Chapter 2

Coming to the Americas: 50,000 B.C. to 1492 A.D.— The Worms and Germs

THE (CHARRED) STICKS and stones of Pedra Furada were not bones, quite the best proof of human presence. There is, however, another human remnant—feces. Under favorable aridity, feces will desiccate to a stone-like consistency and become coprolites—an archaeological term for fossilized stools. Humans without indoor plumbing (like many animals) often have customary places, not far from their habitation, where they relieve themselves. The coprolites can be sectioned to permit microscopical examination of their contents. Food remnants, the eggs of parasitic intestinal parasites, and the resistant cystic stage of intestinal parasitic protozoa (such as that of the diarrhea-causing *Giardia lamblia*) will also be preserved over the millennia. Scientists are beginning to apply the powerful, probing modern immunogenetic technology to the examination of coprolites, as well as to other organic relics of ancient life. In the near future, scientists will surely identify the bacterial and viral infections of our ancestors by mapping their DNA "footprints" in the fossilized feces.

But even with relatively unsophisticated, nonmolecular microscopical techniques a picture of ancient life has been reconstructed from clues in the coprolites. For example, from

the communal privies used by the citizens of tenth-century Winchester and fifteenth-century Worcester, England, large numbers of preserved roundworm and whipworm eggs were found. Those people were heavily parasitized—attesting to the miserable state of British medieval sanitation. From seeds and pollen in the coprolites we know what herbals these people took for what ailed them—the black nightshade, the deadly nightshade, hepbane, self-heal, and the water dropwort. Seven hundred years later, in the seventeenth century, the English still had parasites galore. The great physician-physiologist of that time, William Harvey, departing from his seminal work on the circulation of the blood, spoke of the more mundane intestinal conditions of his fellow Englishpeople by declaring, "Worms in all the guts, nothing so common as worms."

From the parasites recovered in the coprolites and the few American mummies that have been found, we can attempt to construct a likely scenario. The premise: any parasitic worm (or its telltale egg) whose "ancestral home" is Africa or Asia found in American human specimens dated as pre-Columbian indicates that there was human contact between Asia or Africa before 1492.

This was the approach of the Brazilian scientists at Pedra Furada. And feces they found—hard as a rock—at the 30,000 B.C. level of sediment. In these coprolites were the unmistakable barrel-shaped, plugged eggs of the whipworm, *Trichuris.* But this was not proof positive that they were from a parasite of humans, and a more searching examination showed how easy it was to be led down the garden of hypothesis's path. There are several species of *Trichuris* other than that of the human whipworm, *Trichuris trichiura,* and the eggs of all of them look pretty much alike under the microscope. Moreover, closer examination showed that the Pedra

Furada coprolites didn't look "human," that they were kind of kidney shaped in form. The Brazilian paleoarcheologists came to the disappointing conclusion that these were the droppings of a caviid (guinea pig-like) rodent, *Kerodon ruprestris,* that had migrated to South America at the time of the great continental breakup of 40 to 25 million years B.C. The whipworm was a parasite of this animal. *Kerodon ruprestris* still exists in the Pedra Furada area, but when the scientists trapped some of these animals, they found, curiously, that they no longer were parasitized with the whipworm as they had been 30,000 years before. So the worm (eggs) looked the same but the feces were different, and the identity of these humans (if indeed they were present) and where they came from remain a mystery.[2]

Was there truly an ancient "cold screen"? Were the Russian-Siberian immigrants to Alaska free of what we call soil-transmitted intestinal parasitic worms?[3] Thus, the pinworm

2. In this case the parasite eggs looked "human" but the feces looked "animal." In epidemiological sleuthing the opposite can also occur. Some years ago, large numbers of very human looking turds began to appear on the sandy, pristine shores of Kualoa Beach Park in Oahu, Hawaii. The health authorities were very upset because this might be a health hazard and, even worse, a threat to the tourist industry. Sharks are bad enough but feces would be intolerable. The law and political authorities were concerned because they didn't know who was defiling the beach—random vandals, the homeless, or Hawaiian nationalist-royalists making a political statement, so to speak. Examination of these feces revealed that there were numerous protozoan parasites and worm eggs of many types but none were of species parasitic in humans. They were parasites of sea turtles, and these were the "vandals" coming to the beach at night for purposes best known to turtles, in the course of which there was some indiscriminate defecation.

3. The parasites are called soil transmitted because the usual way of transmission from person to person is in fecally infected soil containing the eggs or infective, skin-penetrating larvae. Tourists to the wormy regions of the world may get theirs via the locally grown green salad. There's nothing quite like feces for organic gardening. The other intestinal parasite, the pinworm *(Enterobius vermicularis),* that itching scourge of the collective middle-class anus, doesn't require soil for transmission. Pinworm eggs

could have come over with the original migrants. However, there are no 20,000-year Siberian mummies to verify our assumption. All we have are the modern Russians. And a wormy nation they are. Infection rates, in fact, were so high in Lenin's time that the regime issued the manifesto "Devastate the Worms." This official concern prompted extensive surveys of intestinal parasites to be undertaken throughout the Soviet Union. They showed that the aboriginal peoples of Asiatic Russia, living above 60° north latitude, are free of the two most common intestinal worms, the roundworm *(Ascaris)* and the whipworm *(Trichuris).* A little bit farther south of Siberia, in the Far Eastern zone, the worms begin. But even there, the warm-loving hookworms are absent.

Few pre-Columbian desiccated Indians and/or their fecal specimens exist, but those few support the notion of the clean Siberian coming to America. The ancient North American human mummies and coprolites have come from sites with romantic-sounding names such as Dust Devil Cave (Utah, 6800–4800 B.C.), Big Bone Cave (Tennessee, 500 B.C.), Turkey Pen Cave (Colorado, 700 B.C.), Antelope House (Arizona, 1300 A.D.), and Salmon Ruin (New Mexico, 1300 A.D.). These and other pre-Columbian sites in the Aleutians and the Northwest Coast have, so far, yielded nothing that indicates a soil-transmitted parasite. Our old anal nemesis, the pinworm, was there but that's a hand-to-mouth traveler.

The pre-Columbian South and Central American Amerinds should have been as free of intestinal parasites as their cousins in the North. They should have, in particular, been free of hookworms. Hookworm parasites are transmitted by infective, skin-burrowing larvae in the soil. These tempera-

become infective, embryonated, very rapidly and stick to fingers, bedding, and such. Hand-to-mouth transmission is the usual mode of infection with pinworms.

ture-sensitive larvae would have been quickly frozen had they come across with their human hosts in the Bering Strait migrations.

Thus, hookworms would leave the best footprint of pre-Columbian contacts. Their presence in coprolites and mummies would speak both of contact(s) and where those ancient travelers hailed from. This is because there are two kinds of hookworms in humans and their ancestral "homes" are in different parts of the world. *Necator americanus*, whose name must have been bestowed by a taxonomist with a warped sense of either patriotism or geography, comes from Africa. The other hookworm, *Ancylostoma duodenale*, comes from Asia.

Unlike the North American continent, between the remote, clouded time of 50,000 B.C. and 1492 A.D. the fossil worm record reveals pre-Columbian visitors to the American Southern Hemisphere.

The Brazilian paleoparasitologist L. F. Ferreira and his colleagues of the National School of Public Health in Rio de Janeiro continued to investigate in the Pedra Furada area. At one site they struck metaphoric gold, a treasure trove of human coprolites. Those fossilized stools had been passed 7,320 years ago and they contained hookworm eggs! This was indeed exciting, but the species of hookworm producing those eggs could not be determined. The eggs of both species of hookworm are morphologically identical; one needs the adult worm for those morphological landmarks that distinguish one species from another. Also, it would have been comforting to find at least one more site bearing the hookworm sign of transoceanic pre-Columbian contact.

Confirmation came from a dry mummy high in the Peruvian Andes, a man who had died some 2,800 years ago. In the mummy's intestinal tissue there were helminth parasites

that when examined by scanning electron microscopy, were deemed to be hookworms—*Ancylostoma duodenale* hookworms from tropical-temperate Asia!

But what Asians could have made that seemingly impossible journey so many thousands of years ago? The archaeologists Betty J. Meggars and Clifford Evans believe that 5,000 years ago Japanese from Kyushu were swept by misadventure to Ecuador's shores, bringing with them pottery and, as some parasitologists contend, the hookworm.

In 1961 Meggars and Evans and their Ecuadorian colleagues were working a dig in Valdivia, a seaside town on Ecuador's Pacific Coast. Valdivia has been a site of human occupation for over 5,000 years. Layer on layer of relics give testimony to successive inhabitants. At the lowest stratum, representing a period of neolithic toolmakers, there were mollusk shells, simple tools of bone and stone, *and* pottery of surprising design and sophistication. The pots which "suddenly appeared" were red slipped, incised to make a distinctive decorative pattern, and rimmed by a rising series of ridged castellations. The pots were in fact identical to the pottery of Japan's southernmost island, Kyushu, during the middle Jomon period of 3,000 years B.C.—the same time that carbon 14 dating had given for the age of the Valdivian pots.

The Kyushu people of the middle Jomon period were gatherers of the tidal flats and fishers of the deeper offshore waters. Meggars and Evans believe that a canoe or canoes swept too far out to sea by inclement weather would have been carried by the strong west-to-east current whose path leads to the Ecuadoran coast. It would have been a grueling voyage, but the hardy neolithic Japanese are thought capable of surviving it. It would also have been a one-way trip; there is no alternating current back to Japan. The Kyushans might well have been accepted by the Valdivians who shared a sim-

ple neolithic fishing culture. Thus, the assimilated Japanese would have introduced their pottery and pottery-making technique. But would they also have introduced their parasites? Did they have parasites? Here again we must extrapolate, as we did for the Siberians.

We would not expect that the technologically sophisticated Japanese to have had a Third World level of parasitism. But that was the case of Japan until the mid-1950s. In 1951, 50 percent of those living in Kyushu had hookworms, some so serious as to be fatal. In 1951 alone, hookworm killed 1,261 Japanese. Indeed, until the late 1950s when control programs were initiated, Japan was a parasitologist's paradise. Consider: Every Japanese medical school has a department of medical parasitology. The most pathogenic blood-inhabiting parasitic worm is named *Schistosoma japonicum.* So, it is for good reason that I have my personal tradition of introducing each year's medical school lecture on filariasis (elephantiasis) by projecting a slide of a wood-block print. The print made by Hokusai, that superb nineteenth-century Japanese artist, shows a Japanese gentleman with his enormous scrotum in a sling. And one of the most neurologically damaging mosquito-transmitted viruses is called the Japanese encephalitis virus. These parasitic and microbial infections had been entrenched in Japan for many, probably thousands, of years. This would fit our hypothesis that both hookworm and pots attest to pre-Columbian contact from Japan.

Then there were the transcontinental infections that followed the first migrants to America

When I lived in Honolulu, every mid-April I told my plover that he was an idiot. Why should he fly, nonstop, 4,000 to 5,000 miles simply for sex. "Stay here," I'd tell him. "There are lots of great chicks in Honolulu. Maybe I can fix you up

with that nice Hawaiian stilt I know." But my plover rejected all blandishments. In his new, elegant courting plumage of jet black bib and white shawl, he would, on a late-spring morning, leave his feeding territory of that small patch of grass fronting my condominium's tennis court and wing his way north to Alaska or Siberia. In September, *Deo volante,* he'd be back bug picking on the Hawaiian turf.

In the very far North during the short, warm, humid summer our plover rendezvoused not only with his ladylove but also with the mosquitoes, midges, ticks, and biting flies that awaited his return.

During my many years in sultry climates I have been bitten by tsetse flies, sand flies, blackflies, horseflies, and mosquitoes of many varieties as well as by ticks and mites; but nowhere in the tropics have I been attacked by insects so viciously and massively as when flogging trout streams in the Arctic watershed. The abundance of blood-sucking insects that proliferate during the Arctic's short summer is simply amazing. They make life hell for humans and wildlife. They also transmit viruses that can affect human health. Arthropod-borne viruses are known collectively as arboviruses.

The "natural" hosts of many arboviruses are migratory birds, such as the waterfowl that make epic seasonal flights to their Arctic breeding grounds. Most arboviruses are not too fastidious and can spill over into the mammalian populations—wild, domestic, and human. Some arboviruses are transmitted by ticks (arthropods more related to spiders than insects). Ticks and mites infest the nests of the waterfowl where they have easy access to a blood supply of chicks, which they infect with virus as they feed. Moreover, some viruses can be perpetuated from tick to tick via the tick's egg. If a female tick carries that virus, it can enter her eggs and

lie dormant over the winter. The egg develops; the larval tick hatches already loaded with virus and capable of passing it on to the bird or mammal on which it takes its first blood meals. From the birds without frontiers and the mammals without frontiers and the swarms of vector mosquitoes and ticks at all frontiers, trans-Arctic zoonotic arboviruses probably posed a health threat to the first Americans when they colonized Alaska. They may also have carried viruses in their person or in their accompanying domestic animals that became forever endemic in the Americas. Indeed some of those viruses may have proved highly lethal to the immunologically naive American wild mammals. Shortly after the arrival of humans in North America, many of the large mammals became extinct. Did a human virus or an introduced zoonotic virus from a domestic animal kill them off?

The historical epidemiology of viral diseases is a vexing area of research because viruses are so small and often so mutable. "Here today, gone tomorrow," as well as, "Gone today, here tomorrow," characterizes the changeability of viruses and how they come and go as threats to humans. Lassa fever and, most notably, AIDS are two diseases that came "from out of the blue" in our time. A great disease of the past seemingly without parallel in our present time is the Plague of Athens. That mysterious disease killed one-third of the Athenian population over a 20-year period beginning in 430 B.C. It was a new and unfamiliar plague, swift and killing, striking "like a wolf on the fold" in epidemic proportion. The only clinical description we have is from the philosopher-general Thucydides who was himself stricken but recovered. It was a highly contagious disease giving rise to high fever; respiratory, intestinal, and neurological involvement; a rash; and gangrene of toes, fingers, and penis.

Nothing quite matches the Athenian plague in the pres-

ent clinical logbook or in the subsequent historical medical logbooks. It disappeared with no evident recurrence elsewhere. It has, for many years, challenged diagnosticians who have proposed some 30 causative, mostly viral, agents. I added a thirty-first and speculated that it was a form of Lassa fever (Desowitz, *MD Magazine*, May 1994). Lassa mostly fits Thucydides's account except that Lassa doesn't make your penis fall off; but why quibble over small details?

Then there were the native parasites and microbes of the Americas

When I began to think about the microbes and parasites that were present in the Americas prior to human occupation, I fell into the "only man is vile" trap. I should have known better. The romantic western hemisphere of my brain envisaged a prehuman America as a kind of peaceable kingdom, a pathogen-free land or at least a new world free of human-threatening pathogens. My saner self recognized that this was a crazy, sentimental notion. All living creatures have microbes. Microbes have microbes.

When the world broke up those many millions of years ago, the animals that came to be in the New World undoubtedly had within them a collection of microbes and parasites. In time, isolation from the Old World made these animals evolve into uniquely American species. And as they evolved, so did their viruses, bacteria, parasitic protozoa, and worms also become uniquely American species.

The rich variety of arboviruses peculiar to North America and the tropical Americas is impressive in a frightening way. There is, for example, WEE (western equine encephalitis), EEE (eastern equine encephalitis), and SLE (St. Louis encephalitis), mosquito-transmitted viruses ranging from northern Canada to Argentina in a massive natural reservoir

of infection in reptiles, wild birds, wild mammals, and (now) horses. The virulence of these arboviruses varies from place to place, time to time, and person to person. Arbovirus disease ranges from the asymptomatic to the simple febrile headache to the fatal neurological meningioencephalitis. And not only humans and horses are affected; in 1984 7 of 39 whooping cranes in a captive breeding program were killed by the eastern equine encephalitis virus.

This great reservoir of infection was being silently transacted between wild animal and mosquito many thousands of years ago. As the early Amerindians descended into the mosquito latitudes, they would have encountered one of the encephalitis arboviruses, probably the WEE virus, and it would have gone to their brains. There is a broad range of disease caused by this virus, varying from individual to individual, from simple fever-headache-joint pains to the fatal disease of the nervous system in which there is a progression from drowziness to lethargy to convulsions to coma to death.

The Amerinds, like today's tourists, would have been attacked by new mosquitoes carrying new zoonotic viruses when they came to Central and South America. These viruses with strange-sounding names hint of far-off places—Mayaro virus, Maituba virus, Tacaribe virus, Machupo virus, Tamiami virus; they are relatively mild pathogens that "only" cause headache, fever, and intense joint and muscle pain. A more serious threat would have been the Ilheus and Venezuelan equine encephalitis arboviruses which can cause fatal brain damage. Here again, we do not have proof positive of the extent, if any, that these arboviruses infected the pre-Columbian Amerinds or what impact they had on their health. The modern DNA microbe hunters are beginning to turn their attention to these questions of medical history, and we are

beginning to understand how the early human inhabitants fared in the American viral jungle.

Among the hostile indigenous American pathogens were members of the Hemoflagellate family

The Hemoflagellates affecting humans are divided into three kinds. First, there is the African sleeping sickness family of trypanosomes transmitted by the tsetse fly. The pathogen swims in the blood and has two clans, one in West and Central Africa, the other in East Africa. They are out of our pre-Columbian American consideration so we will leave it at that.

Second, and more pertinent to our story, are the leishmania. Many species of vertebrates including humans have their species of leishmania parasite. I once suggested, not too seriously (*The Malaria Capers,* New York: Norton, 1993), that a leishmania of lizards may have killed the biggest lizards of all, that the dinosaurs may have been exterminated by a leishmania parasite rather than a meteor. There are many leishmania species pathogenic to humans that are spread from the Mediterranean through Africa to the Indian subcontinent and onward to the tropical and not-so-tropical Americas. Although outside the time and place of this chapter, it is worthwhile to note that the leishmania of the Middle East have been of recent threat to American military fighting in Desert Storm. There have been about 40 cases diagnosed from that military operation. Iraq has been, for many, many years, an intense focus of endemic leishmaniasis of both types, the skin invading and the deep organ invading.

All leishmania travel via a minute biting midge, the sand fly. Of all the Hemoflagellate parasites, the leishmania have made the strangest and boldest of adaptations in life style. In their vertebrate-dwelling phase, they have become restricted

to living within the macrophages, the frontline soldier cells of the immune system that have the function of ingesting and destroying foreign bodies and pathogens such as the leishmania. To survive and flourish within the macrophage "garbage disposal" cells of their vertebrate hosts, the leishmania possess a variety of defensive adaptations.

Although under the microscope all leishmania look alike, it is now known from the elegant, exquisitely specific DNA homology techniques that there are many, many species. About 30 species, or types, are peculiar to the Americas. Why so many American leishmania? It is believed that when Gondwanaland began to break up about 250 million years ago and the Western Hemisphere continents began the slow ocean voyage to their present geographical locations, they carried, like some enormous ark, the animals and plants that evolved to become the American fauna and flora. Those animals carried parasites and other microbes, and those too diversified, under conditions of continental isolation like so many Darwin finches (which now have been shown to have diversified very rapidly into new distinct types).

One group of leishmania became "dermatologists," specialists adapting to an exclusive life in the macrophages of the skin tissue. Here they cause an inflammation (which calls for still more macrophages to migrate to the invaded area providing still more "meat" for the parasites) leading to ulceration. Fortunately there is a vigorous immune response to most (but not, unfortunately, all) of these skin-invading leishmania, and the ulcers, in time, heal naturally without the need of drug therapy.

After the ulcers heal, there seems to be a lifelong immunity to reinfection. But the ulcers are, nevertheless, not always all that benign; they are disfiguring and some species

or strains of American leishmania evade or depress the immune system to cause extensive, nonhealing lesions.

Where early Amerindians first encountered sand flies harboring the leishmania is not known. Today, the northern boundary is southern Texas where eight cases of dermal leishmaniasis have been recognized and recorded. The Texan sand-fly vector, that minute midge, has the sinister name of *Lutzimya diabolica.* The real kingdom of the American leishmania is to the south, a vast region from the Yucatan to northern Argentina.

The ecological niches, the "landscape epidemiology" of leishmaniasis within this vast region, are diverse, from the high, dry, cool Andes to, especially, the steamy rain forest. Here natural infectious transactions take place in the trees where the arboreal animals—the opposums, two- and three-toed sloths, and rodents—harbor the sand-fly-transmitted parasite in benign fashion. Humans are intruders in the forest, and the leishmania parasite is one of nature's no-trespassing signs. Thus when the early Amerindians colonized the rain forest, they would have been at risk. Even today, there is the skin ulcer that is the price extolled on the natives collecting the gum of the wild chicle tree in the tropical forest to provide you with the pleasure of chewing gum. These gum collectors, known as *chicleros,* consider the leishmanial lesions so common an occupational hazard that they call it the *chiclero*'s ulcer.

There is, however, a terribly malevolent leishmania of tropical America whose infection in humans does not terminate with a scar of self-cure. This species, *Leishmania braziliensis,* causes the mutilating disease espundia, which would have been a serious threat to the health of the pre-Columbian inhabitants of the neotropical forests.

In the dark ages of medical education when we actually lectured to students, it was microbiology's lot to have our classes scheduled immediately after the lunch break. We were thus confronted by somnolent, Pickwickian students whose blood had retreated, for digestive purposes, from the brain to the deep viscera. One effective revival technique was to project color slides showing grotesqueries of tropical disease. The enormous scrotal enlargement of elephantiasis (caused by a filarial worm parasite) was always good for a waker-upper, but the dictates of the new social or academic order required a more gender-neutral monstrosity—espundia. Espundia begins as a nonthreatening ulcerlike lesion of the skin typical of cutaneous leishmaniasis. And like typical cutaneous leishmaniasis the ulcer heals without chemotherapeutic treatment.

But unlike the typical cutaneous leishmaniasis in which the healing process is complete and even leads to a solid immunity against reinfection, espundia's *Leishmania braziliensis* leaves the skin to metastasize and invade the macrophages of the nose, and mouth or pharynx. It causes horrible destruction of the nasopharyngeal area of the face. The nose and mouth parts literally rot away. It is, today, one of the most feared diseases of tropical America especially so because it is so very difficult to treat chemotherapeutically with the onset of facial involvement. The interval between ulcer and facial involvement may be many months, even many years, and the victim usually makes no connection between the long-forgotten healed skin ulcer and the infection that is now ravaging the tissues of mouth and nose.

The problem for today's physician working in an espundia endemic area is how to treat a patient with a leishmanial skin lesion. Is it a self-curing type that doesn't require aggressive treatment? Is it *Leishmania braziliensis* that can lead to

espundia years later? The lesions look alike; the leishmania recovered from the lesion look alike. Treatment for *Leishmania braziliensis* is most effective when it is aggressively given at the primary lesion stage, but it is long, costly, and unpleasantly toxic. Researchers can by sophisticated techniques, such as karyosome analyses, distinguish *Leishmania braziliensis* from the less virulent skin-invading species. But the techniques require considerable expertise and a sophisticated laboratory and are costly. Like so many remarkably effective diagnostic and therapeutic methods gifted by modern science, they are unavailable to the poor who really need them. It's the old, old question—who is going to pay? Certainly not the impoverished farmer of South America.

Were the early Amerinds at risk to this terrible zoonosis in the forest? The circumstantial evidence for the presence of muco-cutaneous leishmaniasis, espundia, in pre-Columbian times is found in the pottery of a the Peruvian pre-Inca Mochica people. Their terra cotta figures are of heads with extensive lesions of the mouth and nose so reminiscent of espundia. Also, the archaeological sites of the Mochica pottery is in the hot, humid region of Peru where muco-cutaneous is now (still?) highly endemic. That erudite Swiss medical historian–physician-pathologist–parasitologist–linguist, the late R. Hoeppli, considered the anthropomorphic Mochican pottery as depicting people stricken with espundia. But here we find an example of how widely and wildly experts can part. Another, equally distinguished scholar, the late H. Dietschy, looked at the same pots and concluded that the facial mutilations didn't represent the ravages of a parasite but were a tribute to the potato demon. *The potato demon?* Well, the potato originally came from Peru and the pre-Incans so loved the potato that they assigned a god-demon to it. According to Dietschy, the mutilations were made on the pottery faces

(and, maybe, on human sacrificial victims) to give humans a potato-like face as a tribute to the demon. And the potato demon's name was Papamama.

When the Amerinds reached southern Mexico, they would have met what I consider to be the most terrible disease of the Western Hemisphere. The title of the opening chapter, "Tropical Diseases—As American as the Heart Attack," was intended to introduce the notion that North Americans have been beset since European colonization by diseases considered to be exotically tropical. That is a gringo narrowness; in the southern part of the Americas, from Mexico to Argentina, the main avenue to the heart attack, a major cause of sudden death, *is* a tropical disease—Chagas' disease—caused by a parasite of pure American ancestry. Today, within that vast region of entrenched endemicity it is estimated that over 60 million people are exposed to Chagas' and at least 18 million are infected. It is an infection lacking adequate chemotherapeutic cure or protective vaccine and it is coming north; from Texas to Detroit there may be as many as 100,000 cases.

The nineteenth-century South American physicians were confused by a variety of seemingly unconnected common illnesses—some mild, some acute, some chronic—and all of unknown causes. There was an ophthalmic condition in which a puffy swelling appeared suddenly around the eye. This occurred mostly in children but, because of its transient nature, was not considered serious. There was a fatal sickness of children that began with a fever and headache and ended with convulsions and coma. There was a chronic illness of adults and children characterized by prolonged low-grade fever, aching muscles, loss of appetite, and a generalized feeling of irritable "crappiness." And then there was a lot of heart disease, mostly in the middle aged—the irregular fast

arrhythmic beat of tachycardia, the shortness of breath of early heart failure, and, finally, the massive fatal heart attack. Many of those who died in this way were found at autopsy to have grossly enlarged hearts. But the strangest and most frightening disease was one of the intestinal tract, a mega disease in which the colon and/or esophagus seemed to have simply lost power, stopped working, and become enormously distended, flaccid tubes. With digestion impaired and peristalsic waves stopped, the food mass failed to be processed and pushed to its anal conclusion. Feces accumulated within. Nutrition failed and the mega victim died. In 1910 these highly disparate conditions began to be threaded together as a common cause.

By the second decade of this century, parasitology's house was pretty much in order. The causative organisms of the major parasitic disease of humans were identified as well as their modes of transmission. Within this orderly taxonomic edifice, the pathogenic Hemoflagellate group of protozoans were considered to have a neat two-part delineation. The tsetse-transmitted trypanosomes swam freely in the blood whereas the sand-fly-transmitted leishmania were immobilized within the macrophages. To each his own. Or so it was thought until 1910 to 1920 when a Brazilian field researcher in Minas Geraes, his institute Director in Rio de Janeiro, and a Parisian parasitologist of the Pasteur Institute elucidated the Hemoflagellate of the third way—the causative organism of what became known as American trypanosomiasis or more commonly Chagas' disease.

He died in 1917 at 45, but during his brief life Oswaldo Cruz was Brazil's foremost medical scientist–public health authority. Cruz first came to prominence from his effort to control the yellow fever epidemic in Rio de Janeiro which killed some 15,000 people between 1891 and 1894. A grateful

government bestowed a research institute on him (actually it was an old serum therapy factory-like laboratory) that was to become the still-famed Instituto Oswaldo Cruz. Cruz was a fine scientist, and unlike too many scientists-turned-administrators, he had the gift to select talented, innovative people for his staff. One of the Chosen was Carlos Chagas.

In 1910 a railroad was being built in Minas Geraes, a remote region of Brazil. Malaria was taking a high toll of the workers and bringing construction to a near standstill. Cruz dispatched Chagas, then 40 years old, to investigate the problem and apply whatever antimalarial measures might be feasible. Chagas was a scientist-physician of his time, a naturalist who believed that the understanding of human biology (and pathology) could be achieved only though the understanding of the biology of all living things. This spirit of epidemiological pantheism led Chagas to divert his attention from malaria and the anopheline to a bug that was sucking the blood from the peasants. The locals complained to Chagas of an insect, about an inch long, that by day lived in the cracks of the mud walls of their hovels and by night crept out to feed on them as they slept. They had several names for this arthropod vampire: *barbeiro* (the barber) and kissing bug because of its predilection to feed from the face and lips, and assassin bug because of the stealth of its attack. It also had the disgusting habit, later found to be of crucial importance in the transmission cycle, of taking blood at its head end and simultaneously defecating on its host from its hind end.

Charles Darwin, who became a blood meal while in Argentina, gives a graphic description of this reduviid (triatomid) bug in his book *Naturalist's Voyage.*

> At night I experienced an attack (for it deserves no less a name) of the *Benchuca,* a species of Reduvius, the great black bug of the Pampas. It is most disgusting to feel soft, wingless insects, about an inch long crawling over one's body. Before sucking they are quite thin, but afterwards they become round and bloated with blood, and in this state are easily crushed. One which I caught at Iquiqui (for they are found in Chile and Peru) was very empty. When placed on a table, and though surrounded by people, if a finger was presented, the bold insect would immediately protrude its sucker, make a charge and, if allowed, draw blood. No pain was caused by the wound. It was curious to watch its body during the act of sucking, as in less than ten minutes it went from being as flat as a wafer to a globular form. This one feast, for which the Benchuca was indebted to one of the officers, kept it fat during four whole months; but after the first fortnight, it was quite ready to have another suck.

The bug may also have been the death of Darwin. Naturalists, despite the pleasures of their calling, have their trials with nature, particularly as they endure the attention of biting, stinging, blood-sucking, disease-transmitting insects and ticks. Darwin was no exception; during the five years from 1831 to 1836, on the voyage of the *Beagle,* he was repeatedly exposed to the kissing bug and thus at risk to Chagas' disease. He came home to England from his monumental voyage and was sick the rest of his life. Several medical historian–physicians have done a theoretical postmortem on Darwin and have concluded that his chronic lifelong illness—fatigue, irritability, repeated vomiting, flatulence—as well as his final illness and death from heart disease, was caused by a *Trypanosoma cruzi* infection (Chagas' disease) acquired in South America. A first-rate account of the Darwin-Chagas' hypothesis has been given by Jared Haft Goldstein in his article "Darwin, Chagas', Mind and Body" (*Perspectives in Biology and Medicine* 32 (1989): 586–601).

By 1910 there was a growing realization of the role of blood-sucking insects in the transmission of microbial and parasitic infections. In 1896, Ronald Ross showed how the malaria parasite was transmitted by mosquitoes. That same

year, in Africa, David Bruce began to implicate the tsetse fly in the transmission of trypanosomes. In 1901, Major Walter Reed of the U.S. Army and his colleagues demonstrated the transmission of the yellow fever virus by the *Aedes aegypti* mosquito. It had become a standard experimental practice of the field-working microbe hunters of that time to dissect any blood-feeding insect new to them to see what in the way of microorganisms might be lurking inside.[4] In this way Chagas dissected some of the reduviid bugs of Minas Geraes. Under the microscope, he saw protozoan flagellates in the bugs' intestinal tracts that looked like an intermediate, insect-dwelling stage of a trypanosome.

In his bush laboratory, Chagas had come to the end of his technical resources. He did not have the laboratory-bred animals to attempt the experimental infections necessary to determine whether the bugs' flagellates were an intermediate stage of a parasite of mammals or an organism confined to bugs alone. Chagas sent some of the bugs to Cruz in Rio. Cruz fed them on a marmoset. Three weeks later large numbers of strange-looking trypanosomes, morphologically unlike the familiar trypanosomes of African sleeping sickness, were present in the monkey's blood (figures 1A and 1B).

More experimental animals were offered to the bugs, and guinea pigs, rabbits, and puppies became infected. It was

4. Reduviid bugs are still dissected but for a different, diagnostic purpose. In late chronic Chagas' disease, the motile(trypanosome)-stage parasites become very scanty in the blood and are difficult to detect either directly or by test-tube culture. Reduviids are bred in the laboratory and these clean bugs are allowed to feed on the patient. The *Trypanosoma cruzi* trypanosomes, even if present in very scanty numbers undetectable by microscopical examination, will colonize the insects' intestines and be readily identified. This diagnostic method, called xenodiagnosis, is very sensitive but it does not give rapid results; it takes about a month before the bug is "ready" by which time the patient too often has fled or died.

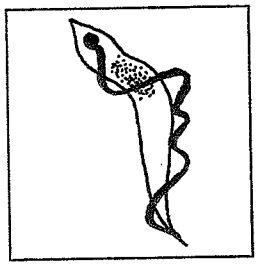

FIGURE 1A
African Trypanosome

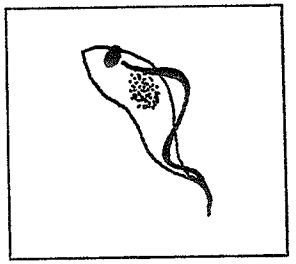

FIGURE 1B
Marmoset's trypanosome

obviously a parasite of mammals and was broadly specific—it could infect many different species. What's more, the parasite was pathogenic—some of the infected animals sickened and died. But did it infect humans?

When the news of the experimental infections reached Chagas in Minas Geraes, he returned to the village where he took blood samples from resident cats and dogs. In the blood of a cat Chagas found the trypanosome, an organism that he was later to name *Schizotrypanum cruzi* (later renamed *Trypanosoma cruzi*) after his admired Master. A few days later Chagas found the trypanosome in the blood of a sick three-year-old girl (who turned out to be one of the lucky survivors; she was alive and well 60 years later). Blood samples from other children were examined in an attempt to connect the trypanosome with a specific disease. Some but not all of the children with the trypanosome in their blood were anemic and stunted in growth. A few children with many trypanosomes in the blood gave a history of convulsions, and these children, Chagas found, died of a neurological disease within weeks or a few short months after he first examined them.

Two years later, in 1912, Emile Brumpt, the parasitologist of the Paris Pasteur Institute, carried out research in Brazil

that proved transmission was *not* by the injection of the trypanosome from the bite of the bug (like all other known arthropod-borne parasites) but by a contaminative route from the bug's feces. One sleeps. The reduviid bug steals from its hiding place and sticks its sticker and sucks up blood. As it sucks, it defecates an excrement containing the infective stage of the trypanosome. Through either a skin wound made by the bug or an existing abrasion, the parasite enters. The sleeper scratches at the offending bug and the trypanosome enters. The bug commonly feeds near the eye. The excreta is rubbed into the conjunctival membranes and soon there is a swelling of the eyelid.

In the next few years two more crucial facts of the American trypanosome's biology came to light. Most extraordinary, the trypanosome entered a variety of tissue cells where, as an intracellular parasite it rounded up to become a leishmania form. The leishmania forms divided asexually to form nests in the tissues. It was like a leishmania but not like a leishmania because it wasn't restricted to infecting only macrophages. Many cell types could be invaded although the predilection was for heart and nervous tissue cells. So here was, much to the surprise of the parasitologists, a unique Hemoflagellate of the Third Way with *both* trypanosome and leishmania stages existing simultaneously in the infected host. Nothing like had been seen before—or has been since. It was purely American. Its family tree is still a mystery; we still do not know from where, when, or protozoologically from whom it evolved. Using the very sophisticated modern techniques of DNA homologies, Herman Heckler of the Swiss Tropical Institute in Basel (even the Swiss have a tropical institute; of the western world only the Americans don't have such a research center) addressed the problem and came up with a paper entitled "Man and Sea Urchin—More Closely Related

Than African and American Trypanosomes" (*Parasitology Today* 9 (1993): 57).

The second fact was that the laboratory animal experiments and Chagas' Minas Geraes cat had predicted the epidemiology of *Trypanosoma cruzi* in the real world. Chagas' disease was proven to be a zoonosis. Many wild and domestic animals were found to be naturally infected, the armadillo and opossum being particularly important reservoirs. I'll tell you about the Chagasic racoons of Maryland when we reach the chapter on our century. However, since we are still in the pre-Columbian period, let us return from this rather long diversion to the Inca in the basket.

She had lived in Cuzco, Peruvian capital of the Incas. Death came when she was about 20 years old, and keeping to the custom of the time, her corpse was placed in a long wicker-like woven basket. Almost 600 years later a team of scientists led by Gino Fornaciari of the University of Pisa's Paleopathology Laboratory and Elsa Segura of Argentina's Fatala Chaben Institute made the long-delayed diagnosis of Chagas' disease as the cause of death. The mummy's viscera still showed the late stage Chagas' mega syndrome. The heart and intestinal tract were greatly enlarged. The dilated colon held an enormous amount of fecal matter. Amazingly, the parasites were also present, albeit in a mummified state, and could be identified by electron microscopy and the unerringly specific staining developed by monoclonal antibody reagents for *Trypanosoma cruzi.* Chagas' disease in Chilean mummies had been suggested, but from this unfortunate lady of Cuzco, Fornaciari and his colleagues noted that this was "the first direct demonstration of this disease [Chagas' disease], and the agent causing it in South America during the Inca empire immediately before the Spanish conquest of the continent."

The story line of this chapter has been rather like a Nintendo game, "Get the Indian to Argentina." You would have to jockey the brave bands of Amerinds down the continents to Tierra del Fuego all the while beset by microbial monsters. Some tribal groups in the game might go blooie, but most would get through to safe havens on the way. Those pre-Columbian Amerindians had their medical troubles, but by and large they were not too bad off. The Americas, in fact, were relatively healthy until that disastrous morning of October 12, 1492, when three sailing ships appeared on the horizon of the Bahamas.

Chapter 3

Who Gave Pinta to the *Santa Maria*? 1492 to 1635 A.D.

THE *SANTA MARIA* was hardly the *Love Boat*, and after a month at sea Juan de Morguer had a acute longing in the loins. He had had a sweetly satisfactory night before departure with his wife; for the sailor whose every voyage was so perilous, sex before sailing was like the last rites. That next day, August 3, 1492, the caravels *Nina* and *Pinta* and the ungainly cargo vessel *Santa Maria* (on which Juan was an able-bodied sailor), which carried them on this mad enterprise, put out to sea from Palos. The wind was fair, the voyage fast, and by August 9 they reached their first destination, the Canary Islands. It was the intention of that jumped-up Italian (some whispered that he was Jewish, despite his almost fanatical Catholicism) who styled himself the Admiral of the Ocean Seas to spend only a few days in the Canaries taking on water and provisions before putting forth to the unknown void of the western Atlantic, an unexplored route that the Italian had convinced the blessed Queen Isabella would take them to Japan and Cathay, the fabulously rich dominion of the Great Kahn.

The *Santa Maria* was such a sow of a boat to sail, slow and constantly breaking down. Well, what can you expect from a rental? A cranky rudder delayed them for a month in Gomera (an island of the Canaries). Finally departing Gomera on