THE NEXT PANDEMIC

ON THE FRONT LINES AGAINST HUMANKIND'S GRAVEST DANGERS

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PublicAffairs
New York

Published in the United States by PublicAffairs™,
a Member of the Perseus Books Group

Library of Congress Cataloging-in-Publication Data
Names: Khan, Ali, MD, author. | Patrick, William, 1948– , author.
Title: The next pandemic : on the front lines against humankind's gravest dangers / Ali S. Khan with William Patrick.
Description: First edition. | New York : PublicAffairs, [2016] | Includes bibliographical references and index.
Identifiers: LCCN 2016001718 (print) | LCCN 2016002627 (ebook) | ISBN 9781610395915 (hardcover) | ISBN 9781610395922 (ebook)
Subjects: | MESH: Disease Outbreaks | Disasters | Internationality | Personal Narratives
Classification: LCC RA441 (print) | LCC RA441 (ebook) | NLM WA 105 | DDC 362.1—dc23
LC record available at http://lccn.loc.gov/2016001718

Editorial production by Christine Marra, Marrathon Production Services.
www.marrathon.net

Book design by Jane Raese
Set in 12-point Apollo

First Edition

10 9 8 7 6 5 4 3 2 1

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A POX ON BOTH YOUR HOUSES

Now the Small-Pox arises when blood putrefies and ferments, so that the superfluous vapors are thrown out of it (forming blisters), and it is changed from the blood of infants, which is like must, into the blood of young men, which is like wine perfectly ripened.

—Abu Bakr Mohammed ibn Zacariya al-Razi,
A Treatise on the Smallpox and Measles

We humans act like we own the planet, when really it's the microbes and the insects that run things. One way they remind us who's in charge is by transmitting disease, often with the help of small animals, including rodents or bats. Seventy to eighty percent of emerging infectious diseases are, in fact, zoonotic. The rest, such as drug-resistant microbes, are completely of our own making.

This does not mean all microbes are bad. We owe them many thanks for the fermenting of wine, beer, and cheese. We've also harnessed them as biological production factories and even as natural insecticides. I have a very healthy respect for microbes. They are 3.5 billion years old, represent 90 percent of all life, can produce thirty generations in a day, and have picked up the nifty trick of rapid genetic evolution by swapping advantageous pieces of genetic material through

transposons and plasmids. In contrast, there is us: humans. Modern humans are about 200,000 years old, we produce a single generation in twenty-five years, and our genetic diversity is defined by localized mating patterns.

And even we are not really a single organism at all, but a hive collective inseparable from our human microbiome.

The human body contains 100 trillion cells, 90 percent of which are microbial cells in the gut and other orifices and on its surfaces. These "passengers" come from about ten thousand different microbe species that comprise the human ecosystem. The complex interaction with this microbiota plays an important role in keeping us healthy. At the same time, it is putatively associated with sexually transmitted infections, obesity, gastrointestinal diseases, diabetes, and rheumatoid arthritis. We already use "good" microbes or probiotics to treat a severe form of neonatal gastrointestinal infection and prevent diarrhea while we're taking antibiotics. Fecal transplants from healthy donors with good microbes are the treatment of choice for patients with a severe life-threatening colon infection. Called *Clostridium difficile,* this disease is associated with antibiotic use that disrupts the functioning of the good microbes in our guts. Finally, there is increasing data that early antibiotic use can lead to later obesity. Researchers now find that they can make obese mice slim by feeding them the bugs from a once obese sibling who became slim after the mouse equivalent of weight loss surgery. There are already provocative studies with fecal transplants from slim persons to those with obesity to test the link between obesity and an altered gut microbiota.

Sometimes microbes go rogue in the hunt for new ecologic niches, akin to us moving out to the countryside when the cities get too crowded. Since the advent of modern science, we've fought back fairly well. Smallpox, which most likely evolved from a rodent virus, was one of the greatest scourges of humankind and undoubtedly changed the course of human history, especially in the colonization of the New World

where the natives were not immune. But, in 1980, a global effort declared that smallpox had been eradicated worldwide. So confident were we that we suspended smallpox vaccination programs. This was possible only because smallpox can't rely on animal hosts or reservoirs, but depends for its survival entirely on person-to-person transmission. If you interrupt the transfer to a new person by finding and isolating the very last human host for the disease, or protecting the uninfected with a vaccine, then you've wiped it out—gone forever. Unless you're keeping some of the virus alive in research labs, of course, which is another story. Unfortunately, with new advances in synthetic biology, the proverbial mad scientist could also readily reassemble it again from the published gene maps for nefarious purposes.

While the danger from native smallpox had been put to rest, there was concern that the ecological niche left vacant might be filled by a less deadly but still troubling disease called monkeypox.

In December 1996, while I was chief of CDC's Epidemiology Unit, Special Pathogens Branch, I took a call from my old friend from the Ebola outbreak in Zaire, Dr. David Heymann of the World Health Organization. He informed me of an outbreak of monkeypox in a cluster of twelve remote villages in the center of the Congo, and he asked for my help.

David had gotten $20,000 from the WHO director general for a three-week investigation, and he wanted me to head a team that included scientists from CDC and from the European Field Epidemiology program, which is the EIS equivalent in Europe.

Monkeypox got its name in 1958, when it was first identified in lab monkeys—crab-eating macaques—captured for use in neurological research. It's caused by a zoonotic virus within the same genus as smallpox, Orthopoxvirus, within the family poxviridae (home of the common wart virus). Despite the name, it is actually more prevalent in sun squirrels and other

rodents, especially Gambian pouched rats. After a one- to two-week incubation period, it causes the skin of people infected with it to break out in deep-seated, firm dome-shaped lesions that can look like vesicles or pustules very similar to smallpox. Fortunately, it is quite rare.

Human monkeypox can be difficult to distinguish clinically from smallpox (to which it is closely related) and chickenpox (to which it is not).

You can test animals for monkeypox antibodies, tell-tale traces left behind when the immune system goes to work against a specific invader. If you find antibodies, you've probably found an animal host for the disease.

After the disease was first reported in humans in 1970 and led to an intense monitoring effort to see if the disease posed a risk to the smallpox eradication campaign. An earlier global yellow fever eradication campaign had been derailed, in part, because the disease was able to retreat into the jungle, sustain itself in animals, then resurface to infect humans. Over the next fifteen years there were only about four hundred cases of monkeypox in equatorial Central and West Africa, mostly in remote villages surrounded by tropical rain forests where people have more frequent contact with infected animals, including the consumption of bush meat. That local menu designation includes monkeys and other wild animals, but Africans eat rodents as well. Monkeypox has a death rate of about 10 percent (smallpox is much deadlier and closer to 30 percent), and a secondary human-to-human infection rate about the same. There is no safe and proven treatment.

The real question for us was, from this large new cluster, had we called it wrong? By discontinuing smallpox vaccination, had we opened the door to monkeypox infection? And were we now going to need to resume vaccination in Central Africa to prevent its spread? But smallpox vaccine is live virus, meant to provoke an immune response in people with healthy immune systems. The problem then was the prevalence of

HIV/AIDS (human immunodeficiency virus/acquired immunodeficiency syndrome) today—which meant that hundreds of thousands of immunocompromised people would have no defense against the live virus, and thus a return to mass immunization could be a disaster. It's always better to prevent a disease than to treat it after you've got it, but at what cost?

The weight of this question and its history was not lost. The largest and ongoing pandemic at the end of the twentieth century was HIV/AIDS, which too had once been a zoonotic disease and an emerging infection. Detailed forensics on the virus genes suggested that it had originated in the 1920s in Léopoldville (now Kinshasa) after successfully making the species-jump from a related immunodeficiency virus of chimpanzees, likely from the handling of bloody bush meat. This was a booming city of trade and commerce with rapid population growth and robust railways that had a million people flowing through the city each year. The similarly booming sex trade and likely reuse of syringes created a toxic mix to amplify the virus and spread it across the continent and farther, via trade and travel routes. Despite potent descriptions of "slim" disease the syndrome was not recognized as a distinct illness in Africa for the next sixty years. This was coupled with a flawed response in the United States due to the politics of sex. The disease is now well established as a human pathogen, with 1.5 million deaths in 2013.

In February of 1997, I returned to the tropical paradise of Kinshasa, which not surprisingly had not improved any since I'd last visited a year and a half before. Chaos and corruption still worked as a tag team to keep everything nightmarish, and the civil war had only gotten worse.

WHO assured us that vehicles would be available once we got into the bush, but first we needed permission from the

minister of health, whose entourage decided that we needed several of their own people on our team; we were not above the speculation that this was so they could earn the per diems. All of a sudden these distant cousins and assorted back scratchers were experts in virology and epidemiology. We were careful to not ask why, until that time they had worked as taxi drivers and clerks. We just hoped that once the negotiations were done, there would be enough room for the people who actually knew something, and not just for the shills.

Ultimately, we were fortunate to put together an excellent team that included people from the Ministry of Health, as well as Dr. Okitolonda Sespi from the School of Public Health at Kinshasa University. A big part of our job would be to take blood from a variety of rodents, trying to figure out which ones had monkeypox. We found an expat zoologist named Delfi Messinger to help us identify the animals.

But then we had to find a plane. The first one we looked at was held together with duct tape, which is somewhat figurative, but I know that it definitely, literally, had fuel leaking out of the wing. The pilot said, "Oh, don't worry. The moment we take off it will pressurize and there'll be no more leaking."

I said, "We're not getting in this," and nobody argued, and we kept looking, even though the delay was costing us time.

Eventually, we found a standard dual-propeller deathtrap and flew to Lodja, about five hundred miles east, and just south of the Sankuru Nature Preserve. This would be our jumping-off point, where we'd rent Land Cruisers and a big truck. This isn't a situation where you drop in at a Budget or Enterprise, put down your credit card, and make sure you get your frequent-user points. This is Do-It-Yourself Rent-a-Car. You track down someone in town who's got a Land Cruiser and say, "How much to use your truck for a week?" You have to put all the pieces together yourself, and if you veer off into a ravine, or rebels shoot it up with AK-47s, that's your problem. There's no insurance company that's going to bail you out after you pay the deductible.

Once we had secured transportation, and rations and supplies, we took off toward our ultimate destination at the epicenter of the Congo's monkeypox outbreak, a village in the Kayembe-Kumbi region called Akungula.

Monkeypox is the kind of exotic viral disease that keeps people like me challenged. The virus can spread not just through direct contact with an infected person's bodily fluids, like Ebola, but also from human to human through droplets in the air, like influenza. The incubation period is ten to fourteen days, and early symptoms include distinctive swelling of lymph nodes (different from smallpox), muscle pain, headache, fever, and a distinctive rash that typically progresses through stages of vesiculation, pustulation, umbilication, and crusting. In some patients, early lesions become ulcerated. The rash and lesions occur on the head, trunk, and extremities, and often even the palms of the hands and the soles of the feet.

But most of all, even if you've eliminated the monkeypox virus in humans, that isn't going to make it disappear. It can survive just fine without us, staying alive in its rodent reservoir. The virus will quietly spread from rat to rat or squirrel to squirrel, year after year out in the jungle, and you'll never know it except for the sporadic human infection. Then suddenly, out of the blue, you've got a new human epidemic on your hands. It can happen anytime, and you've got to be ready when it does.

What scared us about the situation in Akungula was not simply the number of human cases, but the fact that we were able to trace the cases way, way back, sometimes down a chain of eight or more infected persons. This suggested that monkeypox could spread from person to person as easily as a cold in a subway car. We already knew enough about its transmission to expect that people who came in contact with infected rodents would come down with the illness, especially young kids who'd never received the smallpox vaccination, which provides some cross-protection, and who developed their

hunting skills by making snares and other simple traps to capture small animals. What we hadn't expected, and what had us really worried, was how easily the virus could continue to pass from person to person to person, no rodents required.

There were emerging cases throughout the Kayembe-Kumbi area, and the moment we got to Akungula, everybody started telling us what they'd seen and supposedly experienced. All this information had to be sifted through to try to understand what was really going on, and what we really needed to do.

We set up our portable lab in the compound and moved into the hut graciously provided by the chief of the village, Lomange Otshudi.

Starting out from the chief's hut each morning, we would break into small groups, each group taking a vehicle and heading for a village within a thirty- or forty-mile radius. Much of the time, the teams of epidemiologists had to hack their way through the jungle, creating their own roads.

When we arrived in a new region, we usually had the name of a local contact whom we could call on for help. In some larger cities, it might be a Catholic mission where the priest or the nuns could put us up. Instead of camping out somewhere, maybe sleeping in hammocks and eating cold rations, we'd have a hot shower, a regular bed to sleep in, and a nice breakfast complete with Nutella for our bread. It's surprising how luxurious even a spartan accommodation like this can seem, compared to sleeping on the ground, and how much it can cheer you up when you've been bouncing along rutted roads all day in the middle of nowhere. It's from those times that I understood the true meaning of "first-world problems." And the priest, nuns, and various acolytes living in chosen poverty always made me feel blessed and much closer to God.

In some rural areas, there would be a resident *infirmier,* or nurse, a local African who was typically the highest-ranking public health official in the vicinity, and very likely the only medical professional for miles around. They would deliver

babies and distribute medicine, if the government could afford to provide any. They might work out of rudimentary health clinics with a handful of beds—you couldn't really call them hospitals, as they were mostly dreadfully underfunded and poorly equipped. Some of these were remnants of clinics the Belgians had built back in colonial times, when the Congo was the personal property of King Leopold.

In more enlightened times, villagers paid whatever they could afford for medical services, which might be nothing. People with money to spend were apt to get treatment at a real hospital in a bigger town.

Our procedure upon arriving in a new locale was to start by trying to look up any of these *infirmiers* and whatever served as the vestige of a local governance. For example, for the *Zone de Santé* of Kato Kwambe, we met with the supervisor, Omeshango Opanga, the *infirmier chef de santé*, or chief nurse, and the commissioner of that region, Mr. Omandala Odimo.

We also met Sister Jean, who was the nursing director at one of the local hospitals. You need to get the local people involved as you try to sort out what needs to happen and you establish the appropriate relationships in the community to get things done. This is not parachuting in from a plane to a village and saying, "Okay, I'm an American doctor. I'm taking over now." That never works. And why would it? Would you trust an alien with a green pointed head if he suddenly arrived at your local hospital and said, "I have all the answers, and I've come to save you?"

To do the work you really do need to engage with the local community and with the local governing structures to make sure you do the right thing. If you don't do that, the minute you leave, it's all over. Sadly, sometimes that happens even if you did, but we have to try. This is the true definition of global health: striving to improve the condition of people worldwide regardless of GPS (global positioning system) coordinates and an accident of birth.

And that's the big problem with most outbreaks—there's often no sustainability plan, not just for containing the disease itself, but for the basic public health functions, like surveillance.

At each village we would introduce ourselves, look for cases, take blood from people within households, check them for smallpox vaccination scars, and work on getting answers to the study questions. We did school surveys, and we looked at the vaccination history for smallpox over the defined area. This was so important to us because if the epidemiology of the disease had changed, and this was (a) more severe than it had been previously or was (b) being transmitted continuously by people without a need to go back to the rodent reservoir, then that might imply that we needed to resume smallpox vaccination in that area, despite the risk presented by the presence of HIV/AIDS. But that would be a tough call.

In most of these places we were the only outsiders to have shown up in years, and it took great skill from our local team members to earn the trust of the villagers, and then to get blood samples, which were scary and painful, especially for young kids.

For all the high-tech gadgets we now had to track and fight disease outbreaks, some of our most effective tools were almost comically simple. Going from one thatched-roof mud hut to another, looking for suspected cases of monkeypox, we carried old decks of smallpox cards. These were laminated, colored photos of a child with smallpox lesions, which could make the skin from head to toe look like pebble-grain leather. The cards had been used by doctors for years to help people around the world know what smallpox looked like. Given that the lesions were so similar, we figured the cards would be useful in helping people identify cases of monkeypox too.

For years, stacks of these cards had been gathering dust in a closet deep in the bowels of WHO, but we pulled them out and started taking them with us into the field. In villages where we stopped, we'd pass around the cards and ask, "Have you seen anyone who looks like this?"

When we found the telltale pustular rash, fever, and respiratory symptoms, we would take fluid from crusted scabs or vesicles, and swabs or puss from active cases. We counted facial scars, vaccination scars, and noted the age of the individual. The age distribution was mainly young people, although about a fifth were over fifteen years of age, which suggested that they had never been vaccinated for smallpox. It would have been good to know if any of these persons was infected with HIV, but we did not have appropriate approval from the ministry to test them.

Meanwhile, we offered a bounty for villagers to bring in small mammals such as squirrels, bats, monkeys, and rats.

In epidemiology, when we talk about chains of transmission—the paths a disease microbe travels from one host to another during an outbreak—one of the key questions is, will a point come when this chain becomes so long that it's impossible to break? That is, when do you have so many human hosts harboring a communicable disease that it no longer needs an animal reservoir at all? That's the point when you're no longer talking about an animal-borne disease. You're talking about a human disease.

The fancy scientific term is the "basic reproductive rate," which is a proxy for how infectious a disease is. If it is more than one, then people can sustain the disease indefinitely because each case is associated with at least one new person infected. Measles, for example, has the highest basic reproductive number of about fifteen, which is why you need to have extremely high vaccination rates to stop outbreaks. Influenza is about two to three, but it makes up for it with a very short incubation period, meaning the time from infection to illness. (This is the concept I was asked to explain to Kate Winslet and the writers of her film *Contagion*.) With any new disease, it's by calculating this number that you gain some sense of the magnitude of the problem.

In an outbreak like this, if you find that the average infected household has had fewer than one additional case of

infection, then you conclude that the outbreak has peaked. But if the disease's reproductive rate is greater than one—if on average you're finding more than one additional sick person per household—that's a kind of tipping point. It means the disease is capable of sustaining itself in the community. It might even be gathering momentum.

So one of the crucial questions we needed answered was how many additional cases might be in that household. Then we would compile our results to get a big picture of what was going on.

If a virus's reproductive rate stays above one, it can persist in a population forever. This is every microbe's dream and every epidemiologist's nightmare. You have examples of those microbes that stick, you have examples of those that don't stick, and the critical factor that makes them stick. That's a critical issue for us as we think about the next global pandemic. Which ones get to say, "Hey, I made the jump. I never have to go back to the jungle again, slumming inside rodents." Many of our exclusive human diseases have successfully made that jump: measles, seasonal influenza, malaria, and HIV.

Overall, a disease like Ebola may have a basic reproductive rate less than one. But if the infected people are in a community or a hospital where there's effectively no infection control, then it can keep spreading for a long time before it burns itself out. Outbreaks always burn themselves out eventually, but the issue is, how long do you have to wait before that happens, and how much havoc will the community suffer in the meantime?

One of my companions in our Congo adventure was the amazing Joel Williams, of goat-eating notes fame from Oman. Trained as a veterinarian, he was a public health officer in the US Air Force who had a fellowship to study epidemics. He was one of the best epidemic intelligence officers I've ever worked with and a modern-day MacGyver—a TV secret agent from the eighties who could fashion whatever he needed using only a Swiss army knife and whatever junk was lying around.

All day long at the various villages where we stopped, locals would bring us wild animals they'd caught, and Joel would test them to see if they were carriers of monkeypox or any other diseases we were tracking. Essentially, Joel created a biosafety level 3 lab in the middle of the jungle. He traveled with a portable generator he'd bought in the local market in Kinshasa (which we joked was the one we brought from Atlanta but had never arrived with our luggage), a portable centrifuge, and all sorts of other equipment. It wasn't *Star Trek,* but you get the idea. Joel also created work space to dissect animals and put the various parts into canisters of liquid nitrogen. In his little jungle lab, he could do anything we needed him to do with the animals that people brought us. He could take blood samples, or he could professionally dissect the animals and extract whatever organ we needed to examine and send to Atlanta for testing. Joel and I would be up late at night, long after the teams returned from the village, using the light from a portable lantern to get all the animals processed before the next day.

But this research put us in a bit of an ethical quandary. We knew that the most common way people were getting infected was through direct contact with infected animals they were hunting and eating. So should we tell the local people to limit their contact with the animals they were used to hunting to avoid being contaminated? Obviously, we didn't want them to get infected, but at the same time we knew they were going to be hunting these animals anyway, and we really needed specimens. We struggled with this for a while because we could potentially be putting the trappers at risk of infection. In the end, we adopted the pragmatic view that the villagers were already trapping these animals for food and we were simply diverting them for research. We stressed limiting the handling of the animals till they were well cooked, and restricting contact with suspected cases to a single person, preferably the oldest member of the household who had either recovered from monkeypox or had a vaccination scar.

Of course, as we handled these animals, including th blood and body parts, we were concerned about not g ting infected ourselves. We had medical scrubs, rubber glov and masks—although I think Joel was probably more cons entious than I was about steadfastly maintaining biosafe in the Congo's tropical heat. Anyway, we tried to be caref because we were an awfully long way from the nearest full equipped hospital.

As part of his exceptional preparedness, Joel had all kind of emergency gear that I would never have thought of bring ing along. At one point, we noticed that a gigantic swarm o army ants had gathered outside our hut, and an attack seemed imminent. Joel told us, "If those ants get inside, we're done for." Then, out of the blue, he pulled out a huge plastic bottle of heavy-duty ant poison. We were all thinking, Where did that come from? The guy carries this stuff around in his luggage? He sprayed the liquid all around the perimeter of the hut, and the ant invasion never materialized. Joel knew how to keep animals under control. As I said, he was a vet.

Another benefit of traveling with a top-shelf public health officer was that he acted as our de facto restaurant inspector. Of course, I use the word "restaurant" metaphorically. There were never any places to eat—rural Congo is not exactly a tourist mecca. The buildings were mud huts with thatched roofs, and we usually slept on cots we carried with us, but whenever we were going to be in a village for a while, one of the first things we would do was to hire cooks. Our dining area was an open space in front of a hut with a single small table and some chairs. We'd sit there at the beginning and end of the day, and eat the meals our cooks had prepared.

As our food inspector, Joel observed the preparation for the evening meals and, at first, told us only what he felt we needed to know. Breakfast, we quickly noticed, was invariably

leftovers from the night before. After a few days of this, Joel asked me, "Ali, have you noticed any refrigerators around here?"

No, now that he mentioned it, I hadn't. Well, what's a little intestinal distress, especially with ciprofloxacin as your best friend? If you don't think about it too hard, sometimes you can get through it okay.

I am a gigantic carnivore, but as a Muslim I observe certain food restrictions, one of which is that I try to eat only meat that is *halal*, meaning that it's been butchered in accordance with Muslim customs. (Think of it as the Muslim version of kosher.)

Now, it's pretty hard to be a choosey eater when you're roaming around the African interior like a character out of a Joseph Conrad novel. In rural Congo, far from the nearest restaurant with a multipage menu, I got pretty tired of eating nothing but local vegetables day after day. And despite all the rivers in the vicinity, there was not a lot in the way of fish for sale either. So one afternoon I decided, Fine, I'll buy live animals and take care of making them halal myself. I'll do the butchering.

The next morning, a villager brought me a live goat that I'd paid him for. I took a sharp knife, said, "*Allahu Akbar*" to give thanks, then sliced clean through the animal's windpipe and the carotid arteries in one swift motion to minimize suffering. Joel then did the obligatory inspection of the carcass to make sure the animal had been healthy. Mission accomplished. Everyone on the team, including the villagers we'd hire to do our cooking, was delighted—fresh meat! A few days later, I did the same with a brace of guinea hens that I'd bought. We all agreed it was a nice change to have meat in our diet again.

A few days after that, I noticed that my colleagues were more excited than usual. Even the goats tied up nearby seemed excited. I found out that a villager had just arrived with a live suckling pig, and my companions were waiting for me to

butcher it. They were already fantasizing about all the bacon, ham, and pork chops that would be added to our week's menu. I had to tell them, "Look, you've got the process down, but you've completely missed the concept. Pork is simply not on the Muslim menu. Nobody—*nobody*—can make a pig halal." However, I was a good sport and paid for the pig anyway so the rest of our team could eat it.

Despite the fact that my job was all about how *not* to get infected, I admit that even I would be a little lax. Sometimes at night I didn't bother draping a mosquito net over my cot before climbing in. Insecticide-treated mosquito nets are the cheapest and most reliable way to protect yourself from the scourge of malaria, especially if, unlike us doctors, you don't have access to prophylactic antimalarial medication.

The thing about mosquito netting, when you think about it, is that the weave can stop insects a lot bigger than mosquitoes. And some of those things you really don't want in your bed. I recall waking up one morning to the sound of people banging around looking for fuel for the generator. I opened my eyes and saw a fat hairy spider the size of my hand crawling across the mosquito net a few inches from my head. Not a pleasant sight, but far better to find a tarantula on the net than inside the net. That was the end of my days of not always using a net.

Another member of our team in the Congo was the expat mammalogist Delfi Messinger, who was sort of an American version of Jane Goodall. She normally worked at a rescue center in the capital, Kinshasa, that specialized in wild bonobos. These are cousins of the chimps, but much gentler. If you think of a chimp colony as marine boot camp, with a rigid hierarchy enforced by muscle and intimidation, bonobo society is more like a hippie commune, where sex is the ever-present social lubricant that keeps everybody chill. She was quite a colorful character, an animal conservationist who'd lived in Africa for fourteen years. While a Peace Corp volunteer,

she'd volunteered to help WHO with monkeypox once before. During a major uprising, when bullets were flying, she did not flee. Instead, to protect her rescued bonobos, she spray-painted "SIDA" in blood on the entrance of the compound where she worked. (SIDA is the French term for AIDS.)

The animals Delfi worked with had usually been abandoned by their mothers or injured by poachers, who hunt them for bush meat. She was a lovely woman, great with animals, but like Goodall, more identified with the animals than with the humans who made life increasingly difficult for her furry charges. I would try to pin her down about the genus and species of some local creature, and she would know what it was, but it was hard to get her attention long enough to get an answer. It wasn't that she didn't want to be helpful. It was more that she just didn't share our sense of urgency about the mission. She was accustomed to spending her days with bonobos, and bonobos are famously laid back.

The more serious problem we had to deal with was the First Congo War. We knew it had hit home for us when, as I mentioned in the introduction, a kid showed up on a motorbike saying that rebels fighting President Mobuto on behalf of Laurent Kabila, an ethnic Luba from Katanga Province, were less than a day away.

There have been tensions between various ethnic groups in eastern Zaire for centuries, especially between the agrarian tribes native to Zaire and the seminomadic Tutsi tribes that emigrated from Rwanda. Destabilization in eastern Zaire that resulted from the Rwandan genocide was the tipping point that caused numerous internal and external factors to align against the corrupt and inept government in Kinshasa.

Then, in the 1990s, a wave of democratization swept across Africa that put pressure for reform on Zairian president Mobutu Sésé Seko. He officially ended the one-party system he had maintained since 1967, but was ultimately unwilling to implement sufficient reform, alienating allies both at home

and abroad. In fact, the Zairian state had all but ceased to ex ist, with most of the population relying on an informal econ omy for their subsistence. Making matters worse, the Zairia national army, Forces Armées Zaïroises (FAZ), was forced t prey on the population for survival.

Of those who fled Rwanda during the genocide, about 1.5 million settled in eastern Zaire. These refugees included those who fled the Hutu *génocidaires* as well as those who fled the Tutsi Rawandan Patriotic Front, fearing retaliation. Prominent among the latter group were the *génocidaires* themselves, including elements of the former Rwandan army, Forces Armées Rwandaises, and an independent Hutu extremist group known as Interahamwe. They were the guys closing in on us.

After we called the US embassy and they told us to evacuate, we sent villagers out to round up our team. Then we consolidated our samples into a single tank of liquid nitrogen and began the seventy-five-mile trek back through the jungle to the airstrip at Lodja, often floating our vehicles across rivers on pontoons.

The French documentary film crew whose plane was going to pick us up landed in a torrential rain, and as soon as it taxied up, panicked villages hoping to escape Laurent Kabila's rebels swarmed around it, until the security guards fired warning shots.

We were already pretty shaken up, and the weather was nightmarish, which meant that the takeoff from the landing strip was pretty rocky. I noticed that the guy next to me was extremely nervous. Another fellow across the aisle was muttering his prayers. Aside from concern about the plane crashing altogether, there was the matter of stuff that hadn't been tied down well. It was sliding across the plane, so concern that it might hurt somebody or the supplies, causing injury or busting out a door, was always there too.

I turned to my seatmate and told him, "You've lived a good life and if you have no regrets, then dying's not that big of a

deal." I don't see myself as courageous, and I'm not foolhardy but, at the same time, if you're going to go out and help in these kinds of situations, you can't do the job if you're too concerned about your own safety. How do you tell others not to be scared if you're too scared to take action? Not fearing death has always given me clarity of thinking about what to do, because I don't have to deal with my anxiety before getting down to problem solving.

We made it out—barely. But the rebels overran the village a few days after we left and some of the people we'd worked with were killed. Far away or not, the sadness and outrage of finding that good hard-working people had lost their lives as pawns in a power struggle and over mere racism is always overwhelming.

Our work had been disrupted, but still we were able to demonstrate that there was no evidence for person-to-person transmission being sufficient to sustain the epidemic. The long chains of transmission were disturbing, but not surprising given the nature of the disease. Yes, the outbreak had been enabled by the cessation of smallpox vaccination, but we had proved that monkeypox's reproductive rate was still less than one, which meant it wasn't going to become the next global pandemic. It was a serious problem, but it was not the Problem From Hell.

The saving grace of smallpox is that there is no animal reservoir—if you knock it out in humans, that's it. There's also a very effective vaccine that can be combined with "ring vaccination," which means inoculating everyone likely to have come in contact with the infected individual. Then you can form an additional buffer of immunity if you want by also inoculating a second ring of people who may have been exposed to those in the first ring, meaning those directly exposed.

Monkeypox is a different matter. Not only can it recede into the jungle for any number of years before reappearing in humans, but it can be easily transported in the convenient

carrying case known as a rodent. And these days, you can fin the damnedest rodents in the damnedest places.

Oddly enough, I did not leave monkeypox behind when left the Congo. Seven years later, in May 2003, a three-year-old boy turned up in a clinic in Wisconsin with a fever (103°F) of unknown origin, swollen eyes, and a red vesicular skin rash. The child was hospitalized, and when doctors examined samples from his lesions under an electron microscope, they saw a brick-shaped virus, which is a flag for a pox virus. The doctors called the local health department, which called CDC. This was the first time monkeypox had ever been seen in the United States. Which had public health officials scratching their heads. How does a disease never before seen outside central Africa turn up in the American Midwest?

It turned out that the month before, a Texas importer had received a shipment of 762 African rodents from Accra, Ghana. The shipment included Gambian rats, rope squirrels, tree squirrels, brushtail porcupines, dormice, and striped mice. He then shipped these animals to distributors in six states, as well as Japan.

In Illinois, a distributor received the Gambian rats and dormice and housed them with two hundred prairie dogs. This distributor then shipped the prairie dogs to pet stores in Wisconsin, Illinois, Indiana, Missouri, Kansas, South Carolina, and Michigan. They developed lesions resembling smallpox, but for a long while no one noticed—imagine if this had been a deliberate smallpox attack on the United States. The only good news (for us at least but not the prairie dogs) was that we had identified the perfect animal model for monkeypox infections.

It turned out the Wisconsin boy was bitten by a prairie dog purchased from a local pet store.

When CDC got involved, a number of teams were heading out to different states, mostly in the Midwest, where they

would be trying to trace the disease in local rodent populations and follow up on the associated human cases. I asked to lead the Indiana team, primarily because until then I had seen monkeypox lesions only on young African kids. Seeing them on Caucasian adults would be a first, and this was not just idle curiosity. For a clinician like me, this could be useful diagnostic information.

I picked a top-flight deputy team leader, John Iskandar, who had assisted me on my first outbreak with the contaminated ice on the cruise ship. The moment I got to Indiana, I did something that would have drawn a reprimand at CDC headquarters. I said to John, "Okay, you're in charge," and then I jumped in my rental car and—even though I was way too senior to be doing this—drove around Indiana for several days making house or hospital calls on every one of the patients suspected of having monkeypox. You could say I was acting irresponsibly, but I wanted to feel like an old-time epidemiologist again—a disease detective wearing out shoe leather, looking for the facts, sifting for clues. It was also great to visit patients who weren't going to die. In my line of business, I am often the harbinger of death.

Along the way, I gained insight into the world of "pocket pet" people in this country.

I visited one family that had close to a hundred pets, ranging from mammals to snakes. I boned up especially on the world of prairie dogs, and on the world of swap meets, which is often where you go to buy and trade exotic pets, and perhaps to have the fur trimmed on the exotic pets you bought last time.

A lot of times, the people out walking prairie dogs as if they were Chihuahuas were farm families living in trailers. It's a little known fact among America's coastal elite, but it turns out you can drag a giant vacuum cleaner out into the prairie, stick the nozzle down a prairie-dog hole, and suck an animal up out of the ground.

My deputy, meanwhile, was dealing with the bigger issues of epidemiology surveillance, and he was doing it splendidly.

This included continued disease monitoring and a survey in day care center, a school, and two local hospitals.

Of the 200 prairie dogs housed with the Gambian rats and dormice, 94 tested positive for monkeypox virus, including prairie dogs in pet stores in Wisconsin (44 cases), Indiana (24) Illinois (19), Ohio (4), Kansas (1), Missouri (1), and 1 case in New Jersey.

Between May 15 and June 20, 2003, a total of seventy-one people ranging in age from one to fifty-one were infected with monkeypox. Patients typically experienced fever, headaches, muscle aches, chills, and nonproductive coughs. This was followed one to ten days later by a generalized papular rash that developed first on the trunk, then limbs and head. The papules evolved through phases of vesiculation, pustulation, umbilication, and crusting. Every one of these patients reported direct or close contact with a recently acquired prairie dog.

CDC issued guidance on the use of smallpox vaccine, Cidofovir (an antiviral drug), and vaccinia immune globulin (an antibody preparation). Twenty-six residents in five states received the smallpox vaccination. Fortunately, no adverse reactions to the smallpox vaccine were reported.

The case fatality rate for monkeypox is usually between 1 and 10 percent. Although there was one sweet six-year-old with a severe brain inflammation from the virus infection, fortunately there were no fatalities during this US outbreak, which was most likely because this was the milder West African version of the disease than what I had seen in Zaire. But it was a valuable reminder, which is that we are increasingly not immune to a smallpox attack. The deliberate use of smallpox as a weapons is not farfetched due to synthetic biology. One of the great blights on our history is the giving of smallpox-infested blankets to Native Americans.

There's the urban myth of alligators in the sewers of New York, supposedly the result of owners flushing their exotic pets when they realize that a one-bedroom apartment on the

Upper West Side cannot accommodate a large, carnivorous reptile.

Our fear in the Midwest was the prospect of people hearing about monkeypox and releasing their prairie dogs into the wild. We knew that these critters had a fabulous ability to get infected. What we didn't know was what the infection rate was in any given population—what fraction of prairie dogs were carrying monkeypox? Of those that were, how rapidly could the disease they carried spread through a wild population before they themselves sickened and died? If people released their pet prairie dogs only after they showed signs of illness, did that make them more or less dangerous in the wild?

To be on the safe side, the Centers for Disease Control and Prevention banned the importation of all African rodents. The US Food and Drug Administration also issued orders banning the interstate shipment of prairie dogs and all African rodents.

The underlying truth here is that, in the age of air travel, a disease anywhere can very quickly become a disease everywhere.