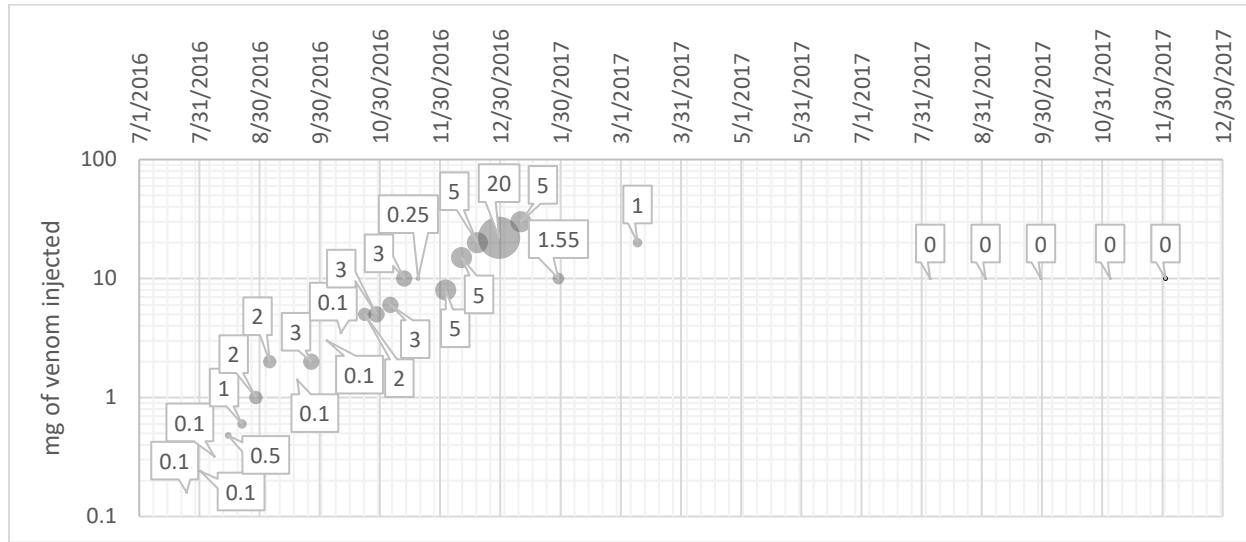


Figure 10 – *Naja haje annulifera* (Snouted Cobra) immunization, log scale. *N. h. annulifera* mdLD50 216.5 mg (dry 1.98 mg/kg). Bubble size callout is peak swelling in square inches. Orange bubbles indicate atopy/anaphylaxis, which in this case consisted of intense itching which is minor. V0005 took antihistamines proactively and also in response to symptoms. Total of 28 injections.

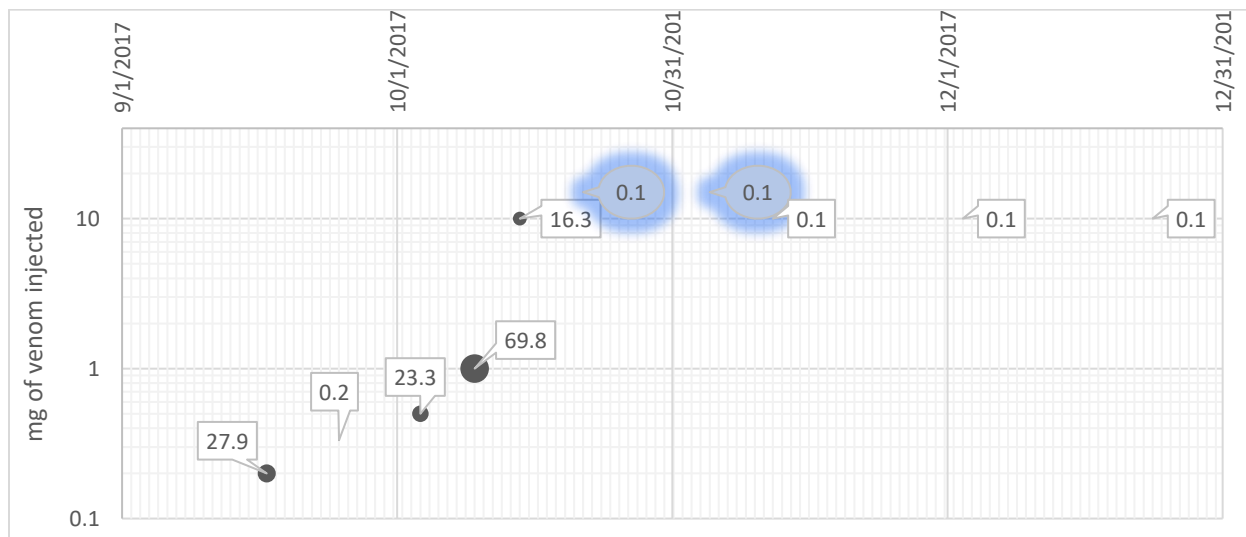


Figure 11 – *Dendroaspis jamesoni* (Eastern green mamba) immunization. *D. jamesoni* mdLD50 91.8 mg (dry 0.84 mg/kg). Bubble size callout is peak swelling in square inches. Blue glow indicate 2 incidents of significant venom effect (drowsiness, ptosis, requiring sitting for an hour). 10 injections.

2.6. V0006 immunization

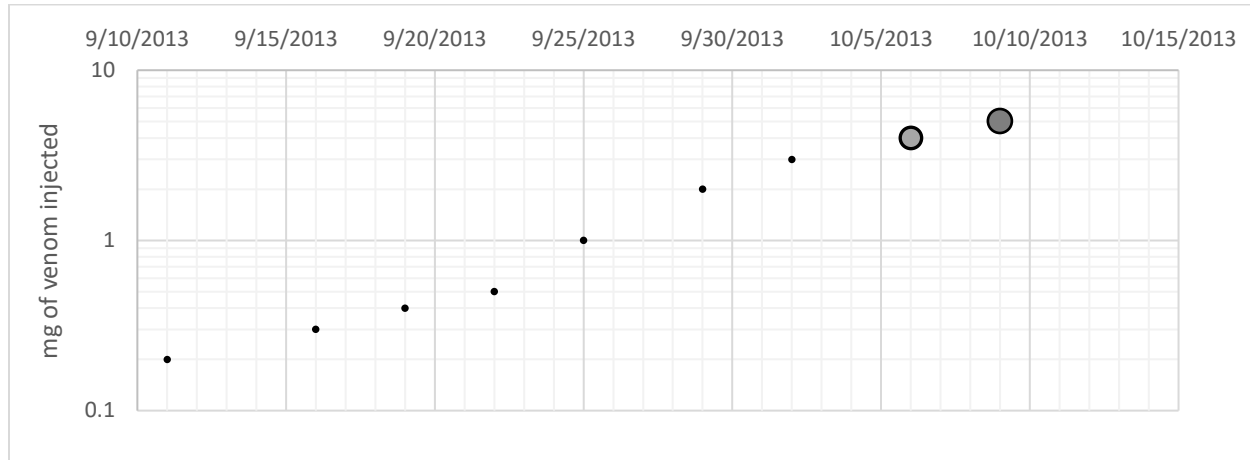


Figure 12 – *Crotalus atrox* (Western diamondback rattlesnake), *Crotalus pyrrhus* (Southwestern Speckled rattlesnake), *Crotalus ruber* (Red Diamond rattlesnake) immunization. *C. atrox* mdLD50 207.7 mg (dry 1.9 mg/kg). *C. pyrrhus* mdLD50 295.2 mg (dry 2.7 mg/kg). *C. ruber* mdLD50 437.3 mg (dry 4 mg/kg). Bubble size is not significant because swelling was not reported. Black outline indicates report of probable sterile abscess needing medical treatment. Total of 10 injections.

V0006 abandoned venom vaccination with this mixture at the end of a month's period, per figure 12. The interval should have been 3-5 weeks between dose increments, not 3-5 days. This indicates there is a place for improving safety by providing better information.

2.7. V0007 immunization

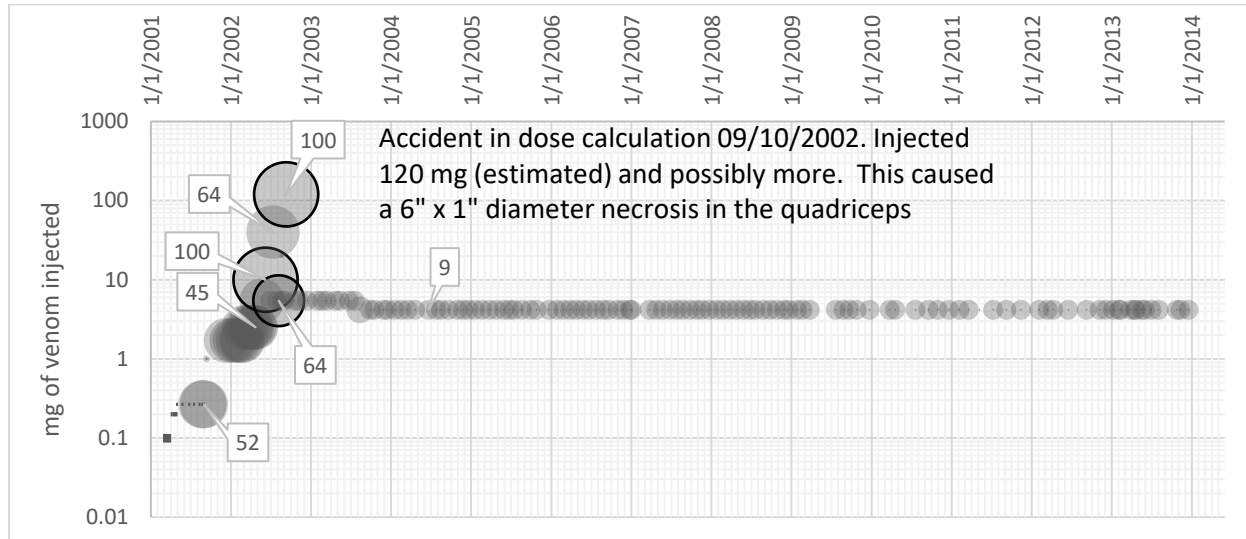


Figure 13 – Mixture of three venoms. *Naja haje* (Egyptian cobra), *Naja kaouthia* (Monocled cobra), *Naja nivea* (Cape cobra) immunization. *N. haje* mdLD50 82.0 mg (dry 0.75 mg/kg). *N. kaouthia* mdLD50 25.0 mg (dry 0.229 mg/kg). *N. nivea* mdLD50 36.5 mg (dry 0.334 mg/kg). Bubble callouts not shown due to density. Median swelling is 9 square inches. Black outline indicates abscess. These sterile abscesses were treated at home. Very early doses had tiny or no swelling. Total of 150 injections.

V0007 has the most data of the cohort, as shown in figures 13-18. The anaphylactic type incidents in figure 14 were the most serious reported, including a degree of closing of airway. An available EpiPen was not used. After 9 repetitions of anaphylaxis, with the last two injections having declining symptoms, the symptoms abruptly ceased.

We think that the anaphylaxis symptoms were probably due to an overly aggressive immunization schedule that assumed more IgG cross-reactivity than there was. Normal immunization schedules start as low as 1 to 10 micrograms. There may also be more cross-reactivity of IgE from the *Naja* species. That there was a high degree of cross-immunity from some type of antibody, most likely IgE, is shown by the fact that aside from the anaphylaxis, there were no significant venom symptoms. It is known that animals

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survive snakebite better with IgE + IgG than IgG alone^[2]. So, IgE is a significant aspect of antibody response to venoms.

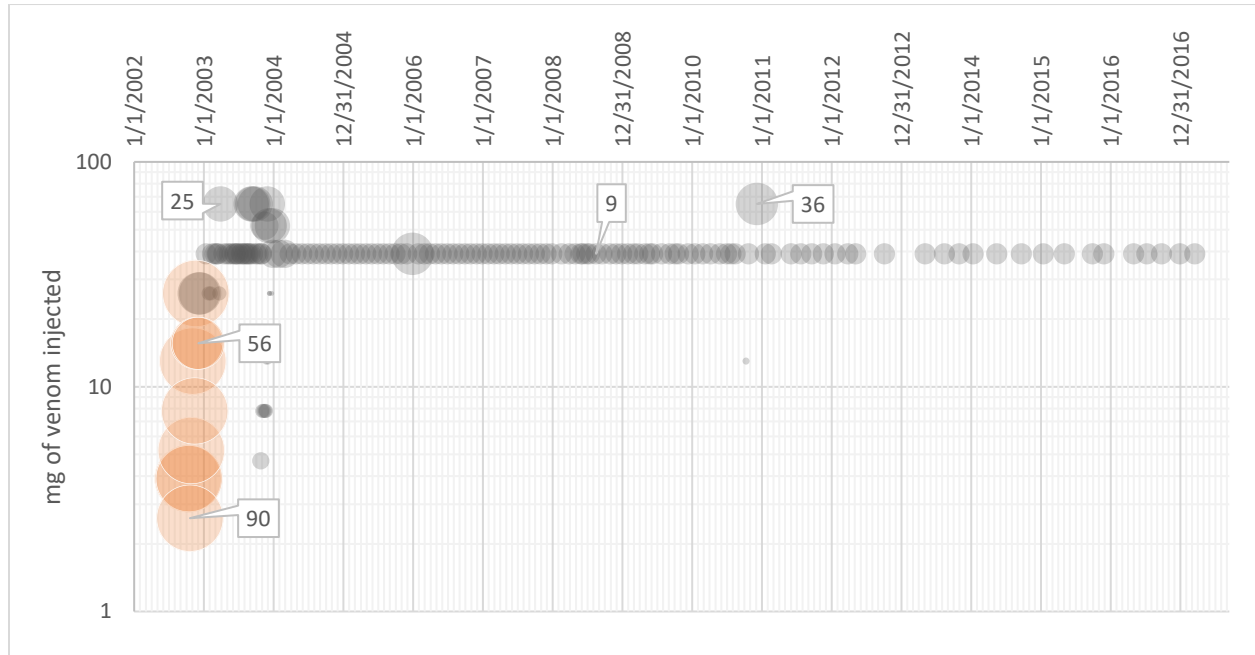


Figure 14 – *Dendroaspis angusticeps* (Eastern green mamba), *D. viridis* (Western green mamba), *D. jamesoni* (Jameson’s mamba), *D. polylepis* (Black mamba) immunization, log scale. Bubble size callouts not all shown due to density. The orange bubbles indicate anaphylaxis that included throat tightening symptoms. *Dendroaspis angusticeps* mdLD50 113.7 mg (dry 1.04 mg/kg). *D. viridis* mdLD50 77.6 mg (dry 0.71) *D. polylepis* mdLD50 35.0 mg (dry 0.32 mg/kg). *D. jamesoni* mdLD50 91.8 mg (dry 0.84 mg/kg). Total of 164 injections.

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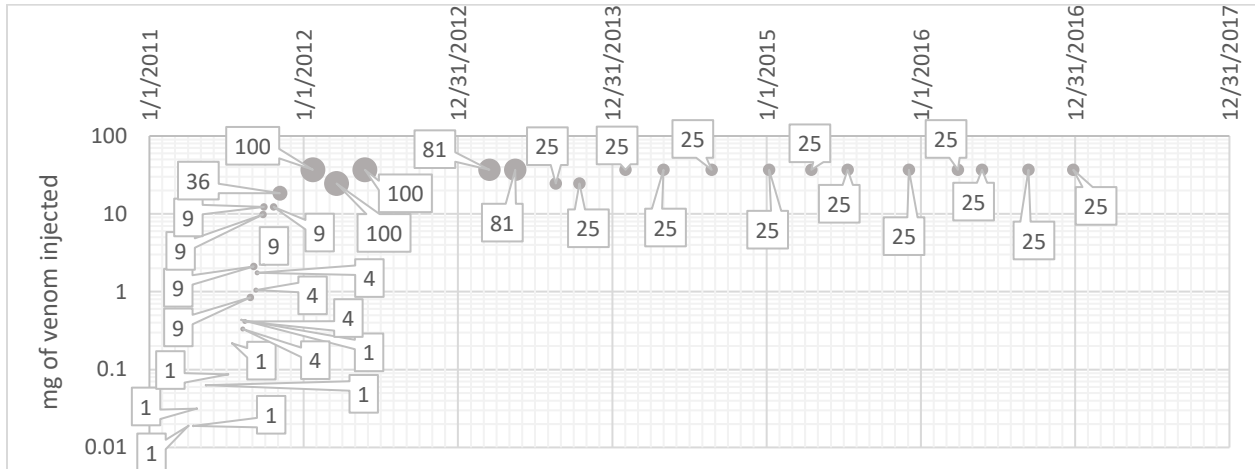


Figure 15 – *Crotalus scutalatus* (Mojave rattlesnake) immunization. Bubble callouts indicate size of swelling in square inches. *C. scutalatus* mdLD50 21.3 mg (dry 0.195 mg/kg). Total of 36 injections.

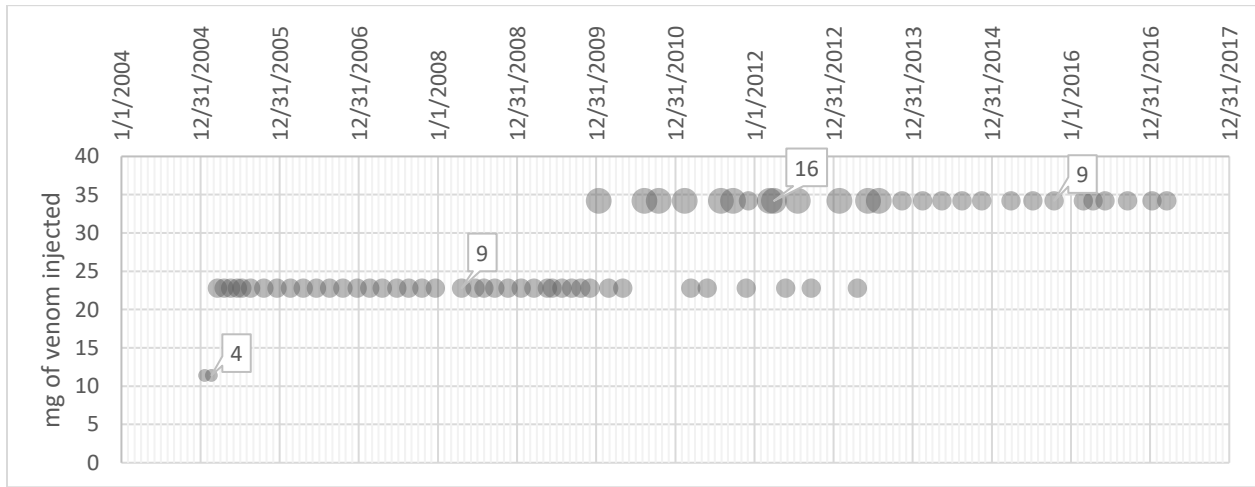


Figure 16 – *Naja haje annulata* (Banded water cobra) immunization. Bubble maximum size is 16 square inches in the top row, low is 4 square inches, median 9 square inches, which is most of the second row and the latter part of the top row. *N. h. annulata* mdLD50 15.6 mg (dry 0.143 mg/kg). Total of 70 injections.

Note that this figure 16 immunization schedule was extremely aggressive, starting with an injection of 11.4 mg of wet venom. It is apparent that this strategy was successful, so the immunizations to 3 other Naja species prior to this one provided protective cross-immunity at a high attack dose. V0007 went to a

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22.8 mg booster level of inoculation after two high dose immunizations and maintained this booster level for 5 years. He later switched to a 34.2 mg booster dose, roughly double the mdLD50.

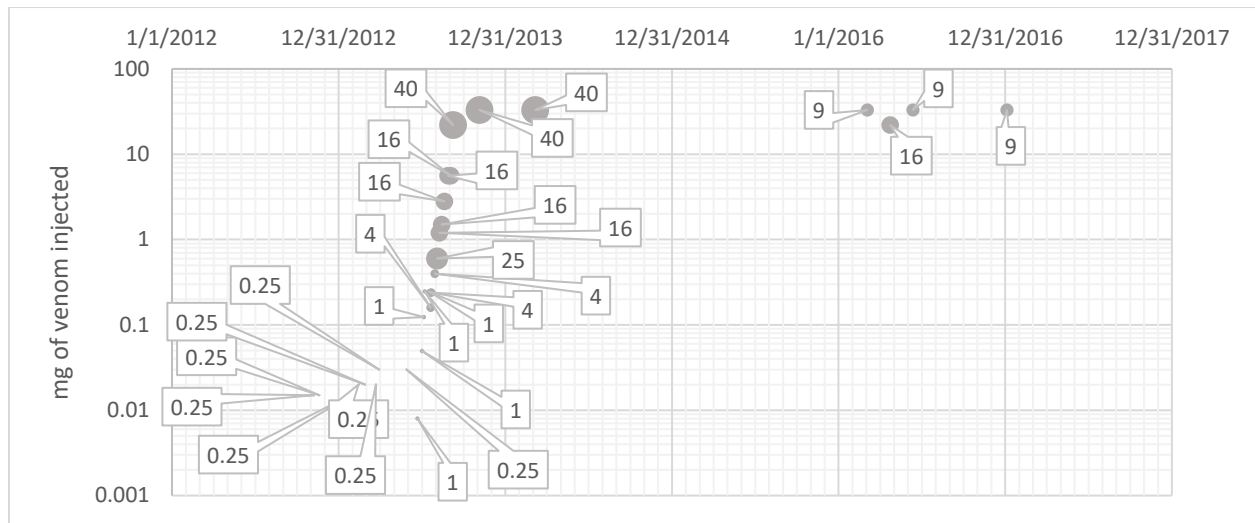


Figure 17 – *Oxyuranus scutellatus* (Coastal taipan) immunization, log scale. Bubble size callouts show swelling in square inches. *O. scutellatus* mdLD50 6.2 mg (dry 0.057 mg/kg). Total of 30 injections.

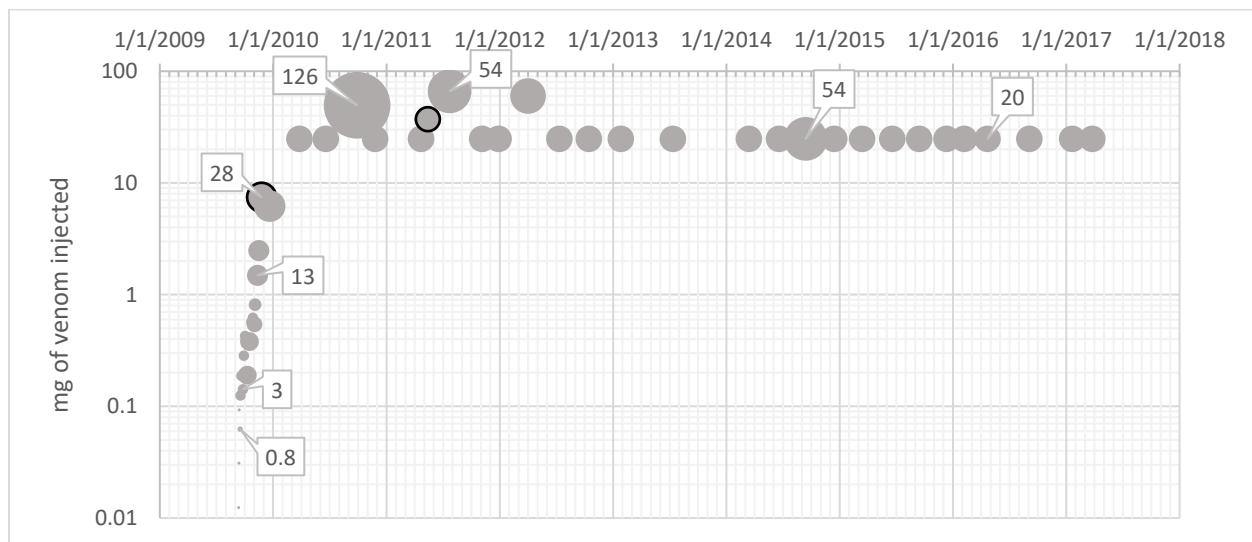
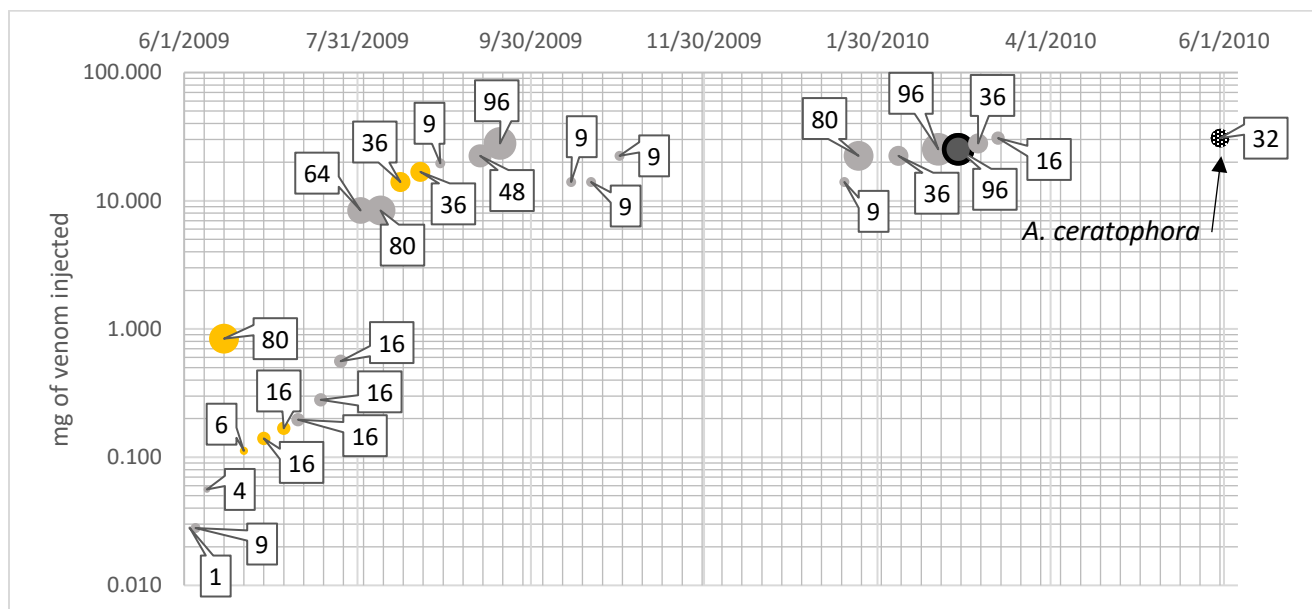


Figure 18 – *Crotalus atrox* (Western diamondback rattlesnake) immunization. *C. atrox* mdLD50 207.7 mg (dry 1.9 mg/kg). Bubble size callouts not all shown due to density. Two minor sterile

abscesses occurred shown with black outlines. The median swelling shown is 20 square inches, with the largest 126 square inches. Total of 47 injections.

This figure 18 series started with 0.012 mg of wet venom. It took 196 days to get to the booster maintenance level. At the time it was started, this participant had been immunizing for 9 years to other venoms.

2.8. V0008 immunization



3. Cohort bite data

3.1. V0001 Bites – *Crotalus atrox* and *Agkistrodon contortrix*

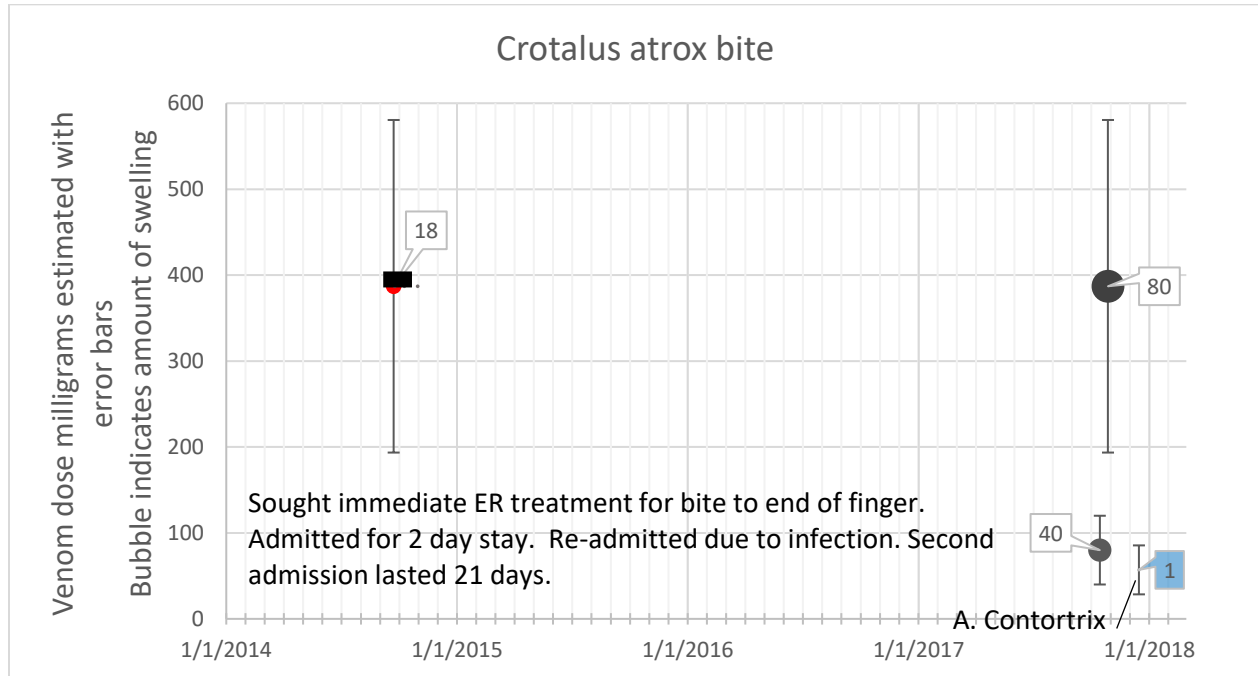


Figure 20 – *Crotalus atrox* and *Agkistrodon contortrix* bites. The first accidental bite occurred after 8 injections, having worked up to 0.5 mg of venom. *C. atrox* mdLD50 207.7 mg (dry 1.9 mg/kg). *A. contortrix* spp mdLD50 101.4 mg (dry 0.927 mg/kg). Red bubble indicates infection. Solid black line indicates hospitalization. Blue callout is *Agkistrodon contortrix* bite all others are *C. atrox*.

The first *C. atrox* bite of figure 20, at day 122 after starting venom vaccination injections, resulted in hospital admission for 2 days during which V0001 received 12 vials of antivenom. After discharge, there was an attempt at self-debridement of a small necrotic area at the tip of the finger. Home collected maggots were applied to the necrotic area of the fingertip. The wound became infected, and he was re-admitted for 21 days. The second stay included 3 debridements. Despite IV antibiotics, an infection persisted. Bacteria cultured were *Proteus mirabilis*, along with *Enterococcus* species and an unidentified lactose fermenter gram negative rod. These are common in wound infections found in hospitals as well as soil and the mouths

of snakes. An infectious disease specialist was consulted, new IV antibiotics prescribed, and the last joint of the finger was amputated.

Infections from rattlesnake bites are fairly rare^[3]. Maggot secretions are antibiotic against gram positive, but less so against the gram negative bacteria found^[4]. That maggot secretions are not effective against those species suggests the maggots as source. And *Proteus* and *Enterococcus spp* tend to be somewhat resistant to Levaquin normally. The bacteria found are nearly omnipresent environmentally and in the mouths of snakes, and V0001 works outdoors with contact with soil.

This case was treated with best practices by the medical facility in the area. The outcome is not related to vaccinations with *C. atrox* venom.

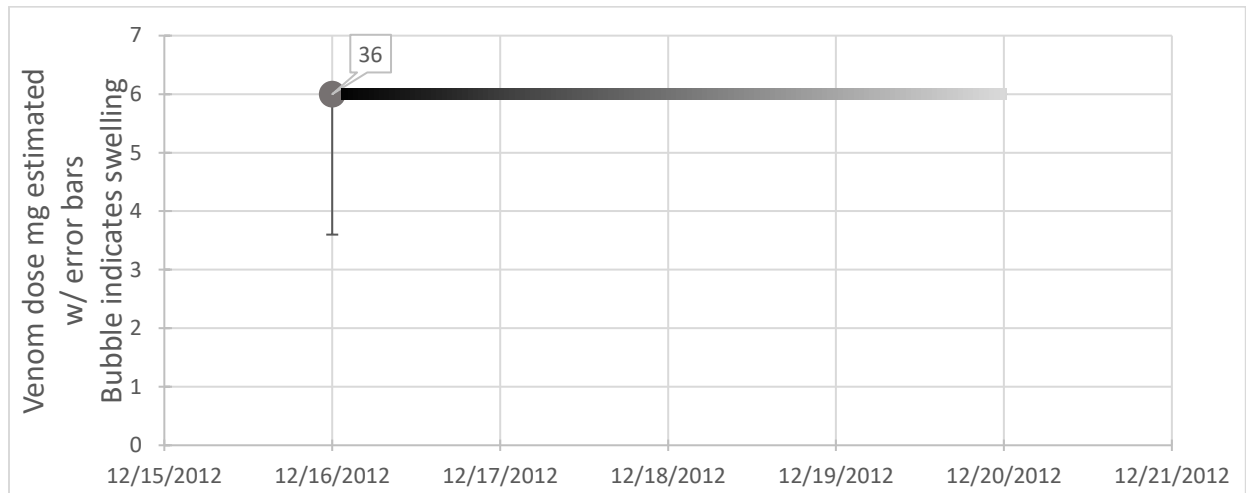
The second bite was 3 years and 22 days (1118 days), 45 *C. atrox* injections, and 102 *A. contortrix* injections after the first bite. The maximum injection received prior to this bite was 30 mg of wet venom. The third bite was 13 days after the second bite. Neither the second nor the third bite was treated with antivenom, and no medical treatment was sought. Swelling and pain began to recede within 36 hours for both, with recovery in 72-75 hours. The single *A. contortrix* bite resulted in very little swelling, roughly the pain of a wasp sting, with complete recovery reported within 2 hours.

3.2. V0002 bites – *Crotalus spp.* Data not shown.

This participant had 3 serious rattlesnake bites, all to the fingers, 2 bites after immunizing and one prior. The first bite to the pinky finger, prior to immunizations, was treated medically with antivenom during 2 days hospitalization, and resulted in a fused joint, scarring and long-term nerve damage. The second bite, which was post-immunization, was treated in hospital for 2 days with pain medication and fluids, but no antivenom. Some skin of the index finger sloughed off a week later revealing new skin. There were no long-term sequelae. Third bite to the middle finger was not treated medically. There was swelling and pain with a small spot of necrosis at the tip. Some nerve damage occurred initially, but this healed within 3 months. Several other dry bites which

did not have significant symptoms were reported. These bites are not included in the cohort totals due to incomplete records.

3.3. V0003 bite – *Agkistrodon halys blomhoffii*



*Figure 21 – This intentional *Agkistrodon halys blomhoffii* (Japanese Mamushi) bite occurred after 42 injections of progressively higher doses across 353 days. *A. h. blomhoffii* mdLD50 694.3 mg (dry 6.35 mg/kg). Gray line indicates recovery time without medical help.*

This bite in figure 21 bite was untreated. V0003 performed his normal work duties throughout his recovery. There was no necrosis, no abscess, no infection, and no anaphylaxis. By 12/20/2012, recovery was complete. Approximately 10 out of 2,000 to 3,000 Mamushi bites per year are fatal. It can cause great distress and significant tissue destruction without antivenom. LD50 can miss significant bite issues.

3.4. V0007 bites

V0007's 132 bites is an extraordinary number. One pair of cobra bites after 9 months after initiating venom immunization, where the bites were received approximately 1 hour apart, required hospitalization (fig. 27). No antivenom has been administered for any bite. This section starts with an observation that was done of V0007 by the primary investigator during a visit to validate that claimed bites were real. V0007 had recently moved and had the snakes in plastic containers with lids. There was no visible attempt to

interact with them in the almost 48 hours prior to the bite. V0007 planned a bite from *O. scutulatus*. The mamba bite that occurred was an accident during transfer of the snake into a display case. The primary investigator watched this from roughly 8 feet, including the strike.

3.4.1. Direct observation and vital signs after a *Dendroaspis polylepis* bite

This first detail of a black mamba bite (*Dendroaspis polylepis*) was observed directly and vital signs taken during the course as documented in figures 22-26. The previous day the same data was taken for a wasp sting.

This observation series included an attempt to compare pain scales between wasp/bee stings and snake bites. On a scale of 1-10, the wasp sting rated a 2 out of 10. Starr rated *Polistes fuscatus* 2 out of 5 in his 1985 paper^[5]. Discussing the difference with V0007, the wasp sting was rated lower because the pain was much shorter in duration, and the peak was not as high.

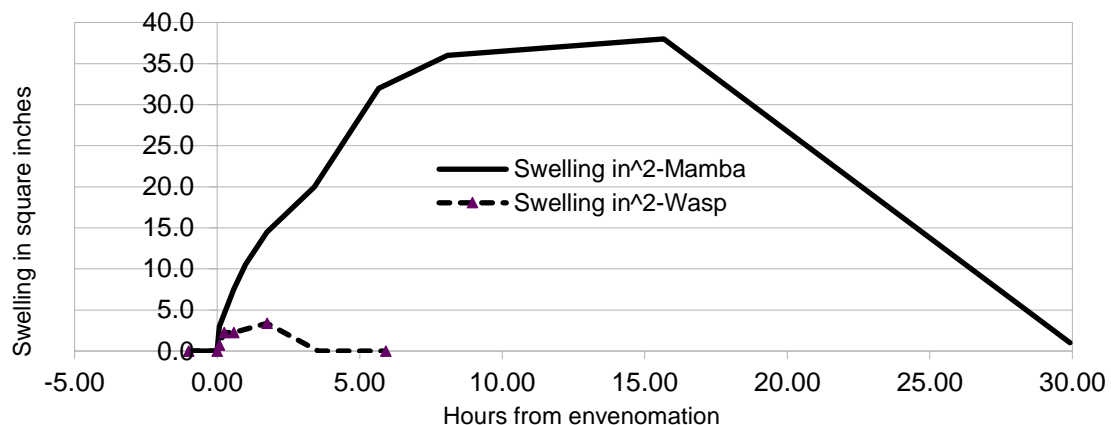


Figure 22 – Comparison of swelling from *Dendroaspis polylepis* (Black mamba) to *Polistes fuscatus* (Northern paper wasp).

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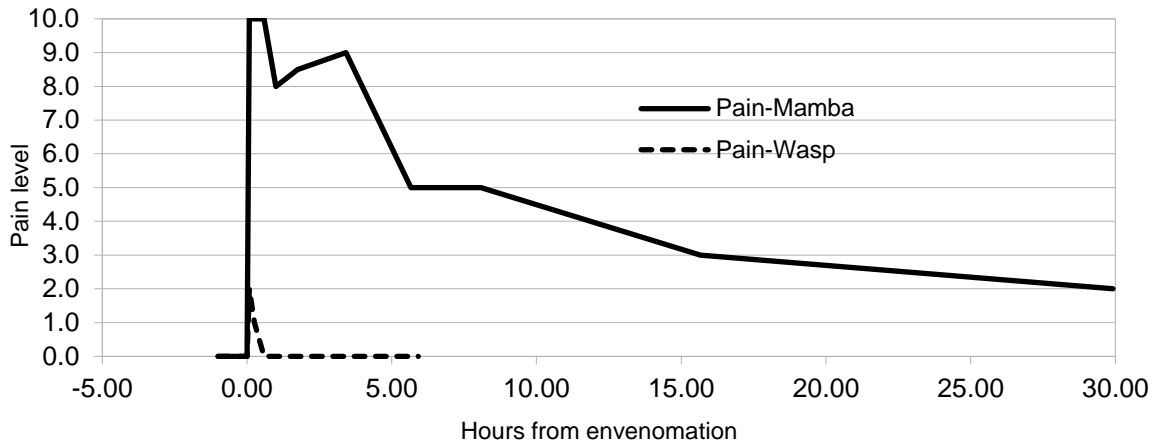


Figure 23 – Comparison of pain scale *Dendroaspis polylepis* (Black mamba) to *Polistes fuscatus* (Northern paper wasp).

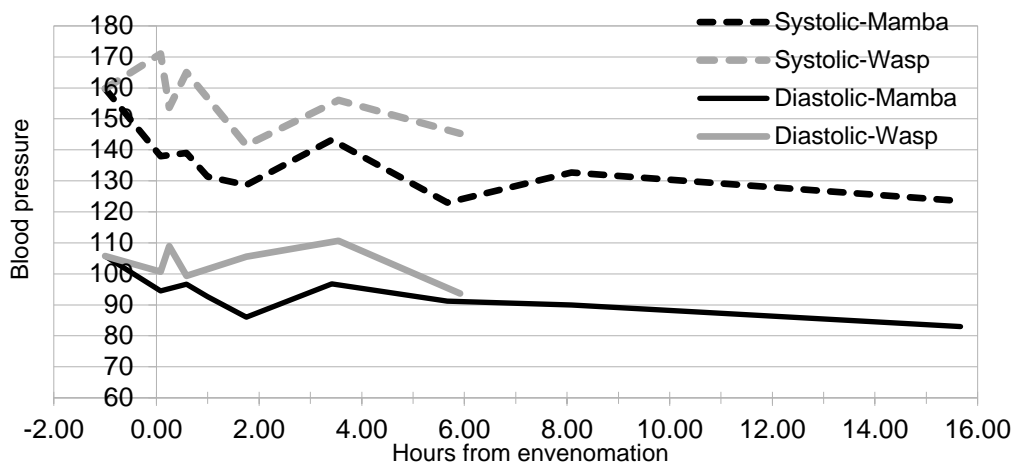


Figure 24 – Comparison of blood pressure, *Dendroaspis polylepis* (Black mamba) to *Polistes fuscatus* (Northern paper wasp).

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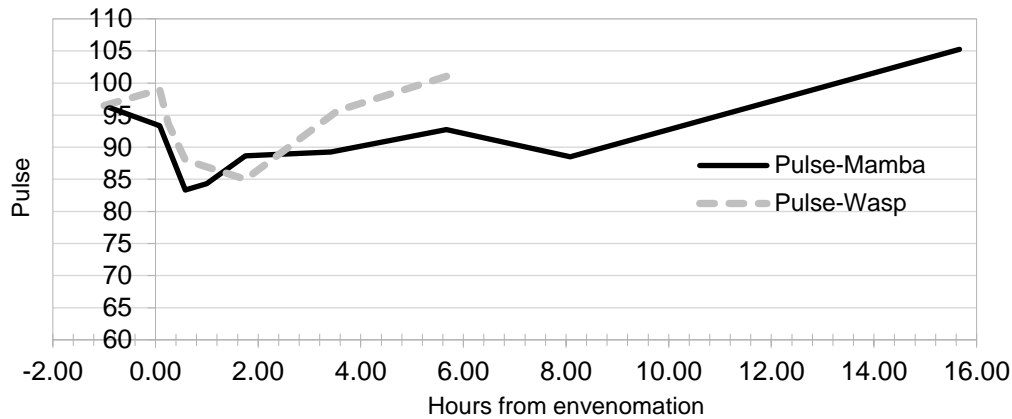


Figure 25 – Comparison of pulse, *Dendroaspis polylepis* (Black mamba) to *Polistes fuscatus* (Northern paper wasp)

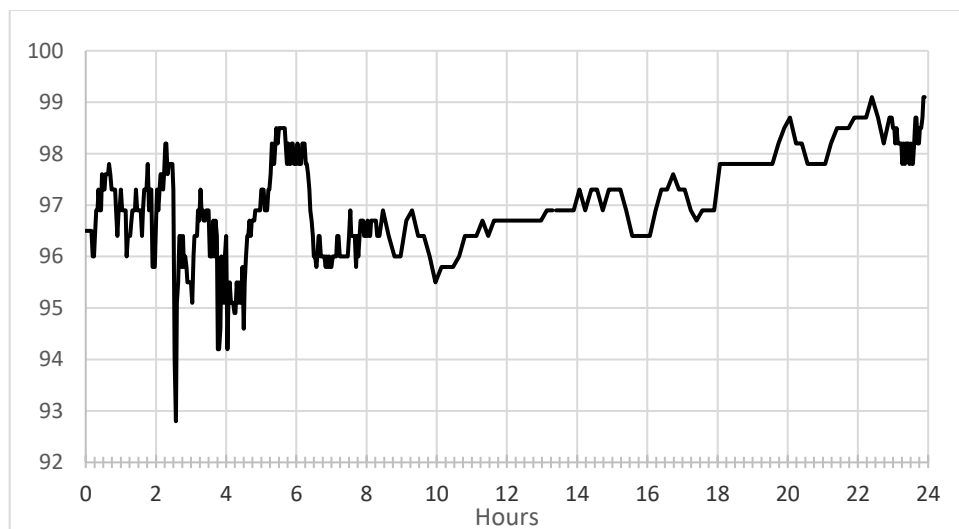


Figure 26 – Armpit temperature in Fahrenheit. *Dendroaspis polylepis* (Black mamba) bite at time zero. Swelling was mostly gone after 25 hours, but full recovery took 48 hours.

Figure 26 temperature data, has ear temperature from time zero substituted for the first 10 minutes instead of the armpit temperature because the patch did not come up to equilibrium for about 10 minutes and the accidental bite was not properly prepared for. Some of the fluctuation is probably movement related. However, the venom appeared to produce some sedative effects in the first few hours.

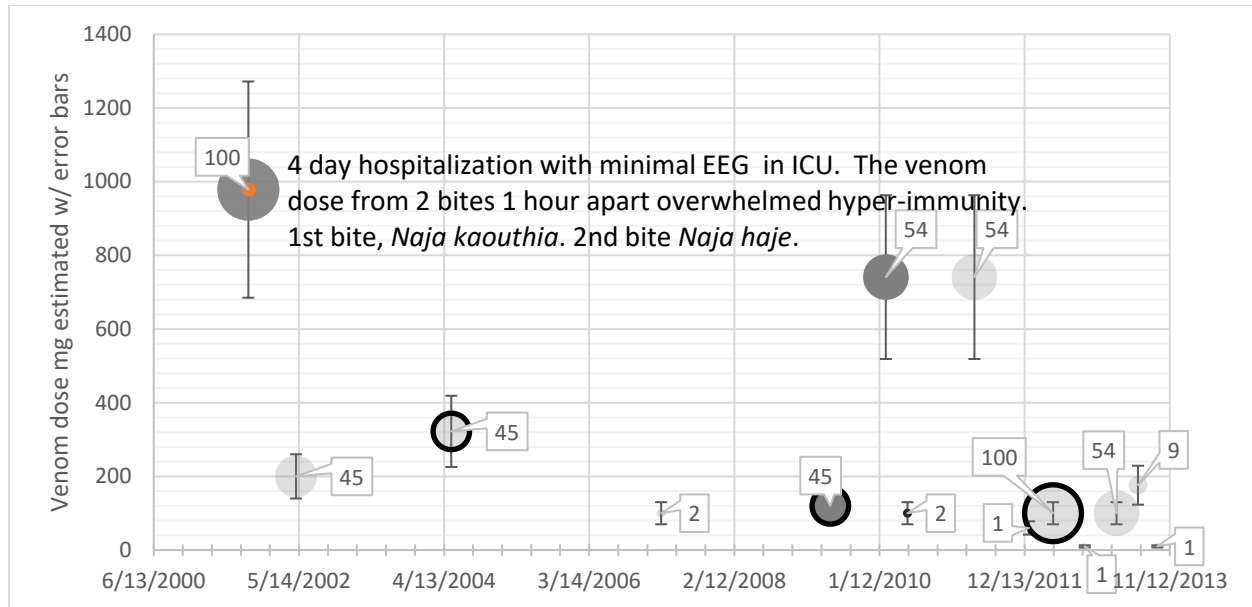
3.4.2. Bites – *Naja* spp.

Figure 27 – *Naja haje* (Egyptian cobra), *Naja kaouthia* (Monocled cobra), *Naja nivea* (Cape cobra) bites. Black ring indicates abscess and necrosis. No medical care was sought for any bites except the first one. *N. haje*. mdLD50 82.0 mg (dry 0.75 mg/kg). *N. kaouthia* mdLD50 25.0 mg (dry 0.229 mg/kg). *N. nivea* mdLD50 36.5 mg (dry 0.334 mg/kg). Total of 15 bites.

The venom dose in figure 27 on the far left that caused hospitalization from the 2 bites 1 hour apart overwhelmed hyper-immunity at this stage. The first bite was intentional, done in milking style into the right bicep. The second bite was not intended. After the second bite, it took approximately 20 minutes for paralytic effect to set in. Recovery of consciousness took 3 days. After discharge it took a month to fully recover from the local effects. Pain scale for these bites averaged 8 out of 10. However, the 4 bubbles in dark gray were rated 15, 13, 12, and 15 out of 10 for pain¹. The small 2 square inch bubble on 5/27/2010 was a finger bite rated 15 out of 10 for pain. Full recovery from local effects of most bites took 2 to 3 weeks. Three sterile abscesses occurred which required drainage.

¹ Despite requests to stay within the boundaries of 1-10, the reporting of pain outside the scale persisted. We take this as a way of communicating intensity and duration. Pain is one of those things that can have new heights one could not imagine before experiencing them. So we decided to accept pain scale assessments that were off the chart.

3.4.3. Bites – *Dendroaspis* spp.

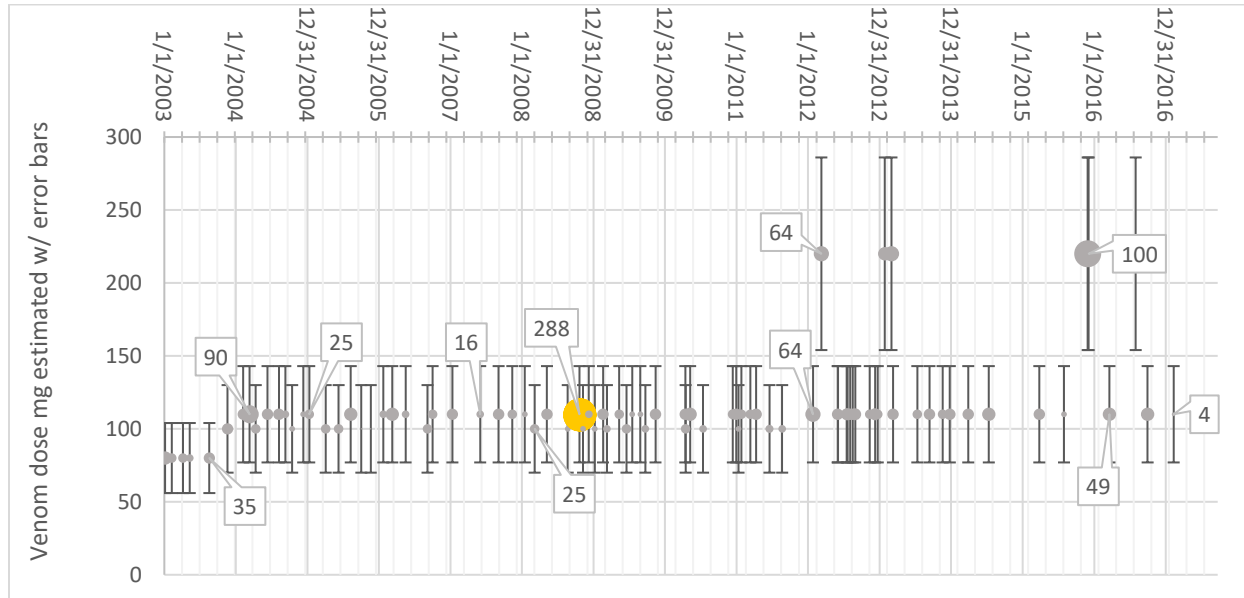


Figure 28 – *Dendroaspis angusticeps* (Eastern green mamba), *D. viridis* (Western green mamba), *D. jamesoni* (Jameson's mamba), and *D. polylepis* bites (Black mamba). Yellow indicates anaphylaxis, severe hives in this case. No antivenom or medical treatment occurred for these bites. *Dendroaspis angusticeps* mdLD50 113.7 mg (dry 1.04 mg/kg). *D. viridis* mdLD50 77.6 mg (dry 0.71 mg/kg). *D. polylepis* mdLD50 35 mg (dry 0.32 mg/kg). *D. jamesoni* mdLD50 91.8 mg (dry 0.84 mg/kg). Total of 92 bites.

Figure 28 shows 92 bites from these 4 *Dendroaspis* spp. These bites averaged 6 out of 10 for pain. However, V0007 rated the anaphylaxis bite as a 15 for pain. Another, visible as the large bubble in the upper series second from right, was a double bite on 12/4/2016 that was rated at 12 out of 10 for pain. The first anaphylactic bite on 12/8/2008 caused large hives for 3 hours. Recovery from these bites took 48 hours. The double bite on 12/4/2015 may have had some IgE component, but aside from swelling it had no anaphylactic signs.

3.4.4. Bites – *Crotalus scutulatus*

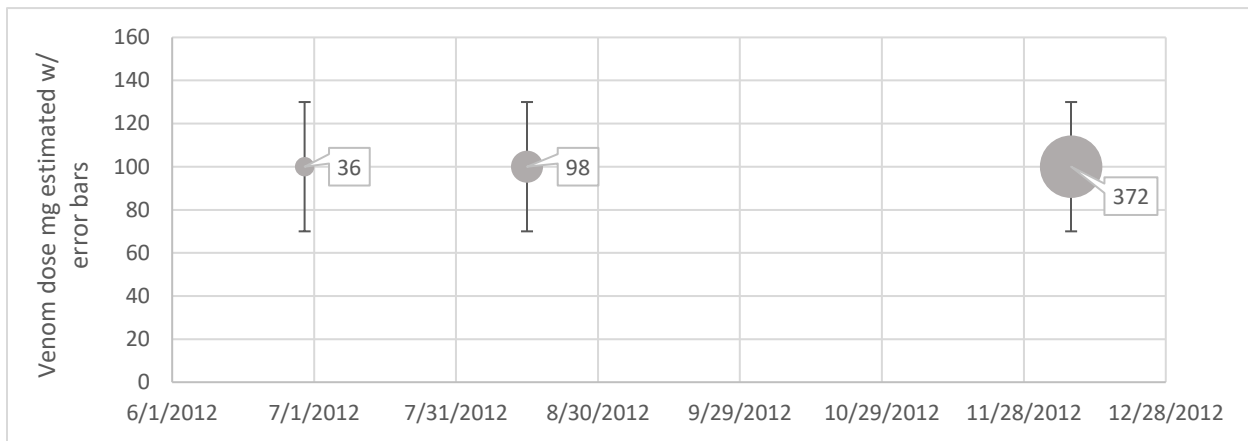


Figure 29 – *Crotalus scutulatus* (Mojave rattlesnake) bites. No medical care was sought for these bites. *C. scutulatus* mdLD50 21.3 mg (dry 0.195 mg/kg).

These 3 *Crotalus scutulatus* bites of figure 29 averaged 8 out of 10 for pain, with range from 6 to 10. Recovery took 24-36 hours.

3.4.5. Bites – *Naja annulata*

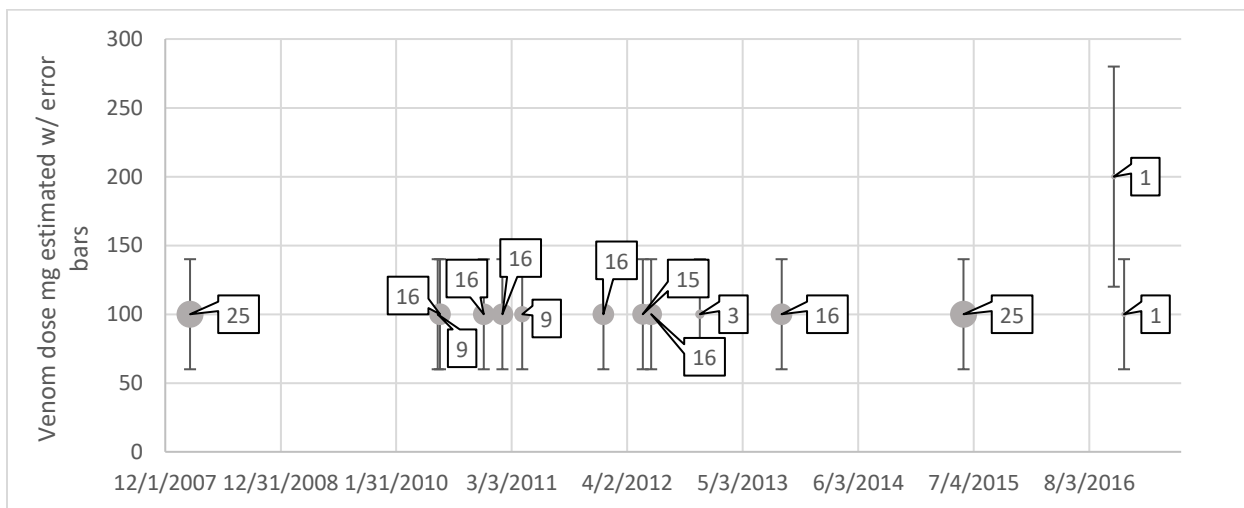


Figure 30 – *Naja annulata* (Banded water cobra) bites. High value is a double bite. *N. h. annulata* LD50 15.6 mg (dry 0.143 mg/kg). Total of 15 bites.

These 15 *Naja annulata* bites of figure 30 averaged 3.86 out of 10 for pain, with range from 2 to 5.

3.4.6. Bites – *Oxyuranus scutellatus*

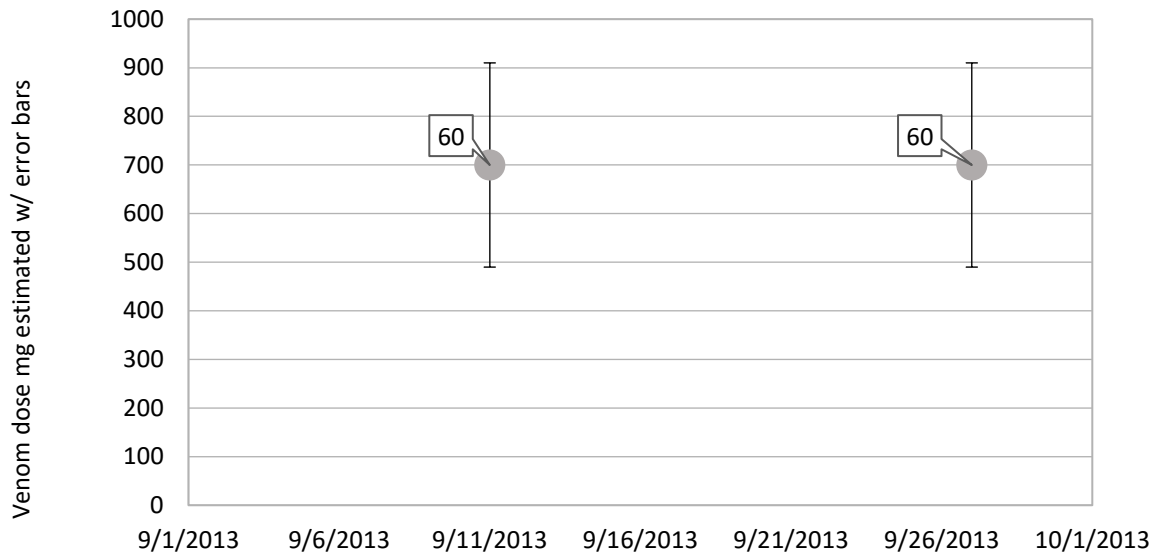


Figure 31 – *Oxyuranus scutellatus* (Coastal taipan) bites. Both of these are double bites. *O. scutellatus* mdLD50 6.2 mg (dry 0.057 mg/kg).

Both of the figure 31 *Oxyuranus scutellatus* bites were rated 8 out of 10 on the pain scale, and both resulted in 48 hours of swelling from knuckles to elbow.

3.4.7. Bites – *Crotalus atrox*

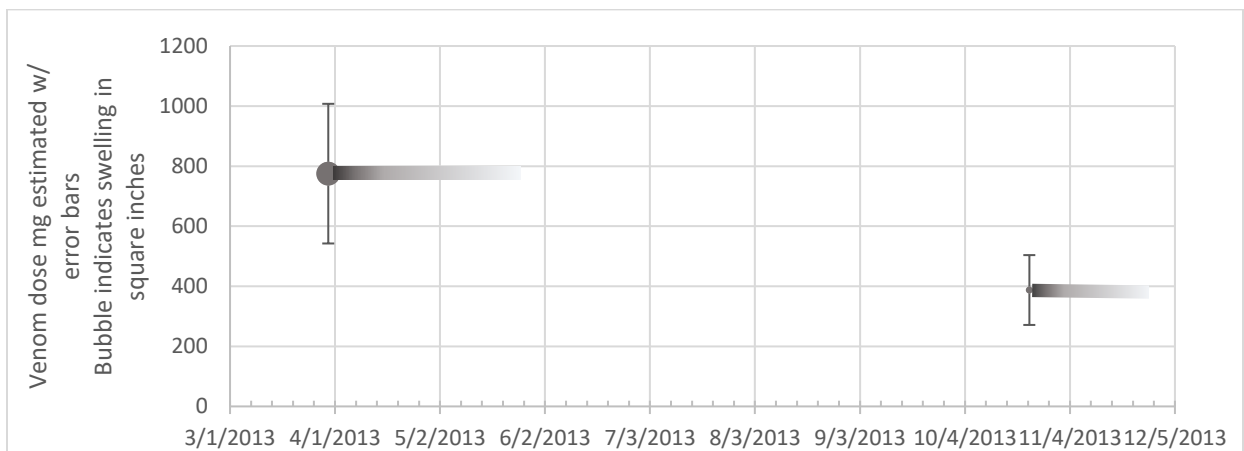


Figure 32 – *Crotalus atrox* (Western diamondback rattlesnake) bites. First bite was a double bite on 4 knuckles. Second bite was a finger bite. *C. atrox* LD 207.7 mg (dry 1.9 mg/kg). Complete recovery time from local effects shown as gray lines.

VIPRBITEM cohort study

The bites of figure 32 were painful, rating 10 out of 10, and had the longest recoveries. In both cases, most effects were over in 72 hours. However, for these bites, complete recovery from discomfort in the affected limb, and feelings of malaise required 30-60 days. For the first bites on 3/30/2013, complete recovery took two months. For the second, a finger bite, recovery took a month. No medical help was sought and recovery was complete. There are no long-term sequelae to muscles, tendons, or joints 5 years later. However, V0007 found Western diamondback bites so unpleasant he has been reluctant to demonstrate immunity from such bites.

3.5. V0008 bite – *Atheris squamigera*

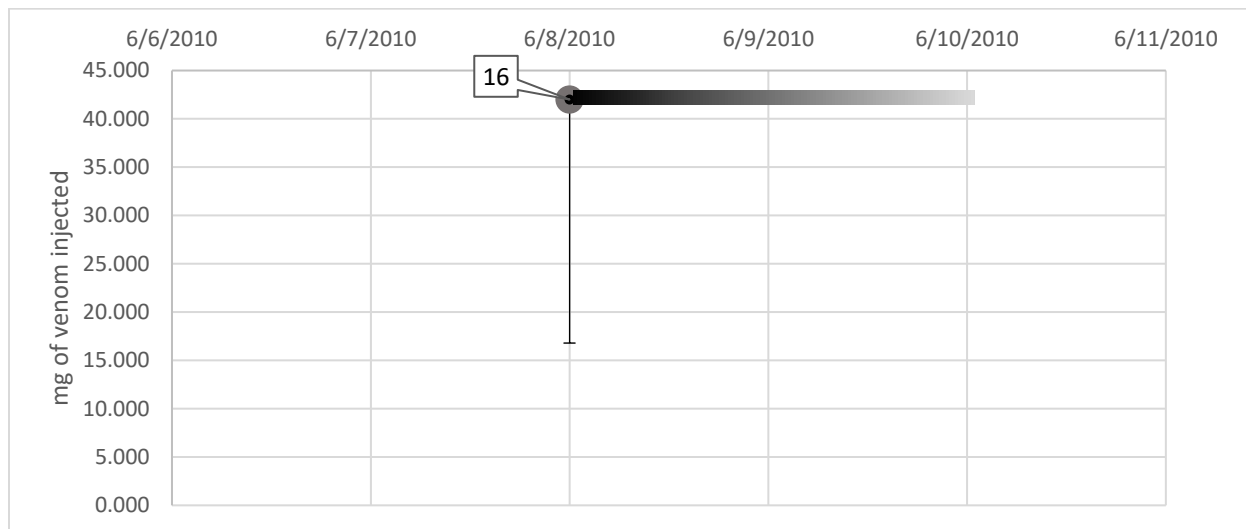


Figure 33 – *Atheris squamigera* (African bush viper) bite. *A. squamigera* LD50 66.8 mg (dry 0.611 mg/kg). Finger bite was rated 10 out of 10 for pain. Gray line shows recovery days.

4. Expanded ethics discussion

Because this type of experiment is not very common, and often misunderstood, an expanded discussion is appropriate. Although we did it, ethics review was not required for this study except for blood draws. We stepped through our data collection with the IRB and received retroactive approval anyway.

First, these are self-experimenters operating independently, Nuremberg principle 5 discusses self-experimentation positively, and Helsinki is built on Nuremberg^[6]. Second, ethics review was created to protect subjects from researchers with unconscionable or dangerous protocols. This cohort is composed of people who had already been practicing immunization with venom, and the investigator did not design their practices, nor direct them to perform these procedures. Thus, there is no place to intervene per the Helsinki paradigm. Third, the study was initiated by request. The input of the lead investigator with the cohort was limited to harm reduction commentary, monitoring, and working with the group to define a spreadsheet format. Protocols were all defined and implemented by the participants which renders them self-experiments.

5. References

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