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### 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 suzerainty? 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 chemico-physiological 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 sub-

stance 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 of 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 ascendancy 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 cre-

ated 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 persevere 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, praziquantel, has shown efficacy and freedom from toxicity in its early trials. If this promise is confirmed, perhaps a satisfac-

tory 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 manufac-

ture 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.