Medical Xpress

# How to save a country from snakebite

December 11 2019, by Yao-Hua Law

Saw-scaled Viper (Echis carinatus). Credit: Wikipedia

The evening that a snake bit Mahfudin was one like any other. The sun had set behind Mount Lawu, to the west of Mahfudin's village in the central part of Java, Indonesia. Crickets chirped in the hedges. Goats

bleated in a shed. An uneven path lit by two dim lamps led to Mahfudin's house: bare bricks and plywood on brown hardened earth, topped by a roof of dried palm leaves. He'd built that house, and once he could afford it, he would paint the walls and tile the floor.

That evening in December 2017, orchards and bamboo thickets melded into a shapeless black shroud around the house. Mahfudin's five-year-old nephew was crying in the living room. A biscuit from the shops would cheer the boy up, Mahfudin thought. He walked out the door, stepped on something soft, then jumped back in a jolt of pain. He slammed the door and looked down at the two puncture holes on his left ankle. "A snake bit me!" he shouted.

Blood oozed from his wound. Mahfudin panicked. He had seen snakes around, and other villagers had been bitten. He tied a T-shirt tightly around his leg above the ankle, just like he'd seen in a movie.

Soon Mahfudin was vomiting blood, and then he passed out. His uncle got him to a nearby community clinic. There was just one nurse on duty and she didn't know what to do. So she cut small incisions on the bite wound hoping it would release some of the venom—then referred him to the larger district hospital.

By the third day, Mahfudin was bleeding from every orifice. His feces and urine ran red. The doctors were as bewildered as the nurse—nothing they did worked. That's when they called her. Maha, the snakebite doctor.

## Maha of Kediri

Tri Maharani—popularly known as Maha—grew up in Kediri, a city in East Java. Her family lived in a simple house on a street of shops. Her father and mother—a military officer and nurse, respectively—couldn't

afford any luxuries. When she was four years old, she met a pastor who taught her "to build a relationship with God and live with God." He changed her life, she says. His teachings nurtured strong empathy in her. She remembers collecting donations to buy a new uniform for a classmate and cooking her pet chicken as a dish to celebrate a friend's birthday; she cried when everyone else ate the chicken.

At 28, she qualified as a doctor and left Kediri. Over the next 20 years, Maha moved between hospitals and universities. She specialized in emergency medicine and completed a Ph.D. in biomedical science, which she'd sold her land to fund.

Maha had researched viruses and chronic inflammation of the arteries, and envisioned a career tackling infectious or cardiovascular diseases. But her life pivoted in 2012 when she attended a snakebite envenomation seminar given by Ahmad Khaldun, a Malaysian emergency medicine specialist. What she heard shocked her.

Worldwide, about 93 million people live near to venomous snakes in rural areas with little access to healthcare. Up to 2.7 million people a year are envenomed by snakes—with about 100,000 dying and many more being maimed. Most victims are people like Mahfudin who work on farms or near forests. But divers and hikers get bitten too, as do people in cities who keep, study or perform with snakes.

In Indonesia alone, snakebites run to the tens of thousands. The country is home to 270 million people and over 70 species of venomous snake. Almost a third of Indonesian jobs are in agriculture, where snake encounters are common.

Yet what shook Maha in that seminar was that everything she had learned about snakebite treatment in medical school was wrong. When Mahfudin tied a T-shirt round his leg, he thought it would slow the blood

flow and stop the venom being carried to his heart. He didn't know that snake venom is a cocktail of toxins, many of which are too large to penetrate our blood vessels. Or that the toxins can enter the lymphatic vessels and move around the body through these instead. Mahfudin's makeshift tourniquet wouldn't have stopped the venom, but would deprive his foot of oxygenated blood—a costly mistake that has forced many doctors to amputate gangrenous limbs. When the panicked community clinic nurse cut into Mahfudin's wound, she wasn't to know she was actually aggravating the bleeding and leaving Mahfudin at risk of infection.

God knows how many snakebite patients we have killed with the wrong procedures, thought Maha. From that point in her career, unable to stomach more mistakes and encouraged by Khaldun, Maha focused on snakebite management in Indonesia, learning the correct treatments through courses and workshops in Malaysia, Thailand and Australia.

It is shockingly rare to find people who know how to treat snakebite correctly—and those that do often don't have the means to do so. Fatalities sometimes trigger a public outcry, but the concern is otherwise sidelined. Snakebite is so common it's a fact of life in low- and middle-income countries like Indonesia, India and Mozambique—yet crucially, it isn't a problem that generally concerns the high-income world.

That's why, in 2017, the World Health Organization (WHO) listed snakebite envenomation as a priority neglected tropical disease. And in May 2019, the WHO launched a roadmap aiming to halve the number of deaths and disabilities caused by snakebite by 2030. The document was drafted and reviewed by a nominated 28-person working group containing just one Indonesian: Maha.

## Mahfudin and the snake

Four days after he was bitten, Mahfudin was transferred to Dungus Lung Hospital in Madiun, where Maha was working at the time. His skin was bluish, streaked with blood both old and fresh.

Venom was destroying the tissues of Mahfudin's body, and could only be neutralized by an antivenom. But first, Maha needed to know what snake had bitten the man dying before her. She had a clue: the flash of green Mahfudin had seen after he felt the bite signaled a green pit viper, either Trimeresurus albolabris or T. insularis, species native to Java that cause systemic hemorrhage. If so, Mahfudin needed an antivenom made by the Queen Saovabha Memorial Institute (QSMI) in Thailand.

But Maha had none—the antivenom is neither registered nor stocked in Indonesia—and QSMI couldn't deliver some in time. Maha was desperate. She fired messages and calls to anyone who might have green pit viper antivenom. Finally, she heard from a snake expert on another Indonesian island who had some in stock, albeit 11 years expired.

Having friends who work with snakes is one of Maha's strongest weapons in her fight against snakebite. She is always roping more people into snakebite management—"I must show them that snakebite victims can be saved"—and she never shies away from making friends and reaching out to those who deal with snakes. Her network has grown out of necessity.

When she first looked for official snakebite numbers in Indonesia, she found none. The country doesn't register deaths from snakebite. So she began asking doctors across Indonesia for snakebite cases. Few responded, likely because they didn't know Maha and because snakebite wasn't a priority. But as Maha expanded her network by giving talks and running workshops on snakebite first aid, her reputation grew, and more doctors asked her for help. Now when she scrolls through her phone, there are too many chat groups to count. Some are unsaved numbers of

doctors who've found Maha's contact details; most are groups of participants from her workshops.

They send her photos: dead snakes, fang wounds, clinical readings, patients' swollen limbs, drooping eyelids. Her phone is always busy, and so is she. She zips across Indonesia to see snakebite patients and conduct workshops. She buys antivenom from colleagues overseas and delivers it free to Indonesian doctors. She talks fondly of sleeping on trains ("flights are too expensive and don't reach small towns") and showering at the stations.

But on this particular occasion, she needed speed. Maha jumped on the only available flight to grab the expired antivenom.

Less than a day later, she gazed down at Mahfudin's agonized face and weighed up her choices.

She knew that WHO guidelines advise that "recently expired antivenom" may be considered as a treatment, but only as a last resort. She'd highlighted that sentence and read it repeatedly. Maha had also consulted a Thai expert from QSMI, who said that an expired antivenom could work and that the worst outcome would be acute kidney injury.

She ordered her staff out of the room. She knew this decision might ruin her career. "If anything bad happens, I alone will bear the blame," she told herself.

Maha tended to Mahfudin for the next two days. She bathed and slept at the hospital. Days later, Mahfudin walked out, fatigued and limping on a swollen leg, but otherwise healthy. His mother prohibited him from working his various jobs: no spraying pesticides in fields, no mixing cement or stacking bricks, no earning to save money. His dreams of painting and tiling his house would have to wait—but he lived to dream

another day.

## A good man named Iskandar

In August 2019, 45-year-old Iskandar was one of four security guards on duty at Cluster Michelia, a relatively up-scale residential community on the western side of Jakarta. The sun was setting. His shift would be ending in 30 minutes. He'd been away from home since 7am, and his wife and three children would be expecting him.

Right before the end of the shift, a resident called asking for help with a snake in the communal garden next to his corner house. The guards didn't expect to be handling snakes in the city, though this was the fourth snake report this year. Iskandar and a colleague responded to the call. They saw the snake, its tail sticking out of a hole, white bands alternating with black saddle-like marks on its back—a Malayan krait, Bungarus candidus, one of the most venomous snakes in the region. Its venom attacks the nerves and paralyzes the muscles that control breathing.

Iskandar and his colleague tried to trap the snake with a broom. But the snake slithered away, so they chased it around the benches and chairs in the compound. When his colleague finally pinned the snake down with the broom, Iskandar grabbed it. Suddenly, the snake whipped around to face Iskandar. He panicked and flung it into the garden. The two guards scrambled to catch the snake again, got hold of it and killed it.

But in the commotion, the snake had somehow bitten or grazed Iskandar's left index finger with its fangs. Residents asked Iskandar to check into a hospital, but he brushed the concern aside. He sucked on the wound and told the others not to worry. Then he sat on a bench, looking pleased with the snake in his hand, showing it to the gathering residents. The resident who reported the snake, however, insisted on taking Iskandar to a nearby private hospital.

Within 30 minutes, Iskandar was nauseous and almost fainted. But the hospital had neither antivenom nor personnel trained to handle a snakebite. They referred Iskandar to the Tangerang public hospital instead, which they said should have antivenom in stock. According to the resident accompanying Iskandar, once they were there he was put on a drip and given Biosave, the only antivenom produced in Indonesia.

Meanwhile, Iskandar's wife Siti was waiting at home without news. Iskandar liked her cooking, but he was uncharacteristically late tonight. At around 9pm, her brother informed her that Iskandar had been hospitalized, and they went to him. By then, Iskandar was aching all over and keeping his eyes closed most of the time. But a doctor told them that he was fine and could go home. "My mind was dark then, and I am not smart. When the doctor say 'go back,' I think it should be OK to go back," recalls Siti. But her brother, worried about Iskandar's deteriorating condition, refused to take Iskandar away.

At around 3am, Iskandar was gasping for air. He tried to talk but could only squeeze out a few words to his wife. He whispered that he would like to lie on his back, and Siti helped him turn over. She never heard him say another word. He stopped moving, then stopped breathing. Iskandar died shortly after 4am.

Iskandar's death shattered Siti's world. In their living room there's a portrait of the two of them huddling with their children, beaming in their matching purple suits. When I speak with her, Siti sits with her back to the portrait and struggles to put her feelings into words. Her loss was too sudden, too deep. The week before, they had celebrated her 38th birthday. Their youngest child was born just eight months ago and is still a baby. "He was a good man. Hardworking and always praying. He makes a good role model for our children," Siti says. Iskandar was the sole bread winner of the family. Siti needs to stay at home to care for the children. Fortunately, she's making ends meet with support from her

siblings. But still, she worries for her children.

Iskandar's death is tragic, and more so because Biosave, the antivenom he was given, is sadly ineffective against Malayan krait venom. The doctors did not know that. They thought it would save him. None of that matters to Siti. Her husband is gone.

Iskandar's story went viral on social media and the news. About ten days later, Maha visited Cluster Michelia to train the guards and residents. She'd jumped on the opportunity to teach people about snakebite, even the doctors in the area (including the head nurse from the private hospital that turned Iskandar away). One guard, Rizky, says he didn't expect to handle snakes, didn't know how, but now is better prepared after Maha's training.

Where snakes and people coexist, people will get bitten. And when severe envenomation happens, doctors can rely only on antivenom to save the patient.

An antivenom consists of many proteins, including antibodies that bind to and deactivate venom molecules. These antibodies are harvested from an animal—usually a horse or sheep—that has been injected with a snake's venom to stimulate an immune response. An antivenom works only against venom from the snake species that has been used to make it.

Even if Iskandar's doctors had known that he was bitten by a Malayan krait, they wouldn't have had the antivenom to save him. The antivenom for the Malayan krait is produced by QSMI. Like most antivenom produced outside the country, QSMI's products aren't registered in Indonesia, and hospitals do not stock them.

A doctor must first identify what snake has bitten the patient to know which antivenom will work. But the correct diagnosis is still futile

without antivenom, says Liao-Chun Chiang, a snake venom toxinologist at Taipei Veterans General Hospital in Taiwan. Taiwan produces about 4,000 vials of antivenom yearly, more than enough to cover the 1,000 local cases of snakebite envenomation that happen each year there. While Maha advises Indonesian doctors to use antivenom only for severe envenomation, doctors in Taiwan use it in every case. Because Indonesia lacks antivenom, its doctors are reluctant to use it freely, says Chiang.

Experts and doctors are calling for more and better antivenom in Indonesia. The sole Indonesian producer, Bio Farma, can produce only 40,000 vials of Biosave a year—far short of the number of estimated yearly cases of snakebite, which Maha says is over 100,000. Moreover, Biosave is only effective against three of the 19 venomous snake species considered "medically important" in Indonesia—it cannot neutralize the venom of the pit viper that bit Mahfudin or the cobras and kraits of Eastern Indonesia. What's more, an independent laboratory report published in *Scientific Reports* in 2016 found that while Biosave can "moderately neutralize" the venom of two of its targeted snakes, it is "weak" against the third. An antivenom that lacks potency means several vials are needed to treat one patient.

Antivenom shortages are further strained by logistics. Biosave is a liquid, must be kept refrigerated at 2–8ºC and has a shelf life of two to three years; storage facilities needed for liquid antivenoms like this are absent in rural areas where snakebite is a big problem. In contrast, freeze-dried antivenom—such as that produced in Thailand, Taiwan and Myanmar—can be stored at room temperature with a shelf life of five years.

## An education

Twenty-four-year-old Hendik liked to hunt palm civets every night in the forest. Not for food or money, he says, but "entertainment." When

hunting, he would walk barefoot—"I didn't want the civet to hear me," he says. He wasn't concerned about the snakes he had seen in the forest. "If the snake is on the ground, I can see it." But he didn't see the green pit viper before it bit his left leg.

His friend sent him to a hospital, where doctors administered Biosave, which was ineffective. They discharged him after an hour. But Hendik's brother, who is a nurse, felt uneasy, and so rushed him to another health center, Marsudi Waluyo Hospital. There, doctors had been trained by Maha four months before. They called their mentor, and she arrived via train a few hours later with vials of Thailand green pit viper antivenom. Hendik survived. "I am scared and can't hunt now," he says, lying on his hospital bed. His mother is standing a few feet away and hopes he never hunts again. "But eventually I will," Hendik says. He appears to have learned only one lesson: "I will wear boots up to my knees."

It is because many Indonesians, like Hendik, either ignore or misunderstand snakebite threats and management that Maha focuses on education. She teaches across Indonesia, not just to doctors and nurses but to farmers, miners, snake hobbyists and hotel workers. Because the Indonesian government doesn't sponsor snakebite management, Maha pays to run most of her talks. She accepts that to promote snakebite education in Indonesia somebody has to be willing to work for free.

Then there's education for her fellow doctors and healthcare professionals. Maha knows that mistakes made by well-meaning but wrongly taught medical staff complicate or delay life-saving treatments. She knows these mistakes are not made out of malice. In Indonesia, medical lectures on snakebite management are few and far between and the contents variable. They often recommend procedures like tourniquets and incisions. These methods—along with suction (to suck out the blood like you sometimes see heroes doing on TV), electric shocks and topical herbal remedies—are described in WHO guidelines

as "harmful and useless" techniques that "should never be used."

Hospitals that mismanage snakebite erode public confidence, says clinical toxinologist Simon Jensen, an honorary research fellow at the Australian Venom Research Unit at the University of Melbourne, who has helped develop snakebite research and management in Papua New Guinea. He wonders if many victims avoid hospitals because their relatives have died there from lack of antivenom. Eventually, "it becomes a tradition to go with traditional healers and not to go with Western medicine."

This article first appeared on Mosaic and is republished here under a Creative Commons licence.