ONE WORLD

In 1998 scientists working independently in Australia and Central America announced that they were finding massive numbers of dead frogs in the forests where they worked. The large-scale die-off was especially dramatic. Global amphibian populations had been declining for some time, but these mounting frog deaths occurred in pristine habitats—places far less likely to have been exposed to toxic by-products of human cities or other man-made environmental threats. Field biologists and tourists alike witnessed the large numbers of dead frogs scattered about the forest floor. This was rare indeed since scavengers quickly eat dead animals. To see so many indicated that the predators already had their fill of free frogs and these were the leftovers. In fact, it was just the tip of the iceberg. A massive and unprecedented amphibian carnage was under way.

The expiring frogs all displayed similar and worrying symptoms. They became lethargic, their skin sloughed off, and they often lost their ability to right themselves if turned over. In the months that followed the first announcements, a number of possible explanations came forth—pollution, ultraviolet light, and disease among them. Yet the particular pattern of death

Frogs killed by the amphibian chytrid fungus. *(Joel Sartore / National Geographic / Getty Images)*

was most consistent with an infectious agent. Animal deaths spread in wavelike patterns from one location to the next suggesting the spread of a microbe, a contagion sweeping through the Central American and Australian frog world.

The solution to the mystery came in July 1998, when an international team of scientists reported the source of the frog disease. The team found evidence that a majority of the frog species succumbing to the die-offs were infected with a particular species of fungus. The fungus they identified was *Batrachochytrium dendrobatidis*, known more simply as the chytrid fungus (pronounced KIT-rid). They found evidence of chytrid, which had previously been seen exclusively in insects and on decaying vegetation, on a number of dead frogs. Tellingly, when they scraped the fungus from the dead and infected healthy laboratory tadpoles with it, they were able to re-create the fatal symptoms. The fungus was to blame.

Since the 1998 report, this fungus is now documented on all continents that have frog populations. It can survive at sea level but also wreaks havoc at altitudes up to twenty thousand feet. And it's a killer. In Latin America alone, chytrid fungus has been linked to extinction in 30 of the 113 species of the strikingly beautiful harlequin toads. Thirty species forever removed from the biological diversity of our planet.

While the spread and devastation of chytrid has now been well documented, much about it remains unknown. The large-scale declines in amphibian populations predated the emergence of the fungus, so it is not the only problem that is devastating global frog populations, but it's definitely among them. Another key factor is the steady decline in available frog habitat as the human footprint has increased over the last hundred years.

The questions of where the fungus originated and how it spreads are largely outstanding. Work done on archived specimens from South Africa shows that the fungus has infected African frogs since at least the 1930s, decades before it hit any other continent. This points to an African origin. Yet at some time, the fungus spread and did so quite effectively. How did it manage to get so cosmopolitan so quickly?

One possibility is the exportation of frogs. The researchers who discovered the early evidence of chytrid in South Africa also noted that some of the species of the frogs infected were commonly used in human pregnancy tests. When injected by lab technicians with urine from pregnant women, African clawed frogs (*Xenopus laevis*) ovulate—which made for an early, if significantly more cumbersome, version of the common pregnancy dipsticks used today! Following the discovery of this human pregnancy test in the early 1930s, thousands of these frogs were transported internationally for this purpose. Perhaps they took chytrid fungus with them.

But *Xenopus* was likely not alone in causing the global spread; since one stage of the fungus's life cycle actively spread in water, that was also a probable factor. Human movement almost certainly played a role as well. Our shoes and boots are at least partially to blame. This small fungus, wanted in the deaths of frogs worldwide, hijacked us.

The chytrid fungus has resulted in global frog deaths and in some cases extinction of entire frog species, a tragic loss for wildlife on our planet. In a 2007 paper, Lee Berger, one of the researchers who first identified the chytrid fungus, used language uncommon in conservative scientific journal articles when he wrote, "The impact of [chytrid fungus] on frogs is the most spectacular loss of vertebrate biodiversity due to disease in recorded history."

What happened with the chytrid fungus also gives us important clues to a larger phenomenon that affects much more than just amphibians. Over the past few hundred years, humans have constructed a radically interconnected world—a world in which frogs living in one place are shipped to locations where they've never previously existed, and one where humans can literally have their boots in the mud of Australia one day and in the rivers of the Amazon the next. This radically mobile world gives infectious agents like chytrid a truly global stage on which to act. We no longer live on a planet where pockets of life persist for centuries without contact with others. We now live on a microbially unified planet. For better or worse, it's *one world*.

How did we get to this point? For the vast majority of our history as living organisms on this planet, we had incredibly limited capacity to move. Many organisms can move themselves over short distances. Single-celled organisms like bacteria have small whiplike tails, or flagella, that allow them to move, but despite their molecular-scale efficiency, flagella will never push their owners far. Plants and fungi have the potential to move passively by creating seeds or spores blown by the wind. They also have adopted methods that co-opt animals to help them move, which explains the existence of fruit and the spores of fungi like chytrid. Nevertheless, precious few forms of terrestrial life regularly travel more than a few miles in the course of their lives.

Among the wonderful exceptions to the largely static life on Earth is the coconut palm. The seeds of the coconut palm (i.e., coconuts), like a number of other *drift seeds*, evolved buoyancy and water resistance, permitting them to travel vast distances through ocean currents. Among animals, some species of bats and birds are masters of space. The best example might be the Arctic tern, perhaps the most mobile species on Earth outside of our own. The tern flies from its breeding grounds in the Arctic to the Antarctic and then back again each and every year of its life. A famous tern chick was tagged on the Farne Islands in the UK near the time it was born in the summer of 1982. When it was found in Melbourne, Australia, in October of the same year, it had managed a twelve-thousand-mile journey in the first few months of life! It's been estimated that these amazing birds, which can live over twenty years, will travel about one and a half million miles in their lifetimes. It would take a full-time commercial jet pilot, flying at the maximum FAA permitted effort, nearly five years to cover the same distance.

Yet despite their wings, most bird and bat species actually live their lives quite close to where they're born. Only a few, like the Arctic tern, have evolved to regularly move great distances. Highly mobile species, whether bird, bat, or human, particularly the ones that live in large colonies, are of particular interest for the maintenance and spread of microbes. Among primates, only humans have the potential to move themselves great distances during a single lifetime, let alone in a few days. That's not to say that other primates simply stay put. Almost all species of primates move every day in their search for food, and young adults routinely move from one area to another before mating. Yet whether primate or bird, nothing on the planet—certainly nothing outside of the sea—matches humans in our capacity to move long distances quickly. The human potential to move, which now includes traveling to the moon, is unique and unprecedented in the history of life on our planet. But it comes with consequences.

Humans started globetrotting in earnest millions of years ago using our own two feet. Bipedalism gave us an advantage over our ape cousins in terms of our capacity to wander. And, as discussed in chapter 3, it had consequences for how we interact with the microbes in our environment. Yet our capacity to negotiate the globe in the amazing way we do now started with our use of boats.

The earliest clear archaeological evidence of boats dates to around ten thousand years ago. Found in the Netherlands and France, these boats (which might be better called rafts since they were made by binding logs together) were probably used primarily in fresh water. The first evidence of sea-going boats comes from a group of British and Kuwaiti archaeologists, who in 2002 reported finding a seven-thousand-year-old vessel that undoubtedly was used at sea. The archaeologists made their discovery at the Neolithic site of Subiya in Kuwait. Stored in the remnants of a stone building, the boat consisted of reeds and tar. Most strikingly, the bits of boat had barnacles attached to the tar, indicating that it was definitely used in the sea.

Employing genetics and geography, we can get a much earlier estimate for the first use of seafaring boats. The indigenous people of Australia and Papua New Guinea provide perhaps the best case for this. By comparing the genes of the Australasian people with other humans throughout the world, we can conclude that people reached Australia at least fifty thousand years ago.

During this time, our planet was a relatively cold place—it was the peak of an ice age. Since more of the Earth's water was locked up in ice, the sea level was lower, revealing pieces of land that connected what are currently islands. Many of the islands in the Indonesian archipelago were joined by these so-called land bridges.

Despite the land bridges that ice ages expose, we know that no one walked all the way to Australia. In particular, the deep-water channel between Bali and Lombok in present-day Indonesia, a channel around thirty-five kilometers long, would have required boats to navigate. So we can infer that these early populations also used at least some form of sea transport.

We know very little about these early Australian settlers, although we know that they traveled at a time before animal domestication so certainly didn't move with animals in tow. Nevertheless, their movements impacted how they related with microbes. When they first crossed from Bali to Lombok, they encountered a completely novel set of animals.

The channel between Bali and Lombok lies squarely on Wallace's Line, the famous geographic divide named after the nineteenth-century British biologist Alfred Russel Wallace who, along with Charles Darwin, codiscovered natural selection.* While the distance between Bali and Lombok was no greater than that between many of the waterways separating the hundreds of islands along the Indonesian archipelago, Wallace noted that animal populations on either side of the channel differed extensively. And while he didn't have the precise models for ice age water levels that we have today, he surmised that this biological divide existed because Bali and Lombok were never connected by a land bridge, something we now know to be true.

Like humans, other animals take advantage of land bridges, but unlike these earlier settlers who had boats, the animal

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* Wallace led a fascinating life. Rather than working from a cushy boat like his contemporary and natural selection codiscoverer Darwin, he traveled on the cheap, selling specimens along the way to fund his expeditions. An excellent scientific biography of him as well as an accessible but detailed discussion of his findings in the Indonesian archipelago can be found in David Quammen's book, *The Song of the Dodo*.

Wallace's Line, and the landbridges that once connected the islands on either side of it. (*Dusty Deyo*)

populations that couldn't fly long distances were largely stuck on one or another side of this deep-water barrier. When the first explorers left Asia for the Australasian continent, making the thirty-five-kilometer hop from Bali to Lombok, they took a fairly short trip by boat but a huge leap for primates. When they crossed this divide, these early explorers entered a world that had never seen monkeys or apes before. They also encountered completely new microbes.

These early settlers would have been hit with novel diseases from Australasian animals and their microbes, infectious agents that had never seen a primate before. Yet the impact of these agents for the human populations as a whole was likely limited, since the small population sizes of the settlers wouldn't have been able to sustain many kinds of agents.

It's hard to know exactly what the first trips across Wallace's Line were like. They may have been colonization events with small groups that were then completely cut off. Perhaps more likely they were short initial forays into new lands, followed by the establishment of temporary outposts, much as we consider colonizing the moon. The actual way in which the new lands were colonized would have played an important role in determining the flow of microbes in either direction. And while these first Australasian humans almost certainly had some connections to the "mainlanders" they left behind on Bali, that contact may have been very infrequent. Yet some new Australasian infections that had the potential for long-lasting human infection could very well have made their first forays into human populations on the Asian side of the divide.

The use of boats to visit new lands would continue with increasing frequency over the forty or so thousand years following this first colonization of Australasia. We have much better knowledge of what later trips were like and how they connected microbially distant lands. Perhaps the peak of boating-based colonization before modern times occurred among the Polynesian populations of the South Pacific.

Among these Polynesian journeys, probably the most incredible was the first discovery of Hawaii, over two thousand years ago.* For the first lucky settlers, finding this island would have been truly like finding a needle in a haystack. To give a sense

* The Polynesians had incredible navigation skills, and though their boats were simple, they were highly seaworthy. At a moment in history when boats in the West rarely went beyond the line of sight with land, Polynesians managed to negotiate huge swaths of the world's largest ocean. They fabricated their ships from two canoes, each dug out from tree trunks, which were lashed to each other with crossbeam planks to form a deck. They used coconut fibers and sap to seal seams.

of scale, the largest island of the Hawaiian archipelago, also named Hawaii, has a diameter of around a hundred miles. And the Southern Marquesas, whose inhabitants were the most likely first colonizers of Hawaii, are some five thousand miles away. To imagine what it would have been like to hit the mark, imagine we blindfolded an Olympic archer, then spun him around and asked him to hit his target—the ratios are about the same. One can only imagine how many boats (and their inhabitants) were lost before the fortunate finally made it.

On their long trips, the Polynesians probably lived largely on caught fish and rainwater. Yet they traveled with a veritable biological menagerie. They brought along sweet potatoes, breadfruit, bananas, sugarcane, and yams. They also traveled with pigs, dogs, chickens, and probably (unintentionally) rats. Having all of these domesticated species meant that the flotillas carried not only life support for the Polynesian explorers, but also minirepositories of microbes, which would spread and mix with local microbes in the places that they discovered.

The boat journeys of the Polynesians, as remarkable as they were for their time, pale in comparison to the global shipping that emerged in the fifteenth and sixteenth centuries. By the time Europeans reached the New World, in the late fifteenth century, thousands of massive sailing ships were plying the waters of the Atlantic and Indian Oceans and the Mediterranean Sea, moving people, animals, and goods back and forth between the countries of the Old World.

The impact of smallpox on New World populations is the most dramatic known example of the way that the connections formed by shipping can influence the spread of microbes. Some estimates suggest that as many as 90 percent of the people living in the Aztec, Maya, and Inca civilizations were killed by smallpox brought by boats during European colonization, a massive and devastating carnage. And smallpox was only one of many microbes that spread along the shipping routes of this time.

Each of the major transportation advances would alter connectivity between populations, and each would have their own impact on the spread of new microbes. The exclusivity of ships as a means for long-distance transport would not hold out forever. The use of roads, rail, and air provided new connections and routes for the movement of humans and animals as well as their microbes. For microbes, the transportation revolution was really a connectivity revolution. These technologies created links that forever changed the nature of human infectious diseases, including, critically, how efficiently they spread.

The use of roads of some sort or another is an ancient practice, far predating the use of water as a medium for transportation. Chimpanzees and bonobos both create and use forest trails to help them move through their territories. I learned this first-hand while studying wild chimpanzees in the Kibale Forest National Park in southwest Uganda. Richard Wrangham, the Harvard professor who introduced me to this work, used these trails to help observe chimpanzees.

Wrangham had done his doctoral work at the Gombe Stream site in Tanzania that Jane Goodall established. He'd critiqued some of the findings from Gombe because the chimpanzees there were habituated by provisioning—to get the wild chimpanzees comfortable with human researchers, the animals were fed large amounts of banana and sugarcane. Wrangham felt that provisioning changed some of the subtle chimpanzee behaviors, so when he started his own site in Kibale, he habituated the animals the hard way—by having his teams follow them until the apes effectively gave up and no longer ran away. He did this by essentially enhancing and extending the natural pathways that they moved along.*

The art of actual road building began in earnest around five to six thousand years ago when cultures throughout the Old World started using stone, logs, and later brick to enable the movement of people, animals, and cargo. The first modern roads followed in the late eighteenth and nineteenth centuries in France and the United Kingdom. These roads used multiple layers, drainage, and eventually cement to make permanent structures permitting regular movement throughout the year.

The rate at which modern roads have spread throughout the world has not been consistent, of course. Some regions in Europe and North America have roads reaching most human populations, while some regions where I work in central Africa have virtually no road access. Clearly, as roads enter into new regions, they bring both positive and negative effects. They are among the top priorities for many rural communities since they provide access to markets and health care, but from the perspective of global disease control, they are double-edged swords.

HIV is among the most notable example of the impact that road proliferation has had on the movement of microbes. In a series of fascinating studies, the HIV geneticist Francine McCutchan, whose lab I worked in at Walter Reed Army Institute of Research (WRAIR), and her colleagues at the Rakai and Mbeya sites in east Africa have examined the role that roads have played in the spread of HIV, demonstrating that proximity to roads increases a person's risk of acquiring HIV. As people have more access to roads, they have a higher chance of getting infected because roads spread people, and people spread HIV.

* Sue Savage-Rumbaugh, a primatologist from Georgia State University, has reported that bonobos go so far as to leave trail markers to help other members find their way when conditions don't permit them to foll other using footprints.

Other than sex workers, the highest occupational risk for acquiring HIV in sub-Saharan Africa is being a truck driver. McCutchan and her colleagues have shown that the genetic complexity of HIV is greater among individuals who have increased access to roads. Roads provide the mechanism for different types of HIV to encounter one another, in a single coinfected individual, and swap genetic information. But roads do more than just help established viruses spread. Roads and other forms of transport can also help to ignite pandemics.

One of the most stubbornly lingering public misconceptions is that we don't know how HIV originated. In fact, our understanding of the origins of HIV is more advanced than our understanding of the origins of probably any other major human virus. As we saw in chapter 2, the pandemic form of HIV is a chimpanzee virus that crossed into humans.* There is no debate within the scientific community on this point. The cumulative evidence with regard to how it originally entered into humans is also increasingly unequivocal. It was almost certainly through contact with chimpanzee blood during the hunting and butchering of chimpanzees. We'll delve further into this in chapter 9 when we discuss the work my colleagues and I have done with central African hunters.

Perhaps the only lingering debate about HIV origins is how it originally spread from the first infected hunter and why it took so long for the medical community to discover it. The earliest historical HIV samples date from 1959 and 1960, twenty years

* As discussed in chapter 2, HIV is a hybrid virus consisting of parts of two monkey viruses that chimpanzees acquired, almost certainly through the hunting of these monkeys. Note: There are multiple HIV viruses that have entered into humans (i.e., HIV-1M, HIV-1N, HIV-2, etc.). Here, when I refer to HIV, I mean exclusively HIV-1M, the dominant pandemic virus that is responsible for over 99 percent of human cases.

before AIDS was even recognized as a disease. In an amazing piece of viral detective work, evolutionary virologist Michael Worobey and his colleagues managed to analyze a virus from a specimen of lymph node from a woman in Leopoldville, Congo (now Kinshasa, DRC).

The lymph node had been embedded in wax for over forty-five years. By comparing the genetic sequence of the virus they found in the specimen with other strains from humans and chimpanzees, they were able to attach rough dates for the first ancestor of the human virus. While the genetic techniques they used cannot pinpoint dates closer than a few decades, they concluded that the virus split from the lineage sometime around 1900 and certainly before 1930. They also concluded that by the time that the woman in Leopoldville became infected with HIV in 1959 there was already a significant amount of genetic diversity of HIV in Kinshasa, suggesting that the epidemic had already established itself there.

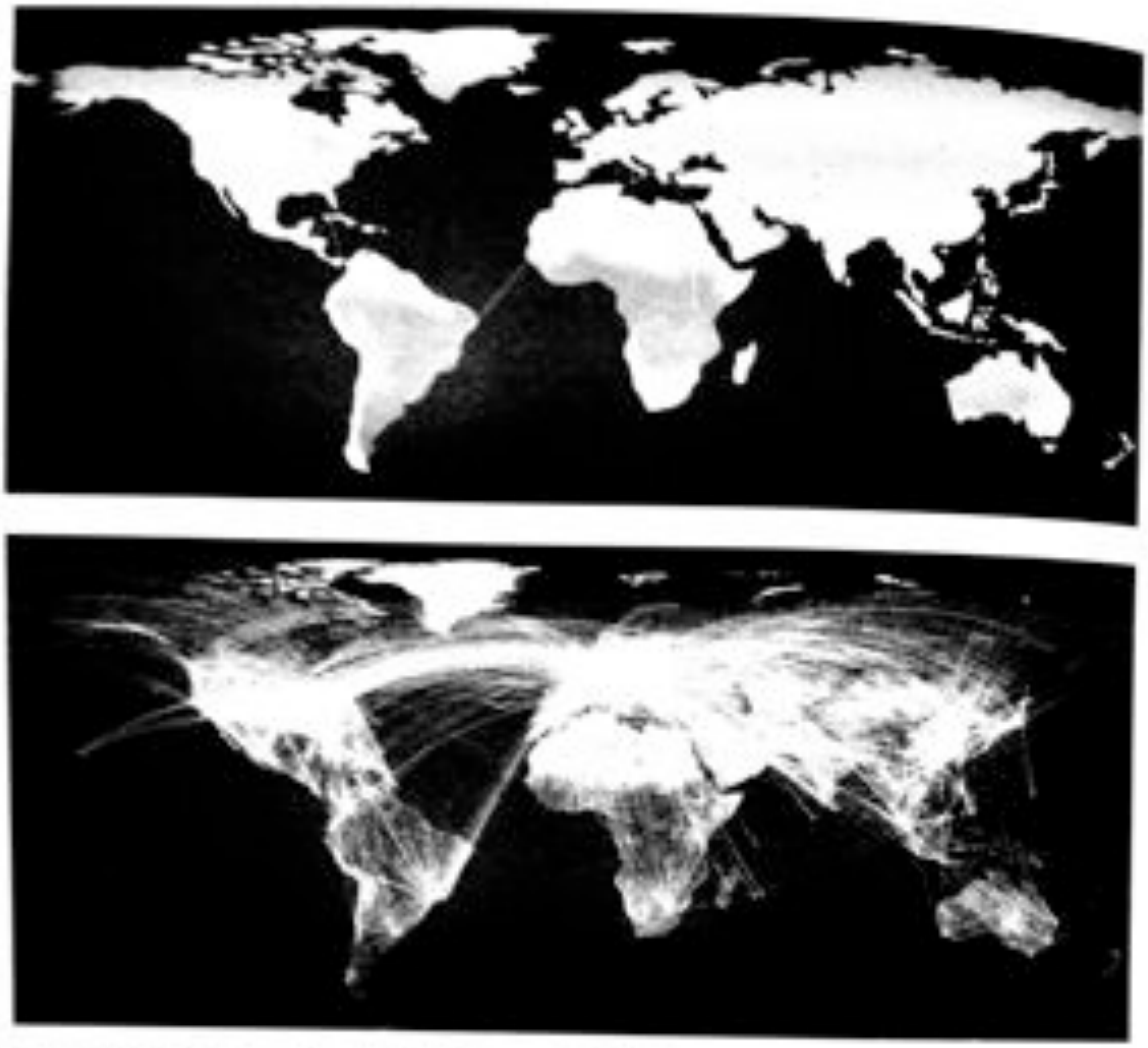
The fact that HIV goes back to 1959, let alone 1900, provides some serious challenges to the medical community. One of the central questions is this: if it was in human populations in the early twentieth century and already constituted at least a localized epidemic in Kinshasa by 1959, why did it take us until 1980 to identify the epidemic? Another key question is what special conditions were present that permitted the virus to start taking off in the middle of the twentieth century?

A number of changes occurred in francophone central Africa, the region where HIV-1 originated, leading up to the period in the 1950s when those first precious samples were taken. The anthropologist Jim Moore and his colleagues at the University of California, San Diego, put together some of the key events in a 2000 paper, the majority of which focused on how easier means of travel influenced virus proliferation. In 1892 steamship service began from Kinshasa to Kisangani in the very heart of the central African forest. The steamship service connected populations that had been largely separated, creating the potential for viruses that previously might have gone extinct in local isolated populations to reach the growing urban centers. In addition, the French initiated the construction of railroads, which, like shipping and road lines, connect populations. This produced another mechanism for viruses to spread from remote regions to urban centers, effectively providing a larger population size of hosts for a spreading virus.

In addition to the connectivity provided by new steam, rail, and road lines, the construction of railroads and other large infrastructure projects led to cultural changes that also had an important impact. Large groups of men were conscripted, often forcefully, to build railroads. Moore and his colleagues note that the labor camps were populated mostly by men, a condition that dramatically favors transmission of sexually transmitted viruses like HIV. Together, the shipping and rail routes and the factors surrounding their construction must have played a role in the early transmission and spread of HIV.

As dramatic as the road, rail, and shipping revolutions were for the transmission of microbes, an entirely new form of transport would add another layer of speed. On December 17, 1903, in Kitty Hawk, North Carolina, a site chosen for its regular breeze and soft sandy landing areas, the Wright Brothers made the first sustained, controlled, and powered flight. Some fifty years later the first commercial jet flew between London and Johannesburg. By the 1960s, the age of jet travel was here to stay.

Airplanes link populations in an immediate way, which allows the transmission of microbes to occur even more quickly. Microbes differ from each other in terms of their *latent period*,



Top: World air traffic, 1933; Bottom: World air traffic, 2010. *(T: Dusty Deyo; B: OpenFlights.org)*

the period of time between when an individual is exposed and when they become infectious or capable of transmitting the agent to others.* Almost no microbes that we know of have

* The *latent period* differs subtly but in an important way from the *incubation period* for some microbes. Where the latent period refers to the time between exposure and infectiousness, the incubation period refers to the time between exposure and the first signs of disease. In the case of HIV, for example, infected individuals become contagious within the first few weeks after exposure, yet at this point they experience only generic symptoms like fever

latent periods of less than a day or so, but many have latent periods of a week or more. The immediacy of air travel means that even microbes with very short latent periods can spread effectively. In contrast, if a person infected with an agent that had a very short latent period were to board a ship, unless the ship had hundreds of individuals the virus could infect, it would go extinct before the ship made land.

Commercial air flights alter in fundamental ways how epidemic disease spreads. In a fascinating paper from 2006, my colleagues John Brownstein and Clark Freifeld of Harvard, one of the new academic breed of *digital epidemiologists*, found creative ways to use existing data to show just how much impact air travel has on the spread of influenza. John and his colleagues analyzed seasonal influenza data from 1996 to 2005 and compared it with patterns of air travel. They found that the volume of domestic air travel predicts the rate of spread of influenza in the United States. Interestingly, the November travel peak around Thanksgiving appears to be of particular importance. International travel also plays a vital role. When the number of international travelers is lower, the peak of the influenza season comes later—because when there are fewer travelers, it takes longer for the virus to spread. Perhaps most strikingly the researchers were able to see the impact of the terrorist attacks of September 2001 on influenza. The travel ban led to a delayed influenza season. The striking effect was not seen in France, which did not enact the ban, providing an excellent control.

During the past few centuries the ease of movement has increased dramatically throughout the world. The rail, road,

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and rash. Most cases of HIV transmission actually occur during this acute infection period rather than after the incubation period for AIDS itself, which is generally some years later.

sea, and air revolutions have all permitted humans and animals to move more quickly and efficiently both within continents as well as between them. The transportation revolution has created interconnectivity unprecedented in the history of life on our planet. It is estimated that we now have over fifty thousand airports, twenty million miles of roads, seven hundred thousand miles of train tracks, and hundreds of thousands of ships and boats in the oceans at all times.

The connectivity revolution we've experienced has fundamentally changed the ways that animal and human microbes move around our planet. It has radically increased the speed at which microbes can travel. It has brought populations together, allowing agents that couldn't previously sustain themselves with low population numbers to flourish.

As we'll see in chapter 8, it has also permitted completely novel diseases to emerge and frightening animal viruses to extend their ranges. These technologies have created a single interconnected world—a giant microbial mixing vessel for infectious agents that previously stayed separate and stayed put. The new microbial mixing vessel that our planet has become has forever altered the way in which we'll experience epidemics. It has truly helped usher us into the pandemic age.