EPISODE 28. SNAKEBITE GURUS REVEAL UNTOLD TRUTHS

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Garry Aslanyan [00:00:08] Hello and welcome to the Global Health Matters podcast. I'm your host, Garry Aslanyan. In this episode, we will be discussing Snakebite. This topic was suggested by one of our podcast fans and a partner organization, Fiocruz, the Oswaldo Cruz Foundation in Brazil. I must admit I was a bit worried about how we can tackle this complex and at times not well known public health issue. But after three very engaging discussions with my guests, all doubt and trepidation have disappeared, as to the importance and relevance of snakebite as a critical global health issue. The World Health Organization (WHO) estimates that 5.4 million people are bitten by snakes every year and nearly 140,000 people die. In this episode, we will be discussing the realities of snakebites at community level, as well as the complexities associated with producing and administering antivenom. I'm joined by Diogo Martins, the research lead for snakebite at Wellcome in the United Kingdom. Later in this episode, you will also hear from two other guests from Brazil and Eswatini.

Garry Aslanyan [00:01:25] Hi Diogo, thanks for joining me today. Really looking forward to speaking to you about this topic. So what struck me most in doing this episode is that very few of us who work in global health would consider snakebite as a pertinent global health issue. Why do you think that is?

Diogo Martins [00:01:49] Hi Garry, good to see you. And let me start by saying you have an incredible microphone. I'm very, very jealous. So it's really nice to give that microphone and the podcast sort of the stage to snakebite and I couldn't agree more with you. Snakebite oftentimes doesn't find the right place anywhere. It is a global health issue in my perspective, because it's an issue that transcends boundaries of countries. So it really transcends, just a disease that happens in an underserved location in country A or B, it really brings together so many of those problems in a way that a person suffering from snakebite, or having had an issue or an episode in their families of snakebite in country A, it will probably going to be replicated somewhere else. And sometimes those problems are addressed by solutions that also transcend those national boundaries. So for that reason, in my perspective, when the problem is global, when the solutions are global, to me, that's a global health issue; beyond countries, beyond just one community, it's an issue that brings in different communities. And snakebite is that. But we have so many different global health priorities, sometimes it's really hard to climb the ladder of priorities in global health because resources are still limited.

Garry Aslanyan [00:03:11] So for that reason, you think it deserves the attention.

Diogo Martins [00:03:14] The burden is quite big. And we do know that in snakebite, about 5 million people are bitten every year. Not all of those bites are venomous bites, more or less 2 to 2.5 are venomous bites, and we do know that out of those 2 million bites, venomous ones, a lot of people will die. We're talking about 100,000 deaths every year and this is most likely an underestimation. And four times more of that will live for the rest of their lives with, unfortunately, amputations, PTSD, and that's a huge burden. And we've done a little bit of desk research about how that compares with many other popular global health issues, and it's actually quite a substantial amount of years lived with disability and it's quite expressive that people just do not know much about it because it feels a little bit remote to many of us, unfortunately.

Garry Aslanyan [00:04:03] And venomous means poisonous, just to be clear?

Diogo Martins [00:04:07] Well, for simplicity, we could say so. If you're talking with an animal expert or a wildlife expert, they'll probably say it's not exactly the same. It's about the way the particular venom or poison is injected. So, for example, snakes are venomous because they have a mechanism to inject you with a venom. For example, if you look at a different species, some of the frogs are poisonous because just by touching the surface of skin, the modus of getting those toxins into your system are quite different. So, for simplicity, let's not overcomplicate because it's already so complex, we don't want to alienate anyone.

Garry Aslanyan [00:04:47] So for this episode, I was able to speak to some champions who are working to address this neglected issue of snakebite. One of them was Dr Fan Hui Wen. She's a scientist and a project director at the Instituto Butantan in Brazil. So this institute is one of the oldest public health funded research institutions in Brazil and is actually quite a big producer of antivenom, both in Brazil and South America. I also spoke with Thea Litschka-Koen. She's from Eswatini. She is the founder of the Eswatini Antivenom Foundation. She's a real forerunner in the community, in the prevention and management of snakebite. So maybe, Diogo, we can start by listening to their stories of how they became involved in this issue. Let's start with Dr Fan.

Dr Fan Hui Wen [00:05:44] Well, my story starts when I was a child and my family used to come to the Institute of Butantan, especially when relatives come from Taiwan, my homeland, in fact. And when they came to visit us, it was a special day at Butantan. It's an exotic place and in such amazing with the very expansive green area surrounded by historical buildings and full of educational activities on science and animal conservation. And then when I finished my degree in medicine, I had the dream to work in remote areas, dealing with vulnerable communities, treating tropical disease and helping people live in the Brazilian Amazonian forest. But at that time I realized that I didn't know anything about snakebiting venom. It's one of the health problems in tropical countries. So for over thirty years, I have been dedicating my career, and more recently, I decided to work in the industrial manufacturing complex of antivenoms because of the commitment of providing good quality products and also to help to increase the availability and accessibility of antivenoms for all that need them.

Garry Aslanyan [00:07:30] And let's also hear from Thea next.

Thea Litschka-Koen [00:07:35] It happened by chance, actually. My son, at the tender age of seven, had a project, his very first project at school, and they had to pull a topic out of a hat, and he happened to pull the topic snakes. Whilst helping him, I came across a website for a company called African Reptiles and Venom, and when I started to research I saw that they do snake handling courses. So I went and I did the snake handling course. A week or so later, I received a photograph of me holding this massive mamba, with a petrified look on my face, in the frame which I just plonked on my desk. And within a couple of days the phone started to ring and the word had spread that I was catching snakes. And the phone would ring, and they'd say, "Please, can you help me, I've got a snake in my house?" And that's how it all started.

Garry Aslanyan [00:08:27] Diogo, I understand you know both Dr Fan and Thea, what do you think we could learn from experiences that they've just shared with us and their passion?

Diogo Martins [00:08:36] Well, Garry, let me start by saying Dr Fan and Thea are both incredible, incredible individuals. I've learned a lot from them, and I've learned a lot about snakebite from them. And it's been really a pleasure over the years to keep doing so and try as much as we can to support the work that they do. And it's so interesting because both of them have similarities in their stories, but also the fact that the contexts are different within the continents where they come from. What I really liked about the stories is that it's sort of a family link, right? It kind of feels like it all started years ago and

unexpectedly. For many of us working in global health, everything is so planned. You go to university, very early on, you do your medical training and suddenly you know that you want to become an infectious disease doctor or a psychiatrist. And it's funny because to me, what I take from these stories is it's pretty much the same the role of chance. I'm from Portugal, I'm a medical doctor by training, and I did not learn in medical school how to treat a snakebite. So that in itself, the role of chance and how that connects with our personal stories, either with family, but also professionally, the unexpected encounters and opportunities that you suddenly just start reading a little bit more and it becomes fascinating. So I started working in snakebite five years ago, and I was working on climate change before, climate change in health, which couldn't be more of a macro type of global health issue, and focusing in snakebite due to the virtue of my personal, professional and then other stories that led me to this space and the kinds of people like Thea and Dr Fan, those were inspirations that sort of end up keeping you engaged with it for a very long time. I particularly chimed with Dr Fan's story when she was thinking in med school she wants to go to the Amazon area to work with underserved populations. I also have that. But probably I thought ten years ago that I was going to be doing it in a completely different way. So I really like how, one, the role of chance, but the role of chance and these happy accidents and that putting the right people in the right place and the right time, and I think that's the case for Dr Fan and for sure the case of Thea.

Garry Aslanyan [00:11:07] Right, right. And the experience that they had that then kind of cemented that passion for them to continue doing what they do. So in doing some research, we realized that availability and accessibility, acceptance of antivenom is still a major challenge, as you said, worldwide. Brazil is one of the few countries with an established national programme where antivenom is free. But even then, they have a lot of challenges and both Dr Fan and Thea shared some experiences about the situation in their respective countries and settings. Maybe we can hear from them.

Dr Fan Hui Wen [00:11:52] In 1986, the Ministry of Health established a programme, a national programme for snakebite control. At that time and since then, we have four public antivenom manufacturing laboratories, and we are responsible to supply the national demands of around 500,000 vials to treat nearly 30,000 patients a year. So the Ministry of Health centralized all acquisition of vials produced by these four laboratories since 1986, being responsible for providing antivenom for states and municipalities in a decentralized policy. And this is what allowed all the universal and free-of-charge treatment for the whole population. Antivenom treatment should be given by a physician. That means that many rural sites are deprived from this kind of health professional and consequently from the antivenom treatment also. So this is one of the big challenges for a country as large as Brazil and also for other parts in the world to give access to antivenom. As we know that time is crucial for the outcome of the snakebite envenoming, our reality nowadays is that the patient may take several hours or even days to reach a health care unit. We may need to have the antivenom vials, but it's not enough to solve the problem of snakebite envenoming. We also need to know how to administer and have health professionals to be aware of all knowledge. In summary, my opinion is that having good distribution of antivenom and well-trained health professionals are essential components for the success of the problem of snakebite envenoming control. It's a challenge that we have to face.

Garry Aslanyan [00:14:05] Thea builds on what Dr Fan shared and highlights the situation with antivenom on the African continent.

Thea Litschka-Koen [00:14:13] In addition, a lot of the clinicians have no faith in antivenom, and it's something that we have taken many years to overcome, and it's simply because of the ineffectiveness of the antivenoms that are currently on the market. There is no regulation with regards to the effectiveness of the antivenom. To produce antivenom is not difficult. To go through the pre-clinical trials, it is incredibly costly. I had no idea how difficult and costly and cumbersome it was to actually

produce this product. If it does happen, it needs to be very well regulated. It needs to go through the processes, it needs to be monitored, otherwise we're going to go back ten years and we're going to be in the situation again where the doctors say, what's the point of using antivenom, it doesn't work. So yes, countries can start producing their own antivenom, they should start producing their own antivenom, but with that comes a lot of responsibility and ethics and planning. We have to plan this very well. But I think as the African continent, I do think we have the ability to produce our own.

Garry Aslanyan [00:15:32] So just like you said in the beginning, very different settings, but a lot of challenges when it comes to this, Diogo. What do you think is needed to overcome these challenges, and do you know if there are any innovations, new options that are on the horizon and might be coming soon and be available?

Diogo Martins [00:15:53] That's the million dollar question, isn't it? Sort of, how can we overcome this? I always, when I reflect about this and talk to colleagues about this, and I've spoken to Dr Fan, for example, many times about this, we're always quite conscious that we're not here as new partners and trying to reinvent the wheel or completely ignore the fact that a lot of these things have been discussed for decades and even the current way treatments are produced, it's based on the technology that is over 100 years old. We come into the space with a lot of humility, with open eyes, open ears. Over the past few years, I've been looking into the therapies in more detail. There are promising things that happened over the past five years to make sure that, for example, the treatments that have been produced in the same way, using forces, are then produced in a way that improves their safety profile and improves the efficacy profile, we can actually do clinical trials with those. We know that, for example, within sub-Saharan Africa there's only been about five different clinical trials for antivenoms, and we know that at the moment there are at least 18 different antivenoms in the market. So, as Thea said, it's severely under-regulated. A lot of these technologies were introduced in markets before any regulations even existed. So there's a lot of things to do in terms of the traditional antivenoms, but also in terms of the new technologies. So things that might be a little bit more advanced, talking about, for example, small molecules that might be repurposed have been produced for one particular disease area that might be used for snakebite, we can repurpose them depending on the different types of syndromes. Or we might be talking about recombinant monoclonal antibodies that do not need necessarily an animal to be produced, they are a little bit more similar copies to human antibodies. So there's a lot of progress and how far those things are, as you were asking Garry, from being a reality is still a little bit far away. We're talking about five, ten years, if not more. Clinical trials take time, for example, if you're looking at conventional antivenoms. But there are promising hints that the field is moving in that direction. One thing that I'm particularly excited about and I'm happy to talk about it, Garry, if that's of interest, is the other part of the delivery. So not necessarily the science, but then we have these shiny improved technologies. How do we make them accessible? WHO, with its own strategy, has talked a lot about finding ways to expedite delivery, to make sure that countries can look for the right interventions for them and access them at a cost or at a price. I'm really excited about this because it really tells us that the importance of having an end-to-end approach. Really good science, really good delivery, but most importantly, Garry, in my perspective, and this might not sound new, especially with COVID being so fresh in our minds, it's all about coordination. We don't need only prevention, we don't only need treatments, we don't only need community engagement, we need a coordination of all of this. And I think a laser focus in making sure that that really happens. But some of the innovations, I would say, just to summarize, are a little bit more short term, but maybe some of the new technologies might take a little bit longer.

Garry Aslanyan [00:19:18] And you really think that some of those innovations have like access in them by design already thought through? Are they thinking about that as they think of the innovations?

Diogo Martins [00:19:30] I think it's inconceivable to be working in global health these days and not really think about these things really seriously, not really thinking about, for example, if there is a contract in the future with a public or private manufacturer, are they thinking about IP? Are they thinking about access? Are they thinking about focusing on low- and middle-income or more resource-limited settings? In the first instance, are we talking about pricing strategies that are going to be sustainable in the long term for the manufacturers, but most importantly for the populations? So I think so, and I think the majority of partners who are in this space are really looking at this very, very seriously. Snakebite, Garry, as you probably know in terms of the market failures, does suffer from other issues that, for example, other disease areas did not suffer in terms of scale. You don't really have that kind of scale. (market) Precisely. So it's in my perspective, it's about finding ways to keep the supply and demand on board, but obviously, front and centre are the patients. You know, it's inconceivable that you can continue in five, ten years time, having patients having to pay $100 in many geographies to solve one episode of a snakebite. Again, we cannot have individuals that earn $1.50 a day and have the unfortunate circumstance of crossing paths with a venomous snake and suddenly all of their savings are gone, to not even mention other impacts socially and economically.

Garry Aslanyan [00:20:58] Snakebite is not only a significant health care issue, but also has socio-economic and psychological repercussions for communities. Thea highlighted the lived experience of this very well. Let's listen to her.

Thea Litschka-Koen [00:21:13] I really appreciate this question that you are asking. It is an aspect that is very seldom considered when it comes to snakebites. The focus is usually on the snake has bitten, we need to treat the patient and that is challenging enough as it is here in Africa, but we very seldom look at the consequences it has on the family and on the livelihoods of the people that have been affected. I see this time and time again and two cases come to mind when you ask this question. The first is an old man who used to be an "indvuna" his area. That means he was a leader or a chief and he was sleeping when he got bitten by a Mozambique spitting cobra and he unfortunately lost his leg. I got to know this old man in the hospital. He was there for many, many weeks. I built this relationship with him and he went from a proud subsistence farmer who used to help his community, to somebody who couldn't walk, couldn't fend for himself and couldn't grow his own food. And he died a lonely and broken, broken man, all because of snakebite.

Garry Aslanyan [00:22:26] So in the face of this shortage of antivenom and in the context of many barriers to its administration, Thea developed a very effective community-based response strategy. So let's hear from her a bit more, Diogo, and maybe you could reflect on that after.

Thea Litschka-Koen [00:22:46] I've been involved with snakebite and snakebite conservation for almost 20 years, and I was a very slow learner, I must admit. I would do a lot of education and I would stand there and I would preach and I would discuss snakes and the importance of snakes. This went on for many years until one day the light came on and I thought to myself, I'm out there doing all this work and I spend hours and weekends and weeks out in the communities talking to people and talking to people and I just get these blank looks most of the time. And then I thought to myself, Why don't we train volunteers from these rural areas, from these communities, so that they can take ownership of the problem themselves and that they can themselves assist their own communities. They trained 52 community rescue volunteers and we had them here for a week. We did a lot of training, practical training, theoretical training, we gave them the PPE, a mobile phone and data on their phone, and we said, Alright, let's give this a bash. And they went out into the community and so proud, so incredibly proud, and we started to immediately see a change in the response to these community guys who are out there. They are living in those rural areas with no electricity and no telephones and no roads. They understand the problem so much better than what I do, even though I thought I did and I had spent so

much time in the field working and all of a sudden there was a change and the message was received with so much positivity. They believed the message and they slowly but surely started to change the perceptions in these rural communities. They go to schools, they go to cultural activities, they go to road shows, and they just speak about the importance of conservation. They take snakes with them, and that's very, very important, and the people get to hold the non-venomous snakes. We teach people, when you see a venomous snake, how do you react? We talk about how you prevent the snakes from coming to your home. That's been so effective, besides the conservation message that's going out there. It's the correct first aid. What do you do if a snake bites you? What do you do to try and preserve life and limb? Remarkably, over the last three years, we've managed to reduce the snakebite incidence by 27%. This simple project now we've got close to 100 community volunteers out there. But this simple approach has been life changing. Absolutely life changing.

Diogo Martins [00:25:33] That's such a great story and I can really hear their emotion as they are explaining how it all started. And the particular sad story about, unfortunately, the gentleman in the community who did not survive. How some of those very difficult stories then are the start of something really special and important. The part that I really liked the most, and my biggest takeaway, is really that when you really start a particular project, especially in the communities and really well-intentioned, you've put in the hours, you're really trying your best to do something that is useful for the community, but then you realize many times your contribution there might not be what your contribution is best located. And being able, and having your eyes and ears open and really listen and observe how sometimes you're probably not the right person to be in front and to lead a particular community project. And we do know from other countries as well, the model where you have members from the community being part of the solution generates in itself positive outcomes when it comes to generating jobs, giving them purpose. It's sometimes with the most simple of things; a phone, mobile data and magic happens. So I think to me it's kind of the start of this whole project with a story of, unfortunately, the gentleman who did not survive and leading on to something that is quite robust, 50 volunteers in then up to 100 and then being able to bring down incidents by almost 30%. So you could even argue within snakebite, community engagement is ever more important because, again, it doesn't matter how shiny your intervention is, how well thought through your policy framework will be, if the folks who are supposed to be benefiting from this are not aware, do not understand what's going on, do not understand their role, do not know what they need to do, it's all work that will not do what it's supposed to do. This story to me is quite special and I also liked hearing Thea's emotions on the positive way and how proud she is of this project. It is very humbling.

Garry Aslanyan [00:27:48] Yes, it was actually one of those moments when I was talking to her, I said, I'd like to see that actually one day, but it was really interesting to observe that particular achievement that they've made there. Diogo, as we draw to the end, maybe we can explore a few more strategies by which an issue like this can be addressed. So one of them was mentioned by Dr Fan in the value of South-South collaboration and partnerships between countries. Maybe we can hear what she had to say about that.

Dr Fan Hui Wen [00:28:24] In Latin America, many antivenom manufacturing laboratories are public institutions and some established more than a hundred years ago as Butantan is. Of course, as one of the oldest manufacturing laboratories, Butantan has a responsibility and a commitment to solve health issues and to work with other partners in this way. Recently, in 2018, we established a network among the 13 public antivenom manufacturing laboratories in Latin America. Because of that, we know each other for a long time and we feel that we need to work in partnership, not only in partnership within the network. So the Pan-American Health Organization, through the Panaftosa Center (the Pan American Center for Foot-and-Mouth Disease) agreed to coordinate this network. It was, 2018 was the year where the WHO established the goals or the plan to reduce as they fight environment, disabilities and mortality,

so it was the opportunity to join all players in this initiative. And we started sharing experiences, organizing seminars, trainings, preparing guidelines and also developing or preparing for clinical, epidemiological and clinical studies to be performed. Some of them, strongly supported by Wellcome Trust, the charity agency in the UK that is very committed to this plan, this big plan, to reduce the burden of snakebite in the world. So I would say that solidarity is the hallmark of the public antivenom laboratories in our region. It's part of our job for decades or even more than a century. We think that not only providing antivenom is a possibility, but also the model of how we have been working for these years in our region is also a way that each country in other regions can achieve or can develop their own learning curves in terms of how to control and prevent snakebite envenoming, considering their local and cultural aspects.

Garry Aslanyan [00:31:34] Diogo, in your work at Wellcome, you work on supporting and facilitating this kind of cross-country learning and sharing. How does that work?

Diogo Martins [00:31:43] When we took on the challenge of looking at snakebites, we're looking at not only supporting really good science, good research, but also looking at all the factors around it that will make it successful. All the enabling factors. We talk about policy, we talk about regulations, we talk about networks, we talk about working with countries. And there are a few examples that Dr Fan was just talking about now in her contribution about a network in Latin America, for example, where the public manufacturers, which respond directly to, in the most part, to the ministries of health in terms of forecasting, in terms of the needs, in terms of distribution models; that network has been around for a few years before COVID, they came together during COVID even stronger, so we do some work on supporting that enabling network activity, which is all about the countries being on the driving seat, telling what the priorities are, making it really clear what the resources would be that would make a difference, and also making sure and we try as much as possible, try to fertilize those ideas and try to bring that message and that learning to other countries, both within the region, but also, for example, Brazil works a lot with the African continent, which is quite exciting. And also Asia works a lot with the African continent and so on and so forth, and from that perspective, try to spill over the positive effects of that collaboration and that process of building good science. Dr Fan shed really good light on the incredible work, I have to say, gold standard work that is taking place in the Latin American context in the Pacific.

Garry Aslanyan [00:33:22] Right. And you mentioned there are some other similar initiatives in, let's say, in Africa. Where are they now in that process?

Diogo Martins [00:33:30] That's a good question. So, for example, as we look at the different regions, it's very clear to me that, for example, Latin America has huge experience with manufacturing of antivenoms, in the model that is mostly based on public laboratories that are somehow connected to the ministries of health. Without Brazil, São Paolo, Rio, all of them have a history of coming up with antivenoms, the conventional ones as we know them, really started in so many aspects in that continent. If you go to, for example, Africa, we have unfortunately only one regional manufacturer of snake antivenom in South Africa that only produces antivenom for that continent, and as we do know, having tremendous issues with that supply alone. So we don't have a similar network. But what's happening, what's been created recently, is in particular countries where there has been historical support for snakebite research, for example, that's the case in Nigeria, in Ghana, in Kenya, some networks are being created into a platform that focuses a little bit less on the manufacturing but building a research agenda for public health, which is a lot more on the implementation side. So how do you create the evidence, epidemiological evidence, that gets you really good data for how big the problem is and how much of a solution is required. So those sorts of networks are accelerating a lot within the African continent, both implementation research but also clinical trials. If you go to Asia, for example, the ASEAN network and

a lot of the countries in South-East Asia working very closely on health economics. They have tremendous health economist at universities in Thailand, in Malaysia and many other countries as well, including countries that unfortunately are going through difficult times, political instability still being very, very active on this, looking at epidemiological data, linking with WHO regional offices, trying to bring more of that economic element, understanding the impact, a tremendous amount of literature being published in the last few years on this in particular. So I do see a future where in different parts, different continents contributing with different fields of expertise and models of collaboration, but I expect hopefully in the next 5 to 10 years to see even more of that and a little bit of a different snapshot of what snakebite looks like.

Garry Aslanyan [00:35:58] Well, that's very hopeful and promising, I'm sure when we look at this in five years, the picture will be different. Some of the challenges we unpacked today are very unique, and I'm hoping our listeners have learned a lot through these discussions. So thanks so much, Diogo, for joining me today and having this discussion, and best of luck with your future endeavours.

Diogo Martins [00:36:22] Thank you, Garry. Obrigado.

Garry Aslanyan [00:36:26] Snakebite is a complex and neglected issue that requires a multifactorial strategy, including conservation, community engagement, scientific research and robust health care delivery. As highlighted by my guests, antivenom is a scarce commodity in most settings. One way to address this issue is through strong cross-country and regional partnerships and networks.

Claudia Chamas [00:36:57] Hello, I'm Claudia Chamas, a researcher at the Oswaldo Cruz Foundation. I'm thrilled to share a remarkable podcast that I wholeheartedly recommend to both health professionals and the general public, Global Health Matters. Under the guidance of Dr Garry Aslanyan, the podcast brings together experts from diverse countries and backgrounds to explore an array of compelling topics. These discussions span crucial subjects, such as access to diagnostics, climate change's impact on health, the empowerment of women in science, health diplomacy, and an extensive range of other pressing issues. I invite everyone to listen to the third season. This initiative offers a unique opportunity to broaden our knowledge and engage in meaningful conversations about global health.

Garry Aslanyan [00:37:53] Thank you Claudia Chamas for your message. Thank you for being a fan of the podcast. To learn more about the topic discussed in this episode, visit the episode web page where you'll find additional readings, show notes and translations. Don't forget to be in touch via social media, email or by sharing a voice message with your reflections on this episode.

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