A Personal Essay on Venom Allergy

Brad Metz

Since a warm Spring Day in 2006, I can tell you the exact number of stings I've taken: eight. But I have utterly lost count of the number of times I've been voluntarily injected with purified honey bee venom, taken epinephrine, or popped a couple of pills and sat quietly in the dark, hoping I don't have to call an ambulance, losing a day's worth of work, and a shocking amount of money. If you haven't guessed, I have developed an extreme allergic response to being stung by honey bees, and yet I remain a honey bee researcher.

I'm writing this because I have a big mouth; whenever I talk long enough about my work with bees, my allergy comes out. Inevitably, then, I get questions about this difficulty of mine. Refreshingly, in an audience of fellow beekeepers and researchers, the "whys" are rare. If you know, you know, and beekeepers know. Increasingly though, I've bumped into people who have suffered like I have, and either stay on the sidelines or have regretfully left the game behind. But after years doing the latter, I was finally convinced by my colleagues, friends, spouse and future boss to get treatment. Many of the questions I get are about that. So, in the hopes of helping anyone going through what I did, understand the honey bee allergy from the patient perspective, here's my story.

I came up working bees in Texas, where highly defensive bees are the norm. We took stings regularly; zippered veils and long sleeves underneath our suits couldn't entirely prevent the pugnacious little buggers getting through a tight fold, a seam edge, or sweat spot. We even had annual sting parties, taking turns to tag each other so we would get that first higher reaction out of the way after the dearth months of Winter gave our immune responses time to build up. For the first years of my graduate studies, my stings were familiar to any of you. There'd be some pain, a little redness, and some swelling. Nothing that a swift scrape of a card, bee tool or handy scalpel (and swearing) wouldn't fix. Over time, though the swelling increased, and the redness intensified. I counted knuckles, if the swelling passed a knuckle, I'd take a Benadryl, if the swelling didn't go down after a few hours, I'd take another. If the swelling ever crossed two knuckles, I was supposed to take an epinephrine shot and call a doctor. Finger knuckles are short, so that didn't count – so I told myself. If the swelling ever passed my wrist, I'd go for help. There'd be days when my whole hand swelled so badly, I couldn't get into a glove. But being stung in other places, the swelling wasn't debilitating, and didn't cross two knuckles, so I took Benadryl and kept at it. I proceeded this way for years. I loved my work. Like most graduate students, I had an obsessive drive fed by the similar obsessions of those around me. We wore our stings like badges of pride. In a bar full of net-wielding geeks and white-coated pipette jockeys, we smelled like smoke and had war wounds. But nevertheless, the annoyance of being stung gave way to "concern" over the next one. That made me a worse beekeeper, which exacerbated the stings. I kept on, but the shine was wearing off and I started running from my hives after working them to take deep breaths, hiding in bushes to get away from the engine drone of angry workers. Towards the end of my PhD, the bee work lightened up and my interactions with bees came fewer and farther between. That seemed good for someone who was increasingly a liability in the field, but that was the final straw for my immune system.

I was working a colony at our lovely lakeside apiary. I was being quick about it because I had a bunch of cages to take care of in the trailers, and I was nervous. Two stings hit right to the inside of my elbow where the elastic from the glove pinches the sleeve. I only had a T-shirt on underneath – it was so hot, and I didn't have it in me to layer. Immediately, I knew something was wrong. I tasted blood and my head started ringing, by the time I got back to the trailers and got to my phone, I couldn't see anymore. I remember the woman on the 911 call yelling at me to stay conscious, but it wasn't happening. Next thing I know there's two paramedics slapping me awake and asking questions I didn't understand. When I could talk, I asked them to carry me to the restroom. By the time I took the ambulance ride to the ER, I felt fine, exhausted, but fine. I was annoyed because I'd left an experiment running and the timing, while not ruined, wouldn't be as clean as I wanted. The doctor told me I couldn't possibly have had an allergic reaction because I wasn't still dying. He recommended I see an allergist and sent me on my way.

A few weeks later, the allergist – I remember he had huge hands, so I trusted that he worked hard – told me that he couldn't provoke an allergic reaction with his skin tests. Whatever this was, wasn't an allergy, so I went back to work. When the inevitable happened, my academic big brother drove me to the ER while I vomited out the side of our lab truck. Once again, the fact that I was returning to a normal state of being by the time doctors saw me was cited as fact that I wasn't having an anaphylactic reaction. Further consults with my allergist led to discussions of a vasovagal syncope, which was described to me as what brides do at weddings. I was offered an anti-anxiety drug as a potential remedy. My own foolhardy relationship with psychiatry, along with the "good ole' boy" doctor's disdainful discussion of my "reaction" meant that we ultimately did nothing. Insofar as I understood, no medical remedy existed.

For the next two years, my life went thusly: I'd work bees, get stung, pass out in the field, wake up, vomit, and go back to work. Sometimes people were around; sometimes they weren't. I learned that after taking a sting, I had forty seconds to get somewhere safe before losing consciousness. Once I miscalculated and landed on a fire ant nest. My main innovation during this period was that if I could elevate my legs, I could keep the blood pressure to my brain high enough to retain consciousness. This left me helpless, but at least vocally so. Needless to say, I planned my exit from bee research, and it was a short hop to phasing out of research altogether. My story was set to end there, I began a teaching career, and figured I was terminally separated from bees. I returned my lab-issued suit and veil. I put my mead-making supplies into storage. I stopped going to bee meetings.

It was seven years later that I moved to North Carolina. I'd raised my children through their infant years, and they were ready for school; they didn't need a stay-at-home dad anymore. It was a lark that I found that Dr. David Tarpy at NC State was hiring a research position. I was shocked by how much I missed the work. My wife and I argued; she didn't like the idea, but ultimately agreed that I'd been missing some "spark" that she'd known for so long. I figured as long as I was honest with him, Dr. Tarpy could make the choice about whether I'd still have any utility in a bee lab, given that I couldn't touch bees much. Luckily, he had a project on drones. We figured the one honey bee that couldn't sting, shouldn't do much damage. I became the drone guy; but Dr. Tarpy also hired me with a qualification: go see an allergist again. It seemed a reasonable enough request; maybe I could get some cheap epipens and peace of mind.

Meeting Dr. McWilliams was the first time I'd seen a physician visibly angry during an appointment. While describing my experiences, she kept coming back to a single point: my lack of local reaction. Once I started fainting, I no longer swelled up, there was no need to count knuckles, and there was little local pain. To Dr. McWilliams, this was a sign that despite the oddities, what I was experiencing was an anaphylactic reaction, and one that she'd expect any physician to recognize. The next step was to prove it through allergy tests. I sat in a room hooked up to monitors for several hours as I was injected with miniscule doses of honey bee venom, and then waited, nurses at the ready with injections of epinephrine and their "crash cart," just in case. The ascending doses left me nonplussed, nurses at attention, but starting to wonder if anything would happen. I didn't swell, no redness, barely any reaction. We reached the maximum standard testing dose without any reaction, and so we went further. At nearly a full sting, I went horizontal mid-sentence. When I came to, we had our diagnoses and could start doing something about it. Crucially, getting my life back was the goal. Dr. McWilliams never once told me to quit working with bees; instead, she said: "since avoiding bees isn't an option for you, let's get you to where you're safe." This meant everything to me. At the time, I was told the process could take around six months before I could take a full sting, with the completion of the immunotherapy in around three years. Little did I know that it would take me seven to life.

Venom immunotherapy is a fairly straightforward process, although it takes a great deal of care and monitoring. Essentially, we went about training my immune system to ignore honey bee venom as much as possible. This goes a little against what both the venom and the immune system is designed to do. Honey bee venom has proteins to invoke a massive immune response, tear cells and membranes open to spread itself, and deploy histamines – the very communication molecule our cells use – to provoke a reaction. All of this to make sure that any mammal that gets stung is properly repulsed. Our immune system, on the other hand, responds aggressively to anything that isn't supposed to be there, and there are a wide variety of cells involved in the recognition of such things and coordinating the appropriate response. In an allergic reaction, the recognition molecule is IgE – a class of antibody and the major coordinator cell is the mast cell. These mast cells are packed with signal amplifiers, histamines among them, and release these to recruit an ever-wider array of responsive cells and protein pathways. This can result in a cascading response that, like a nuclear meltdown, builds upon itself in extreme and unpredictable ways. In my case, it drops my blood pressure to the point where I no longer can maintain oxygen to my brain, losing consciousness. That's why laying down with my legs up worked, using gravity when my circulatory system couldn't do the job.

To complicate matters, I have a condition called mastocytosis – which means I produce an overabundance of mast cells. Like most people with this disorder, I have a fairly benign version that manifests in a higher propensity towards allergies and the need to take bone marrow stimulants to maintain bone density: I use my marrow extensively to make all those mast cells. But the real kicker is that one of the most common symptoms of mastocytosis is *an extreme allergic reaction to venom!* Because of this, I was prone to sudden and extreme reactions, and the only response was to scale up my venom dose very slowly. A normal progression would involve a weekly shot of diluted venom in an ascending concentration of about 30% each iteration until a maintenance dose of about two stings worth of venom is reached, at which point the shot frequency is slowly increased to once a month. At this point, most people can conclude treatment with no further ill effects. In my case, we had to increase the frequency of the shots at first and increment the dosing at much lower rates, going so far as to repeatedly inject the same dose for a few weeks before attempting the next. Even with this, I occasionally lost consciousness in the office and once, terrifyingly, on the drive home. Every time I fainted, we had to start back over again at a lower dose and work back up. Happily, more quickly than the last time. My immune system was a slow learner, but it *was* learning. In 2019, I reached maintenance dose for the first time, with a great deal of pride. The next step was to stretch out the doses, which I had to do a single day at a time, because any more than that knocked me out. So now I was operating on a strange rotating schedule that had to work carefully around weekends and other commitments, but we got through it to monthly shots: maintenance. It wasn't until 2020 that I got my first test of the efficacy of the treatment.

A young researcher primarily focused on interactions among

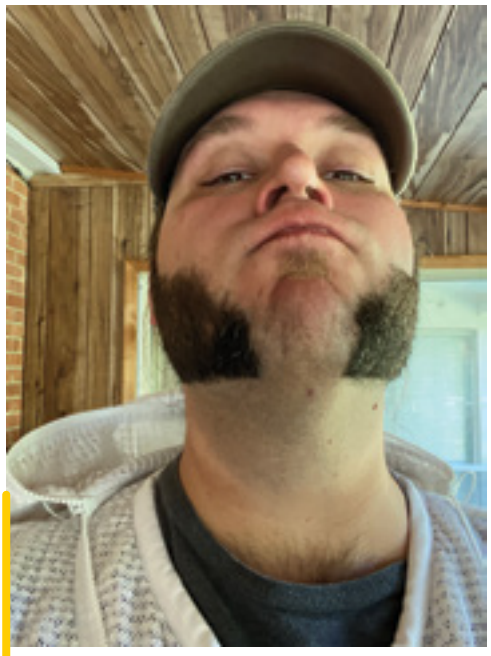

Figure 1. The author, thirteen minutes after being stung, demonstrating both the efficacy of venom immunotherapy and the foolishness of pressing one's face up against their veil to get a real good look. Some things, doctors can't fix.

pollinators at flowers often used our facility as an observation site. Not being a beekeeper, they rarely considered defensiveness in their dress or approach, relying on the gentleness of most insects at flowers as protection. But in June (robbing season here in NC) their long hair managed to capture a half-dozen bees while walking between patches, right through a flyway between colony groups. When they ran (barefoot) into the house where I was paint-marking my drones, I could do nothing other than help. Despite my care, I took two stings to the back. They were minor, through cloth, the stinger didn't stick, but immediately I was alert. I felt my pulse quicken, a familiar light-headedness set in, the taste of iron on my tongue. I grabbed my epinephrine, quickly ate two Benadryl and sat down, legs propped up on the table, bracing until the last possible second to use the epinephrine, because of course THEN I would have to go to the hospital, and abandon my experiment. The years have taught me a lot, but not a lot of sense. But the reaction stopped there, and I felt better in about an hour. I called Dr. McWilliams, and she recommended an extra dose of antihistamines, some monitoring, and otherwise it looked like the immunotherapy was working.

I've been stung three times since then. I'm never so cavalier as I once was. Every sting is accompanied by a cessation of work, a cup of water, and the slow count to forty. But each time, I've stayed afloat, and slowly, I'm back to enjoying working bees. As long as I live, monthly venom shots will be part of my routine, and my purse always has a pair of epinephrine shots in it just in case. My days of carefree independence are over; but I can work bees with a partner, I can go out in the field, and most importantly, I can feed that undying obsession with the whys and the hows of honey bees that put me into the apiary over twenty years ago and kept me coming back despite everything.

Venom allergy presents in about 30% of beekeepers. This can turn that joy of working with our smallest "domesticated" animal into fear or regret. But for the vast majority, there are treatment options that are relatively easy, and effective. Something like 80% of people that suffer anaphylactic reactions can recover with immunotherapy. Those with a less intensive reaction can get by with antihistamines. Anyone who notices changes to their reactions to bee stings should contact an allergist sooner rather than later, since they can provide peace of mind where therapy isn't warranted. In my case, the journey was more fraught, but the lesson here is that sometimes, persistence and a competent second opinion, can get you where you need to be in the end. BC

Author Bio

Brad Metz is a researcher under Dr. David Tarpy of the NC State Apiculture Program. He is the lead scientist in charge of the Honey Bee Queen & Disease Clinic and runs a small research program concerning honey bee male reproduction and quality. He earned his PhD from Texas A&M in 2009 where he studied honey bee chemical communication. Brad is married with two children, both of whom think working with stinging insects is crazy, despite his best efforts to convince his own larvae otherwise.