Chapter 2

A Child Dies in a Small Village

THERE ARE no words to tell you of the heat that consumes the Ganges plain during the months when the winter has left and the monsoon rains not yet begun. No shadow falls from the cloudless sky. Every breath is searing. A torpor settles over the villages strewn throughout the hard, stubbled fields. Children are subdued, adults languish on their charpoy beds, and even the cattle seem immobilized.

On one such burning day in April, in a village in Bihar, Susheela Devi was worried about her sick child. Susheela, a tired-looking woman in a tired-looking sari, is middle-aged at thirty-two years. She was given away in marriage when she was thirteen. Burdened by work, harassed by a bitter mother-in-law, and uncared for by a husband twenty years her senior. That crone mother-in-law still complained that Susheela had not brought sufficient dowry into the family. This was dangerous muttering. Other village wives had fatal "accidents" and were replaced with younger wives and new dowries. Her decision to seek medical help required brave determination. There was the overpowering heat through which she would have to walk, carrying her sick child most of the eight miles to the government health center. The peasant poor of India do not squander their pre-

cious rupees on the luxury of bus or bicycle rickshaw unless there is a great emergency. The child was ill, but not emergency-ill in any of the too familiar life-threatening ways . . . the acute fever and coma of childhood malaria, the rapid wasting diarrhea and death of cholera, or the labored gasps of pneumonia. It was merely that the child seemed somewhat feverish this past month and was becoming emaciated, despite a reasonably good appetite, with a distended abdomen like the children of the failed-monsoon famine years.

Susheela awoke before dawn the next morning; cooked the family's food for that day—some rice and a bit of curried river fish. She led the cow from the stall, which was attached to the house as a kind of guest room, and gave it some fodder. The cow was indeed an honored guest. The mount of Lord Siva as he rode through the cosmos and his audience when he danced, it now gave milk and *ghee* to this poor family. Its dried droppings were the chief source of fuel in the deforested plain. The very substance of the house's mud walls was the excrement from this holy beast.

The fitfully sleeping child was roused as the first light began to appear in the eastern sky. Mother and child left the village to begin the long walk to the health center. They were not long on the road when the sick child could walk no further and the 90-pound mother began to carry her child mile after painful mile. Three hours later, when the sun was rising above the neem trees, the exhausted Susheela arrived at the health center. It was about 9:00 a.m.; already more than one hundred people waited. They filled all the benches on the center's veranda. The overflow, joined by new arrivals, sat on the open ground surrounding the health center.

Susheela sat amongst the outside group. Many were

mothers with their sick children, but more were men. There were men with open wounds. Accidents from road and agriculture take as heavy a toll as malaria and other infectious illnesses. Women were but women; they had to be sicker than men to leave their work to go to the health center. The waiting patients were mostly silent, not unlike the withdrawn silence of our own physicians' waiting rooms. A half hour later the two doctors assigned to the health center arrived. They looked so young and, to Susheela, so different from the young men of her village. And they *were* different. They were born in the city, schooled in the city, medically educated in the city, and clinically trained in city hospitals. Upon graduating, they were forced to work a year or two years at a rural health facility. The shorter time (or no time) if their family was well connected. And as soon as they finished their country time they would be back in the city, scrambling against an excess of physicians to establish a practice. Only a few well-trained doctors chose to serve these non-paying country peasants. Their family would have to be conspicuously "unconnected" to be left in *that* limbo.

The hours passed. The heat intensified. Susheela and her child remained fixed to their bit of ground, afraid to leave even for water lest it be usurped by another of the ailing. Shortly before noon, a health center attendant who had been circulating amongst the waiting people, registering their names, came to Susheela and whispered that within the hour the doctor sahibs would leave for their lunch and would not return since in the afternoon they conducted their business seeing paying patients at their private clinics in the town. However, he confided, for 10 rupees (about 50 cents) he could arrange for her to see one of the doctor sahibs, the smart one, within the hour. Susheela was stunned by the demand, but not surprised; these privileges must

always be bought from the petty government servants. From her small hidden reserve banked in a secret recess of the wall by her pallet she had withdrawn 7 rupees, half her "account," to take with her. She had decided to use it for bus or bicycle rickshaw to take her back home. She felt she just had no strength left to carry her child those eight miles. That would not now be possible, and she offered the attendant all she had, the 7 rupees. He grumbled and reluctantly agreed to accept the bribe, but for such a paltry sum she would not be able to see the smart young doctor sahib who had been at the health center for six months. She would have to be attended to by that ninny who had just graduated from medical school and had been posted to the center only two weeks ago. The precious few coins were handed over, a day's wages for many peasant laborers.

The attendant, fortunately, was an honest man and good to his bribe. Within a short time he called Susheela's name to enter the doctor's cubicle. The young doctor was brusque, unfriendly and uncommunicative. He was unsure of his skills but sure of his importance in being a doctor. He felt alien in this country setting and so he adopted the manners, experienced since childhood, in dealing with social inferiors—brusque, officious, and unfriendly.

He told Susheela to put her frightened child on the bare wooden examination table. This done, the doctor prodded the child's distended abdomen, his fingers sensing the greatly enlarged spleen and the enlarged liver whose boundary was well below the rib cage. The thermometer revealed the child's temperature to be 101°F. Without preliminary explanation he took the child's arm and swabbed it with an alcohol swab, which came away black with grime and sweat, and then, while the attendant took a tight grip on the thin

arm, the doctor stuck a syringe needle into a vein. The procedure really didn't hurt that much, but for the frightened, apprehensive little girl, who had been to this moment so stoically uncomplaining, the sight of blood welling into the syringe barrel produced a shriek, followed by uncontrollable sobbing. A river of sad tears washed the small, pinched face. Susheela did the best she could to comfort her child and was told to wait in the corridor while the blood was sent to the laboratory to be tested.

The health center's laboratory was a small, dimly lit, not very clean room, cluttered with broken but still usable bits of glassware such as microscope slides and test tubes washed innumerable times, and some basic reagents to perform basic, all-important tests: blood counts, staining for malaria parasites, and the presence of abnormal sugar and protein in urine. There was also a microscope of Polish manufacture whose optics, not of good quality to begin with, had acquired a bloom of glass-loving fungus which gave a blurry, chiaroscuro image to the scrutinized malaria parasites, worm eggs, and other microscopic faunal and floral parasites.

The syringe was given to the laboratory technician, who expressed the blood into a glass centrifuge tube. On the floor in a corner of the laboratory, almost hidden in the gloom, sat an old man clothed only in a ragged dhoti. This peon was the centrifuge wallah, and it was now the moment for him to do his work. The health center had no electricity. The microscope was illuminated by the light that filtered through a shuttered window, and the centrifuge—a simple, motorless instrument—was propelled by means of a hand crank and gears. The centrifuge wallah cranked vigorously, spinning the blood tube some 1500 revolutions each

minute. After five minutes, the cranking stopped and the machine came to rest. The centrifuge wallah returned, wordlessly, to his place in the corner.

In the tube, the centrifugal force of spinning had separated the blood into its components, a bottom layer of packed red cells above which there was a thin stratum of white cells. Over the packed sediment of cells was the straw-colored fluid—the serum. In normal, healthy people, there should be an almost 1:1 ratio between the volumes of packed red blood cells and the serum. But in this specimen, the technician noted that the tube contained only about 25 percent in packed cells. The child had only about half the red blood cells that was normal . . . a case of severe anemia. Then the technician transferred a few milliliters of the serum to another tube. To that tube he added a few drops of formaldehyde and vigorously shook the mixture for a few seconds. Within minutes the serum began to solidify into a Jell-O-like clot. This was an abnormal reaction that occurred only when a very great amount of gamma globulin was present in the serum.

To the doctor, the constellation of signs and symptoms could point to only one diagnosis. The prolonged fever, the greatly enlarged liver and spleen, the anemia, the serum that gelled when mixed with formaldehyde, all meant visceral leishmaniasis, a disease that both peasant and physician knew by its vernacular Mogul name of *kala azar*—the "black sickness." Realizing the gravity of what he was about to tell Susheela, his pomposity fell away. The young man had not yet hardened to his role as death's messenger. "Mother," he said gently, "your child is very ill with kala azar." The words made Susheela gasp and her eyes stung as if she had been struck with great physical force. The people of her village and the other villages of the district

were no strangers to kala azar. The disease had reappeared some ten years ago, to begin killing old and young alike, but mostly the young. Before that time, her generation was ignorant of the disease, although the old men of the village spoke of former times, during the days of the British Raj, when great epidemics of kala azar ravaged Bengal and Bihar, the Terai of neighboring Nepal, decimating villages, towns, and cities. Susheela's child was a new victim of the new epidemic.

With urgency, the doctor continued: "It does not mean death. Your child can be cured. You must buy medicine. Then you must come here every day for twenty days so the nurse can inject the medicine. Every day! Not a single day must be missed!"

The word that echoed in Susheela's head was "buy." *Buy?* Buy medicine? She had brought her child to be treated, not to be given a few words of advice. She had walked those miles, sat for hours waiting in the sun; she had paid her bribe—every rupee she had—to see the doctor. Now she was told to buy the medicine that she expected the health facility to provide her.

"Cannot I get the medicine from you, doctor?"

"No," he replied. "We have no kala azar medicine. The state government in Patna gives our dispensary only a few simple medicines to treat a few simple illnesses. Last year we had some kala azar medicine, but there were many people to be treated and our supply was soon finished. We've written again and again to the central medical stores in Patna for more drugs, but they do not even reply to our letters. Now everyone must buy the medicine where they can and as best they can."

"What will it cost?"

"That I cannot tell you. If the pharmacist has a good

stock, it will be cheaper; if not, it will be expensive." He scribbled a prescription on a scrap of paper and, reverting to his customary brusqueness, thrust it at Susheela, peremptorily dismissing her with "Unless you get the medicine there is nothing more I can do for you. Go now!"

Susheela made her way through the crowded market until she found the druggist's shop. She handed him the scrap of paper on which the doctor's prescription was written and the druggist told her that she was indeed fortunate because there were only two bottles of the kala azar medicine left. Many people in the district had the disease and needed the medicine.

"How much is it?" Susheela asked fearfully.

"Mother," replied the druggist, "I know that you are poor and your child is ill. For you, I will give you a bottle of the drug, enough for her whole treatment, for three hundred rupees [about $15]. Others I would charge five hundred rupees."

Three hundred or 500 rupees; it made no difference. It was an astronomical sum, more than the family's income for some months. Susheela picked up her child, turned from the pharmacist, and began the long walk back to her village.

It was well after dark when she reached home. There is no purpose in recounting the abuse she received from her mother-in-law and her husband for being away from her duties for an entire day . . . that was too customary. Later, as they lay on their sleeping mat in the darkness, Susheela told her husband what had happened that day. They must buy the medicine. But how? Sell the cow? If they did that, then surely the family would starve. Borrow from the landowner from whom they leased their small plot of rice paddy? Impossible. They were already in debt to him for almost

half the future crop to pay the lease rent and to repay the loan he had advanced to buy seed and fertilizer. There were no family resources. Each relative was as poor and indebted as themselves. Even if by some miracle they could buy the medicine, there was no way that Susheela and the child could travel those long miles to the health center for twenty consecutive days. Not only, she knew, did she lack the strength but the monsoon rains would soon begin and it was essential that she help prepare the soil and plant the rice. The family's precarious survival required the labor of each member at planting and harvest. No, for the child they would have to do the best they could. They would pray to the gods. They would consult the "doctor" in the adjoining village, a man who practiced Ayurvedic herbal medicine.

In the weeks that followed they prayed at the small village shrine, leaving offerings of food, as if the gods too were petty bureaucrats who had to be bribed. The Ayurvedic doctor did not miss the diagnosis of kala azar and for a few rupees gave the child some herbal medicine that for over a thousand years had been prescribed for fevers. And indeed, for a short few days after taking the draught, the child's fever abated and she brightened. But in the end, as the weeks passed, she became progressively more ill: she grew even more emaciated, her skin turned a dusky gray, her hair became brittle, small bleeding sores covered her body, and the abdomen, burdened with a grossly enlarged liver, distended even further.

One day, some three months after Susheela's visit to the health center, the child began to cough and gasp for breath. During the night, the little girl died.

The mourning family carried the small body on a wooden plank, draped with a bit of cloth and adorned with mari-

golds, to the banks of the Ganges. There at the burning ghats the body was offered to the fires. A fragment of life sacrificed for want of $15.

For the family there was some comfort. There were seven other living children. And, by good fortune, it was not a boy that had died.

Chapter 3

How the Government Disease Came to India

THE INSTRUMENT WHICH consigned Susheela's daughter to the funeral pyre was a tiny midge, no weightier than an eyelash. In Patna, the capital of Bihar State, fifty miles from Susheela's village, Dr. A. K. Chakravarty was holding a cage in which these silver-winged insects were quietly resting on the screened walls. "They look so innocent" was his brooding observation on the treachery of appearances. Chakravarty is the chief of India's National Institute of Communicable Diseases' Kala Azar Unit, based in Patna. He is a large man, well over 6 feet tall, and despite his determined, rather ferocious countenance, he is of gentle nature: a devout Hindu, given to philosophic enquiry into human spirituality; veterinarian-researcher (more later of why a veterinarian should be in charge of a unit conducting studies on a human disease) who treats his animal and human patients with a delicate, kindly courtesy. The objects of this disproportionate encounter between man and insect were the blood-sucking sandfly midges, *Phlebotomus argentipes*. As the anopheline mosquito is the biologically required transmitter of human malaria, the phlebotomine sandfly is the purveyor of another killing parasitic protozoan, *Leishmania donovani*, the cause of kala azar.

Of all the parasites, great and small, that make our bodies home, the *Leishmania* may well be the most peculiar and intractable. To the invaded host, a parasite is a foreign body calling for a response. A major effector mechanism of immune defense is the killing and devouring of the parasite by specialized wandering and fixed cells, the front-line soldiers of the immune system, known as phagocytes. The *Leishmania* have the effrontery not only to evade digestion by the phagocytes but actually to invade them in an obligate fashion to become intracellular parasites.

The parasite was but one factor that led to the funeral pyre of Susheela's child. Her tragedy was an interweaving of parasite and its sandfly transmitter; climate and culture; society, medicine, and politics. Let me take up the thread of this complex of interrelationships by examining the history of the *Leishmania* and the disease it causes—kala azar.

To understand the history of kala azar (or any other human disease), we must keep in mind that our "files" go back only a few thousand years . . . to the beginning of written language, the beginning of the human documentary. There are a few mummies and ancestral bones from which the medical archeology detectives have gained sparse clues into the nature and epidemiology of ancient illnesses. However, humans must have thought about their health from that imperceptible time when they became truly human—an animal with the cognitive sense of well-being, and of illness and the certainty of death; an animal with the gift of foresight. Health and disease was an issue to our ancestors as it is to us today. When the ancients devised the written word, they wrote about their illnesses—in hieroglyphics—in Sumerian, Babylonian, Arabic, Greek, Latin.

All early written languages seem to have had their

"medical books," although notions of disease causation were very different from ours. Microbes and such are new to the medical profession. Before the first microbe could even be discovered there had to be a good microscope to see them by, and not until about 1825 were achromatic microscope lenses available. Then someone with extraordinary insight had to put two and two together to recognize, for the first time, that so minuscule an organism could be the specific agent of a specific disease. Only in 1875 was a protozoan shown to be a pathogen. This was *Endamoeba histolytica*, the cause of amoebic dysentery and amoebic liver abscess. This "tropical" parasite was described by F. Lösch from Russian patients living in the balmy latitudes approximately a hundred miles south of the Arctic Circle. Viruses are newer still. The first virus to be discovered was a virus not of humans but of plants. It was the tobacco mosaic virus described by the Russian D. Iwanowski, in 1892. The yellow fever virus, discovered in 1900 by the U.S. Army Commission led by Major Walter Reed, was the first viral disease of humans to be identified.

While the pre-Pasteur doctors may have had some peculiar ideas on the causation of disease—demons and devils, humors and miasmas—they weren't all that bad as descriptive clinicians. They recorded the signs and symptoms of their patients' complaints with sufficient accuracy to allow us to identify some of those illnesses in modern terms. Malaria, for example, with its cyclical, regular periodicity of rigor-shakes and fever-sweats, was recognized as malaria by physicians of ancient and medieval Europe, the Middle East, and Asia a thousand or more years before November 6, 1880—the day that Alphonse Laveran, a French Army médecin-major 1re classe, posted to Algeria, saw under his microscope the malaria parasite within the

blood cells of a feverish, twenty-four-year-old artillery man. Thus we can look back with reasonable confidence and make historical-epidemiological judgments, saying that malaria was the scourge of ancient Rome and that it has persisted in southern China for at least two thousand years.

Kala azar, however, is different: it has not yielded its past origins and epidemiology to the modern historian's search. This is peculiar because the disease is distinct enough that had it been present it should have been descriptively remarked upon in the early medical writings. It is not an indolent disease that would have gone unnoticed. Kala azar frequently occurs in epidemic proportion, killing thousands during its apogee. Nor can we attribute this narrative absence to an observational gap solely on the part of India's ancient writers. Visceral leishmaniasis (kala azar) is not confined to India but is now known to occur in a vast area of China, in Russian Turkestan, in the Sudan and Ethiopia, in Mediterranean Europe (southern Spain, France, and Italy, Greece, Malta, Crete, and Yugoslavia),[2] in North Africa, and in the New World as foci of infection along the coast of Brazil. Except for Brazil and the Sudan, these are regions with a rich written record spanning at least fifteen hundred years. In that record we can see the past epidemics of plague, typhus, malaria—but nowhere do we find an account of a disease that could be interpreted as kala azar. To the best of our admittedly imperfect knowledge, kala azar seems to have made its first attack on humans in Jessore in 1824. It was like a new scourge, as AIDS is in our time. And like

2. The tourist and guide books certainly do not mention the risk of contracting kala azar at these European tourist meccas. The odds are admittedly very small. Still, a tourist stands a greater chance of getting kala azar in the French Côte d'Azur than breaking the bank at Monte Carlo. And while it is hardly a tourist resort, special and timely note should be made of kala azar's entrenched endemicity in Iraq.

AIDS, its true epidemiological origins may never be satisfactorily traced.

In recent times, Jessore has been a pawn of political events. It is now in Bangladesh, but its spirit defies national boundaries; it remains a city of Bengal. The Bengalis of Jessore may worship Allah, yet they recite the poems of Tagore with the same passion as do their Hindu cousins a short march to the west in Calcutta. Now a sleepy market city near the Indian border, Jessore was an important commercial center during the Mogul Empire. From the mid-1700s it was successively administered by the East India Company and then by the British government itself. Jessore probably hasn't changed that much since the first British East India Company agent-administrators, appropriately known as Collectors, were posted there in the 1750s—except that in the 1750s there weren't any Chinese restaurants, a favorite cuisine of modern middle-class Bangladeshis. Many of the Collectors were honest men of noble intent who had real concern to alleviate the lot of the tax-oppressed peasants. One Collector of Jessore, with the unlikely name of Telman Henkel, was so popular that the locals made an effigy of him and worshipped it. That doesn't happen to Indian political administrators today. The Collectors would certainly have noted and reported in their journals the presence of a killing epidemic of the dimensions that kala azar was about to become. Moreover, by 1764 the Collectors were joined by civil and military surgeons of the newly established Indian Medical Service in their district.[3]

It began in the village of Mohamedpur, thirty miles dis-

3. Hospitals were established very early in the East India Company's rule: in 1664 in Madras, 1676 in Bombay, and 1707 in Calcutta. The British doctors in the Company's employ earned the princely annual wage of £36.

tant from Jessore. In the last months of 1824 the people of Mohamedpur began to die. Their color darkened to a clayey gray. The flesh fell away and the abdominal veins stood out, like enlarged blue cords, on wasted bodies. An overwhelming dysentery or pneumonia were the common final events that terminated their lives. With frightening progression the "black sickness" engulfed Jessore District and then enveloped the entire Gangetic plain. By 1832 it had spread from Jessore into what is now Indian West Bengal. The disease progressed by the arteries of road and water as if it were a systemic infection of a dying land.

Even before the Mogul conquests, the capital of Bangladesh (then Dacca, now Dhaka) was a thriving river port city. A network of rivers from upcountry feed into the great Jamuna (the lower Brahmaputra) in the Dhaka District. Lateen-rigged sailing barges with brilliantly colored sails and pole-propelled craft of all sizes on which whole families and crews live under cramped thatch cover continue to crowd the riverbank at Dhaka, bringing produce and manufacture from all over Bengal-Bangladesh. Although it is some two hundred miles from the Bay of Bengal's Ganges estuary, in the Jamuna that flows by Dhaka and its environs one can see the river porpoises, giving the appearance of monstrous, fabled sea serpents as their bodies roll in the water.

In 1862, one of these boats from upcountry brought a consignment of rice to Jageer, a populous town near Dacca. For over six months the entire crew had been ill with an intermittent fever and lassitude. Economic necessity had required them to pole-push and tow to Jageer, the men straining along the riverbank's towpath at the length of rope attached to their heavily ladened boat. It was to be their last trip. In Jageer, their condition rapidly deteriorated, and one by one they died. It is believed that these boatmen

from upcountry were the "spores" that introduced kala azar to the Dacca District. Over the next four years the mortality in Jageer was incalculable. Perhaps only descriptions of bubonic plague epidemics compare. The dead lay where they died, abandoned in their homes, or were thrown into the rivers or *beels* (the artificial irrigation ponds in most Bengal villages). Four years later, Jageer as a living community had ceased to exist. Today it is no longer on the map, and the curious traveler cannot exactly locate its remnants.

In 1876 an Indian physician, Dr. G. C. Roy, published an account of that time. His words, written before the discovery of the cause and transmission of the disease, remain a model of clinical-epidemiological observation: "The mode of attack of the villages one after another is very peculiar. In the first year, the villages adjacent to an epidemic-stricken locality will show at the close of the rains more of ordinary fever cases and greater mortality than usual, but this being nothing more than they are accustomed to in some fever seasons, will not create any alarm or grave apprehension." Roy then notes that with winter the number of cases declines and "the people congratulate themselves on the change." The full brunt of the epidemic begins with the second year's rainy season. The disease "becomes more general and the village is panic-stricken. Deaths from acute fever run high. The suffering being general, there is seldom any person spared in a family to attend to the sick."

Roy's observations of despair are confirmed in the journal of a British civil surgeon of that time, a Dr. French. He writes of whole villages "in which not a healthy person was to be met with, while repeated relapses of fever, the daily deaths, the loss of their children, the increasing depopulation of their village, the absence of all hope for better times,

had so demoralized the population that they neglected to avail themselves of medical and other aid, unless brought actually to their homes."

The British make no apology for their imperial period. They speak with pride of their high purpose as colonial custodians in freeing the peasantry from the excesses of despotic native rulers; in endowing their former colonies with a judiciary, a sense of fair play, cricket, and a democratic government. The French, on the other hand, endowed their colonies with the ability to bake wonderful loaves of bread. Making a current comparison between the former colonies of those two powers it would often seem that good bread has proved to be more sustaining and enduring than hand-me-down parliaments. Less often mentioned, and of equal importance to the ultimate character of these colonies-become-nations, was the fervor with which the British built the avenues of communication—roads, railways, and waterways. This was particularly true in India where, in the first half of the nineteenth century, they built the Bombay-Agra Road, the Bombay-Calcutta Road, and the Grand Trunk Road from Calcutta to Peshawar. Three thousand miles of new roads—all paved. They also built a canal-irrigation system for the Ganges and its tributaries that when finished was the most extensive in the world.

The Brits were not the Mad Ludwigs of road building, nor were their motives purely altruistic. Commercial prosperity (or "exploitation," if you consider colonialism to be a four-letter word) demanded the means to collect and distribute the produce of the country and the manufactured goods of the motherland. Commerce also demanded a pacified dominion. The pacified dominion, the Pax Britannica, required the roads, the railways and waterways to deploy the troops and administrative officers where needed.

Unfortunately, what was good for the business of colonial rule was also good for the pathogens. The new corridors that brought the rice and lentils, the Manchester bolts of cotton cloth and cooking pots, were also passageways for the dissemination of infectious disease.[4]

Kala azar was a stowaway traveler to Assam, carried there in 1875 by the British steamers that began to ply the upper Ganges and Brahmaputra rivers. When the infection broke out in Assam, the inhabitants recognized it as something new to their experience and somehow associated the disease with the activities of their new masters, the British.[5] With remarkable epidemiological insight, they called their new affliction *sakari bemari*, "the government disease." Now Assam was ignited, and during the next twenty-five years kala azar in some districts killed 25 percent of the population. Some villages lost two thirds, or more, of their people. From Assam to Tamil Nadhu, kala azar had established a permanent residency in India.

4. An account of the untoward effects of road building on disease could fill a book. Not only do roads facilitate the dissemination of infection, as was the case of the kala azar epidemic in India and of sleeping sickness in tropical Africa, but the ecological consequences of road building frequently are the creation of habitats favorable for the breeding of insect vectors. The breeding of malaria-transmitting anopheline mosquitoes in the collections of water on rutted roads and their verges is but one example.

5. Assam, as much a part of Burma as India, was not originally included in Britain's Indian "package." This wild hilly country of thick steamy jungles inhabited by fierce naked tribes fell to the British as a spoil of war with Burma in 1826.

Chapter 4

In Search of Kala Azar: Bedbugs and Other Red Herrings

WHEN THE CENTURY turned to 1900 the epidemic in the Gangetic plain began to wane.[6] After kala azar's merciless half-century hold in Bengal, Bihar, and Assam, the demoralized and depopulated land slowly began to return to a more secure and prosperous life. Kala azar did not completely disappear; cases continued to occur, but at much lower, non-threatening numbers. However, when the epidemic ended, an inquiry could be pursued that was impossible when the disease first struck Jessore in 1824. Between 1824 and 1900 the concept of the causation of disease had undergone a radical change. It was as if medical science, during this brief period of time, had emerged from the long medieval night into the enlightenment. Louis Pas-

6. Most epidemics of infectious disease seem to have a natural cycle of activity. After various lengths of time there is a decline in intensity even when there is no apparent human intervention or alteration in ecological or behavioral factors. The mechanisms that govern the rise and fall of these epidemics are still imperfectly understood. Mutational changes in the pathogen to a less virulent form, acquisition of a herd immunity on the part of the populace, or, simply, that so many people have died that the pathogen can't get around much anymore, are all possible explanations. But mostly, as in the case of the 1824–1900 kala azar epidemic in India, it is the X factor . . . the unknown. Kala azar seems to have an epidemic cycle of fifteen to twenty years.

teur ushered in the new science with his studies on the microbial causation of "sick" beer and silkworms. By the 1870s he was extending his studies to the microbial pathogens of animals, and then to those of humans. It was not long thereafter that the Germans entered the game, led by the giant intellect of Robert Koch. Now microbial pathogens were being discovered almost monthly—cholera, plague, boils, diphtheria. It seemed then that microbes were everywhere; that all disease had a microbial etiology. There was an enormous excitement and vigor in the pursuit of the pathogen. The *Zeitgeist* of the period was expressed by old Dr. Gottlieb in Sinclair Lewis's novel *Arrowsmith*, who "anoints" the young scientist with the benediction, "May Koch bless you!" Parasitic pathogens were also being discovered during those years; Laveran (as noted earlier) unearthed the malaria parasite in 1880, and J. E. Dutton found the trypanosome in a human sleeping sickness patient in 1902. Science and tropical medicine were being brought together. Paul Ehrlich's work in Germany on dyes and drugs began the search and discovery of synthetically created, powerful chemotherapeutic agents. Diseases were beginning to yield up their secrets *and* they were yielding to cure by man-made drugs.

The diseases of the tropics were studied by scientist-physicians who were truly *engagé*. Some of the best minds that the ruling country had to offer went to the colonies. They watched birds, catalogued the fauna and flora, sat up nights in flimsy *machans* to kill tiger. They played polo, shot snipe—and pursued their microbial quarry with a tenacity that by today's standards of paid-for-by-project research seems almost quixotic. So, when the old Queen went to her reward in 1900, there was already in place in India a medical research establishment staffed mainly by

military men of the Indian Medical Service. Other excellent research was carried out by medical men, such as tea estate physicians, working in remote areas under primitive conditions. It was at this time and in this climate that these men (and one woman) took off in hot pursuit to discover the causative agent of kala azar. It was a pursuit that would follow many false trails and scents before the *Leishmania* was bearded in its macrophage and sandfly dens.

It seems strange from today's retrospect that the first false trail was laid down by a worm—the hookworm.[7] The ancients were ignorant of the hookworm but aware of the disease it caused. Almost one thousand years ago a Chinese medical commentary epitomized it as the "able to eat but too lazy to work" disease. In 1838, a Milanese physician, Angelo Dubini, described the numerous small worms that he saw attached to the intestine of a dead Italian peasant whom he had autopsied. He saw the worms but didn't understand what they could do. That was left to O. Wucherer, a physician born in Portugal of German descent and practicing in Brazil. In 1861 the Benedictine

7. There are two hookworms of humans, *Ancylostoma duodenale* and *Necator americanus*. The adult worms are attached by fanglike mouthparts to the inner wall of the small intestine, where they assiduously suck the blood from small, ulcerous lesions at their attachment site. In time, with enough worms (and often compounded by other conditions such as iron-poor diet, malaria, and pregnancy), the constant loss of blood leads to a severe anemia—even death in the worst cases. Hookworms are both temperate and tropical in their geographical distribution. At one time they almost bled the American South white. The hookworms also caused great debility to miners because the then unsanitary conditions in mines and tunnels were highly favorable for hookworm transmission. Hookworm eggs pass out with the feces onto the soil and hatch into larvae which remain quiescent until trod on by the unshod human foot. They then penetrate the skin of the foot and make their way through the body to the intestine, where they grow to adult size, mate, and suck blood. In the tropics the barefoot boy is just as likely to be palely anemic as brown-cheeked.

monks of Bahia, with true Christian charity, called Dr. Wucherer to attend to a dying black slave they owned. The wretched man was at death's door, so severely anemic that his blood was almost water. The next day the slave died, and over the strong objections of the monks, Wucherer did a postmortem examination and found masses of "Dubini's worms" clamped to the intestinal wall. From this he made the association between the parasite and the "hypoaemia." Thus, in 1890, when a commission was sent to Assam to investigate the cause of kala azar, they searched for the then known agents that could cause severe anemia, and they thought of hookworm. Hookworm was a natural prime suspect. And when the investigator in charge, Dr. Giles, examined the feces of inhabitants of kala azar-stricken villages, he did indeed find the characteristic thin-shelled eggs of the hookworm under his microscope. "Kala azar is hookworm," said Dr. Giles.

"Not so," said Surgeon-Major Dobson, also posted to Assam. Dobson's choice was that malaria caused kala azar. It was conceded that hookworm would cause anemia, but in kala azar not only was there an anemia but there was also a big spleen, and splenic enlargement was not a consequence of hookworm disease. Malaria caused anemia *and* splenomegaly. Kala azar was malaria.

"Not so," said Dr. Giles. The big spleen didn't count. Practically everyone in Assam had or had had malaria. There were a lot of people without kala azar walking around with a big spleen. Besides, the fever of kala azar was not like that of malaria, it was more sustained and unremitting, and there was that progressive downhill slide to death that was atypical of malaria.

The malariaphiles (by 1896, Dobson was joined in his views by others) continued the forensic with the rebuttal

that practically everyone in Assam had hookworm but not everyone had kala azar. Kala azar was a *special* form of malaria—a malaria cachexia (a progressive wasting condition). Meanwhile, wiser heads maintained that kala azar's cause was neither hookworm nor malaria but a pathogen yet to be discovered. When that pathogen *was* discovered in 1900, it turned out to be a microbial organism, a pathogenic protozoan, entirely new to human knowledge.

If you have to go to Calcutta, and if you have to fly there, you will land at Dum Dum Airport. It is a terrible place. Noisy, unbelievably crowded, unbelievably confused, and retrieving your luggage (if it beats the odds and actually arrives on your flight) is an exercise exemplifying Darwin's principle of the survival of the fittest (and the pushiest). One hundred years ago it was also a terrible place. The town of Dum Dum and the British cantonment there (about ten miles from Calcutta) was so beset by kala azar that the vernacular name for kala azar throughout Bengal was "Dum Dum fever." In 1900 one of those stricken was an Irish British soldier from the military cantonment. There were no drugs then for kala azar, although he may have been given quinine in the mistaken belief in the malaria cachexia hypothesis. The soldier was invalided to the military hospital in Netley, England, where he died. His body was autopsied by a Dr. William Boog Leishman, formerly of the India Medical Service. Leishman—bald, beaky-nosed, military moustached (for some reason I think him a handsome man)—was a physician possessed of the spirit of scientific inquiry present in so many others of his IMS colleagues. He was also on the hunt for the causative organism of kala azar. Leishman excised a bit of tissue from the dead man's grossly enlarged spleen, stained the samples (with a stain later called Leishman's stain; we still use it to

examine blood for malaria and other blood parasites), and examined the preparation under his brass-barreled microscope. There under the microscope lens he saw the numerous, ovoid-shaped forms within the macrophage cells that populate the spleen. The sporelike bodies were minute, not much bigger than a bacterium.

This British soldier, nameless in medical archives, unwittingly gave his life for science. His body yielded up the secret of his last enemy. But what was it? Now began the biological-taxonomic pursuit that was to occupy tropical medicine specialists, parasitologists, and entomologists for the next thirty years. Even though the causative organism had now been observed, false trails continued to lie ahead. Leishman had once seen trypanosomes[8] in the blood of an Indian rat, and although his kala azar organisms were intracellular and much smaller than the trypanosomes, there were some similarities in structure. Putting two and two together (which, unfortunately, turned out to add up taxonomically to three), Leishman erroneously concluded that kala azar was caused by trypanosomes, and that the "bodies" within the splenic macrophages were actually degenerate forms of trypanosomes that had been ingested (phagocytized) and partially digested by the host cells.

Now others began finding the "Leishman bodies," the first confirmer being Charles Donovan in Madras. Unlike Leishman, Donovan studied the sick rather than the dead. He began a diagnostic practice that is still used, of sticking quite a large needle through the patient's skin, through the

8. Trypanosomes are the cause of African sleeping sickness. Other species of trypanosome parasitize a wide variety of other animals from frogs to primates. They are microscopic "fishlike" protozoan organisms swimming in the bloodstream by means of a lashing flagellum. They belong to the larger group of hemoflagellates, and *Leishmania* are of this group—first or maybe second cousins to the trypanosomes.

abdominal wall, and into the body of the spleen. Donovan expressed the plug of splenic tissue captured in the needle onto a glass slide, stained it, and examined it under the microscope. The organisms which Leishman had described were seen only in the splenic tissue of patients with symptoms typical of kala azar.[9] By 1904 the organisms were recognized as being protozoan in nature. They were given the name "Leishman-Donovan bodies," and later the taxonomic designation of *Leishmania donovani.*

But nomenclature is not an end in itself. The tidy housekeeping of biology demands that any newly discovered creature or plant be classified according to its affiliations—its family ties—siblings, near and distant cousins, the near and distant relatives of its extended family. In more exact terms, it would need a sorting placement within genus, family, class, and phylum. In 1903, *Leishmania donovani* was still a taxonomic orphan in search of its nearest relatives. Of more crucial importance, however, was the unsolved question of how *Leishmania donovani* got from A to B . . . from an infected person to its next host. The disease could not be effectively controlled unless the manner of its transmission was known. The spread of kala azar from household to household, and from village to nearby village, clearly indicated that it was an infectious disease. Was it carried in the air from the breath of the infected to the uninfected? Was it carried in the drinking water contaminated by the excretions of the sick? By touch? By sex? By giving nursing care to the stricken? Or by another route that in 1903 was beginning to appear as a new possible mode of transmission—the blood-sucking insect?

9. The discoveries made in India were the "main event" of the investigations on kala azar, and what happened, and is happening, in the Indian subcontinent is the theme of my story. However, as noted earlier, kala azar (visceral leishmaniasis) occurs elsewhere too and early research was carried out in those endemic regions. In 1903, Marchand described the parasites from a British soldier who died during the fighting near Peking. That same year Pianese found the organisms in smears from the spleen and liver of children dying of "splenic anemia" in southern Italy.

In 1876, (Patrick Manson) who was to become the father of tropical medicine), working in Amoy, China, as a physician to the Chinese Imperial Customs Service, discovered that the filarial worm, the cause of elephantiasis,[10] was transmitted by the mosquito. Then, in 1898, Ronald Ross in India and G. B. Grassi in Italy made the great discovery that malarial parasites were also transmitted by mosquitoes.[11] So, by analogy, there were those who hypothesized a blood-sucking insect as the means by which *Leishmania donovani* got from A to B.

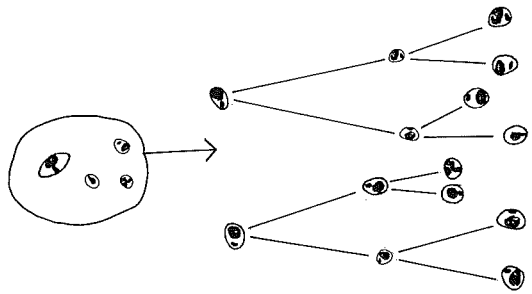
One of the first clues to both transmission and taxonomy came from the "test tube" cultivation of the parasite. It is all very routine today: you go to your doctor with your sore throat or other infected part, and a sample is taken for cultivation on artificial medium, the organism grown out, identified, and its sensitivity to various antibiotics determined so as to select the most efficacious one for your treatment. In 1903, when microbiology was in its lusty infancy, cultivation techniques were just being devised. It was essential to isolate, propagate, and identify the microbe in culture for research on the origin and treatment of infec-

10. It is said that Manson's first encounter with elephantiasis was a Chinese peanut vendor whose scrotum was so large that he used it as a counter to display his merchandise.

11. That a parasitic organism living in a warm-blooded host will undergo a profound morphological and physiological transformation to complete its cycle in the completely alien milieu of the invertebrate is a truly remarkable adaptation. We still have no real understanding of the cues and the consequent genetic activation that bring about these transformations.

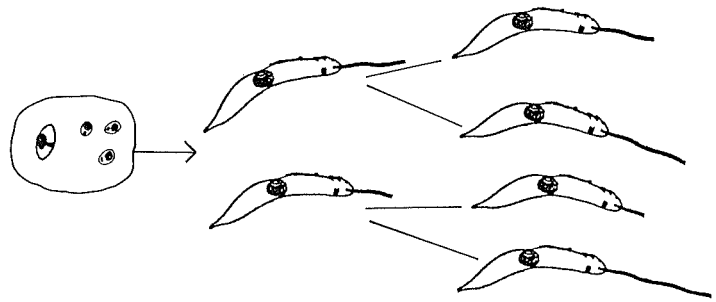
tious diseases. In each case, the discovery of a new pathogen was quickly followed by an attempt to grow it under laboratory conditions. Sometimes it worked. Sometimes it didn't. It was not, for example, until some seventy-five years after the discovery of the malaria parasite that the trick of getting it to grow in the "test tube" was worked out. For some microorganisms and parasites the culture trick has still not been elucidated.

Thus, when *Leishmania donovani* was identified as the cause of kala azar, the next natural step was to grow the organisms in man-made culture medium. In 1904, a year after Donovan's confirmation of the causative organism of kala azar, Sir Leonard Rogers, working in Calcutta, put some spleen tissue from a patient into a simple salt solution nutriment "soup," Sir Leonard must have been dumbstruck with surprise when, a week later, he peered down his microscope at a drop of the culture fluid. What he would have expected, if the culture was successful, was a multiplication of the Leishman-Donovan bodies, like so:



But that was not what Sir Leonard saw. The Leishman-Donovan bodies had *transformed.* From a minute ovoid form, they had become, in culture, spindle-shaped bodies

some ten times the size of their midget Leishmanial parent, each bearing a single threadlike flagellum at the anterior end. These flagellated forms were multiplying by an asexual division in the culture fluid, like so:



This meant that the Leishman-Donovan bodies within the macrophages of kala azar patients were but one stage in the life cycle of the parasite. Culture had revealed that there was a flagellated stage also, and this made it a cousin of the trypanosome, relatives within the larger family of tissue and blood-dwelling flagellates collectively known as the hemoflagellates. Protozoologists had seen the same spindle-shaped flagellate organisms (we now call this stage/form the *promastigote*) elsewhere—within the intestinal tract of a variety of flies and bugs. It was therefore most likely that what happened in culture represented what would normally occur in the gut of a blood-sucking insect. Ergo! Transmission of *Leishmania donovani* from person to person was by the bite of an insect infected with these flagellate forms. A good and sound assumption; but culture provided no clue as to what the insect—or insects—might be. Another thirty years of intense research were to pass and many more false trails laid before the innocent flies of Dr. Chakravarty were proven to be the guilty party.

The bedbug, even when dignified by its Latin name of *Cimex lectularius,* is a loathsome creature. During the depth of night it creeps from its hiding places—whether the cracks of mud-walled hovels in the tropics or the steam pipes and crannies of North America's tenements—to feed on its sleeping blood supply. It's not nice to have bedbugs. The scarred feeding marks on the bodies of poor children will attest to that. Logic would have it that any bug with as disgusting, blood-sucking habits as the bedbug must be a carrier of disease-causing microorganisms. And, God knows, there was no shortage of bedbugs in India. Thus, the bedbug became an early prime suspect as the vector of kala azar.[12] Those who incriminated the bedbugs became highly partisan in their belief and there was, for some twenty-five years, the tantalizing but not quite conclusive experimental evidence that was to keep them steadfast to the bedbug red herring.

The chief champion of the bedbug-as-vector was Dr. W. S. Patton, who was conducting his researches in Madras. For five years, from 1907 to 1912, Patton fed bedbugs on kala azar patients. In the intestine of a few of the bedbugs that he dissected several days after their blood meal, he observed the flagellate "culture" form of the parasite. However, although the Leishman-Donovan bodies from the patients had transformed in the insect's intestine, the flagellate-stage parasites could not be found in its salivary glands or mouthparts (by analogy, the infective form of the malaria parasite is in the mosquito's salivary glands). Those glands would have to be the repository of the parasite if they were to be transmitted during the feeding process.[13] Well, reasoned Patton, et al., if they don't spit *in* you, they shit *on* you—transmission was by the infective route. The flagellate bodies were voided in the insect's feces and made their way into the human body by abrasions on the skin or the small puncture made by the feeding bedbug.[14]

12. Over the years, the bedbug has been suspected, incriminated, and condemned as being the transmitter of a variety of parasites, bacteria, and viruses, but has always been proven innocent. As far as is now known, the bedbug's bite does not transmit any infectious pathogens to humans. Lice were also an early suspect as the vector of *Leishmania donovani* but it was pointed out that the Bengali was clean of his person and rarely lousy. The bedbug, on the other hand, would bite the sleeping washed and the sleeping unwashed without partiality.

Meanwhile, the bedbug was giving researchers a considerable amount of trouble. The flagellates tended to disappear from the bug's gut after a few days and those organisms that did remain were mostly dead and dying forms. As for the feces, it was difficult to recover viable forms that would "return to life" in test tube culture medium. Not a candidate vector to bet one's career on. Then, in 1922, the bedbug was dramatically rescued by a Mrs. Helen Adie. Mrs. Adie was a protozoologist working on kala azar in

13. Salivary juice, "bug spit," is essential to the blood-sucking insect. It contains powerful anticoagulants (which causes the itch and to which one can become allergically sensitized) that prevent the blood from clotting, and clogging in the small-bored "hypodermic-needle" mouthpart.

14. By analogy, this was not a totally unreasonable hypothesis. There is an allied disease present in the American tropics, Chagas' disease, caused by *Trypanosoma cruzi.* It's an untreatable infection that affects hundreds of thousands of people and may lead to death by heart failure or other cardiac abnormalities. It is transmitted by another blood-sucking bug, the Triatomid, which can slip its stiletto mouthpart into the sleeping person so artfully that its familiar names are the "kissing bug" and the "assassin bug." The infective-stage forms of *Trypanosoma cruzi* are in the bug's feces. When the Triatomid feeds, it takes in blood at one end and simultaneously defecates on the skin from the other end. The sleeping host may unconsciously scratch the bite and rub the parasites into the body through a lesion to effect transmission of the infection.

Calcutta[15] who claimed to have actually found the *Leishmania* in the bedbug's salivary glands. This would be almost positive proof that *Cimex lectularius* was the One True Transmitter. It was summer and the government and health officials, anybody who was anybody, had moved to the hill stations. Mrs. Adie sent a telegram to the government sitting in Simla telling of her great news, and a few weeks later that telegram was published, *in toto,* in the *Indian Journal of Medical Research.* Adie's finding greatly buoyed Patton's cause. Later that year, he announced to the Indian Science Congress that the bedbug theory was now nearly complete.

In the meantime, Mrs. Adie's microscopical preparations of the infected bedbug salivary glands were sent to other experts and their judgment caused the rapid deflation of the bedbug-as-vector theory. The organisms in the glands were not *Leishmania* but rather a completely unrelated protozoan parasite, *Nosema,* that had a superficial morphological resemblance to it. *Nosema* was known to be a common parasite of insects and even played a role in Pasteur's formulating the germ theory of disease from his finding the protozoan in sick silk worms. Even after all these years I can feel so sorry for Mrs. Adie . . . as would any other scientist who can appreciate the pain and embarrassment of having a great finding, a breakthrough, proved false because of a technical experimental error. I am happy to report that Mrs. Adie carried on. Two years later we find

15. Try as I might, I have been unable to trace the person of Mrs. Adie. She was a medical protozoologist, as were several other distinguished women scientists in the era between the two world wars (and also today). She had, however, the singular distinction (as far as I know) of being the only woman scientist of that time actually to work in the tropics on tropical diseases. She must have been a wonderful character and I wish I had known her.

her publishing an article on a malaria-like parasite of pigeons, a subject that could not excite great controversy or strong passions except amongst a small coterie of purists.

As the bedbug theory was being discredited, others were casting about for new candidates. One of the men who was to put his formidable energies to the effort was Major John Sinton of the Central Research Institute's Medical Entomology Section at Kasauli. Sinton, a North Irishman, was to become renowned not only for his stature as a malariologist but also because he would be the only person to hold both of Britain's highest honors, the Victoria Cross for military galantry and Fellowship of the Royal Society for scientific achievement.[16] At that time, it was not beneath the dignity of physicians to study insects, and most of the foremost medical entomologists were doctors who combined an expertise of medicine and zoology. In considering the kala azar vector problem, Sinton did what any good military man would do: he looked at maps. The map of kala azar showed its restricted range in eastern India, from Madras to Assam. When distribution maps of the blood-sucking biting insects were overlayed on the kala azar map, the range of one species neatly coincided—*Phlebotomus argentipes,* the silvery sandfly. In 1924 and 1925, Sinton published papers advancing his theory that the sandfly was the vector of the kala azar parasite, *Leishmania donovani.* The pursuit of the sandfly was now joined. It would take another twenty years

16. During a somewhat careless life in the tropics and elsewhere, I've had several outstandingly frightening experiences—for example, with a hippo who thought I didn't belong in his water, and the confrontational terrors of the African road. But perhaps the most unnerving experience was, as a very young graduate student, to be the bridge partner of Brigadier John A. Sinton, V.C., F.R.S. "The Brig," a wonderfully kind man, would bid with the same panache that won him his V.C. Mostly three no trump, as I recall. And heaven help his partner who didn't make the contract, no matter what cards he held.

before the final piece of conclusive proof was put into place. But at least the trail was now true.

The Calcutta School of Tropical Medicine had an additional piece of epidemiological evidence incriminating the sandfly—Ward 14. Ward 14 of Calcutta was largely populated by another product of British colonial rule, the Anglo-Indians. Merle Oberon and Ava Gardner's Bhowani Junction apart, the Anglos led unromantic lives in an ambivalent subculture that was neither quite English nor quite Indian. In expiation for their sins of miscegenation, the parental English virtually bequeathed the Indian railway system upon their mixed-race progeny, and it was run by them with great efficiency. The Anglo-Indians, in making a somewhat distorted cultural alignment, built homes which they thought of as being typical "mother country"—large, morose-looking wooden houses within a compound of thickly shadowing foliage. In 1925, the Anglo-Indians of Ward 14 were dying of kala azar. Their distant Hindu cousins of Calcutta's northern wards were barely affected by the disease. Searching for the reason for this difference, the Calcutta School of Tropical Medicine scientists headed by Robert Knowles noted that the dark rooms of the Anglo-Indian houses, "lumbered with family furniture," humid from the surrounding dank vegetation, were optimum conditions for the livelihood of *Phlebotomus argentipes*. The Anglo-Indian houses held large populations of this sandfly, while the simpler, more open shacks and homes of the Indians did not. In the poorer Indian wards there were lots of fleas, lice, and bedbugs, but relatively few sandflies. This finding encouraged the Calcutta School group to begin the demanding transmission experiments.

None of us likes sandflies. They are extremely finicky to breed and maintain in the laboratory. Identification of

their species often requires such expert practice as dissecting out their genitalia—and they are very small creatures with very small genitalia. Despite these difficulties, which were even more rigorous in 1925 than now, the Calcutta scientists managed to establish a thriving colony of *Phlebotomus argentipes*. Knowles began to feed these "clean," laboratory-bred sandflies on kala azar patients; then, day by day, he took the flies apart. On a glass slide under the microscope each fly was carefully dissected and searched for the presence of the flagellate form of *Leishmania donovani*. There was a considerable sense of excitement when these forms were seen in the gut of flies that had been fed on the patients three or four days earlier. Twelve days later the flagellate forms had multiplied and were now in the "throat" of the sandfly. This was great progress, but it still didn't prove actual transmission. The crucial A to B experiment had yet to be performed: an infected sandfly had to bite a human "guinea pig," and that human had to come down with kala azar.

The protracted transmission studies were now largely undertaken by officer-scientists deputed to the Indian Kala Azar Commission. The original trio, who set up shop in Assam, were Colonel Rickard (later Sir Rickard) Christophers, Major Henry Edward Shortt (later Professor Shortt), and a Mr. P. J. Barraud whom we don't hear much of as a "later." Knowles communicated his findings to the Commission, and Christophers, et al., quickly confirmed the Calcutta group's findings. Looking into their overly optimistic clouded crystal ball, the Commission predicted in their First Report of 1926 that "Only experimental transmission by the sandfly would therefore now seem to be necessary to prove finally the *role* of this insect in the transmission of kala azar." Little did they then know that the

successful A to B experiment would take another fourteen years.

Henry Edward Shortt, the only one of the trio to stay the course, would never carp over what must have been frustrating years. He was a man who pursued, and pursued, his quarry. He loved the hunt. As an Indian Medical Service officer, he shot tiger. As a professor at the University of London's prestigious School of Tropical Medicine and Hygiene (where he was to discover the missing "liver" link of the malaria parasite's life cycle), he taught his graduate students, at teatime, how to stalk and kill houseflies by creeping up on them with two extended fingers. As a retired visiting professor emeritus in Africa, he hunted agamid lizards (to study their malaria) with a blowpipe he made from glass laboratory tubing and modeling clay as the pellet missiles. No Jivaro could have been more accurate than this deceptively mild-looking man of modest stature peering at his prey over half-glasses. At the age of one hundred he caught his last trout and died, leaving his widow, his beloved Hobby, to survive him for another year until she joined him in death at age one hundred and three (Knowles had been the best man at their wedding in India those many years ago). Shortt knew that it was now no trick to produce infected flies; but try as he and his colleagues did year after year, time after time, the bite of those flies did not produce infection in human volunteers. Some experimental technique, some trick, was missing. When the trick was *finally* discovered, it seemed so simple; it also showed how scientists could be snookered for so long behind entrenched, plausible—but erroneous—assumptions.

The assumption was that the sandfly was rather like a small mosquito in its dietary habits. The male mosquito and the male sandfly, gentle souls, are vegetarians, feeding

exclusively on fruit juices and other plant material. They partake of no blood. Only the ladies are blood feeders. This is certainly true of mosquitoes but, as it turned out, not quite true of the sandfly. In 1939 a physician-cum-entomologist, Dr. R. O. Smith, established a laboratory in Bihar to study sandflies, beginning the research that was so important in unraveling the transmission knot. First, Smith showed that the female sandfly would readily feed on fruit (Smith gave them raisins) after taking the initial, infecting blood meal.[17] Next, he showed that when the usual procedure was carried out of maintaining the flies on "clean" blood feeds (as in malaria transmission techniques with mosquitoes), the second blood feed would, for some inexplicable reason, halt the multiplication of the flagellate *Leishmania* parasites. It caused them to lose their vitality, and sometimes even wiped them out from the sandfly.

Even more startling was Smith's observation that the raisin diet following the infective blood meal caused the flagellates to thrive and multiply so enormously that the sheer numbers of organisms formed a plug in the sandfly's pharynx. It was these "plugged" or "blocked" sandflies that constituted the potential transmissive danger. When they tried to feed again, the plug of parasites occluded the throat and made feeding impossible. The sandflies made violent efforts to ingest blood or other fluids, and in doing so, some of the flagellates of the plug became dislodged. It was these

17. My wife says that one of her most prominent memories of a sabbatical year I spent at the London School of Hygiene and Tropical Medicine was the scene at the morning coffee break, the "elevenses," where from time to time she joined me and the other faculty members. The entomologists, she vividly recalls, would turn up in the coffee room with cages of mosquitoes strapped to their arms and legs. They would nonchalantly have their "elevenses" of coffee while the female mosquito companions had theirs of blood.

dislodged organisms that might be capable of infecting a human when the "blocked" sandfly tried to feed. Shortt and all the other researchers had been following the malaria-mosquito experimental procedures of successive blood feeds. With the sandfly *Leishmania donovani*, this gave rise only to non-infective parasites.

In 1940 an Indian physician-scientist, C. S. Swaminath, and Shortt made the successful A to B experiments.[18] Swaminath collected six Indian volunteers from a hill district of Assam and fed the "raisined" infected flies on them. Three of the volunteers contracted the disease. The sandfly, *Phlebotomus argentipes*, was finally confirmed as the vector of kala azar. Thirty-eight years to prove a point! Only the post-game criticisms customary for new discoveries had still to be dealt with.

There was one bit of sniping that was amusing and would be impossible in modern science's impersonal, peer-reviewed publication policies. In 1944, a Dr. Malone published a letter in the *Indian Medical Gazette* in which he advanced his doubts that Shortt and Swaminath had proved their case for the sandfly transmission of kala azar. A few weeks later Shortt makes his Shorttian reply in the *Gazette:* He knows Dr. Malone to be a disciple of George Bernard Shaw, therefore the opinions of a fervent Shavian socialist cannot be accepted. Finis. At a much later year, Shortt was to refer to a well-known but not-quite-first-class scientist as "The Bishop" because he was always confirming others (including Shortt's recent discovery of the liver phase of the

18. From the 1920s onward it was not all a "one-man show" of British scientists; many competent and distinguished Indian physicians were engaged in kala azar research and often took precedence in publication. Shortt always spoke highly of his former Indian colleagues, although he might occasionally grumble that in the midst of a crucial experiment they would depart on a holy pilgrimage for an indeterminate period.

malaria parasite). Knowles, in his lecture notes from the Calcutta School, sums up the protracted search with a kind of eulogy of exhaustion:

> The story of the discovery of how kala azar is transmitted from man to man is one of the most amusing, also perhaps one of the sorriest in tropical medicine. It is a history of almost twenty years of wasted effort, of individual workers starting off with the highest hopes and ending in despair; of false starts and erroneous conclusions; of acute controversies and the flow of much ink; of wasted effort and the absence of co-ordinated enquiry.

BY THE SAME AUTHOR

New Guinea Tapeworms and Jewish Grandmothers: Tales of Parasites and People

The Thorn in the Starfish: The Immune System and How It Works

The Malaria Capers

More tales of parasites and people, research and reality

Robert S. Desowitz

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