appropriate experimental probe. Miller is excited by the prospect that he can isolate each merozoite's specific receptor and use it as a vaccine to produce what should be a solid immunity. That isolation will be a very tricky business, but he speaks enthusiastically of exploiting the new, remarkable techniques utilizing hybridomas (certain kinds of tumor cells made into producers of specific antibodies by fusion with antibody-producing white blood cells) and recombinant-DNA technology. I'm a rather old-fashioned malariologist, and I tell Lou, who is a close personal friend, that this is Buck Rogers stuff. But in my secret heart I wish I had done those experiments.

6

THE FLY THAT WOULD BE KING

One African tyrant does not attend political councils, is not a member of the Organization of African Unity, and has not palavered with roving diplomats, and does have a personal air-transport system—the tsetse. Holding Africa in thralldom since ancient times, this parasite, known as a trypanosome, is only six ten-thousandths of an inch long, but it has affected the economy, social institutions, and even the religious complexion of the continent.

During the mid-nineteenth century, Muslim Fulani cavalry swept from their near-desert West African Sahel kingdom into the savanna to the south and east, conquering and converting the animist tribes with whom they came into contact. But in their progress through woodlands and rain forests they encountered a formidable adversary, the tsetse. Swarms of these flies attacked and bit the horses, transmitting the parasite to them. It caused a lethal form of animal trypanosomiasis, and in rapid order the cavalry became a disarrayed

infantry. On foot, the Fulani were virtually powerless; their invasion was halted before it could reach the great population centers of the Benue and Niger river valleys. Thus was Islam, with its concomitant sociopolitical influences, prevented from infiltrating this vast densely peopled region of Africa for more than half a century.

The popular notion of trypanosomiasis is represented by the image of a lethargic human suffering from the "sleeping distemper," to use the words of an English observer some two hundred years ago. Not a form of distemper at all, the infection is caused in man by one of two closely related parasitic organisms, *Trypanosoma gambiense* and *T. rhodesiense,* and in animals by *T. brucei, T. congolense,* and *T. vivax.* (*T. gambiense* was thought to be restricted to man, but researchers have recently implicated the pig as a reservoir host.) Both animal and human trypanosomes are transmitted by the tsetse, a bloodsucking fly of the genus *Glossina.* Tsetse flies inhabit Africa only south of the Sahara, from approximately fifteen degrees north to twenty degrees south latitude, although they once had wider distribution, as evidenced by the discovery of a fossilized tsetse in the Oligocene shales of Colorado. While human trypanosomiasis continues to be a public-health problem, being responsible for some seven thousand deaths each year, it is the infection in domestic animals that has had the greatest impact on African development.

The tsetse belt encompasses more than six million square miles of land denied to livestock production, mixed farming, and in some regions, human settlement. It is an area that could potentially provide 125 million head of cattle to the protein-starved continent. The disease has forced herdsmen to concentrate their stock on the limited amount of fly-free pasturage, and this practice has led to overgrazing and attendant soil erosion. When cattle are trekked to distant markets through fly-infested country, some 25 percent may die before reaching their destination. And yet, a less anthropocentric view might hold that by preventing overexploitation of this enormous area, the tsetse and the trypanosome are the most stalwart guardians of the African ecosystem and its magnificent wild fauna.

The manner and degree of transmission of trypanosomes involves complex interactions of parasite, host and fly vector. With this in mind, let us consider the scenario and dramatis personae of *The Fly That Would Be King,* an African spectacular with a cast of millions.

Act 1 is set in a forest in Africa. On stage is the host—a man, a cow, or an antelope. A closer, microscopic examination reveals the second character, the trypanosome, swimming about in the blood of the host by means of an undulating membrane and a lashing flagellum. A sound of angry buzzing comes from off stage. Enter a tsetse, a brown insect not much larger than a housefly. The tsetse smells and sights the host, then strikes and bites, sucking in its trypanosome-containing blood.

Act 2 takes place inside the tsetse's gut, where the trypanosome elongates and multiplies by simple asexual division. After about four days it migrates to the fly's salivary glands; there, over the next fifteen days, further transformation takes place, until it assumes the short, stumpy appearance of the metacyclic stage—the terminal developmental form, in which it is capable of infecting a new host.

Act 3 opens in the forest twenty days after act 1. The original host lies obviously ill on the stage floor. Enter another host. The infected tsetse strikes, delivering the

metacyclic parasites to the blood stream of the new host and completing the cycle. Curtain.

While this plot is essentially the same for all African trypanosomes, the details for each species differ in important respects. In man, the disease caused by *T. gambiense* is chronic and malignant, and gives rise to the torpor and eventual coma and death classically associated with sleeping sickness.

The pathology of the disease is largely unknown. Over the course of time, the trypanosomes tend to leave the blood and enter, first, the lymphatics, and later, the spinal fluid and the tissues of the central nervous system. The patient becomes comatose during this latter phase, and dies after several years if he has not received chemotherapeutic treatment.

Whereas Gambian sleeping sickness results in a slow death, that caused by *T. rhodesiense* kills within weeks or months. The two infections differ not only in degree of virulence but in other respects as well. Gambian trypanosomiasis is essentially a human disease, cycled from person to person, while the transmission cycle of Rhodesian trypanosomiasis includes a third host—the wild antelope—which acts as a reservoir of infection. By all biological criteria, *T. rhodesiense* is a parasite of the wild ungulates, rather than man. Evolution has resulted in a state of equilibrium in which the parasite produces no overt disease in the animal host. Man, for the most part an accidental host, has not attained this accommodation, as the intense virulence of the human disease indicates. The manner by which the antelope modulates the infection remains a mystery; its elucidation might aid in devising a means of similarly stimulating a protective state in man.

The ecological setting—the landscape epidemiology—is different for each of these disease varieties. Gambian sleeping sickness is generally restricted to the humid forests bordering the lakes and rivers of West and Central Africa, the obligatory habitat of *G. palpalis*, the tsetse species that transmits this form of the disease.

Because rural African populations rarely have the means to obtain water from distant sources, communities tend to form along the banks of rivers and lakes, and village activities—bathing, washing, drawing water, and fishing—take place at the water's edge, making for intense man–fly contact. Epidemics flare from time to time, but generally the disease level is low because this tsetse is, biologically, a relatively inefficient vector. Trypanosomes can readily multiply in *G. palpalis* only shortly after the fly emerges from the pupal stage. Very few older flies are able to act as vectors after feeding upon infected humans.

Sleeping sickness caused by *Trypanosoma rhodesiense* is endemic to the dry savanna woodlands of East and Central Africa, the habitat of both the *G. morsitans* vector and the great herds of antelope that serve as reservoir hosts. Human infections occur when people settle in the savanna or intrude to hunt, gather wood, or graze cattle. The species of vector that transmits this form of the disease is not an equal-opportunity biter; and it prefers to take a blood meal from mammals other than humans. When game becomes scarce, however, the fly will feed on humans. Apparently attracted to large, slow-moving objects, it becomes confused when these sometimes turn out to be vehicles rather than antelope, and it will feed on the passengers. In this curious way, a package tour of East African game parks occasionally includes trypanosomiasis.

There is, then, an intimate relationship between the

nature of the ecosystem and the epidemiology of trypanosomiasis. The history of Africa, however, is characterized by continuous ecological change—with felled rain forests succeeded by grasslands and savanna woodlands, an advancing or retreating desert, and shifting distribution or concentration of human inhabitants and wild fauna. These environmental changes have played a crucial role in the epidemiological patterns of the Gambian and Rhodesian forms of trypanosomiasis, particularly where their ranges overlap in east-central Africa.

The activities and diseases of both Africans and colonial expatriates have also contributed to the epidemiological status of trypanosomiasis. Before the nineteenth-century colonial period, trypanosomiasis was confined to a relatively few smoldering foci. Internecine warfare and lack of roads restricted communication and prevented the spread of the infection. The rapid dissemination of sleeping sickness can be traced to the opening up of Africa by the colonial powers. It was the *Pax Britannica* as much as the tsetse that was responsible for the broadcast of infection. How this complex of changing environmental and human factors has influenced epidemicity of the two types of human trypanosomiasis is illustrated, par excellence, by the events that have occurred along the Kenya and Uganda shores of Lake Victoria.

Prior to human settlement, the lake was surrounded by a tropical high forest. Primitive farmers migrated to the lake's shores and felled forest tracts for their shifting agriculture. Forest-inhabiting tsetse were present, but human trypanosomiasis was absent. Eventually, deforestation progressed to such a degree that grassland replaced large areas of forest. The grassland then

attracted a second wave of migration—Nilotic pastoralists (that is, herders who originated in the Nile basin) and Bantu cultivators. The combined pressures of grazing and agriculture suppressed forest regeneration and thus maintained a fly-free area beyond the forest that fringed the lake.

In the nineteenth century the society along the lake was devastated by the twin pestilences of smallpox and rinderpest, and agricultural activity diminished. Before the population had time to recover, savanna woodland succeeded the grassland. At the close of the nineteenth century the ecological stage was set for sleeping sickness. The shores of the lake were bordered by a rain forest infested with *G. palpalis,* the tsetse vector of *T. gambiense.* Beyond the forest *G. morsitans,* the vector of *T. rhodesiense,* inhabited the savanna woodland. Still the trypanosome had not made its debut.

The parasite is thought to have been introduced when Sir Henry Morton Stanley, employed at that time in the Congo by the Belgians, mounted an expedition in 1887 to the area of Lake Victoria. Natives in Stanley's retinue, probably infected with *T. gambiense,* may have carried the seeds of the epidemic that was to decimate the population for the next ten years.

By 1910, when the Gambian sleeping sickness began to burn itself out, the number of inhabitants in the area had declined from 300,000 to 100,000. Before the epidemic, the large size and number of human settlements had had the effect of suppressing the faunal population; but as people died of the disease or fled the stricken area, the game reservoirs of *T. rhodesiense* increased and moved into the adjacent savanna woodland. The final epidemiological link in the chain of Rhodesian sleeping sickness—from game to man through

woodland-dwelling fly—was now present, to complete the cycle. When government-inspired resettlement was attempted in the 1940s, the migrants rapidly became infected with this highly lethal disease, and once again the inhabitants deserted the land. Today, this potentially rich region is virtually abandoned, occupied only by a few fishermen who are at high risk of contracting the infection.

When I joined the West African Institute for Trypanosomiasis Research in 1951, the entire infected population of Nigeria lay, so to speak, before me, but I was to be introduced to the human disease in a much more personal way and under circumstances that gave me a first glimpse into the meshing of the fly, the trypanosome, the ecosystem, and human behavior.

My friend Dan Quaddo, a Rukuba and in the epithets of that unregenerate colonial era, a pagan (being neither Christian nor Muslim) was the household "small boy" (the domestic of all work, age notwithstanding). He was a small, cheerful, but unbeautiful man; his name meant Son of the Frog, and West African "village" names are bestowed with deadly accuracy. The only maggot in Dan Quaddo's otherwise optimistic disposition was his unfathomable terror of "teef men" (pidgin for burglars, not dentists), and even during the hottest nights of the hot season he would barricade himself within his quarters. I once tried to reason with him: "Dan Quaddo, why do you do this? You are so poor and have so little, why would anyone want to teef you?" I vividly recall his reply, in which he explained with the patience of someone describing an immutable law to a small, rather dense child: "Suh, anyone who teef me be so bad he not need a reason."

A short time after this illuminating conversation he returned to his nearby village, on the slopes of the Bauchi Plateau, and spent several weeks there attending to "family affairs." A few weeks after returning he once again locked, bolted, and shuttered himself within his house, this time complaining not of "teef men," but of devils of fever and headache. The American reaction would be to exorcise these with aspirin, but in Africa, where malaria is commoner than the common cold, the first resort is routinely to the magic of antimalarial drugs. After a time the fever abated, but the headache persisted and Dan Quaddo became uncharacteristically eccentric and surly. He took to putting nonperishables in the refrigerator—theater tickets, tennis balls, my wife's brassière (the "small, small vest for chest"). There was no disputing that what ailed Dan Quaddo was not malaria and that he needed medical attention. In the tropics the microscopic examination of the blood takes pride of diagnostic precedence, and I remember peering into the microscope and seeing, for the first time outside a laboratory classroom, the trypanosomes of a human swimming in the microscopic field and the dancing movement of the red blood cells as they were disturbed by the thrashing parasites. We later found that Dan Quaddo's infection had progressed to the stage where his lymph glands had also been invaded by the Gambian trypanosomes, but fortunately the disease was caught before the central nervous system became involved. He was successfully treated and made an uneventful recovery. However, I was curious about how he had contracted the infection, since we were supposed to be outside the tsetse belt. Inquiry revealed that Dan Quaddo was actually one of the last victims of a cataclysmic sleeping-sickness epidemic, beginning some ten years earlier, that had brought his tribe to the verge of extinction.

In former times the outliers of the typical high forests

bordering streams and rivers had penetrated the dry savanna, and these outliers had provided a suitable ecological niche for the tsetse vector. The Rukubas had cut down most of the outliers, but each tribe preserved near its village a small area of forest that was sacred, the *tsafi* grove. The flies had retreated to these groves and were concentrated there in great numbers. Every seven years the elders and the young boys went to their sacred grove for a religious retreat, during which the youngsters were initiated into manhood. The secrets and mysteries of the Rukubas were passed from the old to the young, and the genealogy of the tribe was recounted. Circumcision rites were performed, and the elders harangued the initiates about morality. During these religious retreats man and fly were in close contact, but until the early 1940s the trypanosome was absent. The infection is believed to have originated with a farmer who, taking advantage of the relatively new state of intertribal tranquility imposed by the colonial government, traveled to the south of the plateau, an area of endemic trypanosomiasis. On his return, this farmer participated in a manhood initiation rite and was a source of infection to the fly and consequently to his coreligionists. The human infection slowly built in intensity, and by the mid-1940s one-fourth of some village populations had been stricken. When the first medical teams were sent to the area, the Rukubas either fled or hostilely ejected them from the villages. In 1944 they were finally convinced of their plight and accepted mass drug treatment and tsetse-eradication campaigns. By the early 1950s the epidemic, except for a trickle of infection, had been brought to a halt. My unfortunate friend Dan Quaddo, whose "family affairs" had really been a *tsafi*-grove ritual, was one of the last to become infected, and he had

almost been "teefed" of his life. The trypanosome was indeed, so bad it didn't need a reason to rob him.

The trypanosomes that infect domestic animals are not restricted to any particular forest ecosystem; animal trypanosomiasis exists wherever there are tsetse flies of any species. The presence of wild-game reservoirs—along with the fact that the flies, in all probability, carry the trypanosomes (*T. brucei, T. congolense,* and *T. vivax*)—contributes to a level of transmission so intense and ubiquitous as to effectively preclude stock production in one-fourth of Africa. Nomadic and semisettled cattle-owning tribes have been forced to pasture their animals in the fly-free zones in and near the arid Sahel. As the dry season approaches, the Sahel is no longer able to sustain the herds and the annual trek into the fly-infested Guinea savanna begins. Losses to trypanosomiasis always occur, but where nutrition is adequate and the density of flies not too great, the stock may manage to survive, if not flourish.

The breed of cattle favored by the African pastoralist is the zebu, a large, humpbacked longhorn, well adapted to semiarid conditions. Although it produces relatively high yields of milk and meat, the zebu has the unfortunate disadvantage of being susceptible to trypanosomiasis. There are smaller, even dwarf, breeds of cattle, such as the N'dama and Muturu, that possess remarkably high resistance to or tolerance of the trypanosome. Studies carried out at the Nigerian Institute for Trypanosomiasis Research have proved that the resistance of these breeds is due to a highly efficient immune response. Two conditions are necessary for the attainment of this level of protective immunity. First, the animals must be born of a hyperimmune dam, and second, they must receive an early and continuous

infection of trypanosomes, so that they produce a protective antibody.

These tolerant breeds have not as yet been economically exploited, probably because of their small size, although the N'dama is large enough to be used for meat. Crossbreeding with zebu or European breeds does not result in offspring capable of developing hyperimmunity.

Combating trypanosomiasis calls for heroic measures, but because of the severity of the side effects, the remedies may not be practicable. The battle against the disease has included massive alteration of the environment, social dislocation, wholesale slaughter of wild fauna, and the mass administration of toxic drugs. A commonly employed means of control has been to deny the tsetse its required habitat by selective or large-scale deforestation. Fly-free zones can only be maintained by intensive land use, brought about by the collectivization of the population into large agricultural villages and townships. This forced dislocation from the traditional, stable life in small, scattered tribal groups has resulted in a disturbing upheaval of the social order.

Perhaps the most controversial control measure was the game-destruction program carried out in East Africa during the 1950s. Designed to open up land to human settlement, this scheme was faultless in its logic. Game animals harbor *T. rhodesiense* and are the main source of blood for the tsetse; therefore, destroying the large fauna means good riddance to both trypanosome and fly. After the campaign, however, small mammals survived in sufficient numbers to support the fly population. Also, as the game was decimated, herdsmen moved their cattle into the cleared areas, the fly began to feed on the livestock and the pastoralists, and the

result was continued and intensified transmission of both animal and human trypanosomes. Finally, revulsion against the studied slaughter brought the program to a halt.

Another possibility is to control the spread of the disease by means of insecticides. Ironically, one researcher, Dr. Walter Ormerod, has proposed that the use of insecticides was a major, if not prime, contributor to the great drought that recently ravaged sub-Saharan Africa. The reasoning of this hypothesis is as follows: Increasing urbanization and prosperity in West Africa precipitated a demand for meat. Traditional cattle-owning tribes increased the size of their herds to match the market. Widespread, government-sponsored aerial spraying of insecticides, in conjunction with mass chemoprophylactic injections of cattle, followed, permitting growth of herds not only in the Sahel but also in the adjacent Guinea savanna. The large numbers of cattle overgrazed the meager stands of grass and other plant life in this fragile ecosystem, resulting in a higher reflectance of sunlight from the denuded land. There is good evidence that such a situation causes a decrease in rainfall, and in this region matters did indeed proceed to a point where the result was climatic havoc.

Despite more than seventy years of research and effort, the freeing of Africa from trypanosomiasis has not been realized. The effective, practicable means of control now available are too harsh. Except for limited areas, insecticide spraying is too costly. Governments of the new African nations are often too poor in economic and technical resources to maintain the anti-trypanosome and anti-tsetse programs begun during the colonial era.

Drug treatment of infected people has brought about

a decline in human trypanosomiasis, but the trypanosomes can develop resistance. Confronted with this impasse, scientists have long sought the biological "magic bullet"—immunization—as a solution of the problem. Vaccination has brought many of the great scourges of mankind, such as smallpox and yellow fever, under control without necessitating changes in the environment or turmoil in the socioeconomic order. But unlike the immunologically amenable bacterial and viral pathogens, the trypanosome has confounded all attempts to induce protective immunity. The reason for this failure stems from the parasite's ability to elude the host's immune defense by a process known as antigenic variation.

There is currently great concern over the antigenic shift of the influenza virus, a phenomenon that seems to occur about every ten years. A trypanosome undergoes the same process, but a new antigenic variant arises every five to ten days. This is tantamount to the host's being assaulted by a new, personal epidemic each and every week.

During the course of a trypanosomal infection the host may develop an antibody that eliminates most, but not all, of the trypanosomes. The survivors are of a different antigenic character from the others, so the antibody fails to recognize them. The variant trypanosomes then begin to proliferate in the blood stream. The host responds by producing a new specific antibody. The process is repeated over and over, for the trypanosome possesses the remarkable ability of producing a large, probably infinite, number of antigenic variants.

The underlying mechanism responsible for antigenic variation has been the subject of a long controversy between those who hold it to be a selective process,

which presupposes a starting parasite population of one predominant and many minor variants, and those who believe that antigenic variants arise by mutation. There are difficulties in supporting either of these explanations by experimental evidence. Electron microscopy and immunochemical analysis suggest that the trypanosome antigen—the face the parasite presents to its world—is a glycoprotein coat, or pellicle, situated outside the trypanosome's limiting plasma membrane. Apparently this coat is periodically shed, and the parasite, acting as its own couturier, designs and makes a new antigenic garment.

T. vivax, the important pathogen of livestock, seems to have developed still another maneuver to survive in the immunized host—antigenic mimicry. This trypanosome may be able to absorb a coat of host serum protein that disguises its alien status and also acts as a protective shield against any antibody that the host may produce. A similar phenomenon, the absorption of host substances to the external parasite surface, occurs in the schistosome blood flukes of man. Antigenic disguise may thus be another important adaptive evolutionary strategy that permits some parasites to exist in the immunized host.

New methods for dealing with human and animal trypanosomiasis are urgently needed. However, the extent of research and the amount of resources invested are minuscule compared to the magnitude of the problem. A new trypanocidal drug has not been added to the chemotherapeutic armamentarium for twenty years. Pharmaceutical companies candidly admit that the high cost of development and the potentially poor profits from selling to the generally impoverished underdeveloped nations have virtually taken them out of tropical-

disease research. I feel confident, however, that improved means of combating the infections will eventually be forthcoming. A quality of biomedical science is its incurable optimism that all things are possible, given time and support.

But it may well be that Africa's real problems will commence with the effective control of trypanosomiasis. Scientists and the administrators carrying out the practical applications of research often fail to recognize that they are engaged in a gigantic chess game. As one enemy piece is captured, other pieces move to threaten. As trypanosomiasis is conquered, overgrazing, soil erosion, social disruption, and faunal extinction may result. Until the time comes when scientists and their technical-administrative partners appreciate the grand strategy of acting sanely and effectively to protect the well-being of all Africa's citizens, both two-legged and four-legged, we may applaud the cosmic wisdom that has made the tsetse, rather than man, Africa's custodian.

7

RIVER BLINDNESS

> Information has reached me that the village of St. Pierre has disappeared; all that is known of it is that the houses are completely deserted and broken down.
>
> —A. Rolland, 1972

In 1963 a small band of settlers, driven by hunger, left their overpopulated and infertile land in the savanna of West Africa and migrated to the banks of the Keralie River, a tributary of the Black Volta. There, they built the village of Saint Pierre and began to farm the rich valley land.

Five years later, 75 percent of these pioneers had developed ocular lesions. Some were already functionally blind. Finally, life and sight became too precarious and they fled. By the time epidemiologist A. Rolland made his report, Saint Pierre had become one more ghost town of the West African savanna—another community crumbled by the parasitic filarial worm *Onchocerca volvulus* and its vector, the blackfly *Simulium damnosum*.

The disease onchocerciasis, familiarly known in Africa as river blindness, has a quality of gothic horror

falls, the liver is adversely affected, and the number of platelets (those small, round cells in the blood intimately involved in coagulation) plummets. The substance or substances responsible for this pathological cascade have defied isolation so far.

One hypothesis is that the reaction somehow arises from the union of antibody with the worm antigen. A blackboard in my laboratory has lists of all the findings and arrows that show the possible pathways and relationships. From time to time a graduate student or visitor will contemplate this *Gemisch* of data and draw in another line. The blackboard has begun to look like a Jackson Pollock painting. Meanwhile we are experimenting empirically with known blocking agents that act on certain pathways, hoping that chance will favor our prepared minds. We are not even certain that the events occurring in the dog also occur in the treated human. But at least we have some idea of what to look for when we move from the laboratory to field and stream.

In one of his more enlightened manifestoes, Lenin once exhorted, "Devastate the worms!" But the revolution, in the form of more effective and safer drugs and larvicides, is yet to come for the tropical proletariat under the yoke of onchocerciasis. Until that jubilee day, means will have to be found to implement the measures now available, and the planners of great schemes will have to adopt the physician's guiding principle: first do no harm.

8

CONTROLLING THE SCHISTOSOME AT A SNAIL'S PACE

There is a hilarious episode in the movie *The Apprenticeship of Duddy Kravitz* that makes a sly comparison of the rituals of savage and sophisticate. Duddy, a young entrepreneur with a surfeit of chutzpah, is engaged in the business of filming the weddings, bar mitzvahs, and suchlike events that punctuate our lives. As the scene opens, Duddy and his director, a man slightly unhinged, are screening their latest epic. It shows a bar mitzvah. Present at the screening are the beaming parents, the boy who recently became a fully fledged member of Judaism's fraternity, and the rabbi who officiated at the event. Duddy's movie begins in an orthodox enough fashion, with the boy intoning the portion of the Torah, and then, with surgical suddenness cuts into a scene of a pagan rite. Savages. Wild men screaming and carrying on in demonic fashion. Then a cut back to the serenity of the bar mitzvah, and then back to the pagans—the shifting ritualistic counterpoint continuing

until the end of the film. The lights go on, and we see the stunned parents looking to the rabbi for judgment of this unexpected offering. The rabbi, after thinking for a moment—perhaps seeking guidance from the Higher Critic—pronounces it to be an avant-garde milestone in the art of bar mitzvah films, and the tension eases visibly.

The scene stuck, with nagging persistence, in my thoughts. Upon later reflection I decided that this was because during my years in Africa and Asia I had perceived a commonality in all ritualistic celebration, whether by the tribe of Israel or the tribe of Ibo. I think this commonality is particularly shared by the rituals that mark the coming of age—that beautifully magic formal moment when a society recognizes the signs of passage from childhood to the obligations of adulthood. But in Africa there is one frightful marker of impending sexual and social maturity that is blessedly absent in the temperate world; at puberty the urine of the African youth may turn red with blood. This is so common an occurrence that in many parts of Africa it is considered to be a kind of male menstruation. The offender, in fact, is a parasitic worm living within the veins surrounding the bladder, whose clinical expression usually begins, for reasons not fully understood, during the early teens of the infected host. This blood fluke, *Schistosoma haematobium,* and the two other species commonly infecting humans, *S. mansoni* and *S. japonicum,* impose a burden of debility in the tropics second only to that resulting from malaria. The infection is water-associated, transmitted by fresh-water snails, and it is essentially a disease that humans bring upon themselves: it is now increasing in range and intensity as a result of agricultural and water-impoundment projects.

Like malaria and other infectious diseases, schistosomiasis has played a role in human history, and at least once in our generation it influenced the political destiny of a region.

In 1948 the Nationalist armies of Chiang Kai-shek, having met defeat at the hands of the Communists, fled, along with thousands of civilians of similar political persuasion, to refuge in Taiwan. It was a chaotic moment, marked by political and military uncertainty. The American ship of state had not yet sailed to protect these troubled waters, and the Communists intended to consolidate their victory by taking Taiwan. They rushed some 200,000 troops from northern China to encampments along the lower Yangtze River to train for an amphibious assault.

One hundred years before, in 1847, the physician Dariji Fujii journeyed to the Lacquer Mountain, Katayama, in the Hiroshima prefecture of Japan. Dr. Fujii was the first to describe the affliction of the local people during the rice-planting season. The first sign, which appears after the victim had waded in the rice paddies, was a relatively innocent rash of the legs. Not long after, the disease announced itself with fever and bloody diarrhea. Some of those affected continued to waste away, and died. Dr. Fujii noted in his diary that to his frustration the medicines for "boosting spirits," for the "four-times-rebellious disease," and for "poisoned people" were of no avail. The cause of Katayama disease was to remain a mystery for another sixty years, until another physician, Katsurada, proved its symptoms to be the early manifestations of *S. japonicum* infection.

This set of symptoms, still known today as Katayama disease, struck the Communist troops. Northern China, where these troops originated, is schistosome-free, but

the lower Yangtze River was at that time one of the most massively and intensely endemic areas of japonicum schistosomiasis. Within weeks of their arrival the men were paralyzed with fever and diarrhea. Some came running, but few went marching. An assault by troops so weakened by illness was out of the question, and the invasion was postponed. During that respite, American policy solidified. Taiwan became our protégé. Our navy steamed offshore. We had made the commitment to Asia.

But what would have happened if the schistosome had not been in the Yangtze Valley or the Communist troops had not fallen to the sickness of the Lacquer Mountain? Would the United States have turned its back on the East and ceded to the Chinese their traditional suzerainity? Would we have become involved in Vietnam? Would our present entente with the People's Republic of China have come to be, or would it have come about even earlier? We shall, of course, never know, but I strongly suspect that scholars would be writing a different history of Asia and America if not for the primitive flatworm.

The mantle of schistosomiasis is enormous. However, *S. japonicum,* which for countless centuries was highly endemic in Asia, has now receded, largely as a result of a herculean control effort by the Chinese and of the destruction by the Japanese of snail-breeding sites (some of the most important former habitats are now housing estates, factories, and golf courses). Intense foci of japonicum schistosomiasis still exist in some islands of the Philippines and in the Celebes, in Indonesia. A parasite resembling *S. japonicum* has recently been discovered infecting humans living along the Mekong River in Laos, where it is, as far as we can tell, localized. There

is, however, concern that if the Mekong River project is ever completed, new habitats for the snail host will be created and the infection will be disseminated along extensive stretches of the river.

S. mansoni is highly prevalent in Africa, extending from the Nile Delta south through the greater part of the continent below the Sahara. And Mansonian schistosomiasis is also entrenched in Latin America, having been introduced, as if for revenge, by African slaves. It was tropical America's bad luck and the schistosome's good fortune that suitable snail hosts were awaiting the arrival of these slaves. Today, schistosomiasis is a major, unresolved health problem in Brazil, Venezuela, Surinam, and many Caribbean islands, including Puerto Rico.

In Africa, *S. haematobium* covers much of the same geographic range as *S. mansoni.* It is also present in the Middle East (in Iraq, Syria, Saudi Arabia, and Iran). Until it was eradicated about a decade ago by ecological measures and treatment of infected individuals, there was a small focus of urinary schistosomiasis along Israel's Yarkon River, perpetuated by orthodox (and infected) oriental Jewish women who took their ritual *mikveh* bath in the river and its tributaries.

That is the where of the schistosome. The why of the parasite is rooted in the complexities of its life cycle. And a complex life cycle it is—a marvel of development but a plague to student and reader (to whom apologies are made on behalf of author and schistosome). But in the Great Worm War we must ferret out the most subtle and secret facts of our enemy's life, so as to devise an effective battle plan. Knowledge of the developmental cycle allows our scientific counter intelligence corps to discern the weaker links in the transmission chain.

Understanding of the parasite's chemical physiology provides (theoretically at least) a means of developing effective chemical and pharmaceutical weapons. If we know the mechanisms underlying the immunopathological process we may be able to prevent infection and disease by modulating the human host's natural defenses. Also from this intelligence base, we may be able to anticipate the kind of blunders by our own political and technological high command that would cede the advantage to the parasite. So for these reasons let us examine the lives and loves of the schistosome.

The schistosome is an uxorious worm. The relatively stout cylindrical male, three-quarters of an inch long, has a grooved canal along the length of its underside. In this canal the female lies in constant embrace; they are monogamous and mated for life, which may be as long as thirty years. The worm's homestead is within a vein, where it is fixed to the vessel wall by means of two holdfast suckers at its anterior end. Each species of schistosome has adopted a venue in a particular compartment of the venous system; *S. mansoni* lives in the veins draining the lower intestine, *S. japonicum* in the veins of the upper intestine, and *S. haematobium* in the network of veins surrounding the bladder.

The female is a superefficient reproductive machine, daily producing approximately 3,500 eggs, each containing a fully formed larva, the miracidium. To continue the life cycle the egg must pass first through the wall of the vein and then through the wall of the bladder or bowel. How the egg broaches these formidable barriers is still uncertain. It is equipped with a spine, which evidently helps catch it on the vein's lining and protects it from being swept away by the circulating blood. Electron microscopy reveals that the egg has

many minute pores, like a sieve, and the miracidium is believed to secrete a digestive enzyme that passes through these pores to the tissues and acts as a kind of meat tenderizer to facilitate passage. Only about 30 percent of the eggs make it to the lumen of the bowel or bladder, to be voided with feces or urine. Some eggs remain entrapped within the wall of the vein, or of the intestine or bladder, while some are carried by the blood stream to other organs, notably the liver, where they are filtered out into the surrounding tissues. As we shall see, it is the eggs that remain in the tissues that are the primary exciting agents of acute disease.

Shortly after the egg reaches the water, it hatches; the miracidium is released. The body of the larva is covered with "rowing hairs," the cilia, and for a brief period it lives free in the vastness of its water environment. But it must find a snail host within twenty-four hours or die. It was once believed that the miracidium came to the snail only by chance, but recent research has shown that there is a guidance system. The snail's "body odor"—emitted by a secretion of amino acids, fatty lipids, and possibly certain metallic ions—acts as a powerful attractant. Homing in on this chemical beam, the miracidium contacts the snail and by means of enzymatic secretions and vigorous drilling movement penetrates the snail's foot or antenna and migrates to the innards.

While this system helps the miracidium locate potential snails, it is not highly refined, and the secretions from suitable and unsuitable species of snail are equally attractive. But the schistosome's requirements for a host, like those of most vector-borne parasites, are very specific. *S. mansoni* will develop in *Biomphalaria* snails but not in species of *Bulinus,* while *S. haematobium* develops in *Bulinus* but *Biomphalaria* is refractory. Even more

exacting limitations exist; over their broad geographic range, schistosomes and their snail hosts have evolved to a degree of narrow interdependence. For example, the species of genus *Bulinus* that is the vector of *S. haematobium* in Egypt cannot be infected with the West African strain of that parasite. It is even possible, by careful selective breeding in the laboratory, to isolate from a normally susceptible species of snail a subpopulation that will be resistant to infection. Susceptibility and resistance appear to be controlled by only one or two genes, but what chemicophysiological determinants are programmed by these genes is a secret that scientists have not yet been able to unlock.

However, let us return to our lucky miracidium, which has found and entered a compatible snail. I think what has always attracted me to animal parasites (fortunately the attraction hasn't been mutual; only on one occasion have they been attracted to me) is their remarkable, almost magical ability to transform, like Nature's Merlins, anatomically, functionally, physiologically, and antigenically as they proceed through their life cycle. It is as if they become entirely different creatures at each stage of development. In keeping with this phenomenon, the free-living miracidium transforms within the snail into an elongated sac, the mother sporocyst, whose sole function is asexual reproduction. The wall of this sac is lined with germinal cells that give rise to miniature replicas of itself. These daughter sporocysts grow and in turn reproduce—not other sporocysts, but the infective stage of the parasite, the tadpolelike, forked-tailed cercaria. This proliferation is staggeringly prodigious; as many as 250,000 cercariae will result from a single miracidium.

The cercariae leave the snail in daily waves, usually

between 8 A.M. and noon. Again, time is a critical factor for survival, for each cercaria must find its final host within two to three days. Enter (into the water) the fisherman, the housewife doing the family wash, the bathing child, the rice farmer, or your author, who has gone to retrieve a pygmy goose for dinner, and contact is made. The cercaria can also meet its host in drinking water. Upon contacting the mucous membrane or skin it flicks off its tail and penetrates, aided by enzymatic secretions from specialized glands. It rests from its labor for a day or so in the skin tissue, and during that time transforms into a juvenile worm, the schistosomula. Then it gets its migrational motor in gear and enters a small blood vessel, which carries it to the liver by way of the heart and lungs. It pauses for a mandatory sojourn in the liver, where it grows into a sexually mature female or male adult. Then this blind, unthinking worm migrates, with the certainty of a traveler holding a confirmed booking, to the venous compartment for which it is, as a species, destined. In the veins, boy schistosome meets girl schistosome, but how this liaison is brought about is not fully understood. There is now some evidence that parasitic worms secrete a powerful aphrodisiac, possibly similar to the pheromones of insects, that may guide the schistosomes to their sanguine tryst. One to three months after the cercariae have made that fateful meeting with their host—the exact time varies with the species—the female schistosome's genital assembly line begins cranking out her daily quota of eggs.

Let us review the stages of the life cycle, observing how they cause disease. Trouble for the host can begin with the pinhead-sized cercaria's penetration of the skin. The parasite's proteolytic secretions may cause a transient rash. With repeated exposure many individu-

als become sensitized and cercarial penetration incites an intense itching, accompanied by blister formation. Actually, cercarial dermatitis is not confined to the tropics; it has been a bothersome plague to bathers and other human aquatic waders in many parts of the world. Numerous animals, including water birds, have "their" species of schistosome. The cercariae of these animal parasites will penetrate the skin of the human, although they can mature no further in that abnormal host. In some places, bird schistosomes can cause reactions as intense as those produced by the human-schistosome cercariae. The description given by a man inflamed with cercarial dermatitis after bathing in a lake near Seattle is typical: "While drying myself with a towel I noticed that my skin turned red, and in a few minutes my arms and legs burned as though on fire."

Once the cercaria is under the skin it transforms into a schistosomula. This stage excites no pathological reaction. In fact, the schistosomula is the stage most vulnerable to the host's immune defenses. In an "immunological virgin," such as a tourist or young child, the schistosomula migrates and matures more or less unmolested. But in an experienced, immunologically primed host, the slaughter of most of the schistosomulae is accomplished by a complex co-operation of antibody and of specialized cells. Antibody and a serum protein "binder" (complement) coat the surface of the schistosomula. Certain cells, a subpopulation of lymphocytes and mast cells, send out a chemically signaled call for help to another type of white blood cell, the eosinophil. Eosinophils swarm to the scene and bind to the antibody which is bound to the parasite. The eosinophils, now blanketing the schistosomula, give the parasite the kiss of death by discharging a toxic substance into it. A few of the parasites escape; why they should be so privileged is not known.

The adult worm and the schistosomula share a number of antigens in common, and it struck researchers that, unaccountably, the immune response stimulated by these antigens killed the young schistosomulae but left the adults completely unaffected. The mystery was solved several years ago when it was discovered that the schistosome is yet another parasitic artful dodger masquerading as a human being. The developing schistosomes acquire host red-blood-cell and certain serum protein antigens on their surface. So when the immunized host's antibody molecules and killer cells come in search of the alien parasite, the schistosome responds, in effect, "There ain't nobody here but us humans."

There is little, or no, host reaction to the adult worm. The parasite isn't killed, but it doesn't excite an inflammatory response. It is the eggs, not disguised by host antigens, to which the host responds vigorously, and these are the chief cause of pathogenicity. You will remember that more than half the eggs become entrapped within the tissues. The antigens, the excreted products of the living miracidium within each egg, are what cause the host to react and overreact. Masses of immunocompetent cells—specialized white blood cells and nomadic macrophages—are mobilized, and surround each egg. Dr. David Wyler, of the National Institutes of Health, has shown that the egg antigens also call forth, and induce proliferation of, fibrocyte cells. In time, the egg becomes encapsulated in a thick coat of fibrous material. The immune system at this time is as hyperactive as the broom of the Sorcerer's Apprentice; it doesn't switch off after its mission has been accomplished. The mass of fibrous reactive tissue about the

egg gets bigger and bigger, replacing the host's normal tissue. The heavier the infection, the more numerous the eggs and the greater the loss or organ tissue. In infection by *S. haematobium* there is early bleeding (the source of the blood in the young men's "menstrual" urine) as the eggs break through the ulcerated bladder wall. As the inflammatory response proceeds, the bladder loses its muscularity, becoming thickened and toneless. Urination in these advanced cases is painful and difficult.

While the pathological changes in the bladder and intestinal wall are undoubtedly serious, the most debilitating effects stem from the *S. mansoni* and *S. japonicum* eggs that are carried to the liver, where they are filtered out into the tissues surrounding the small veins. The egg-induced fibrosis surrounding these vessels can become so extensive that if the liver were cut open it would appear to be transected by a mass of thick white pipes. In fact, pathologists refer to this condition as clay-pipestem cirrhosis. These perivascular collars narrow the vein, and blood flow is impeded. The body's pipes are blocked, and its fluid, the blood, produces a back pressure—portal hypertension. The blood itself also backs up, through the venous connection, and the spleen becomes engorged and enlarged. The lungs may be similarly affected. When the pulmonary blood vessels are obstructed, the burden of the back pressure falls on the heart's right ventricle. The heart makes an effort to compensate, but if the condition is not ameliorated it can be fatal.

If this train of pathological events were to continue, many, if not most, of those infected would ultimately die. Fortunately, the immune system has a regulatory component that dispatches another group of specialized

white blood cells, the suppressor cells, which emit chemical signals to switch off the process. Certain antibodies probably also act as a modulating feedback mechanism. But for some it is already too late when the immune system decides "enough, already," and these individuals either die or remain seriously disabled. *S. japonicum* is particularly virulent, not only because of the high fecundity of the female, but also because the suppressor arm of the immune system seems immobilized in infections with this species. There is also some evidence that for some unknown reason people with blood of group A are more likely to develop severe hepatosplenic schistosomiasis than are infected individuals of other blood groups. Factors such as malnutrition and the presence of other infections also enhance the schistosome's pathogenicity. And always, the children and young adults suffer most.

The "compensated" cases survive and are fit enough to carry on, meeting their modest personal needs. But even in this large group, the parasites exact their subtle toll in human energy. It has, for example, been variously estimated that Egypt loses somewhere between 4 percent and 35 percent of its productivity to the schistosome. The parasite robs each infected Filipino of an estimated $50 to $100 each year, no small amount considering the meager average annual income of the peasant. In a Tanzanian sugar estate where a bonus for extra work was used to measure the effect of antischistosomal chemotherapy on productivity, it was reckoned, at the end of the study, that out of a total labor force of 1,700, the schistosome was in effect deducting 38 laborers.

Water, poverty, and unsanitary habits are the basic ingredients for schistosomal endemicity. The poor of

the tropics will be with us, if not forever, at least for the foreseeable future. Their unsanitary customs are unlikely to change until their economic fortunes improve. But while poverty and habit have perpetuated the infection, they have played only a small part in its intensification. It is the manipulation of tropical water resources, ostensibly for the national good, that is responsible for the spread and increased prevalence of schistosomiasis today. That schistosomiasis will be a consequence of any tropical water-impoundment project constructed for agricultural or hydroelectric purposes is almost axiomatic. A listing of the condemnatory evidence would fill several single-spaced pages. Let us use as representative case histories two of the biggest and most disastrous projects, the Volta project in Ghana and the Aswan scheme in Egypt.

Here is how the Ghanaian industrial-political complex trashed the Volta. Shortly after World War II a treasure in aluminum was discovered in the savanna of what was then a West African British colony, the Gold Coast. The great industrial groups proposed not only to mine the ore but also to construct the means to smelt it within the country. A few years later, when the Gold Coast gained independence and exercised the mandatory prerogative of liberation by changing its name, the president-for-life and self-styled "Saviour of the People," Kwame Nkrumah, seized upon the scheme as a means of propelling Ghana into an age of economic opulence and into political ascendency among the African nations.

The smelting of aluminum ore requires an enormous amount of electrical energy, and the potential for this high wattage lay hard by the ore deposits. The Volta River was to be dammed. Behind the dam would be created the largest artificial lake in the world. It was, at that time, the most ambitious engineering project ever proposed for tropical Africa.

The Volta has a vast watershed, extending to the west, north, and east of northern Ghana. The river enters Ghana as the Black Volta; after flowing some distance along the western border it is joined by tributaries to form the Volta, which courses, half a mile wide, through the equatorial forest. The river then emerges from Ghana's green mansions between two ranges of hills. Through a succession of turbulent rapids, the river descends two hundred feet within a few miles. Below the rapids, the river calms to flow through coastal plains, and finally it divides into a great deltaic system, before debouching into the Atlantic.

In 1966 the dam, two hundred feet high, was completed. Behind the barricade at the Adjena rapids a lake, ultimately 200 miles long, 8,500 square miles in area, with a 4,000-mile shoreline, began to form.

Before the lake was created, schistosomiasis was almost absent in the area. A survey in 1959 revealed that less than 0.3 percent of those living along the upper Volta and its tributaries were infected. The snail vectors along this stretch of river, *Bulinus globosus* and *B. (truncatus) rholfsi,* were not well adapted to rapidly flowing water. The consequently low numbers of snails would account in large part for the low level of infection. In contrast, the delta was like a huge aquarium filled with snails. *B. rholfsi* was abundant in the fresh-water lagoons, and in some delta communities 90 percent of the people were infected with *S. haematobium.*

With the filling of the lake a series of ecological changes occurred, producing a snail-schistosome chain reaction that triggered an infective explosion. The lake

covered an area that had been savanna forest, with many hardwood trees. After inundation the trees died, and the dead trunks acted as a natural underwater palisade, braking wave action toward the shoreline. The resulting still waters were ideal for water weeds, and within a few years the inshore part of the lake was covered with a massive carpet of submerged weeds, predominantly *Ceratophyllum.* The vegetative growth was to provide food and shelter for the snails that were to make their way to the lake. The pioneer snail was *B. rholfsi,* which had lived in the small streams of the upper tributaries. As if sensing an abundance of food and shelter, snails of this species migrated to the lake, and within a short time changed in behavior from stream dwellers to lake dwellers. Now the snail population became massive. Enter the schistosome.

Fish colonized the lake, and fishermen colonized the lake shores. Farmers arrived to farm the lands about the lake. Villages and towns burgeoned, each settlement discharging copious amounts of solid waste (containing the schistosome eggs from infected fishermen). The organic matter encouraged further growth of aquatic weeds, which encouraged further growth of snails, which became infected by the miracidia hatched from the schistosome eggs. The infective cycle had been established.

As the lake filled to its final level the character of the shoreline changed. Where there had been only open beaches, many small coves and inlets began to form. Weeds (and snails) grew unmolested within these pockets of sheltered water. It was in these inlets that the fishermen beached their boats, and here they brought their catch on market days. Great crowds came each market day; villagers would wade into the water to buy fish and, unwittingly, to contract schistosomiasis.

But the children suffered most. The typically water-loving youngsters would come to the lake each day to play and bathe. Their contact with the water was intense. Daily, they were torpedoed by cercariae. By 1969 all—*all*—children between the ages of five and nine in many lakeside villages had *S. haematobium* in their pelvic veins. With puberty the telltale urine tinged with blood gave sign that they had come of age. Their bladders had been bartered for beer cans. And even that sacrifice was for almost nothing. The aluminum production failed to meet expectations, and Ghana's bright dreams of prosperity and political ascendancy faded.

On the other side of the continent another government, that of Egypt, was seeking to attain power and glory from a colossal water-impoundment scheme, the Aswan project. This project was bedeviled from its inception, first by politics—John Foster Dulles in pique denied American funding—and later by the havoc wreaked by ecological-epidemiological consequences. The Soviet Union came to the financial and technical rescue, and a dam 364 feet in height was built at Aswan, behind which the impounded water formed a lake 310 miles long, extending into the Sudan. The Nile was trapped and the river sickened, with bloating in the middle and dryness in the delta.

From its source in Lake Victoria, the Nile flows 3,500 miles to the sea. At Khartoum, in the Sudan, it is joined by the White Nile and this union enters the bleak Nubian Desert; then it flows into Egypt through the gorges and cataracts of Aswan, past the solemn ruins of Luxor and Karnak. It begins to widen as it courses through the fertile valley to Cairo. Below Cairo the great river disperses into a lacework of channels to create the delta that extends 150 miles from Port Said to

Alexandria. The Nile Valley and the delta have, since ancient times, formed one of the most populous and fertile areas of the world.

Into this cradle of civilization, the Nile—swollen by monsoon rains at its headwaters—has overflowed each autumn, bringing with unfailing generosity the rich organic silt that will nourish the next year's crops in the river valley and the deltaic basin. The early Egyptians, in homage to the river's fertile, life-giving force, depicted Hapi, the god of the Nile, as a physically feminized male—an amalgam of male strength and female bounty. The schistosome was present even in those ancient times. Mummies of the Twentieth Dynasty (1200–1075 B.C.) have been found to have mummified parasites within them. The pharaoh's daughter was undoubtedly at risk when she went to fetch the infant Moses from the waters of the Nile. However, until the building of the Aswan High Dam, the schistosome was largely confined to the delta; some 98 percent of the fellaheen there are infected, but as late as 1961 a survey revealed that no more than 5 percent of the population along the upper reaches of the river had schistosomiasis. The river's environment above the delta did not support a large population of snails, and at any rate the current was too swift to allow good contact between cercaria and human. Even in the endemic area of the delta there was an annual relief during the winter season, when the irrigation canals were allowed to dry out for about forty days and the silt, along with the snails, was dredged out.

In 1971, with the completion of the great dam at Aswan and the filling of Lake Nasser behind it, the epidemiology of schistosomiasis in Egypt changed radically. To begin with, the dam made continuous

irrigation possible; the winter closing of the canals was no longer necessary. Year-round human activity and year-round fecal pollution intensified. This led to constant risk of superinfection and since the degree of pathological effect in a person depends in large part on the number of worms harbored, the people became yet worse stricken. In addition, the snail population now began to burgeon. The opaque, silted water of former times had tended to discourage the vegetation growth required by the snail. After the dam was completed the floods of yesteryear were no more and the waters ran clearer. Sunlight could now penetrate the water of the lower Nile, and that part of the river became colonized by masses of floating vegetation, cattails, and other reeds—a wonderful watery world for the snail. *Bulinus (truncatus) rholfsi,* the vector of *S. haematobium,* began to breed even more prolifically. What was even more disturbing, the population of *Biomphalaria alexandria,* the vector of *S. mansoni,* which was formerly present in only modest numbers, also began its explosive increase.

Finally, the upper Nile also became diseased. The water slowed. There was more vegetation and a consequent increase in the number of vector snails. Today, the prevalence of infection is still increasing in the growing communities along the Nile. In Lake Nasser an algal bloom has appeared, and snails, many of them already infected, are beginning to move into the area and establish themselves. It is only a matter of time before the lake becomes heavily schistosomatized.

The beneficiaries of the Aswan project were the snail and the schistosome; they flourish. Certainly the land was not a beneficiary; it lost its yearly rejuvenation of silt and became less fertile. Nor was the suffering sardine, which for reasons not completely understood all but dis-

appeared from the Mediterranean waters near the mouth of the Nile after completion of the dam. The failure of the sardine fishery meant the loss of an important protein food source, and has brought poverty to thousands of fishermen. Nor were the fellaheen beneficiaries; they assumed an even greater parasite burden. But governments will have their dams, and as long as the chic of Araby have their way with the world's petroleum resources, hydroelectric power will be a seductive alternative, despite the capital costs for construction, staggeringly high to the energy-poor Third World. Unfortunately, the (hydro) electric bill too often contains a high schistosomal surcharge.

If schistosomiasis were present in Sweden or in the United States it would not be tolerated. The infected would be treated and hospitalized when necessary, with the costs taken care of through the national medical services (in Sweden) or through health insurance, Medicaid, or a second mortgage (in the United States). Lakes, rivers, ponds, and streams would be patrolled and warnings would be posted to the effect that "defecation in this water is a punishable offense." An army of scientists would be turned to the problem. No expense or effort would be spared in extirpating the worm from the citizenry. But schistosomiasis does not exist in affluent nations; it is an infection of the poorest people of the poorest nations. The peasant farmer and fisherman cannot afford Thomas Crapper's ingenious invention, the flush toilet, and will continue to relieve themselves in lake, river, and rice paddy. Present-day drugs are too expensive and noxious to be administered en masse by the usually inadequate and underfunded medical services. How then to loosen the schistosome's grip on its impoverished domain?

Prior to World War II the main emphasis in the control of vector-borne diseases, including schistosomiasis, was on personal and environmental sanitation; actions for this purpose ranged from sleeping under a mosquito net to draining swamps. Hygiene and sanitation were relatively effective but required constant attention and, often, large amounts of manpower and community participation. The postwar discovery of effective antimalarials and insecticides radically altered the strategy of control. If great masses of people could (theoretically) be protected by antimalarial drugs, why could they not be given schistosomicidal pills? If the anopheline-mosquito population could be reduced to an extent that interrupted transmission, why couldn't the snail population be similarly reduced by molluscicides? In the 1940s and 1950s a crossroads was reached in the development and selection of control measures, and the main road followed was paved with chemicals. The paths to control by biological means, environmental measures, or the development of methods to afford immune protection, diminished to relatively insignificant byways.

The synthetic promise offered by the antimalarials and insecticides was never fulfilled for the control of schistosomiasis. There is nothing comparable to the antimalaria pill that can be routinely taken at breakfast. I can bear personal witness to that. When I finally emerged from my nine-year sojourn in Africa, a routine medical examination revealed that I had acquired a light, asymptomatic infection of *S. mansoni.* At that time there was some evidence that Mansonian schistosomiasis caused or predisposed to liver cancer. The issue has been debated for many years without decisive resolution; there is a stronger case for the relationship of bladder cancer to urinary schistosomiasis. My friend and

physician Alan Woodruff, professor of clinical tropical medicine at the London School of Hygiene and Tropical Medicine, is a cautious man, and with a "no nonsense from you, Desowitz," he had me admitted to the London Hospital for Tropical Diseases. He also assured me that he was in possession of a new sovereign remedy, a new form of antimonial compound that was free of the adverse side effects usual to antimonial drugs. The antimonials are organic preparations of the heavy metal antimony; they have been the sheet anchor for the treatment of schistosomiasis. But they have a medieval quality in that they kill the parasite just before they would do in the patient.

I entered the hospital hale and hearty to have a two week-course of drug infiltrated into the nether region of my person. The "nontoxic" drug produced an almost unbearably itchy rash and constant nausea, and made my heart's electrical circuitry do a few abnormal flip-flops. I had never felt so miserable. Since that time, drugs have been discovered that are somewhat freer of those side effects—but somewhat less effective. The point of my tale is that I had the closest and best medical attention, as well as the intellectual understanding to accept and perservere through the therapeutic course, while the average infected peasant, by contrast, would have none of these support systems. Probably, the severely affected persons of all economic and cultural strata would agree to treatment. However, if there is to be any impact on public health, all egg passers must be treated, and many of them are asymptomatic. Among those without symptoms, willingness to undergo treatment is very limited. At least one new drug, praziqantel, has shown efficacy and freedom from toxicity in its early trials. If this promise is confirmed, perhaps a satisfactory degree of control can be achieved, providing cooperation can be obtained from the untutored masses.

Except in limited demonstration trials, molluscicides have not proved to be any more effective than the drugs. Today's chemical snail killers have not been able to suppress vector populations over long periods of time or in large bodies of water. Except for the two-sexed vector of *S. japonicum,* all the snail vectors are hermaphroditic, so the few snails that survive molluscicide application can rapidly repopulate a body of water once the chemical pressure is removed. New, more potent molluscicides are in the works, as are baits to attract and concentrate the snails around the chemical depot. Undoubtedly some of these compounds will prove splendidly effective. They will also undoubtedly be staggeringly high in cost, particularly those of petrochemical derivation, and the invoice's bottom line will almost certainly deny science's bounty to those in greatest need of it.

Unlike most of the other afflicted nations, the People's Republic of China decided, almost thirty years ago, to bite the bullet rather than await deliverance by research's promised missiles. According to the Maoist bestiary the threatening creatures—tigers, Americans (at a less amicable time), and schistosomes—have a dual nature. These enemies are at once formidably real and vulnerably weak. It was Mao's view that all of China's adversaries could be felled by the irresistible strength emanating from the collective will of the people. I think it a telling insight into the Chinese revolution that among the first targets to which this strategy was applied were the schistosome and the snail.

For many hundreds—probably thousands—of years, japonicum schistosomiasis had been one of China's most

important health problems. In 1940 it was estimated that over 100 million people were at risk and at least 10 million infected. Whole villages were debilitated by hepatic schistosomiasis, and since these were mainly agricultural communities the economic loss to the entire country was serious. In 1949, within a year of taking power, the revolutionary government decided to launch an antischistosomiasis campaign, not only to improve health but also as a primary step in politicizing the populace by collective action. The Chinese realized that their industrial base was weak. They did not have the chemical industry to produce drugs and molluscicides in sufficient quantities for a national campaign. But they had people power; what they lacked in capital and technology was balanced by the labor potential from hundreds of millions of workers. In 1950 the "People's War against the Snail" opened with an intensive educational broadside. Peasants were informed about the disease and the strategy of the coming campaign by posters, radio talks, and lectures to village communes by the first barefoot doctors (the handbook given to these auxiliaries exhorted them to "be brave and not afraid of hard work"). During the next year hundreds of thousands of farmers, joined by teachers, students, soldiers, and factory workers, began the labor of dredging canals, draining ponds and swamps, building embankments, and even removing snails, one by one, with chopsticks. Snails of the genus *Oncomelania* (the vector of *S. japonicum*) were buried and suffocated beneath the dredged mud. Later in the campaign, molluscicides of local manufacture were applied to areas where the snails persisted. Mass fecal examinations were carried out and the individuals found infected were treated with the drugs that had been given priority of manufacture by the nascent pharmaceutical industry. But of paramount importance was the stern sanitation discipline imposed. Indiscriminate defecation was no longer permissible under the socialist way of life. A simple, odorless water-seal latrine was devised, in which worm eggs—not only of schistosomes but of all intestinal parasitic worms—were killed in the sedimented sludge. This simple sanitary device provided multiple benefits: it was a great success in reducing parasite transmission, the processed excreta were recycled as fertilizer, and the methane gas from the sedimentation tanks lit homes and cooking fires.

Although these measures have greatly reduced schistosomiasis in China, to a point where it is no longer a serious menace to health, the infection has still not been completely eliminated. The low levels of residual infection and snails are a slumbering threat. During the height of the antischistosomiasis campaign, Chairman Mao was moved to write the poem "Farewell to the God of Plague." The constant effort of community action keeps this malign god at bay in China, but in other parts of the world the health of millions continues to be sacrificed at his altar.