A REPORTER AT LARGE

NATURE'S BIOTERRORIST

Is there any way to prevent a deadly avian-flu pandemic?

BY MICHAEL SPECTER

Early last September, an eleven-year-old girl from Kamphaeng Phet, a remote village in Thailand, developed a high fever, a severe cough, and a sore throat. She lived with her aunt and uncle in a one-room wooden house—not much more than a hut on stilts. The family had fifteen chickens, which wandered freely beneath the plank floor, where the young girl often played and slept. Then, at the end of August, the chickens died. Within days, the girl was sick, too. Her aunt took her to the hospital, but the fever kept rising. The girl's mother, who lived near Bangkok, where she worked at a factory, rushed to her bedside; sixteen hours later, her daughter was dead. In keeping with Thai custom, she was cremated immediately.

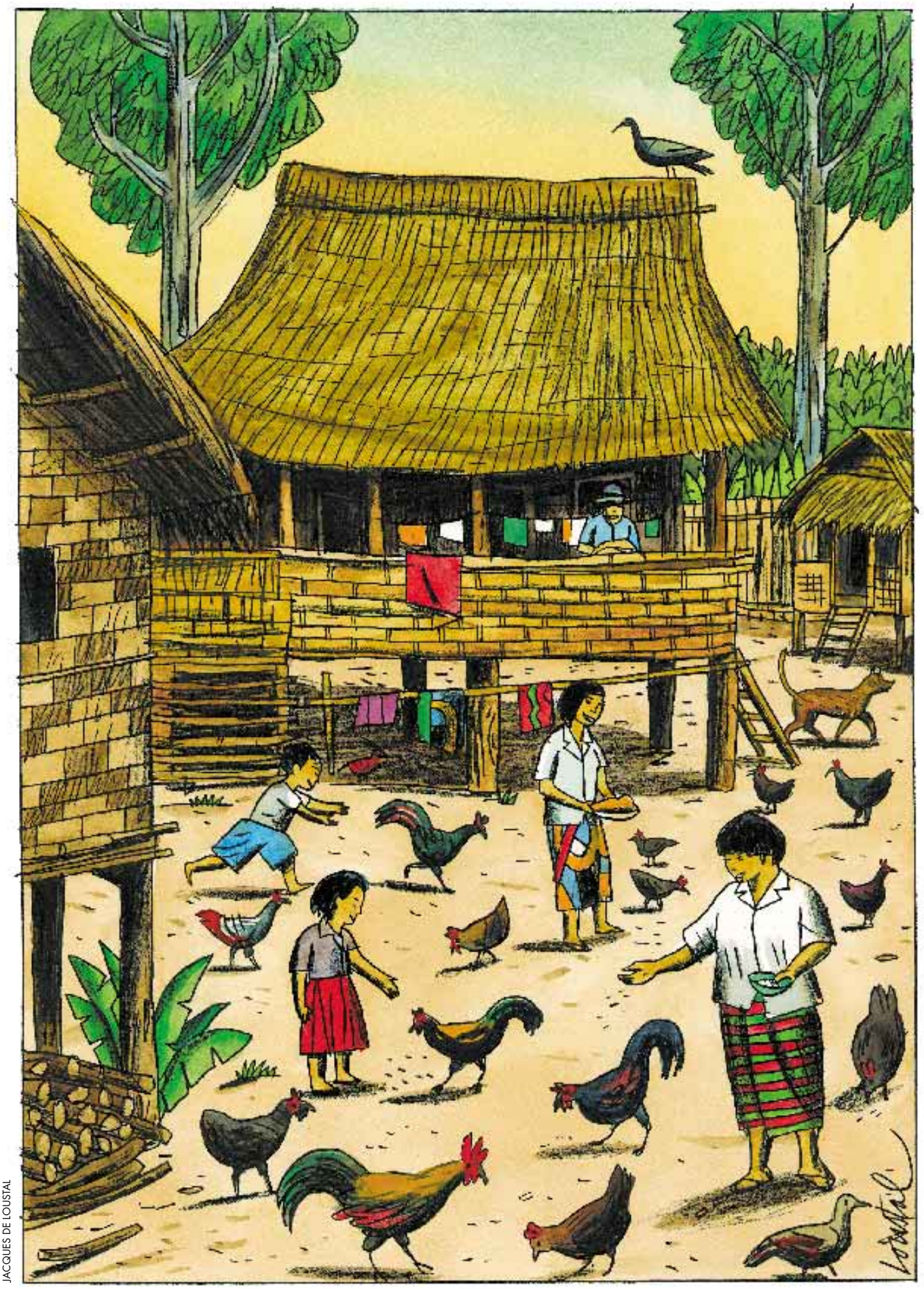
Avian influenza is nothing new in Thailand, or anywhere else where poultry are raised. Veterinarians often refer to it as the fowl plague, because in one form or another the disease has killed millions of chickens, turkeys, and other birds over the years. In 1983, the virus raced so rapidly through the Pennsylvania poultry population that health officials there were forced to slaughter nearly every chicken in the state. Until recently, however, humans rarely became infected with this type of virus. It had happened fewer than a dozen times since 1959, and in each case the illness was mild. But the strain that killed the girl from Kamphaeng Phet is different; in the past two years, it has caused the deaths of hundreds of millions of animals in nearly a dozen Asian countries. No such virus has ever spread so quickly over such a wide geographical area. Most viruses stick to a single species. This one has already affected a more diverse group than any other type of flu, and it has killed many animals previously thought to be resistant: blue pheasants, black swans, turtledoves, clouded leopards, mice, pigs, domestic cats, and tigers. Early in February, nearly five hundred open-billed storks were found dead in Thailand's largest freshwater swamp, the Boraphet Reservoir. And the disease is no longer limited to Asia. In October, customs officers at the Brussels airport seized two infected eagles that had been smuggled from Thailand and destroyed them, along with the other animals held in quarantine at the airport.

This virus also kills people—so far, forty-two have died, including thirteen Vietnamese since Christmas. Those deaths represent more than three-quarters of all known avian-flu infections—an ominous mortality rate. Strains of influenza are named for two proteins on their surface that latch onto respiratory cells and permit the virus to invade them, and, if this strain, known as H5N1, becomes capable of spreading efficiently among humans, it will kill millions. Public-health officials in Asia, still reeling from the crisis created in 2003 by SARS (severe acute respiratory syndrome), have struggled to contain the burgeoning epidemic. Yet the task is immense. SARS was caused by a virus that turned out to be less deadly, less contagious, and far less aggressive than the flu. The threat was never as great. There are six billion chickens in Southeast Asia, and millions of households depend upon them, for income as well as for food; preventing this flu virus from spreading has become all but impossible. By early February, during Tet, Vietnam's biggest holiday, officials began posting livestock inspectors on major highways. Last week, officials banned poultry-raising in Ho Chi Minh City.

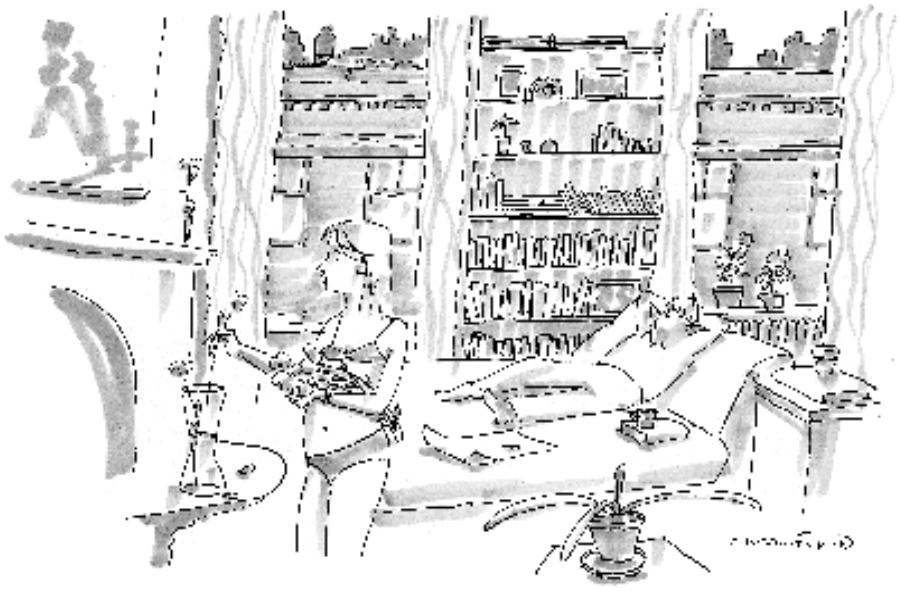
Vigilance is one of the few weapons available. Two weeks after the girl died in Kamphaeng Phet, Thai epidemiologists were asked to visit a hospital near Bangkok, where a woman had symptoms that matched those caused by the virus. It turned out to be a false alarm, but while the investigators were there a nurse took one of the doctors aside and mentioned that another woman had just died of similar flu symptoms. The death hadn't been reported, but the victim's last name sounded familiar, and so did the name of her village.

"It was just a fluke," Scott Dowell told me not long ago over tea in his office, on the sprawling campus of the Thai Ministry of Public Health, in the suburbs north of Bangkok. "Sure enough, the woman was the mother of that eleven-year-old girl. We would never have known if that nurse didn't happen to mention it." Dowell is the director of the Thailand office of the International Emerging Infections Program, which was established by the Centers for Disease Control in 2001. The group, which was among the first to identify SARS when that new virus appeared, is a front-line outpost dedicated to preventing the spread of infectious disease in a world where modern travel, global commerce, and porous borders mean that any new pathogen—whether a lethal strain of influenza, H.I.V., or the synthetic creation of a bioterrorist—may be no more than a plane ride away. Thailand is not nearly as poor as some of its neighbors, but its fertile climate and lengthy borders with Cambodia and Laos—neither of which has a credible public-health system—produce a continual stream of odd, and often deadly, infectious diseases. The Nipah virus, which is named for the village in Malaysia where it was discovered, in 1999, has been endemic; so have dengue and leptospirosis, a bacterial infection that affects humans and animals. Thai-

"One day, they're all alive and healthy," a Thai chicken farmer said. "The next day, they're dying by the thousand."



JACQUES DE LOUSTAL



"It's been weeks since you bought me exculpatory lilies."

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land also has serious epidemics of tuberculosis and H.I.V.

Now there is little on people's minds but the flu. "Our Thai colleagues called us and said, 'Hey, do you want to go to Kamphaeng Phet?' " Dowell said. "And on the way up there they told me the story. And I just said, 'We absolutely have to get hold of this virus.' This could be the first clear case of person-to-person transmission, the beginning of something very significant, something terrifying. So the girl had died and been cremated, and the mother was dead and embalmed. She was literally at the wat, awaiting cremation. The Thai doctor who was riding in the car with me was calling on his mobile phone to the team there, telling them to do whatever they had to do to hold that embalmed body out and take some blood or a tissue sample."

A pandemic is the viral equivalent of a perfect storm. There are three essential conditions, which rarely converge, and they are impossible to predict. But the requirements are clear. A new flu virus must emerge from the animal reservoirs that have always produced and harbored such viruses—one that has never infected human beings and therefore one to which no person would have antibodies. Second, the virus has to actually make humans sick. (Most don't.) Finally, it must be able to spread efficiently—through coughing, sneezing, or a handshake. For H5N1, the first two conditions have been met; it's new and it's deadly. On the ride to Kamphaeng Phet, Dowell couldn't stop wondering whether the virus had met the third condition, too.

If so, there would be little time to distribute medicine, develop a vaccine, establish quarantines, and plan to care for the millions—maybe tens of millions—of sick and dying people throughout the world. "That was why it was so important to get blood or tissue samples, for us to be able to know how this woman died," Dowell said. "Then we get up to the province and we go to the hospital where the girl was and the mother is dead and in comes the aunt and she has had a cough and fever for five days and she is complaining of a sore throat." Dowell and his colleagues grew even more alarmed. What had at first seemed like a coincidence now looked more like the start of an epidemic. "It really had to be human transmission, because there were no other cases in the village," Dowell told me. "Nobody tested positive for the virus. All the chickens had been killed, and the mother didn't even live there; she never encountered a chicken. There was just no other way for her to get sick."

Infectious-disease experts talk about pandemics the way geologists talk about earthquakes; the discussion is never about *whether* "the big one" will hit. Pandemics have recurred in cycles for centuries. The great flu of 1918 killed at least fifty million people and infected hundreds of millions of others. In the United States, it took more lives than all combat in the twentieth century. Hospitals and medical staffs were overwhelmed. Treatment of other diseases stopped. Less severe pandemics occurred in 1957 and in 1968, but each killed millions. The evidence in Thailand seemed to point toward a single conclusion. As it turned out, however, the virus was contained. The third condition for a pandemic had not been met: the aunt, who eventually recovered, and the mother, who did not, almost certainly became sick because each had spent so many hours with the girl; the virus had not mutated in such a way that it could pass easily among people.

Now, speaking in his office, Dowell was calm. "The world just has no idea what it's going to see if this thing comes," he said. Then he stopped himself and started over. "When, really. It's when. I don't think we can afford the luxury of the word 'if' anymore. We are past 'if's. Whether it's tomorrow or next year or some other time, nobody knows for sure. The clock is ticking. We just don't know what time it is."

On October 14th, the four hundred and forty-one black-striped Bengal tigers at the Sriracha Tiger Zoo, near Bangkok, began to die. They had been fed raw chicken carcasses from a local slaughterhouse. Each day, four or five developed symptoms of severe influenza. By the end of the month, forty-five were dead; more than a hundred others were infected and considered a danger to the remaining tigers as well as to the humans who tend them. They, too, had to be destroyed. Until 2003, tigers had never been susceptible to avian influenza. H5N1 was evolving rapidly and with unsettling implications.

I had stopped at the offices of the World Health Organization, in Geneva, on my way to Thailand. The scientists there were holding a meeting to discuss the feasibility of developing a

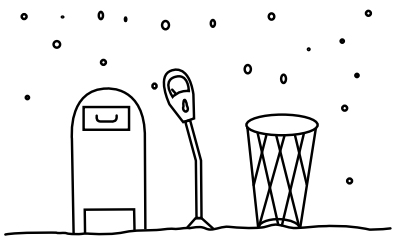
vaccine that would lessen the impact of a pandemic. The man in charge of the W.H.O. influenza program, Klaus Stöhr, was worried. Despite the mounting signs of danger, few countries or companies had taken the possibility of a pandemic seriously, and there was little interest in developing a vaccine. Stöhr has one of the trickiest jobs in the world of public health: remaining unruffled while racing to prepare for the worst. It is never easy to sound the alarm for an epidemic that might or might not soon sweep the earth. When I asked if Stöhr, who trained as a veterinarian, could assess the danger that H5N1 posed for humans, he sat down and sighed. "Let's take a step back for a moment," he said. "We know that during the last three pandemics—1918, 1957, 1968—all these viruses had genes that derived from animals. In 1918, the virus had consisted almost wholly of avian genes. Now we have a very powerful animal virus circulating in Asia that is already moving into humans. It is very widespread. The virus has changed its characteristics over the past few months. It is now highly pathogenic to chickens. It is infecting an increasing number of species—we now know that cats are susceptible. And they don't just start coughing and sneezing, either. They die."

He went on, "We know that the virus may have got a foothold in ducks, many of which, unlike chickens, appear to stay healthy. That's good news for ducks, but it can be very bad news for us, because controlling a disease that is spread through a hidden reservoir of highly mobile birds is much more difficult." Ducks are particularly dangerous, because they can carry in their digestive systems each strain of the virus—there are fifteen—that affects humans. Stöhr compared them to Trojan horses deployed throughout the world. I asked whether any of this information suggested that the virus was on the verge of a global assault on humanity. "Well, we can't say with certainty," he replied. "But take the example of a football player. Maybe he is even a bad football player. So he's kicking the ball ten, fifteen, twenty times toward the goal before he scores. And a good player does it once. This virus is not a good scorer. But even the worst scorer is going to make it one time. And in this game it's going to take only one goal for the virus to win."

It is hard to overstate the damage that the death of sixty million chickens has caused to Thailand's national psyche. Until last year, the country had been the world's fourth-largest exporter of poultry. That ended with the first reliable reports of infection. Both the European Union and the United States have suspended imports from several countries of Southeast Asia. (China, which may have an even more serious problem, no longer exports poultry.) In Thailand, although there are many commercial producers, a large part of the poultry population remains with families and in small households. The Food and Agriculture Organization of the United Nations has estimated that two hundred million farmers in the region keep an average of about fifteen birds each—ducks, chickens, geese, turkeys, and quail. Most of these birds are free to scavenge in their yards, making them prone to infection from the migrating fowl that travel the seasonal flyways from Siberia and northern China.

There is a natural tension between the people who are responsible for a country's commercial agricultural production and those whose job is to safeguard public health. Chinese leaders, worried about trade and tourism, lied about SARS for months when it first appeared—ensuring that the virus would spread. Thailand has just put more than a hundred million dollars into the fight against avian influenza, but when early reports of an illness characteristic of the virus first surfaced there, more than a year ago, that government, too, was reluctant to act.

"It was difficult to persuade officials in this country to take the problem seriously," Prasert Thongcharoen, one of Thailand's most distinguished microbiologists, told me shortly after I'd arrived in Bangkok. We met one morning in his spartan office at Siriraj Hospital, on the Chao Phraya River. "I believe the Department of Livestock at first covered it up. I talked to farmers. At the very first sign of a problem, the department told the public that the chickens had cholera. But farmers said it wasn't cholera. If a chicken has cholera, you give it antibiotics and it gets better. These birds got sick one evening and the next day they were dead. That's not cholera. So I believe it was known, and it spread here at least from October, 2003. One year ago or more. And why didn't the veterinarians realize that? It's not difficult to make that diagnosis. They didn't do the right thing. I'm not saying it would have stopped an epidemic, but they didn't do what they should have done."



The next morning, I went with a woman from the World Health Organization to visit some farmers in Suphan Buri, a province about sixty-five miles north of Bangkok—a straight shot on the wide-open, recently completed freeway. Water buffalo grazed by roadside thickets of bamboo. Acres of bright-green rice paddies bent low in the breeze. Suphan Buri is a relatively prosperous province, thanks to the efforts of Banharn Silpa-archa, the former Prime Minister, who is from the area and whose political party long controlled agricultural development. It is a center of the Thai poultry industry and has been devastated by the epidemic. In Suphan Buri, chickens and ducks had been living in groups of between five thousand and ten thousand, often in long wooden coops spread out on stilts, and perched on top of a pond.

Finding a chicken in Suphan Buri proved to be a challenge. Farmers had been forced out of the business and were unwilling to talk. Most of their flocks had been killed. The government compensated the farmers generously, but the money didn't make up for their losses, or persuade many to switch to a more regimented way of raising birds: coops now have to be built on land, where chicken feces can't contaminate the water. It's hard to change the habits of a nation, particularly when it costs a great deal and may be futile. After driving for about an hour—from empty

farm to shuttered coop—we came upon a seventy-year-old farmer working a fishpond next to an abandoned chicken house. The man had deep-brown skin and a remarkably youthful face. He wore a long-sleeved white shirt and black knee-high rubber boots over clay-colored cotton pants. He had a dark-blue baseball cap on his head. Like many of his neighbors, he was a contract farmer who raised chickens for one of the conglomerates. Influenza had ruined him, he told me; all forty thousand of his chickens had died. He hired an earth mover to stuff the chickens into their coffins—giant blue-and-orange feed bags. "I could put thirty chickens in each bag," he said. He then used a crane to lift the bags into mass graves next to a copse of bamboo on his property. He pointed to a low rise and shook his head. "It's damn hard to watch," he said. "One day, they're all alive and healthy—the vets were here the week before to check them—and the next day they're dying by the thousand. It happened so quickly. They started shivering, thousands of them at once. And then they started to fall. Every one of them. They just fell over, dead." He said that he's stopped raising chickens, and that he's fed up with the government. He can't afford to switch to the enclosed system of housing poultry that Thailand now requires. "I'm too old, and you have to inspect everything every day," he said. "It's ridiculous. Under the new rules, you have to change clothes even when you go into one of the chicken houses. Who do you think is going to do that?"

I asked who he thought was responsible for the current situation. "Well, the bird flu came here from Hong Kong, like most diseases do," he said. "And SARS, too. But once it's here I'm not sure how you get rid of it. And I'm not sure how you keep it from coming. They have killed millions of chickens, but are they going to kill every single one?"

The farmer is not entirely out of the business; he still raises birds for cockfighting, which is a big sport in Thailand. It is also a dangerous one when an avian virus is loose. These animals are often sold in the market, their cages rarely disinfected. People move from farm to farm to buy them. And, now that such activity has become harder, middlemen are often paid to do it. Thousands of people attend cockfights. The government has tried to crack down, citing the ease with which the birds pass viruses to one another and to other animals in the marketplace. But it has not been very successful.

The man shrugged. He is now resigned to raising fish. "Chickens you had for forty days and then sold," he said. "Fish we have to raise for five months." He has sixty thousand fish in his pond. It's hard to know how much food to give them and how to keep birds from swooping down at feeding time and stealing it. "This whole thing is not for me," he said. "I want it back the way it was."

After leaving his farm, we were turned away at several others. The longhouses in the paddies all seemed empty. Eventually, for fifty baht—a little more than a dollar—I persuaded a man on a motorcycle to lead us toward the tree line, across a small bridge, and into a deep-green pasture next to a brook. The field was filled with some two thousand dark-brown long-billed ducks, penned in by a white picket fence. The din was enormous, even with the car windows closed. The man watching over the birds was protective of the owner, but he finally told us how to find her.

Saijai Phetsringharn is a forty-year-old woman who wears diamond rings on her fingers and gold bracelets on her wrists. As a wholesaler of duck eggs—she earns about two baht apiece—Phetsringharn is something of an avian activist, and she has strong opinions about how to stop the epidemic, which she has voiced frequently in public protests. "Vaccinate the animals," she said. "The government needs to vaccinate the chickens."

Vaccines for chickens do exist, but there are no consistent guidelines on how to use them. Both China and Indonesia—which do not export poultry—vaccinate their birds. But, so far, the Thai government has refused to adopt the practice. There are legitimate reasons for that: it takes time for the vaccines to work, and they may not always prevent the birds from becoming infected or from passing the virus on. In theory, that means humans could be exposed to healthy-looking birds that nonetheless carry the virus. Still, many public-health officials, including Scott Dowell, of the C.D.C., told me that it was time for the Thai government to reconsider the policy. Some villages are taking matters into their own hands, using herbs on the chickens, which many think will protect them.

"The government seems to think they can solve this problem just by killing birds," Phetsringharn said, mentioning that eight thousand of her ducks had recently been killed. "They are wrong. If they do that, the virus will persist but our industry will die."

She may be right, but recent genetic studies of the virus have determined that, while the ducks remain healthy, they are now shedding larger amounts of the virus and for longer periods than they did just a year ago. Last week, the government proposed a vast new culling—of three million free-range ducks.

"And this light here lets you know when the camera is obsolete."

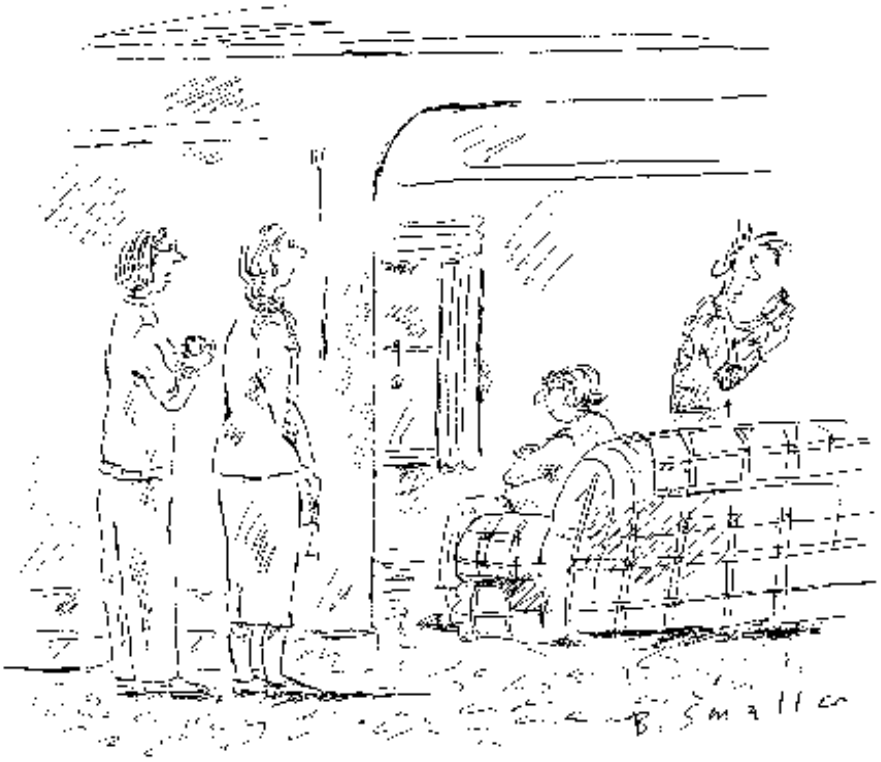
"Ducks are not like chickens," Phetsringharn said. "They need their freedom." She was standing in a garage stacked high with trays of large brown eggs. Many boxes of fowl-cholera vaccine were lined up on the floor. She is at least the third generation of her family to raise ducks. "We did it before I was born. Before my mother was born." She has three children, who are four, ten, and thirteen, and she expects them to enter the business, too. "If there is a business," she said, frowning.

Influenza is the sixth-leading cause of death in the United States, and it is responsible for even more damage in less-developed countries. During most flu seasons, as much as twenty per cent of the American population becomes infected, about thirty-six thousand people might die, and more than two hundred thousand are admitted to hospitals. Few viruses have endured as long or done as much damage. Records of respiratory ailments that appear to have been influenza go back to ancient Greece and Rome. The word "influenza" derives from the Latin *influentia*—"influence"—reflecting the common belief that the epidemics it caused were due to the influence of the stars. People—often even doctors—refer casually to any respiratory infection as "the flu," but most are not. Influenza is caused by an orthomyxovirus, which comes in three types, designated A, B, and C. The B and C forms can infect people and make them sick, but they're not common and they're rarely serious. Type A is the virus we worry about. Every influenza virus has hundreds of microscopic spikes rising from its surface. Most are made of a viral protein called hemagglutinin, which can latch onto cells that the virus seeks to enter. The other spikes are called neuraminidase, an enzyme that helps the virus spread. These two proteins are the reason that flu viruses are labelled with the letters "H" and "N." Type A influenza has been so successful for so long because it is among the most mutable of viruses, capable of swapping or altering one or more of its eight genes with those from other strains.

Because this virus evolves so quickly, an annual flu shot is at best a highly educated bet on which strain is most likely to infect you. The vaccine stimulates antibodies that should provide protection from the particular strain of the virus that epidemiologists think will predominate this year. But, if you are infected with a flu virus whose surface proteins have changed, your antibodies won't recognize them fully. That new strain could edge its way past the human immune system's complicated defenses and establish a new infection, and—though you might have some resistance, depending on how the strain had changed—you would need an entirely new set of antibodies to fight it. This goes on throughout our lives, and these small changes on the surface of the virus—the antigen—are called "antigenic drift."

The eight viral flu genes are put together in segments a bit like a line of connected Lego blocks, and they are easily dismantled, changed, and reassembled. When animal strains of influenza mix with human strains, there is always the possibility that the result will be an entirely new virus. That is called "antigenic shift." When large fragments of genetic material are replaced with genes from other influenza subtypes, or with genes from other animals, like pigs or chickens, the outcome is something that the human immune system will be unable to recognize. And, even with the sophisticated tools of molecular genetics, we cannot predict how a virus will change or when or whether it will become more or less dangerous. We don't even know if survival of the fittest, when it comes to viruses, means survival of the most virulent: a virus so powerful that it kills all its hosts couldn't last long.

The elaborate transportation system for a flu virus adds to the chance nature of its evolution. The midpoint between Thailand and the Northern Hemisphere is Guangdong province, in southern China. Migrating birds often stop there, which may be one reason that so many epidemics begin in the region. The chances that an animal virus will jump the species barrier are greater in places with constant contact between humans and animals. Sixty per cent of the world's people—and billions of its animals—live in Asia. There are eighty-six million people in Guangdong alone—more than the population of



"I'm in the sandwich generation—my parents don't approve of me and my kids hate me."

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Germany. Every day, tens of thousands of chickens are moved by truck from Guangdong to Hong Kong. Agriculture, too, plays a role. Rice, the ubiquitous crop of Asia, needs water. Farmers raise ducks on the rice farms and on their ponds, and wild waterfowl can transmit their virus to domestic ducks there. The ducks can then pass it along to chickens and pigs, which often serve as a mixing vessel for human- and animal-flu viruses, because the receptors on their respiratory cells are similar to ours. In such an environment, one sneeze from a pig could be enough to start a pandemic.

When the Bush Administration's Health and Human Services Secretary Tommy Thompson announced his resignation, in December, he cited a potential epidemic of avian influenza as one of the greatest dangers facing the United States. The World Health Organization has put a "conservative estimate" of the deaths from such an event at between two and seven million people and expects that as many as a billion people would fall ill. Other numbers are even more sobering: Michael Osterholm, the director of the Center for Infectious Disease Research and Policy at the University of Minnesota, has made calculations based on the 1918 epidemic, taking into consideration general improvements in health care. Applying those fatality rates to the world's current population, Osterholm suggests that at least a hundred and eighty million people would die in a pandemic of similar severity. Shigeru Omi, the W.H.O. official in charge of Asia, recently arrived at similar conclusions, stating that an H5N1 pandemic could infect between twenty-five per cent and thirty per cent of the world's population. Economic losses would be in the tens of billions of dollars.

Robert Webster, who holds a chair in virology at St. Jude Children's Research Hospital, in Memphis, has been studying avian influenza for decades. Nobody knows more about the origins of the virus, how it changes, or what those changes might mean. "This is the worst flu virus I have ever seen or worked with or read about," he told me when we spoke recently. "We have to prepare as if we were going to war—and the public needs to understand that clearly. This virus is playing its role as a natural bioterrorist. The politicians are going to say Chicken Little is at it again. And, if I'm wrong, then thank God. But if it does happen, and I fully expect that it will, there will be no place for any of us to hide. Not in the United States or in Europe or in a bunker somewhere. The virus is a very promiscuous and efficient killer. That much we have known since 1997."

Pandemics seem to occur every thirty or forty years. On May 21, 1997, three decades after the previous outbreak, a three-year-old boy in Hong Kong died from what doctors were fairly certain was the flu. The most densely packed city on earth, Hong Kong has often served as a cauldron for viral diseases and a transit point for epidemics. In 1894, a plague killed more than a hundred thousand people there after arriving from China. The two flu pandemics that swept the world in the past fifty years each appeared first in China, then in Hong Kong. In 2003, SARS originated in China, incubated in Hong Kong, and then fanned out across the globe. Health authorities in Hong Kong have every reason to be vigilant about unusual signs of illness.

The boy's doctor had forwarded a routine sample of his respiratory secretions to researchers at the Department of Health. Something about the structure and arrangement of the viral strain seemed strange to them. Clearly, it was a flu virus, but not a strain the Hong Kong scientists had seen before. They sent samples to research centers in England and the Netherlands and to the C.D.C., in Atlanta. It took three months before specialists at the three institutions could agree on what they were looking at through their microscopes. It was H5N1, which until then had affected only poultry. Not even farmers who handled sick birds every day had become ill.

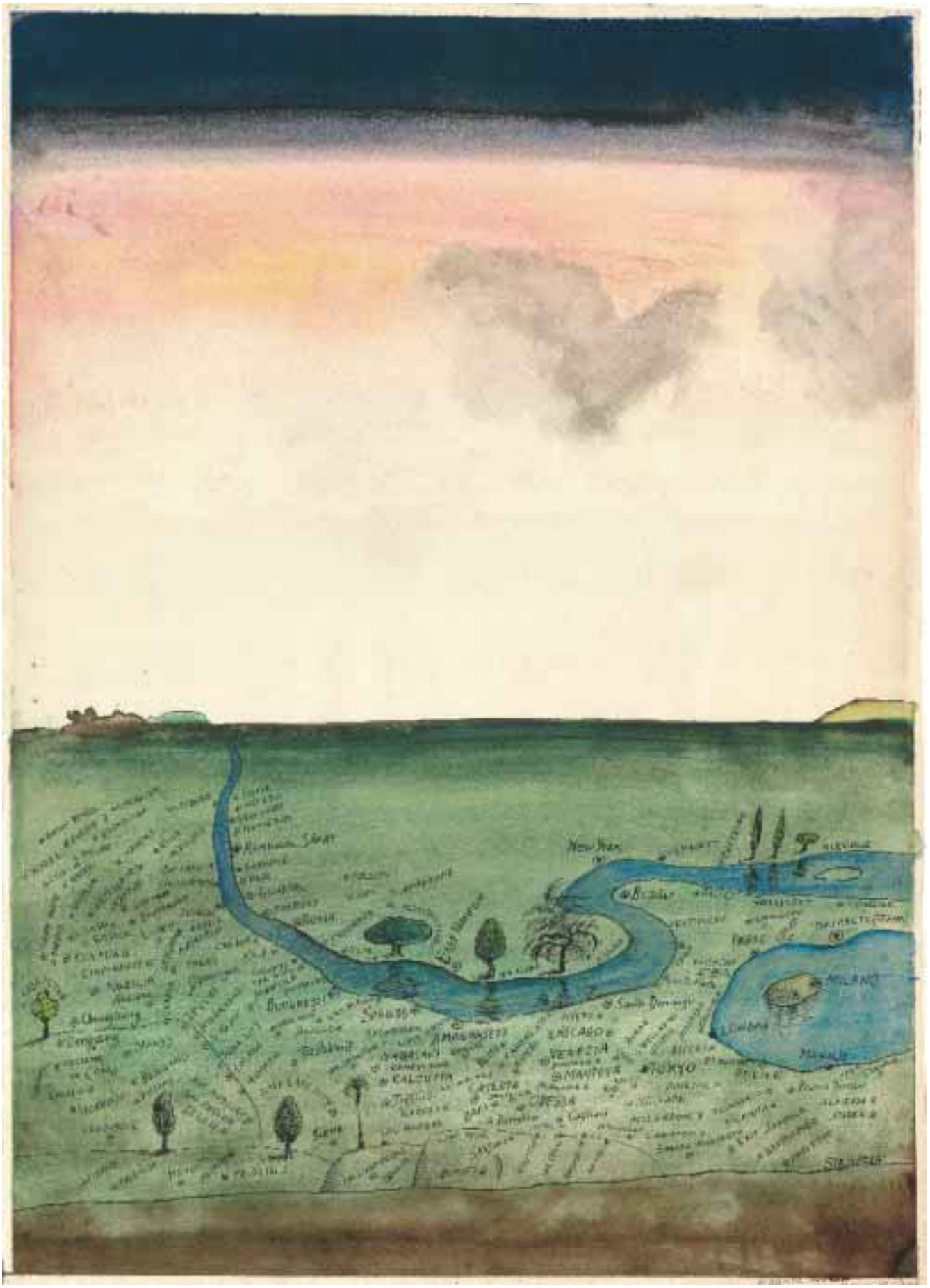
As soon as the strain was identified, Keiji Fukuda, the chief flu epidemiologist at the C.D.C., left for Hong Kong. The possibilities frightened him, but he was also excited by the opportunity to investigate a genuine medical mystery. How could that virus have infected a three-year-old child? Fukuda and his colleagues from the C.D.C.

PORTFOLIO

MAP OF *SAUL*

Never sure of his beginnings, the late Saul Steinberg invented the Romanian city of Râmnicul Sărat as a place "for me to be born in," and put it downstream from Hatteras, and not far from Laramie, Waikiki, and Juneau, in this 1966 drawing of the wandery river of his life. The piece, designed as a *New Yorker* cover but not run, appears at last in a new book, "Steinberg at *The New Yorker*," by Joel Smith, and at the current exhibition of the same name at the PaceWildenstein Gallery, each celebrating a unique conjunction of artist and institution. During a fifty-eight-year outpouring of eloquent surprises that did not quite end with his death, in 1999, Steinberg produced eighty-nine covers for this magazine, along with six hundred and fifty cartoons and drawings, and five hundred-odd spreads and multi-page features. Maps became a favorite Steinbergian theme—as did handwriting, labels, punctuation, numbers, sounds, Americana, thoughts (a fat, blocky capital "E" seeing itself in svelte Caslon type, with French accent), taxis, and alligators. That 1976 map of the United States as seen in narrow view from Ninth Avenue is his best-known (and most pirated) drawing, but other readers might recall a chart of the artist's wiggly route across some back roads of Massachusetts while he tries to follow the dying thread of Mozart's "La Clemenza di Tito" over his car radio. Steinberg called the magazine "my refuge, *patria*, and safety net," and rewarded us with his ceaselessly astounding best. One can picture an afternoon in downtown Râmnicul Sărat, which honors its favorite son with daily parades, grand avenues, pedestals, florid proclamations, statuary, rubber-stamp Indians, thought-laden artists, drum majorettes, and airborne music and exclamation points, all by Saul.

—Roger Angell



SAUL STEINBERG, "AUTOGEOGRAPHY" © THE SAUL STEINBERG FOUNDATION

spent a month in Hong Kong, turning over every piece of evidence they could find. But they saw no other indication that the virus had moved into the human population. "It had not spread to even one other person, so we just wrote it off as a freak occurrence," Fukuda told me when I went to see him in Atlanta. Fukuda is wiry, quiet, and intense—characteristics that underscore his deadpan presentation of facts. "It was weird and a little scary," he told me. "But it was so unexpected to find it in a human being that we eventually decided it must have been one instance involving that boy and that would be the end of it."

The team returned to the United States and moved on to other work. Then, later that year, a fifty-four-year-old man was hospitalized in Hong Kong with the bird flu. By December 5th, he was dead. Fukuda returned to Hong Kong with the same troubling question that would eventually preoccupy his colleagues in Thailand. "I wondered if this virus was now acting like other strains—maybe its genes had mixed with human genes and it was moving freely among people. I remember sitting on the plane and thinking, If this is really happening, my God, what are we in for?" By late December of 1997, eighteen people had become infected in Hong Kong, and six of them died—a remarkably high mortality rate. Researchers couldn't figure out how the virus was getting to humans. In the past, scientists had believed that such mutations required pigs to serve as a mixing vessel. These new cases suggested that H5N1 didn't need an intermediary host; it seemed that the virus had acquired the ability to move directly from birds to people. "I don't know why I remember this, but I do," Fukuda told me long after the events had taken place. "Christmas that year was on a Thursday," he said. "It was a very bad day. There were too many reports of people getting sick. The city just had this bad feeling to it. A heavy feeling."

Fukuda thought that only drastic measures would stop an epidemic, and he said so. The Hong Kong agriculture department, realizing that the virus was spreading rapidly within the poultry markets of the city, agreed. Many bird species were housed together in the markets, an ideal environment for genes from different viruses to mix and mutate. On December 29th, city officials began to kill every chicken in Hong Kong. One and a half million birds were culled, then disinfected and buried in landfills. "All these trucks driving up to a medium-sized poultry farm," Fukuda recalled. "Everyone is covered with protective gear—moon suits and all. They put the birds in bags and then used gas on them. Then they were deposited in the landfills." The decision was risky, but it seemed to work. No one else became ill, and many public-health experts believed that the slaughter in Hong Kong had prevented a horrifying epidemic. For several years, there were no other reports of the virus infecting a human being; some people even dared to hope that H5N1 had been vanquished. Fukuda was not so sure. He knew how risky—and potentially dangerous—such assumptions about infectious diseases can be. Then, in early 2003, Fukuda's fears were confirmed. A nine-year-old boy and his father were hospitalized in Hong Kong with the bird flu. The boy recovered, but on February 17th his father died.

That month, officials from the World Health Organization's rapid-alert team began hearing reports of a "strange contagious disease" that had attacked scores of people in Guangdong province, which borders Hong Kong. A month earlier, geese had suddenly started to die in several Hong Kong parks. Klaus Stöhr, of the W.H.O., happened to be attending a meeting in Beijing to help China develop a national flu-vaccine strategy. As Stöhr listened to each province report its general-health information, he became increasingly alarmed. Finally, an official from Guangdong stood up and spoke about an outbreak of what seemed like an unusually powerful flu. People were dying, and it was difficult to understand why. "I just put two and two together and it added up," Stöhr told me a few months later. "I thought this must be H5N1 coming back in precisely the way we had all feared. It was our worst nightmare—and the world's."

In the end, the illness that the Chinese were talking about turned out to be SARS, and scientists throughout the infectious-disease community, though concerned about the dangers of the new virus, took a deep breath. But the confusion was understandable. The early symptoms of SARS seemed a lot

MEMOIR

Orwell says somewhere that no one ever writes the real story of their life.
The real story of a life is the story of its humiliations.
If I wrote that story now—
radioactive to the end of time—
people, I swear, your eyes would fall out, you couldn't peel
the gloves fast enough
from your hands scorched by the firestorms of that shame.
Your poor hands. Your poor eyes
to see me weeping in my room
or boring the tall blonde to death.
Once I accused the innocent.
Once I bowed and prayed to the guilty.
I still wince at what I once said to the devastated widow.
And one October afternoon, under a locust tree
whose blackened pods were falling and making
illuminating patterns on the pathway,
I was seized by joy,
and someone saw me there,
and that was the worst of all,
lacerating and unforgettable.

—Vijay Seshadri

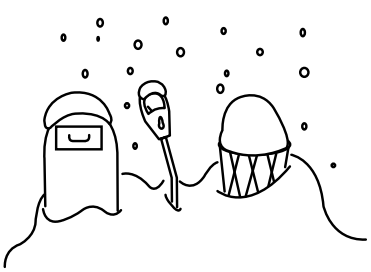
like those of the flu. And nobody expected this entirely new virus. Hong Kong went into economic, social, and psychological shock. Taxi-drivers disinfected their cabs (and advertised the fact on banners that flew from their windows) each time they dropped off a passenger. Subway ridership plummeted, and people who were brave enough to use the system wore white cotton masks—which, like antibacterial hand lotions, were selling briskly at every kiosk in the city. Restaurants and hotels were either shuttered or nearly empty. Headlines flashed constantly across every television set: "Outbreak," "In the Shadow of the Virus," and "Fear Across Asia." For the first time, the W.H.O. issued a global health alert that advised travellers to avoid Hong Kong and Guangdong province unless they had no choice. Billions of dollars in revenues were lost, unemployment reached record levels, tourism vanished, and the epidemic pushed the city of seven million to the edge of its third recession in a decade.

Since SARS first appeared, it has killed fewer than a thousand people; during that time, a larger number drowned in bathtubs and swimming pools in the U.S. The fears weren't altogether irrational, however. SARS was the first serious, easily transmitted disease to emerge in the twenty-first century, and the first in decades to move from animals to humans while also mutating into an illness that could be spread simply by breathing. More important, perhaps, coming not long after the anthrax scare of 2001, SARS reminded a world of something that it seemed to have forgotten—how easily it could be disabled by disease.

Early one morning, I drove to Sa Kaeo, a province about two hours east of Bangkok, on the Cambodian border. There, and in a province near Laos, Scott Dowell's C.D.C. team has established a sort of radar defense system for microbes—the International Emerging Infections Program. The idea came about simply enough: the United States wants to protect itself from foreign threats, and in the nineteen-nineties—after confronting a series of new viral diseases—public-health officials argued persuasively that such unexpected infections posed a threat that the United States was not prepared to meet. Zoonotic diseases—animal illnesses that infect humans and make them sick—caused particular concern. Since the viruses often appear in densely populated Third World countries, the C.D.C. set up its first operation in Thailand. A second office opened last year, in Kenya. "The feeling was that maybe if we were out there with our ear to the ground, listening and watching, we might be able to catch something before it's too late," Mark Simmerman, who is with the C.D.C. in Bangkok, told me as we drove. "So we decided to look very carefully at the residents of these two provinces."

The I.E.I.P. team has more than a million residents under surveillance for signs of pneumonia and other bacterial infections. (The theory is that if you look at lung X-rays and blood work closely enough to detect pneumonia you are also likely to detect other significant problems.) Every morning, in every hospital, a surveillance officer reviews the previous day's admission logs. Whenever there is a questionable notation in the reports, doctors review it further. Technicians in the field are equipped to scan the X-rays and send them electronically to labs where more sophisticated analysis is possible. There have already been some successes: the program has helped raise the profile of influenza, which had traditionally been ignored by most Thais; it has made it easier for the provincial leadership to convince people that sick birds can be dangerous to humans. The team helped identify SARS, of course, and Dowell was one of the authors of the initial report characterizing the virus.

The C.D.C. selected Thailand as the first country for the program in part because the government there was agreeable and committed. But there are other reasons. Health care is good. There are emergency rooms, antibiotics, and clinics. That is not true in neighboring Cambodia, however. Each day, thousands of Cambodian workers surge into Thailand—and often return home within forty-eight hours. The movement is never one-way; gambling is illegal in Thailand but not in Cambodia. Travel from Bangkok has increased markedly during the past three years. "This is sort of the classic situation we are facing in the world today," Nancy Cox told me before I left for Thailand. Cox is the chief of the influenza branch at the C.D.C., and she has been a strong advocate for establishing these listening posts, which are modelled on several that already exist in the United States. "We have Laos and Cambodia, which have fewer resources and much less of an infrastructure to deal with something like avian influenza or to do surveillance than they do in Thailand. And that really poses a perpetual danger, because they could be having outbreaks there that we simply are unable to know about. We are dealing with a difficult situation, and one that, unfortunately, looks like it will be with us for some time."



Our first stop was a village about forty kilometres from the border. It was a hot, airless day, and people weren't moving unless they had to. Seventy-five per cent of the residents keep birds. Thailand has nine hundred thousand volunteers to watch over the health of its provincial villages. Each volunteer is responsible for a few households, and tries to monitor the health of the people and even of the animals in his or her domain. A weekly bird census is taken—when I was there, there were 84,563 birds in the district. "Paying close attention this way may make the difference," Simmerman told me. "Maybe this will be the place where we will, in the end, see a cluster where the virus has begun to change. And, if so, we can hope to contain it far earlier than if we waited to see something like that in Bangkok or Hong Kong."

I spent some time with one of the health volunteers, a woman named Samorn Santhhape, who was wearing a yellow polo shirt and a floral-print skirt. We sat for a while on the stoop of a house and watched the chickens clucking and strutting about on the barren

ground in front of us. There were about ten houses within sight, and at all of them the scene was the same. Each family owned about twenty chickens.

"These people are worried about this flu," she told me. "But they are more worried about losing their birds and the way they live. They are sometimes resentful of government announcements that tell them what to do." Animals have been kept in this way in Thailand for centuries, and many villagers feel that a basic right has come under attack. Yet any government that ignored such a severe threat to its animals and its people would be negligent. "What did we do wrong?" the woman at whose house we sat asked. She offered us tea, then rice and fruit. "We love our animals and treat them as well as we can." That seems to be true. Santhhape told me that there was a feeling of hopelessness. "When the chickens do get sick, they are dead before we even have time to notice," she said. "Sometimes it feels like we are trying to halt what we cannot even see."

If the avian epidemic does move widely into human populations, as many scientists have predicted, it will mark the first time the world has been able to anticipate a pandemic. For thousands of years, people have rarely known the causes of their illnesses; they have certainly never been warned that an epidemic—whether smallpox, plague, cholera, or influenza—was imminent. Viral genetics has changed that. We can follow the evolution of a virus on a molecular level and gauge its power. Researchers at the C.D.C. have just begun crucial experiments in specially protected laboratories where they will attempt to juggle the genetic components of the H5N1 virus. There are two ways to do that. First, the team will infect tissue with both the bird virus and a common human flu virus and see what grows. They will also use the tools of genetics. Molecular biology now allows scientists to break a virus down to its genes; the researchers will disassemble H5N1 and mix it in a variety of combinations with human flu viruses. Then they will test the results on animals.

There are other preparations under way, too, of course, but they face significant financial, ethical, and political obstacles. The Bush Administration has put hundreds of millions of dollars into flu preparedness. Largely, that commitment reflects a world after 2001, in which it is not hard to convince leaders that if a natural virus can move quickly from Asia to America so could one that is produced by terrorists. Vaccines would provide the most effective protection at the lowest cost. Yet even vaccines won't solve a crisis. First, the world does not yet have the capacity to produce hundreds of millions of doses of an annual flu vaccine at the same time that it prepares for a pandemic strain like H5N1. In fact, this year the United States had trouble simply producing the annual vaccine. That became painfully apparent last October, when the government was forced to announce that a plant owned by one of its two principal manufacturers—Chiron Corporation—had been shut down by British licensing authorities. This delayed annual shots for millions of Americans. Currently, the world can produce three hundred million doses of flu vaccine a year—but there are more than six billion people, and in 1957 the pandemic crossed the globe in less than eight months. The ideal solution would be to develop vaccines that could offer protection from all influenza subtypes. Many public-health officials argue that such a vaccine should become a basic goal, like finding vaccines for AIDS, tuberculosis, and malaria. Without that, even if we could produce a billion doses of a new flu vaccine, which would we make? H5N1 might evolve so rapidly that a shot that would protect us today could prove useless six months from now. And who would get those vaccines? The most rational public-health approach would be to vaccinate those who would first be exposed—health-care workers and people in the region where an epidemic has struck. That is unlikely to happen. "Can you see the developed world shipping all its vaccine to Vietnam in a genuine crisis?" one senior U.S. public-health official told me. "Who are you kidding?"

The antiviral drug oseltamivir phosphate should protect against avian influenza. (It binds to one of the surface proteins and prevents the virus from multiplying.) The U.S. government has enough of the drug to treat 2.3 million people. It's made by one company, and a course of treatment costs more than sixty dollars. If the infections were spreading in Chicago or London, flooding the city with the drug might help. But in Thailand, Cambodia, or Vietnam? Not many people in those countries could come up with that kind of money—or find the drug even if they could. "This is where we can really have a remarkable effect," Bruce Gellin told me. Gellin is the director of the U.S. National Vaccine Program Office, and he spends most of his time these days trying to persuade governments and public officials to make the possibility of a pandemic a priority. "We need to realize that the stuff will be in short supply but that we can use it effectively," he said. "My analogy is a spark and a squirt gun. If you aim properly, you can get the spark and be done with it. If you miss, though, the fire is going to spread and there is nothing you can do to stop it."

What if the world did pay enough attention to what seems like an obvious threat? With the current knowledge about viral genetics, can we think about preventing the transmission of an epidemic of H5N1 from animals to people, or from Africa or Asia to Europe and America? Or could we contemplate achieving similar success with the Ebola virus or hemorrhagic fevers or Nipah or a new form of a hantavirus or some other exotic, and unidentified, disease? If you look at the ProMED daily report on the Internet—most infectious-disease experts read it every morning—the answer would appear to be no. The report, compiled by the International Society for Infectious Diseases, collects and forwards information about novel or important outbreaks of infectious diseases wherever they are found. And they are found everywhere: in the past several weeks, papaya ring-spot virus has ap-

peared in southern India, Newcastle disease has returned to the chickens of Japan, and in January the Canadian Food Inspection Agency reported two cases of mad-cow disease. A woman with melioidosis, which is endemic in Southeast Asia, died on the southwest Indian Ocean island of Mauritius, the first known death there from the disease. There is no information about how the bacteria—often cited as a potential agent for biological terrorism—travelled five thousand miles.

"We are certainly better than we ever were at detecting viruses," Supamit Chunsuttiwat, who is one of the senior infectious-disease officials at the Thai Ministry of Public Health, told me. "But we are also much better at spreading them. A hundred years ago, the Nipah virus would have simply emerged and died out; instead, it was transmitted to pigs and amplified. With modern agriculture, the pigs are transported long distances to slaughter. And the virus goes with them." Few, if any, organisms have benefitted from travel more than viruses have. For nearly fifty million years, the earth has been separated into distinct continents. Those continents were essentially walled off by geographic barriers. A virus could emerge, evolve, and move between species. But it could never pick up and move from, say, China to Montana. When smallpox emerged, three thousand years ago, it would have killed the population around it and stayed where it was; but in the fifteenth and sixteenth centuries sailing vessels carried smallpox—and measles and yellow fever—between the Old World and the New World.

These kinds of health problem were supposed to have been dispensed with by now; by the late nineteen-sixties, the Surgeon General had even announced that it was time to close the book on infectious disease. Polio, measles, and tuberculosis, major causes of death for centuries, no longer posed a serious threat in the United States. Good nutrition and living conditions helped; so did clean water. More important, immunization had taken many common diseases off the map, and the discovery of antibiotics had provided almost miracle cures for others. By the time the World Health Organization declared that smallpox had been eradicated, in 1979, cures had come to be expected.

"Don't think of it as a conspiracy charge. Think of it as a buddy trial."

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Yet infectious diseases may present more of a danger than ever before. Late last week, for example, the W.H.O. reported that scores of miners had died of pneumonic plague over the past two months in the Democratic Republic of Congo—the largest such outbreak in decades. And in 2003 alone, in addition to the SARS epidemic, monkeypox broke out for the first time in the Western Hemisphere (monkeypox causes symptoms that are similar to those of smallpox, but—at least for now—it is not nearly as contagious); West Nile disease continued its insidious spread across North America; and mad-cow disease appeared for the first time in the United States.

Other parts of the world, too, are experiencing the effects of infectious diseases that have never before been encountered. Rift Valley fever, an acute viral disease, suddenly infected hundreds of people in Yemen and Saudi Arabia in 2000—the first time it had been seen outside the African continent. Epidemiologists were amazed. "We never thought we would study viruses in Arabia," a senior researcher at the C.D.C. told me. "There is nothing there. We always called it the empty corridor." However, there has been a lot of traffic in animals there, and, in the case of Rift Valley fever, wind may have been enough to spread the virus. New viruses are not the only problem. Yellow fever, which crossed the world in the water barrels of ships, almost stopped the construction of the Panama Canal. The virus remains endemic in the tropics despite many attempts to eradicate it.

Travel, transportation, trade, pollution, and ecological disruption all play a role in assuring the constant flow of disease from one part of the world to another. Last year's tsunami has pushed the world's public-health agencies to their limits. It's not clear how they could respond to a sudden global epidemic as well.

When I was in Sa Kaeo, I sat for a while in the district office with several provincial health officials. On the wall was a giant poster filled with avian-flu information. "Chickens used to live in our back yards—they didn't travel much. Now, throughout the world, farms have become factories," Charun Boonyarithikarn, the chief of social medicine for the district, told me. "Millions of chickens are shipped huge distances every day. We can't stop every chicken or duck or pig. And they offer millions of opportunities for pathogens to find a niche." He shook his head, and smiled. "People around here fly to Hanoi and Phnom Penh and Paris. They visit China. They travel. Well, we have to realize this and accept it: take a plane ride to Paris and you may be taking an epidemic along with you." ♦