## Avian Flu: Barbarians in the Coop

"Without chicken, there will not be a banquet." —Chinese Proverb

For an ancient and yet nasty poultry virus, H5N1 has created a lot of pandemonium. First came the televised bird holocausts that featured solemn men dressed in ghostly killing gear. Reports of dying or dead peasants soon followed. Politicians then blamed the viral trade killer on wild migratory birds and ordered the draining of wetlands. After white coats at the World Health Organization in Geneva added up the dead (nearly 100 poor people), virologists started to fret about another global influenza pandemic like the viral blizzard of 1918 that dispatched 50 million people. Meanwhile Chinese authorities did what the modern Chinese do best: They issued a flock of denials about the pandemic's authentic birthplace, Guangdong.

An eerie Hitchcockian spell soon infected Internet blogs, public health officials, and poultry lovers everywhere. The hullabaloo trailed H5N1 wherever it popped up. In Egypt fearful peasants culled their chicken flocks, whether infected or not, and dumped their primary source of protein into the Nile. When dead birds fell from the sky in northern Iraq, people ran away as though nearly struck by God. The wary German government dispatched Tornado reconnaissance jets to locate hundreds of swans felled by flu along the shores of the Baltic Sea. The fastidious Dutch declared an emergency and moved all their poultry indoors. The French, whose proud national symbol remains a rooster, suffered an identity crisis. The Hong Kong authorities warned bird-loving citizens not to kiss their feathered pets. And governments everywhere started to publish pandemic preparation plans by the dozen.

But before avian influenza set the global village on fire with a rare gallinaceous fever, Mark Dekich met and did battle with the invader in a crowded Saudi Arabian chicken factory. The year was 1998. At the time Dekich's exploits in the oil kingdom didn't get much notice. In fact, Dekich went to criminal lengths to keep them quiet. The global poultry industry doesn't really like talking about its factory-made infections. But Dekich's exceptional story partly explains how a plain avian virus became a feared global menace and eventually worked up a hurricane of human hysteria.

Eight years ago Dekich held a good job at Fakieh Poultry Farms, one of the biggest chicken producers in the oil-rich kingdom. When not taking care of Fakieh's birds with mass vaccinations and medicated feeds, the Georgia-born bird doctor spoke at symposiums on factory chicken diseases and even testified for the U.S. Department of Agriculture on key livestock matters. As a

longtime poultry expert, Dekich knew that "fowl plague" comes in two forms: mild maimers that clog up chicken lungs, and strains of "highly pathogenic avian influenza" that kill. Any maimer can morph into a killer and clean out a factory of 40,000 birds with 100 percent mortality in hours.

A pathogenic strain works with a certain demonic precision: It simply overwhelms meat birds the same way Ebola melts Africans. The invader commandeers every organ and tissue of a bird, from the top of its comb to the tips of its ammonia-burned feet. The broilers bleed from their eyes, beaks, and anuses. One moment they are pecking away; the next they fall over dead. In the end they just "melt out," resembling rubber caricatures of themselves. An outbreak not only eats up profits and creates unsightly piles of dead animals but generally shuts down a bird factory for weeks.

Like most people working in the global chicken trade, Dekich had nervously watched a viral outbreak crash and burn hundreds of thousands of birds in Hong Kong's high-density poultry farms and live markets in the spring and fall of 1997. The sudden plague wiped out between 70 and 100 percent of the ducks, chickens, and quails it encountered. Then a three-year-old boy played with a chick at a day-care center and came down with an unusual bout of the flu. The disease shut down his lungs, kidneys, and liver. He died six days later in a coma. When virologists identified this viral citizen as H5N1, they started to pace at night: The strain had never assaulted or outgunned the human immune system before. H5N1 was supposed to be a stable avian predator, not a pioneering human one.

Six months later the deadly virus emerged again after weeks of wet weather. It immediately went on another chicken-killing spree. After five more children and adults got caught in the viral crossfire and died of overwhelmed immune systems, Hong Kong's public health authorities took draconian measures. They sent out four-person teams to kill 1.6 million birds in the city's farms and "wet" markets, the bustling clusters of stalls where vendors of live birds and fish clean the streets by pouring buckets of water down them. The avian assassination squads broke necks, cut throats, and gassed birds in bags. When the masked killers came home at night, they did not kiss their wives or touch their children.

As Hong Kong battled the outbreak, Dekich penned a prescient paper for the journal *Poultry Science*. After 30 years of breeding "big, economical and fast growing chickens," wrote Dekich, the profitable commercial broiler business faced a number of health risks, including unreliable vaccines and "increased poultry house density." Giving chickens less space than a page of typing paper to live on just heightened the "potential for spread of endemic diseases through large naïve populations of birds." A "naïve" bird is an immunocompromised animal with no natural disease resistance.

Shortly after penning the warning, Dekich learned that some of his broilers at Fakieh's factories were keeling over from a mild strain of avian influenza. It wasn't H5N1 but H9N2, a weaker and rapidly evolving cousin that had started to rattle chicken cages in Asia, Europe, and the Middle East in the 1990s. H9N2 (every avian virus has what Mike Davis, author of *The Monster at Our Door*, quaintly calls a "genetic license-plate number") sickened factory chickens

with lung problems and outright killed birds burdened by other infections. Because virologists then regarded H9N2 as one of the world's most abundant bird viruses, they placed it "high on the list with pandemic potential" for humans. Given the growing hysteria about H5N1 in Hong Kong, Dekich knew that any public revelation of the outbreak would result in serious investigations, trade restrictions, and multimillion-dollar losses. The same invader had already raised hell in Iran's chicken flocks.

So Dekich did what every major factory farmer and broiler-friendly government has done since avian flu first invaded the global chicken coop: He kept the barbarian under wraps. "With the world health publicity about avian influenza, it was a priority of the company to keep confidentiality. The human epidemiological consequences can be severe if this H9N2 virus is allowed to continue to replicate and re-sort its genome (genes). Fakieh Poultry Farms must go avian influenza negative and protect that negative status," he later wrote in one company memo.

After consulting with a well-known poultry specialist at the University of Delaware about his fluish flocks, Dekich arranged for a struggling biotech firm, Maine Biological Laboratories, to secretly produce a vaccine. Dekich then smuggled a sample of the chicken killer into the United States. MBL mislabeled \$900,000 worth of its product as a vaccine for Newcastle disease (another viral menace) in order to evade detection by U.S. authorities.

Until Dekich and six employees of MBL pleaded guilty seven years later to mail fraud, virus smuggling, or making false statements to the government (among other crimes), no one knew much about the mail traffic in poultry killers or Saudi Arabia's avian flu outbreak in 1998. Upon sentencing Dekich and his accomplices in July 2005, U.S. District Judge John A. Woodcock, Jr., called the corruption "insidious, enticing and aggressive." The judge's verdict could easily have been applied to the global spread of avian flu.

Bird flu is now poised to sweep through humans like a viral tsunami. Most members of the world's unhappy flu-watching fraternity now debate only the severity of the next pandemic. Will the virus heat up and kill 1 in 50 people, setting off an economic collapse, or cool down and dispatch 1 in 1,000 people, setting off a global panic attack? Or will it simply fade away, leaving citizens with nothing more than a bad case of H5N1 fatigue and governments with expensive stockpiles of antiviral drugs, like Tamiflu?

Whatever its future course, H5N1 has already changed the world forever. It has done to chickens what AIDS did to sex, and it has visited upon Asia's poor the same kind of calamity Katrina dropped on the indigent in New Orleans. But that's just the beginning. The invasive opportunist has endangered the world's number two source of protein, accelerated species extinction among wild birds, impoverished more than 100 million rural families, demonized backyard chicken keepers, cost Asian taxpayers \$20 billion, and added another layer of vulnerability to modern life. Like it or not, H5N1 has become another global mischief maker with a universal passport. Earl Brown, a University of Ottawa virologist, believes more viral mayhem is on the way: "Welcome to the beginning of the new normal."

The Great Chicken Pandemic, which has buried more than 200 million winged creatures, is another unadvertised by-product of globalization. Its source, pure and simple, is our gluttonous appetite for cheap, industrially produced meat. Crowded bird factories, rampant bird smuggling, bad vaccines, and duplicitous governments have all played a role in fouling the proverbial nest. Medical professionals may not like to admit it, but avian flu is a fairly predictable man-made plague, or what scientists cryptically call a "deliberately emerging microbe." Even the UN Food and Agriculture Organization (FAO) has repeatedly concluded that avian flu owes its global reach to "the intensification and concentration of livestock production in areas of high density human populations." H5N1, in other words, is a factory-acquired infection.

It is also a bona fide biological invader and a member of the fast-and-furious club. Anthony McMichael, a well-known Australian public health expert, has long argued that the roller-coaster pace of global trade and travel selects for troublemakers by disrupting their natural homes or ecosystems. As a result the world's r-species, true die-hard globalists such as fungi, viruses, and bacteria, are once again looking for new homes. Unlike k-species (apes and humans), the r-species reproduce quickly, do little parenting, and excel at spreading their numerous offspring. Trade, travel, city making, and chicken factories smile on "these small opportunistic species," says McMichael. Biologists just call them invaders.

Avian flu has been waiting for an opportunity to go global for a long time. This ancient virus has dwelled harmlessly in the guts of wild ducks and other migratory waders for millions of years. There it hijacks a duck's intestinal cells to make more evolutionary anarchists and gene spreaders. Whenever the duck defecates, the viral freeloaders enter ponds and lakes where they can survive happily for months at a time. It's telling that 10 billion virus particles can be found in a single liter or quart of water. In the scheme of things, God probably made ducks to breed and transport viruses.

Wild fowl visit ponds inhabited by domestic poultry. Here wild ducks share their viral cargo, much the way careless suburbanites share gastrointestinal trouble in hot tubs or ecotourists share measles with apes. Just a gram (0.03 ounce) of infected duck feces can infect a million chickens. Depending on the strain of influenza that the wild fowl transmit to them, the domestic birds can gain immunity, start sneezing, or fall down dead.

As the world's oldest pathogenic entrepreneurs, viruses are always looking for opportunities to expand their domain. This explains why influenza now comes in four major and often troublesome tribes: A primarily dwells in wild fowl but occasionally makes forays into several mammals, including horses, humans, and pigs; B, a tamer tribe, mostly dogs humans but has been found in seals; C can produce mild colds in humans and pigs; and Thogoto remains largely a tickborne virus in Asia and Africa. All the tribes can occasionally swap genes and evolve in unpredictable ways, but only A and B can author a pandemic that turns human lungs and brains into a bloody mess.

The A tribe can stir up pandemic trouble in as many as 154 genetic combinations or subtypes. Each tribal subtype, in turn, can spawn hundreds of different strains. (Like fashion models, influenza viruses are always changing shape.) H5N1, for example, has mutated as many as 20 times already. The subtypes can be told apart by the position of two creative proteins on the surface of the avian virus: hemagglutinin (HA) and neuraminidase (NA). Their arrangement helps to shape a virus's ability to break and enter into a cell. All of these subtypes call birds home, but certain ones—H1, H2, and H3—stick pretty well to human lungs while others, such as H7, prefer horses. Until H5N1 popped out of Asia, scientists generally thought that no member of the A tribe could make a bad case of the flu without first swapping genes with other tribal groups or at the very least passing first through pigs, the world's best viral mixing medium. But H5N1 surprised them.

Like most RNA viruses, the avian clan tend to be sloppy and capricious reproducers. During "viral sex" they make all sorts of rude copies and in the process create innumerable mutants. A heavy load of flu virus (say, 50,000 particles) can make up to 50,000 mutants. In a chicken factory, a strain of avian flu will quickly evolve from a benign hitchhiker into a nasty killer. Crowds encourage the selection of deadlier and stickier forms of influenza, explains Earl Brown. "The virus responds to its environment, and the highest yielding virus on the barn floor wins." The winner is usually a formidable chicken killer.

Italians first described an outbreak of the "fowl plague" in 1897, but it wasn't until 1955 that scientists identified the culprit as a member of the avian influenza tribe. Although fowl plague killed off a fair number of domestic birds early in the century, it didn't really gain strength until we foolishly separated the chicken from viral evolution in wild birds.

That separation occurred when American ingenuity malled the chicken. After World War II the age-old practice of rearing a couple of feathered friends in the backyard got dumped for the four horsemen of the flu: density, efficiency, drugs, and big money. The principles of factory farming were simple: Take a sturdy and desirable stock, breed out qualities such as disease hardiness, and breed in a genetic disposition to grow fast on less feed. Then crowd the efficient meat producers into cages by the thousands. Add indoor lighting and air conditioning. A small number of companies supplied all the chicks and feed to "keepers," contractors who fattened the birds for automated slaughtering plants. By 1965 one man alone could operate a factory producing 40,000 chicks a day. Today one-fifth of the world's 100 billion birds are genetically uniform broiler chickens.

The industrialization of the once noble chicken had several effects: It made eggs and chicken meat much cheaper, displaced thousands of farmers in North America, and generated a series of appalling chicken epidemics. First came coccidiosis, an intestinal parasite that preyed on young chicks awash in too much of their own waste. Next appeared Newcastle disease. This novel virus leaped out of imported Hong Kong pheasants into California's poultry flocks in the 1950s. Since then Newcastle disease, an agent almost as infectious as avian flu, has developed a taste for factory birds around the world. An infamous 1972 outbreak resulted in the "stamping out" of 9 million chickens in California alone at a cost of \$57 million.

Page Smith, an American journalist and chicken historian, found that poultry holocaust deeply disturbing: "Chickens are not people, but perhaps the destruction in our age of millions of human beings who were thought to carry a kind of racial virus in their genes has inured us to the horror

of killing so many living creatures and left us equally indifferent to the strange developments which make such a solution seem inevitable." Smith had no idea that gallicide would soon become a regular staple of the global poultry trade.

To stamp out one pathogenic invader after another, the chicken business resorted to the usual quick fixes. It doled out antibiotics, vaccines, and medicated feeds in an effort to keep stressedout, immune-blasted birds upright. (Most broilers are now so breast-heavy that many are lame or prone to heart attacks.) After desperate Hollywood housewives, broiler chickens are probably the most drugged denizens on the planet. Whenever a virus or bacterium gets into a factory and threatens feed schedules or weight gain, the "units" are routinely rounded up and rubbed out. Frank Perdue, the American chicken magnate, wasn't kidding when he said, "It takes a tough man to make a tender chicken."

Avian flu has played a major role in toughening up the poultry business too. When turkey farms unfortunately located under the migratory pathways of wild birds in California, Minnesota, and Ontario came down with bird flu in the 1960s, the industry responded by moving the birds indoors. When the disease hit chicken jails in the 1980s, many factories adopted an "all in, all out" system to keep the virus out. Instead of trucking the fowl around to different feeding locales, they now raised meat birds in one spot until slaughter. "They keep changing farming practices to keep ahead of avian flu," explains Brown.

Before the Asian outbreak, avian flu had "officially" visited the poultry industry only 21 times since 1959. The most memorable invasion took place in 1983, when a mild strain of H5N2 invaded Pennsylvania's chicken factories. After it mutated and started to swell chicken brains, authorities ordered the destruction of 17 million birds at a cost of \$61 million. The epidemic affected three states and raised the price of chicken across the country. South of the border, it also raised hell. In an attempt to stay ahead of the invader, the Mexican authorities set up a rigorous poultry vaccination program. In spite of the program (or, some argue, because of it—many of these vaccines were substandard), a mild strain of H5N2 slowly morphed into a highly pathogenic killer that plucked the feathers from Mexico's chickens. The progenitor of this invasion jumped into the wild birds of Mexico, where it smoulders, waiting for another dinner. Meanwhile Mexico's industrial chickens have required 2 billion doses of vaccines in the last two decades in order to make it to the supermarket.

Avian flu isn't the only frequent microbial visitor at chicken factories. In recent years every Tom, Dick, and Harry of the avian disease world has come calling on industrial piles of meat. Six-hundred-page books and entire journals with dry titles like *Avian Diseases* are now devoted to a seemingly endless list of chicken predators, including cholera, fowl pox, infectious coryza (a sinus clogger), Marek's virus (a tumor maker), infectious bronchitis virus (a SARS relative), and retroviruses that behave like AIDS. Given that the movement of people, equipment, and vehicles can effortlessly spread these invaders, it's not surprising that many factory-minted pathogens are beginning to spill over into wild birds too.

In 1994 American bird lovers discovered wild house finches with crusty eyelids and impaired vision at backyard feeders. A common factory poultry scourge, *Mycoplasma gallisepticum* (MG),

had attacked them. Scientists have yet to identify its source. The epidemic wiped out tens of millions of songbirds and spread like wildfire throughout the eastern seaboard. (Blinded by the infection, the hapless finches couldn't see to eat.) The plague's remarkable speed so impressed scientists that the journal *Emerging Infectious Diseases* declared that MG "illustrates how rapidly a pathogen can be disseminated throughout a large geographic area within a highly gregarious and mobile host population." Then came the Asian outbreak of avian flu.

It all started with mountains of poultry. In the last decade Asia's domestic bird population jumped from 4 billion to 16 billion. Between the 1970s and the mid-1990s, the volume of animal protein devoured in China and environs grew three times faster than it did in North America and Europe. As the middle classes of Hong Kong, Shanghai, and Mumbai got more cash in their pockets, they wanted more chicken in their bowls. Sitting down with a pile of meat, after all, is a badge of progress toward good living.

But Asia's burgeoning chicken trade ignored some basic epidemiological facts. For starters, Asia has been the epicenter of influenza pandemics for thousands of years. You can't crowd people, pigs, and poultry together without building a better market for viral commerce. China's Guangdong province, which virologists call the "birthplace of influenza," teems with 86 million people, tens of millions of pigs, and about 250,000 birds per square kilometer (about 650,000 per square mile). One public health expert recently told the *Los Angeles Times*, "Charles Darwin could not have set up a better genetic re-assortment laboratory if he tried." Since 1900, Guangdong has probably been the seedbed of two human influenza pandemics. But it's not the only flu nursery. When pigs, wild fowl, and crowded U.S. military camps turned Iowa and Kansas into mini-Guangdongs in 1918, the flu that sprang from the American midwest infected half of the world's population and killed more than 50 million people.

Robert Webster, a prominent influenza scholar at St. Jude's Children's Research Hospital in Memphis, Tennessee, has repeatedly warned the world's chicken growers that they shouldn't fool with the flu. In particular, the virologist has explained that feeding pigs and chickens in the same neighborhood assists viral exchanges; that live bird markets, where as many as 276 bird species mingle, give flu viruses ample opportunities to re-sort themselves; and that commercial poultry farms offer "an optimum number of susceptible poultry for rapid viral evolution."

Michael Osterholm, a well-known American public health advocate, has made a similar point. In a 2005 issue of the *New England Journal of Medicine*, Osterholm noted, "It is sobering to realize that in 1968, when the most recent influenza pandemic occurred, the virus emerged in a China that had a human population of 790 million, a pig population of 5.2 million, and a poultry population of 12.3 million. Today these populations number 1.3 billion, 508 million, and 13 billion respectively."

But the chicken trade has made more friends in government than it has among grumpy doctors obsessed with overcrowding. Take Thailand, for example. It banked on the broiler chicken to elevate its economy and make it "kitchen to the world." Before its avian ambitions transformed the tropical nation into a global chicken exporter, most peasants depended on hardy native fowl for pocket change and protein. These farmers kept, on average, about 15 hardy chickens, geese, and quails that foraged freely for food. The owners didn't fuss about medicated feed, vaccination, or medication. The birds also mixed with their wild migratory cousins, ensuring that avian influenza repeatedly immunized their stock with mild strains of the disease or occasionally culled them with deadlier versions.

However, Asia's livestock revolution changed that bucolic scene by escalating viral evolution several notches. In Thailand the government and the Charoen Pokphand Group (CP Group), a conglomerate run by ethnic-Chinese entrepreneurs, adopted the bigger-is-better model, or what the Asian media call the "Guangdong syndrome." Inspired by American-style poultry factories, the CP Group promoted "chicken farming estates" in closed buildings that housed between 10,000 and 100,000 birds each. The CP Group lent money to farmers, sold them chicks, feed, and antibiotics, and bought the finished birds to export to Japan and Europe.

Outside of Bangkok, a megalopolis of 10 million chicken eaters, the volume of domestic fowl slaughtered for export grew from 410 million to 890 million birds in just one decade. Most of this expansion took place in poultry factories. Thailand, a relatively small country, miraculously became the world's fourth-largest poultry exporter. Similar chicken concentrations have piled up outside Hanoi, Manila, Guangzhou, Shanghai, and every major Indian city.

Not all the Asian economies chose chicken as the miracle maker. China and Vietnam invested in ducks and boosted production threefold in the last two decades. The two countries now house three-quarters of the world's ducks. According to Samuel Jutzi, director of the FAO's Animal Production and Health Division, this swarm of 1 billion ducks and geese unfortunately developed on less "than .5% of the earth's terrestrial surface," where excess phosphates from chicken waste had already polluted 30 percent of the farmland. He's not at all surprised that the cackling concentration of domestic geese and ducks provided "an effective breeding ground for the myriad of avian influenza viruses circulating in wild waterfowl."

Although government and industry officials still pin the origin of the Asian pandemic on wild fowl, most scientific experts at the FAO don't think it spilled from "the flyways to the highways and byways." Migratory birds have surely played a role in transporting the virus (as have the poultry trade and live markets), but the pandemic didn't begin with them. A weighty 2005 report for the FAO by two New Zealand epidemiologists concluded that the virus probably "arose through a recombination process between viruses in the influenza epicenter region of Asia involving interchange of viruses among a number of species of domestic birds." In other words, all the trouble started on the byways and highways around factory birds and then flooded wild flyways.

The big viral party probably began in the 1990s when highly pathogenic strains of avian influenza struck commercial poultry factories throughout southern China. In 1996 domestic geese started dying in heaps in busy Guangdong province, where millions of people and billions of fowl live cheek by jowl. It then spread to domestic ducks and eventually spilled over to broiler chickens and quails bound for Hong Kong, one of the world's most densely populated cities. When the indomitable Hong Kong virologist Yi Guan later traced H5N1's lineage back to China, his lab was temporarily closed for violating "state secrets."

The first human casualties appeared in 1997 as avian influenza ripped through the Hong Kong's poultry operations, infecting 18 people. After six citizens dropped dead, the city declared an emergency and mobilized 2,000 government workers to stamp out the plague. In what would soon become a repetitive scene, men in ghostly moon suits bagged and gassed the birds at 160 farms and 1,000 wet markets and buried the fowl in landfills. Hong Kong then banned all aquatic fowl from its markets and mandated two cleanup days a week, when the markets would be scrubbed down and disinfected. China maintained its sorry record of secrecy and issued the usual polite denials.

H5N1 created quite a buzz among virus researchers. It reproduced much faster than its innumerable relatives, killed wild birds (something avian influenza shouldn't do), and mowed down domestic chickens more quickly than any avian invader encountered before. It had also jumped species and appeared to have pandemic potential. H5N1 wasn't supposed to infect humans, let alone kill them. "We thought we knew the rules," Stephen Morse, director of the Center for Public Health Preparedness at Columbia University, later told *Newsweek*. "And one of those rules was that H1, H2 and H3 cause flu in humans, not H5. This is like the clock striking 13."

But H5N1 wasn't the only avian invader making headlines. In March 2003 the Netherlands, a country with its own "Guangdong syndrome," got a visit from one of H5N1's less virulent cousins, H7N7. The Dutch epidemic began after free-range chickens picked up the virus, probably while mingling with some wild swans on a pond in the center of the country. The virus then hitched a ride on contaminated litter, vehicles, and the clothing of poultry workers. As it worked its way through uniform chicken "units," the virus heated up and became a chicken eater. More than 400 farm workers and slaughtermen exposed to infected poultry got a bit of the flu and came down with conjunctivitis and the sniffles. One veterinarian died when pneumonia filled his lungs with fluid. The Dutch called out the military and slaughtered 30 million chickens on 255 premises, nearly one-third of the nation's 100 million birds. Police even raided the homes of pet lovers, who tried to hide their beloved chickens in the bathroom. To protect the chicken killers, the government handed out Tamiflu, face masks, and goggles. The barriers did not prevent an outbreak of depression, anxiety, and "emotional aggravation" among farmers and vets. The virus spread to Germany and Belgium too, where another 3 million birds got the ax.

Back in Asia, the feared H5N1 strain continued to make the rounds in China's congested poultry factories. It took up residence in healthy domestic and wild ducks in the coastal provinces and southern cities. It, too, did some gene swapping with pigs. When scientists inoculated domestic chickens and mice in 2003 with samples of the latest version of the virus, their laboratory patients dropped dead. So too did ferrets, a species with a high tolerance to flu. "Clearly," concluded the understated researchers, "H5N1 influenza viruses are continuing to evolve in Asia."

The Chinese inadvertently helped the virus along. First, they started to douse chicken factories with the human antiviral drug amantadine. This explains why H5N1 mutated and has appeared in drug-resistant forms throughout Asia. Then they hit their city-sized flocks with a sloppy and

frenzied vaccination program that used bad batches of inactivated virus from 20 different medical facilities. "Initially they were not matching the virus to the vaccine," explains the virologist Earl Brown. These poorly matched vaccines simply drove H5N1 underground. Although the birds looked healthy, they still shed the virus in feces, infecting unvaccinated birds in "silent epidemics."

The Mexicans conducted a similar uncontrolled experiment in viral evolution in their flocks from 1980 to 2004. Their industrious 20-year vaccine campaign tempered the virus but did not eliminate the disease. In fact, the *Journal of Virology* recently reported that the strain merrily kept on evolving under vaccine pressure—a development that scientists call a source of "concern for the effectiveness of vaccination strategies within the poultry industry." (Incredibly, the use of Mexican-made vaccines in Japan has now been linked to several outbreaks of avian flu.)

Thanks to China's haphazard interventions, H5N1 learned some new genetic tricks and started to kill other fowl in 2002. It flattened a flamingo, an egret, two gray herons, and other waders in a Hong Kong zoo. Within short order it was killing ducks, something an avian virus had never done before. Pigeons and house sparrows soon began to pile up in Hong Kong and Bangkok.

In August 2003, evolution hit a new high in Thailand, Indonesia, and Vietnam as a highly pathogenic strain (genotype Z H5N1) started to explode through factory farms and backyard operations. (Indonesia, like most governments, didn't officially recognize the epidemic for another six months.) This latest mutation of H5N1 directly attacked chicken brains. Some birds laid misshapen eggs before dying; others flopped around like drunks. Most just dropped dead.

In Vietnam the first wave unsettled large commercial farms along roads. A second wave in March 2004 devastated the Mekong Delta, a poultry and human beehive. In Thailand the virus jumped from free-grazing ducks on rice ponds into chickens and back again. In Indonesia it raced from island to island. According to the Indonesian Poultry Information Center, an illegally imported vaccine from China may have helped to spread more silent epidemics of H5N1.

Throughout Asia despairing farmers protected their avian assets as best they could. In Indonesia, where the famed Kampung chicken is every family's cash cow, ordinary people concealed their troubles, one poultry official explained later. "Farmers feel shame if their birds are infected by AI [avian influenza], [so] they try to keep the information to themselves. Farmers also feel scared that if government knows they have AI, they must stamp out their birds and have no pay. So they try to sell the birds as soon as they can in order to save their capital." Not surprisingly, wet markets became distribution points for the bird flu.

By now the virus was taking advantage of every man-made opportunity and poultry habit. Major festivals, such as the Chinese New Year and Tet, brought birds and people together in markets in huge numbers. In Thailand fighting cocks, players in the country's most popular sport, transported H5N1 from village to village. A good rooster can command as much as \$20,000, so millions of Thais predictably hid their fighting birds from murderous government officials intent on protecting the export trade.

In the midst of the avian pandemonium, H5N1 startled virologists once again by jumping species. After it killed 45 tigers and clouded leopards in Thailand, zookeepers belatedly removed

raw chicken from their diets. When infected tigers passed on the disease to other tigers, authorities euthanized another 102 animals. Captive tigers, leopards, and lions died in heaps in Cambodia and China. By now H5N1 had shown "the widest host range" of any avian virus ever seen. In Holland researchers proved that household cats fed raw chicken could transmit the virus too. During a human pandemic, cats could become silent spreaders.

Then people started to drop dead, just like ducks and tigers. In a small village in Thailand where all the local chickens succumbed, 11-year-old Sakuntala Thongchan developed a fever and stomachache. She coughed up blood until viral pneumonia suffocated her lungs. Her 26-year-old mother died of avian flu shortly afterward. In Vietnam three brothers toasted one another with glasses of duck blood; one died, one fell ill, and another lived to tell the tale. After slaughtering a chicken, a 21-year-old farmhand named Nguyen Si Tuan battled the flu for 82 days and lost a third of his body weight. In Thailand a cockfighter sucked the mucus from a bird's throat in order to revive his prized possession and died a week later. In Indonesia entire families perished after slaughtering old laying chickens. And in southern Vietnam a four-year-old boy and his sister died of diarrhea and acute brain swelling after bathing in a duck pond. British researchers marveled at H5N1's versatility: "The virus is progressively adapting to mammals and becoming more neurologically virulent."

In a belated effort to control the pandemic (which now affected 10 Asian countries), governments orchestrated the killing of millions of birds in early 2004. Bare-handed workers, farmers, and soldiers all became reluctant chicken killers. In Vietnam they burned chickens alive; in Thailand they packed 11 million birds into fertilizer sacks and buried them alive. To get rid of the "evil spirits" affecting their fowl, Indonesians barbecued flocks on pyres. The poorest of the poor, however, did what they've always done: They ate their diseased livestock.

To help out, the United Nations printed pamphlets on chicken disposal that offered this useful nugget: "It can be extremely difficult to remove dead birds from their cages once rigor mortis is established." Infectious disease experts watched the slaughter on their television screens with alarm: "They are trying to eliminate the animal reservoir, which is what we want, but if they are exposing themselves to the virus while they're doing that it might defeat the purpose," declared one official at the World Health Organization.

Many of the world's influenza experts were almost beside themselves. An influenza virus must meet three conditions to start a wave of human trouble. It must be novel—something to which people don't have immunity. It must kill with ease, and it must spread easily from person to person. H5N1 had now fulfilled the first two conditions. The flu expert Robert Webster repeatedly called H5N1 the "worst flu virus I have ever seen or worked with." Greg Poland, an infectious-disease expert at the Mayo Clinic, likened the whole affair to "watching a train wreck in slow motion." Most of Asia's birds, wild or domestic, had become viral factories that manufactured mild or deadly strains of H5N1 for up to 17 days. The virus was everywhere.

In addition to taking advantage of a chronic shortage of vets, laboratories, public health experts, and doctors, H5N1 thoroughly exploited Asia's imbalanced chicken economy. The region's 200 million backyard operations, which are annually seeded with flu strains by wild fowl

influenza, sit next to high-tech commercial factories where feed shipments, workers, egg trays, and live birds move in and out every day. This commercial traffic juggled the virus from backyard operations to factories and vice versa. "The commercial broiler chains may well have played a major role in the seeding" of the virus, according to FAO livestock ecologists. To date the owners of Asia's factory farms have refused to open their disease records for public scrutiny.

As poultry prices plummeted and peasants started eating rats in Vietnam, relatives of H5N1 prompted more killing around the globe. In August 2004 South Africa started culling \$30 million worth of infected ostriches while Maryland officials dispatched 4 million birds. South Korea and Japan also battled outbreaks. After Taiwan dispatched hundreds of thousands of chickens and ducks, an unusually frank editorial in the *Taiwan News* lamented the wave of plagues pummeling the region, from SARS to foot-and-mouth disease: "Regrettably, these major epidemics all came from China. Why? The most important reason is trade and smuggling of agricultural and livestock products."

Europe learned that lesson in October 2004 when a Thai bird smuggler went on a business trip to Antwerp. In a cloth sports bag he carried two rare eagles bought at a bird market in Thailand for a European collector. Had it not been for a routine drug search, the birds would have escaped detection. Both were infected with H5N1. The incident opened a small window on a large and illegal global enterprise: the smuggling of 4 million pet or exotic birds around the world every year. Shortly afterward Taiwan found eight infected birds in a load of 1,000 smuggled birds from Fuzhou, China. And in Port Elizabeth, New Jersey, U.S. Agriculture Department agents seized 12,000 kilograms (27,000 pounds) of smuggled frozen poultry from China.

By now most of the world had witnessed the remarkable geopolitical prowess of avian influenza. When H7N3, a mild relative of H5N1, invaded poultry factories in the Fraser Valley of British Columbia in the spring of 2004, the Canadian government rolled up its sleeves, called out the killers, and culled 19 million birds. The Canadian Food Inspection Agency, a booster of livestock trade, tried gassing the flocks with carbon dioxide. When many birds recovered and walked again, they clubbed them with sticks. They shot peacocks with shotguns and poisoned some duck populations two or three times before they died. The government stamped out rare breeds as well as millions of uninfected broilers. In the interests of international trade, Canada's bird killers elected to kill first and test later.

During the slaughter, neither government nor industry talked about the perils of overcrowding or high-density poultry production. But British Columbia's chief medical officer of health, Perry Kendall, pointed out the obvious: "The intensely farmed birds tend to be very genetically similar. The methods of farming result in them being actually more frail and more vulnerable to diseases, particularly since there are so many of them in such a small volume of space."

Back in Asia, H5N1 continued to gobble up birds and people while governments did what Mark Dekich did: They protected trade and tried to avoid the word *influenza*. The French reporter Isabelle Delforge aptly described Thailand's handling of bird flu as "a saga of cover-ups, incompetence, lies and extremely questionable decisions." The nation's top microbiologist, Prasert Thongcharoen, later told *The New Yorker* that the government's response had been an unmitigated fiasco. "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."

For starters, the country's poultry kings and the Department of Livestock (two largely indistinguishable entities) denied the existence of the disease even after a veterinarian found H5N1 in November 2003. Trade-conscious officials explained at first that the sick chickens were dropping dead "without any medical cause." Meanwhile infected birds were traveling to market by the thousands. Then the government, fearing public panic and trade sanctions, claimed it was dealing with a ho-hum case of bird cholera, a disease treatable by antibiotics. But still the chickens died. The birds would start shivering en masse, then they'd fall over dead. The lies and delays, however, gave industry ample time to capitalize on the rising prices for frozen chicken parts.

When the truth finally came out and the country's \$1-billion chicken trade collapsed, Thailand's president, Thaksin Shinawatra, did what politicians do best: He publicly ate wellcooked chicken. "If Thais don't eat Thai chicken, how can we expect others to buy our chicken?" cooed another panjandrum. The government sponsored chicken festivals and the CP Group gave away thousands of free chicken dinners. While pop stars sang sweet songs about "the kitchen of the world," public relations experts encouraged Thais to eat at Kentucky Fried Chicken outlets, arguing that the fast-food chain served only factory chickens and that factory chickens were virus-free. As European trade bans left piles of raw chicken meat on Thai docks, the government tried to broker an unusual deal with Sweden: poultry for a JAS 39 Gripen jet fighter. Sweden politely declined.

Officials looking for scapegoats found a convenient one in wild birds, the natural reservoir for the virus. Thai leaders gave orders to butcher wild Asian open-billed storks, and the trees they nested in were hacked down. In Singapore the order went out to cull crows and mynahs and to trap and clip the wings of migratory birds. People shunned nature reserves and impulsively released their pet songbirds. In Hong Kong authorities cut down more trees so birds could not nest in schoolgrounds. In Taiwan educators forbade children to visit nature reserves, and in Japan they shot crows. Colin Poole, Asia director for the Wildlife Conservation Society, had never seen anything like it. "Birds had become the enemy."

Although migratory ducks, geese, and swans arguably provided H5N1 a free ticket out of Asia, wild birds didn't spread the invader around China, Vietnam, or Indonesia. A 2006 genetic analysis of migratory birds and factory chickens in southeast China confirmed that the invader started in Guangdong, colonized local areas, and then spread via the local poultry trade. Wild birds are "not the scapegoats for maintaining H5N1 within poultry," the Hong Kong researcher Malik Peiris told the *New Scientist.* "There the cause and solution lies within the poultry industry."

For the last two years, most wild fowl carrying H5N1 have been found dead or dying near chicken factories, and, as many observers have noted, "the dead don't migrate." (Ducks appear to be an exception; they can carry the virus with little misery.) Many bird species targeted by irrational governments, such as open-billed storks, never carried the virus in the first place. As

Poole adds, "no waterfowl spend the winter in southern China and then migrate further south." In sum, "the international movement of poultry and other birds in trade" initially spread a virus lethally served up by factory farms. Yi Guan, the astute Hong Kong virologist, has called the migratory bird issue a "free lunch" for governments that can't or won't control legal or illegal movement of poultry or pet birds. "Each time there's an outbreak they say, 'It's migratory birds. I cannot control them. I cannot lock my sky!"

To many scientists the relentless slaughter of chickens no longer makes any sense on ethical, economic, or ecological grounds. The virus is now here and, given the structure of the modern poultry business, is not about to depart anytime soon. Given the paucity of good viral monitoring and detection, no one really knows how many of the 200 million birds killed, burned, or gassed to date were uninfected or would have recovered. "These animals, whether chickens, ducks or pigs, have lives too, and almost no religion on earth would condone such massacres of living organisms on such a scale, especially with preventative measures," wrote three indignant Chinese scientists in *Nature*.

Dave Halvorson, a University of Minnesota veterinarian and flu expert, also doubts the modern poultry business can "tolerate this expensive, unproven, draconian and dramatic method of disease control much longer." The need for a continuous supply of meat and eggs, he says, has caused many poultry factories "to act in ways that do not contribute to disease control and may actually contribute to disease spread." Although Halvorson argues that it is no longer necessary to "consider diseased or convalescent poultry as evil," global traders and governments have not accepted the message. Nobody, of course, wants to talk about crowding.

Earl Brown, who has spent much of his career studying how population densities govern the virulence of viruses, doesn't understand why chicken numbers still haven't become a priority. "Neither governments nor the media want to talk or hear about it." Without proper research on population dynamics, chicken factories will simply hatch more viral trouble. "We have to know what's happening and figure out the calculus that drives virulence, so we don't repeat it."

Yet the global menu calls for more chicken in greater and greater concentrations. The Great Chicken Pandemic has even strengthened its most efficient incubator: the factory farm. The pandemic has displaced thousands of farmers and is actively replacing the backyard chicken with so-called biosecure corporate operations. Singapore has banned all small-scale poultry farming, as have several cities in Vietnam. In fact most jurisdictions with factory birds want to ban free-range chicken farming or small backyard poultry flocks as threats to "biosecurity." Even Elizabeth Krushinskie, president of the American Association of Avian Pathologists, now regards organic and free-range chicken as a risk to "the increased prevalence of highly concentrated food animal agriculture." Many Asians now suspect that the lively traditional banter of the region's colorful wet markets will eventually be supplanted by corporate slaughterhouses and the Muzak of superstores.

Meanwhile H5N1 continues its quest for global citizenship. In the spring of 2005, the Year of the Rooster, H5N1 killed off 6,000 bar-headed geese on Qinghai Lake in northern China, nearly 10 percent of that species's population. It then started to gobble through domestic fowl across the

country, hitching a ride on untreated poultry manure, smuggled birds, and poultry trucks. After hundreds of outbreaks and probably scores of human deaths, the government announced an amazing plan: the vaccination of 14 billion birds. No one knows what quality of vaccines will be used or whether the vaccination campaign will drive the virus to greater lethal mutations. Yi Guan, the combative Hong Kong truth seeker and virologist, doesn't even think the scheme is feasible. "This is a very crazy, a very stupid idea." He thinks the only way to end the invasion is for all infected countries to shut down their chicken factories and start over.

When migratory fowl started to die in wetlands and lakes in Siberia, Kazakhstan, and Mongolia in the summer of 2005, Europeans panicked. Sweden clamped down on Tamiflu hoarders, Holland and France moved their commercial birds indoors, and the Croatian government ordered its citizens not to eat raw eggs. In England trigger-happy hunters picked off migratory birds flying over the Channel. But in London bird importers blithely mixed consignments of quarantined birds, transferring H5N1 from a batch of Taiwanese exotics to parrots from Suriname and proving once again that migratory birds aren't the only viral carriers.

South Koreans experimented with sauerkraut and kimchee, a fiery cabbage dish, to treat fluish birds. In Japan authorities traced 31 outbreaks of H5N2, a mild relative of H5N1, at chicken factories to an illegally smuggled vaccine from Mexico. As H5N1 insinuated itself into every nook and cranny of the poultry trade, many scientists abandoned their Chicken Little predictions and got philosophical: "We're just in chapter five of a 20-chapter book on avian flu—there is so much we don't understand," reflected one exasperated Indonesian veterinarian.

H5N1 isn't the only member of the influenza tribe looking for diversification opportunities. Pigs, for example, used to harbor two stable influenza subtypes (H1 and H3), but in the last decade, "pig genetics has gone spinning in wild directions," says Brown. Now avian, human, and porcine types are all swapping genes in the world's expanding pork factories. To date the viral invasion hasn't caused much more than a lot of porcine sneezing. "But we have a really varied viral soup in pigs right now," notes Brown.

Dogs haven't been so lucky. With absolutely no warning, a horse flu (H3N8) jumped to greyhound racing dogs in 2004. (Greyhound pups are traditionally fed horse meat.) The outbreak quickly burned through a dozen U.S. states, including New York and Florida. The new canine influenza virus starts with an unusual "kennel cough," then proceeds to a bloody pneumonia for about 10 percent of puppies and older dogs. Canines and felines can also carry H5N1.

None of this frantic viral activity in mammals surprises the famed Dutch virologist Jaap Goudsmit. He argues that viruses are now breaking out of their natural reservoirs in wildlife at unprecedented rates, thanks to persistent human encroachment. Humans now utilize 83 percent of the earth's surface, commandeer 60 percent of the freshwater, and consume a third of all living things in the ocean. That doesn't leave much room for other creatures. "A new phase seems to have begun in the evolution of avian flu viruses," Goudsmit muses in his book *Viral Fitness*. Given that human activity or what we call globalization is rapidly eliminating birds and mammals

at nearly a thousand times the natural rate of extinction, Goudsmit wonders, "Where else other than among humans can a virus family settle down in the coming centuries?" Where else, indeed?

Most experts expect that H5N1 will soon invade North America, where the World Bank thinks it could cause a multibillion-dollar headache for the fast-food business. They also predict that avian flu will deliver an economic calamity in Africa, where backyard chickens are the only capital many women can own. "It's out of the box now," admits Henry Niman, an American flu expert and president of Recombinomics, a biotech firm. Every day Niman publishes an insightful viral evolution of H5N1 commentary on the elegant on the Internet (http://www.recombinomics.com/). Most end this way: "The dramatic expansion of H5N1 in poultry and people is cause for concern as are reports of dead dogs and cats." Niman believes that H5N1 is now so widespread that it can't help but become a human virus. "The only question is, How virulent will it be?" He doesn't think antiviral drugs or vaccines will slow a pandemic down much. He marvels at the weak public health response, the shoddy monitoring, the repeated deception by governments, and the limited number of effective interventions. "People are talking about the avian flu but they're not doing much about it."

The talk has been colorfully pessimistic. Mike Leavitt, U.S. secretary of health and human services, describes the world as a "biologically dangerous place right now." Lee Jong-wook, director general of the World Health Organization, says, "The next pandemic will cause incalculable human misery." The United Nations secretary general, Kofi Annan, warns that "we would have only a matter of weeks to lock down the spread before it spins out of control." Jaap Goudsmit worries that influenza might jump to cattle, while the French microbiologist Antoine Danchin fears we are just reaping what we so dutifully sowed: "It is impossible to separate infectious diseases from our lifestyle or from the structure of our societies, and above all, from venal considerations. Our infections mirror our primary interests and our way of life."

In all of its manifestations, avian flu has reminded men in white coats that influenza is what it is. It moves more like a hurricane than like an invading army. It can act faster than governments or the peripatetic professionals of the World Health Organization. It can hijack a chicken factory, travel with manure into ponds, and take over a flock of migratory birds. It can spread unseen, thanks to the oldest of human passions: trading and smuggling. And it can out-evolve vaccine producers or drug makers. It is, in short, a biological storm gathering velocity and force.

The feathered blizzard of influenza also possesses many ancient advantages. It can travel along the most intimate of pathways: a handshake, a kiss, a cough, or a tear. It can swim in water and sleep in frozen duck meat. It can silently infect poultry workers without illness, leaving only a ghostly antibody behind as a calling card. And it can noiselessly sweep through any crowd. Once a few particles enter the human lungs, influenza multiplies furiously. Within a couple of days, the sick are shedding tens of millions of particles in nasal mucus alone. When an airplane full of globetrotters lost its ventilation for about four hours in 1977, influenza ran through the passengers at lightning speed: nearly three-quarters of them got the flu from just one sneezing passenger.

At a 2005 symposium organized by Deutsche Bank, the well-known influenza researcher Robert Webster wrung his hands as he has done many times in the past. What began as sneezes and low-grade fevers in Guangdong's poultry factories in the 1990s has become, just a decade later, a distinct serial killer of ducks, chickens, and migratory birds. When given to ferrets, animals with a legendary tolerance for influenza, it caused diarrhea, forced breathing, leg paralysis, and death. "This is the first influenza virus that kills ferrets and spreads throughout the body to the brain." Although the virus has killed many human chicken handlers and colonized thousands more with silent infections, it has yet to acquire a real knack for person-to-person transmission with pandemic ease. Webster has no doubt that the evolving virus will master that trick next. "I think that we have to accept the fact that we are sleeping on top of a time bomb."

So far that's the good news. The really bad news is that there is more than one improvised explosive device ticking along the global roadside.