SACRED BOVINES

FROM SNAKEBITES TO SERPENTARIUMS

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What enables science's great achievements? A common intuitive response might be "scientific reasoning, of course." That might include, first, skepticism, even toward dogma. Add theoretical insights. Powerful predictions. The logic of testing. But perhaps this generally revered truism—another Sacred Bovine?—might be subject to critical reappraisal.

Consider our discoveries on the biology of snakebites. In the 1890s, nearly three thousand persons died annually in Brazil from encounters with venomous snakes. Many were illiterate immigrants working on coffee plantations or building the railroads that would help transport the coffee. Few doctors were available in rural areas, and they could only treat the symptoms, not counteract the poisons. Workers relied primarily on local healers with their spectrum of herbal remedies. But were any of them truly effective? How could science contribute to solving this important health problem?

Young physician Vital Brazil Mineiro da Campanha (Figure 1) saw the challenge first-hand. With an eye toward helping his patients in the town of Botucatu, São Paulo state, he wanted to systematically test those purported treatments. Easier said than done. First, you need test animals. Fortunately for him, dogs, goats, and guinea pigs were readily at hand. But next, what about securing the test venom? You cannot theorize or reason snake venom into existence in your lab. You need actual creatures. Along with their real dangers. (And Brazil did indeed start the enterprise with a deep fear of snakes.)

So Brazil's first achievement was to work with local healers to get a snake—a living snake that had been captured, rather than immediately killed as a threat. The first two specimens were mishandled and soon died. If you need snakes, a seemingly trivial task like the proper handling of snakes can ultimately be essential to practicing science. The third snake survived. Next, how to collect a sample of venom without being bitten yourself? Brazil's solution was to present his snake with a mass of cotton as an artificial target, into which the snake released its venom. Then Brazil could do the relatively simple task of injecting an animal with both the toxin and a prospective remedy, and observe the results. Plain trials. No subtle or sophisticated reasoning. Rather, concrete—and risky—work in the material world.

Not surprisingly, Brazil found none of the local remedies effective. But soon he read about work in France that indicated a role for anti-sera instead of herbal treatments. Albert Calmette, following other researchers, had immunized animals to snakebites, then extracted their blood serum to treat other organisms that had been bitten. Calmette's approach was to find the most powerful venom and use its anti-serum against all snakebites, regardless of species. Serum developed from cobra venom was the key, he claimed. Brazil was certainly impressed. But this meant that his research was stymied because he lacked the expensive equipment to extract sera. He endorsed the hypothesis, what good was it without the laboratory where it might be tested? Resources are integral to scientific progress.

Figure 1. Vital Brazil, 1904.

Brazil found a new job and relocated to a bacteriological institute in the capital city of São Paulo, where the director allowed him to continue pursuing his interest in snakebites. He even helped him develop a long-handled device for lassoing the snakes, now known as Lutz's loop (Figure 2). So a core research problem—a practical one—was solved. Brazil began collecting several species of poisonous snakes and immunizing animals to develop anti-sera. He wanted to test a sample of Calmette's cobra serum on the local species, but it was very expensive. Finally, he secured some and tested it, only to find it had no effect on Brazilian snakes.

So Brazil was left to investigate the sera he could make himself. When he tried to find (as Calmette did) which serum was the strongest, the results were unexpected. The rattlesnake anti-sera worked on rattlesnake venom, but not on jaracara venom. Likewise, the jaracara serum worked only on jaracara bites, not rattlesnake bites. Based on the limited materials available for research,

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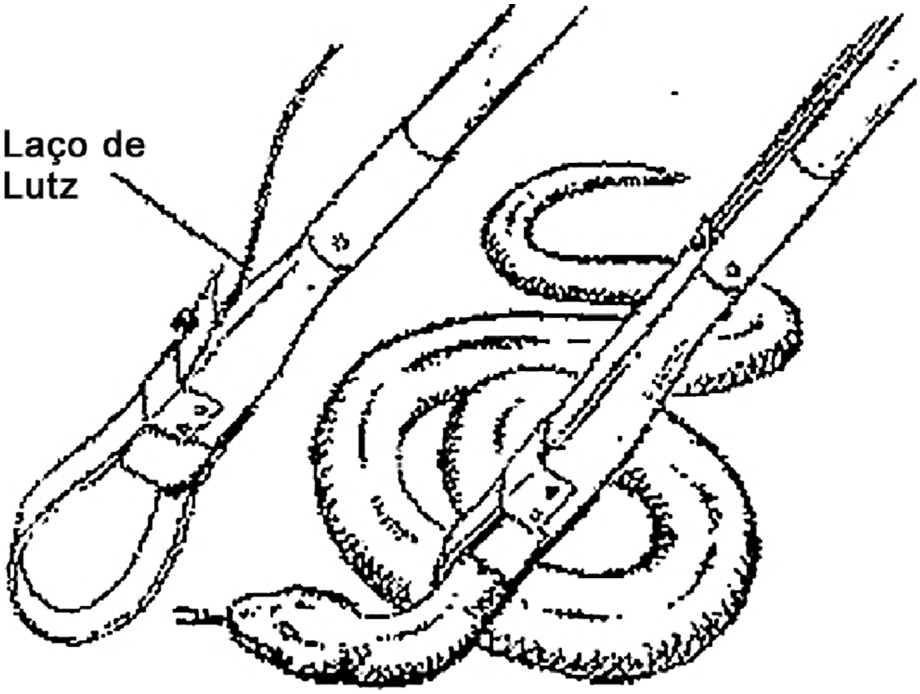

Figure 2. Lutz's loop, or the *laço de Lutz*.

Figure 3. The popular serpentarium at Butantan Institute, São Paulo, Brazil, in the early 1900s.

Brazil had inadvertently discovered the immunological specificity of snake venoms. Calmette's assumption of a common scale of toxicity was exposed and found wrong. That discovery had immense significance for interpreting and treating snakebites.

Ironically, perhaps, the pattern had been simple to discern. There was no theoretical prediction. No grand logical deduction. But the result dramatically changed how immunologists and doctors conceptualized poisonous venoms—of snakes and other organisms.

Brazil was ready to communicate his findings about snake serum specificity with the world, but bubonic plague broke out in a nearby port and his ordinary job duties took priority. Suddenly, he was in charge of producing large amounts of plague anti-sera. That ultimately involved the institute purchasing a large farm outside the city to maintain the horses and sheep that functioned as organismal "factories" for the serum. Two years later, Brazil was able to resume his research on snakebites more earnestly. By then, fortunately for him, the institutional expansion meant that he had more resources for these investigations. He confirmed his findings and shared them with the world.

Brazil's concern was still primarily the individuals who were bitten by snakes. So, in addition, Brazil created an exchange system for keeping an adequate stock of snakes and then distributing the sera. When workers in rural areas shipped him a snake in one of the heavy wooden boxes that the institute provided, he would return several bottles of serum and syringes for the treatment of snakebites. Brazil was also able to persuade the railways to provide free transport. He got the snakes; the workers at risk got life-saving serum. Working concretely to establish that system helped transform an ideal of potential treatment into a sustainable reality. Mortality rates for snakebites dropped from 25 percent to 2 percent. That was science in action and it exhibited substantive work and resources, not just abstract scientific reasoning alone.

Once aware of the material challenges of science, one might wonder how Brazil managed a large population of dangerous snakes. He still had Lutz's loop, of course, to handle the snakes. But where do you keep them safely? Brazil constructed a large *serpentarium*, surrounded by a pit and sheer walls. In time, the small "snake zoo," with its thrilling proximity to danger, became a popular attraction for visitors (Figure 3). The image of the serpentarium, celebrated in postcards, helps underscore the indispensable role of infrastructure in science.

Vital Brazil worked over the next several years to transform the old farm into the Butantan Institute, which continues his work even now, over a century later, addressing major problems in toxicology and immunology. Brazil himself broadened his research to include venomous spiders and scorpions. Today the institute is one of the most important worldwide researchers and producers of sera and biopharmaceuticals. Scientific ideas are one thing, but without the institutions and resources that materially enable research, science would be empty. Vital Brazil's work on snakebites, including building the dramatic serpentarium, reflects that as well as anything.

○ Supplemental Material

Teachers may find an interactive classroom inquiry activity on the case of Vital Brazil & Snakebites online at http://shipseducation.net/modules/biol/brazil.htm.