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MOSQUITOES AND HUMAN HEALTH

J. GORDON EDWARDS

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During the war in Europe, in 1944, we went to sleep every night while being fed upon by bedbugs and fleas, and there was no way to escape them. We heard about "cooties" (body lice) causing typhus, which killed nearly four million people in Europe and vicinity during the first world war, and I had read that Napoleon's army was decimated by typhus while invading Russia, and that 20,000 of his men died while retreating through the town of Vilna, Poland. According to the *Saturday Evening Post,* August 1942, he invaded Russia with 500,000 troops and returned with only 5,000.

One day I was ordered to dust every soldier in our company with an insecticidal powder that had just been received I later learned that material was produced by a German chemist, Othmar Zeidler, in 1874. He made hundreds of chemical compounds but he never suggested uses for any of them. Sixty years later, in Switzerland (1939), Dr. Paul Müller was seeking chemicals that might kill insect pests, and he followed Zeidler's written directions for preparing several compounds. One of them was a compound that Zeidler had labelled dichlorodiphenyl-trichloroethane. Müller called it "DDT" and received the Nobel Prize in 1948 for his work with that chemical. For two weeks I dusted the insecticide on soldiers and civilians, breathing the fog of white dust for several hours each day. The body lice were killed, and the DDT persisted long enough to kill young lice when they emerged from the eggs. Fortunately, no humans were ever harmed by DDT.

Dr. Joseph Jacobs later described his role in producing the first DDT made in the United States. At Merck & Company in New Jersey, he was assigned the task of duplicating Zeidler's procedure, but on a much larger scale. He commandeered a huge glass-lined reactor and produced the first 500 pounds of DDT made here. An Army truck rushed it to an airport and it was flown to Italy, where it halted a developing epidemic of typhus in our troops. The surgeon general telegrammed thanks, from President Roosevelt, and stated "It is estimated that 5,000 lives were probably saved by destroying the typhus-carrying body lice infesting our soldiers."

After the war I entered Ohio State University to study entomology. Insects are the most abundant forms of life on earth. Fortunately, only about 1% of them compete with humans for food, fiber, and space. A small part of that 1% threaten our health with stings or bites, and a few transmit serious diseases.

I received my PhD for research on beetles, and was hired to teach entomology at San Jose State University, There I spent much time studying parasitic insects, and taught medical entomology courses for more than 30 years. In addition to louse-borne typhus, our students were required to learn about diseases caused by mites, ticks, fleas, kissing bugs, black flies, chiggers, sand flies, eye gnats, tsetse flies, and mosquitoes.

Science magazine (9 June 1972) reported that "more than 80% of human infectious diseases are transmitted by insects, mites and ticks." They have caused the death of hundreds of millions of people by infecting them with the pathogens that cause typhus, bubonic plague,

yellow fever, malaria, dengue fever, sleeping sickness, encephalitis, elephantiasis, leishmaniasis and yaws.

In Europe there have been more than 150 typhus epidemics. During the Thirty Years' War typhus reduced the population from 30 million to just 13 million, killing 14 times more people than died in battle.

A Mexican typhus epidemic was being studied by Howard Ricketts, who died of typhus three weeks after becoming ill. In Poland, Stanislas von Prowazek also died of it. Appropriately, scientists named the pathogen that causes typhus *Rickettsia prowazeki.*

A *Saturday Evening Post* article (August 1942) was titled "Blitz Plague." It referred to the body louse as "the mass killer which has slaughtered 200 million people in Europe and Asia alone, diverted the stream of history and done more than any other single factor to determine the outcome of wars." It reported: "This year, in the Polish town of Vilna, where typhus once killed 20,000 of Napoleon's troops retreating from Russia, railway employees were forbidden to approach trainloads of infected German soldiers returning from the Russian front. When infected, a person's fever often reaches 107 degrees, with excruciating headaches and delirium. Mortality rates may be as high as 70%." "American troops may have an edge on the Axis, for they have a promising new anti-typhus vaccine that was developed by Herald Cox at the Rocky Mountain Spotted Fever Laboratory in Hamilton, Montana in 1939. Previously, in typhus research labs, almost every medical laboratory worker was stricken and more than a third of them died of the disease."

In the 14th century, fleas that sucked blood from sick rats ingested pathogenic bacteria that were later named *Pasteurella pestis.* When

those fleas then bit humans, they transmitted bubonic plague to them. That plague (the "Black Death") killed one-fourth of the population of Europe and two-thirds of the population of the British Isles.

But mosquitoes have been the worst of all!

More than 3000 species of mosquitoes have been described in scientific journals. Most of them are in tropical areas, where as many as 150 species have been found in a single square mile. U.S. contains about 170 species, Canada 70, and Arctic lands less than two dozen. In the Canadian Arctic, researchers who bared their arms. legs, and torsos in an experiment reported as many as 9,000 bites per minute. Unprotected humans could lose half of their blood in two hours, and die. Hundreds of cattle and horses have been killed by just such exsanguination, in our southeastern states.

Yellow Fever is caused by a virus transmitted by *Aedes aegypti* mosquitoes. Perhaps the disease was brought into America with slaves in the 1500s, but it could have originated in monkeys in Central America, which still have it.

The name of this disease refers to the yellowing of skin that results. After a 10-day gestation period, there is a sudden onset of fever, with aching, nausea, bleeding from digestive tract, lungs, nose and mouth, and severe vomiting (frequently bloody). Mortality rates from yellow fever often exceed 50% of the cases.

In 1542 Hernando DeSoto suffered with it and almost half of his troops died of it in what is now Florida. In 1741 England sent Admiral Edward Vernon with 27,000 men to Mexico and the Louisiana Territory. They retreated after 20,000 were killed by yellow fever. In

1802 Napoleon's brother-in-law, Charles LeClerc came to the Louisiana Territory with 33,000 soldiers, but gave up after 29,000 of them died of yellow fever.

Napoleon had envisioned a French colonial empire in the New World, but after such severe losses he did an about-face and sold the Louisiana Territory to the American colonists for $15 million, nearly doubling the size of our country. Some historians say that the sale was a result of yellow fever killing 40,000 French troops.

In 1900, in Cuba, the U.S. Yellow Fever Commission investigated the disease, under the guidance of Walter Reed, James Carroll, Jesse Lazear, and A. Agramonte. Their research with human volunteers proved that the fever was transmitted only by the bites of *Aedes aegypti* mosquitoes, rather than personal contacts. See U. S. Army Yellow Fever Commission, in *U. S. Senate Document* No. 822 (27 January 1911) for details. Attempts to eradicate those mosquitoes almost succeeded in Central America and the Caribbean, but failed in southeastern United States, where they still abound. Their larvae thrive in junk yards and auto wrecking yards, where they live in used tires and other small containers of water. Yellow fever vaccines have been available since 1942 but must be kept refrigerated. That is a problem in hot countries, especially since Freon was unwisely banned by our pseudoenvironmentalists. More than 400 million people have been given the vaccine.

In Central America a pretty native jungle mosquito, *Haemagogus spegazinii,* transmits the virus from monkey to monkey in the tree tops. If a tree falls in the jungle and humans are nearby, the *Haemagogus* can transmit the virus to them. Those humans may then serve as reservoirs of the fever in their villages.

Mosquitoes transmit many other kinds of viruses, causing illnesses such as Eastern Equine Encephalitis (EEE), Western Equine Encephalitis (WEE), St Louis Encephalitis (SLE), Japanese B Virus (JBE), Venezuelan Equine Encephalitis (VEE), and West Nile disease. An epidemic of SLE in 1933 devastated St Louis and several other cities as far east as Louisville KY. More than 1,000 cases resulted in 266 deaths. Japanese B Encephalitis has been very deadly in Japan and Korea. In 1924 Tokyo had 6,000 cases, and 3,800 died. In 1948 Japan had 8,000 cases and 4,750 died. The vector, the Asian Tiger mosquito (*Aedes albopictus*) is now well established in the United States. and has already transmitted fever viruses to children in southeastern and midwestern states, and in Texas. Transovarial transmission may pass encephalitis viruses from female mosquitoes to their larvae, via infected eggs.

Dengue Fever is also known as "Breakbone Fever" because the virus causes extreme aching of joints, even the joints between plates in the skull. Many kinds of mosquitoes transmit the virus, but *Aedes aegypti* is the major vector. In Guam, 98% of the American troops were infected. Some of my students served with the U. S. Navy and had been infected with dengue. They told me the pain was "indescribable" and one said: "when I had malaria I was afraid I might die, but when I had dengue I almost wished that I could die." The only medication they had was aspirin, which gave very little relief. In addition to the fever and other symptoms, the dengue virus causes great pain in the eyes, "like someone has his fingers behind your eyeball and is trying to pull it out." A first exposure to dengue is not often fatal, but re-exposures are more serious, with about 15% mortality caused, especially in children

The Asian Tiger Mosquitoes, *Aedes albopictus*, are efficient carriers of the dengue virus. When they first invaded Brazil, there were only 6 dengue cases in Rio (in 1985). In just one year the mosquitoes spread the fever to 350,000 people! In 1985 some of these mosquito larvae were shipped into Houston Texas from Japan, in old automobile tires, They can breed successfully in as little as a quarter inch of water. In Evansville, Indiana, they were also breeding in piles of old tires. The piles were sprayed with insecticides every day, for 11 days, but swarms of adult mosquitoes still emerged. In early July 2001, Tiger Mosquitoes were found in the San Francisco Bay Area of California. They had just arrived from China, in a shipment of live bamboo plants. The larvae had matured in the water surrounding the plant roots. They will probably extend their range from coast to coast, and many encephalitis cases should be anticipated.

MALARIA

Sir Ronald Ross, a British Army Surgeon in India, proved that only in *Anopheles* mosquitoes could the malaria protozoans complete their development, and that those parasites were in the saliva of the mosquitoes. He received the Nobel Prize in 1902 for his research on malaria.

There are over 300 species of *Anopheles* in the world, but only 60 are closely associated with humans. Others feed on snakes, lizards, rodents and birds. Avian malaria is a major cause of bird deaths. When marshes were sprayed with DDT to kill mosquitoes that bothered people, bird populations in the marsh frequently increased very rapidly, because the adults and the nestlings were no longer getting malaria.

Humans have suffered from malaria for centuries.

In Babylon, on 28 June 323 BC, Alexander the Great died of malaria. He was 33 years old and had already conquered Egypt, Syria, Persia, Arabia, and Northern India. Alaric, King of the Goths, conquered Rome in 430 AD, but then died of malaria.

That Old World disease was brought to this hemisphere many times, but perhaps first by Columbus' sailors.

During the construction of the Panama Canal, William Gorgas used massive amounts of oil and other poisons to eradicate the mosquitoes from 100 square miles of jungle. Malaria was reduced from a frequency of 800 of every 1000 workers in 1906 to only 16 per 1000 workers, by 1916.

The California Mosquito Abatement Program was established in 1911, to control a malaria epidemic near the Sacramento River delta that had wiped out half of the residents. In 1914 U. S. had 600,000 cases of malaria, most of which were in California and Florida.

According to the *WHO Newsletter*: several thousand malaria cases developed in 1919 near Archangel, Russia (64 degrees North Latitude), and in 1923, Russia had 5 million cases of malaria, with over 60,000 deaths.

In the United States, in the 1930's, there were still more than six thousand malaria victims every year. People at greatest risk protected themselves by swallowing bitter quinine pills three times a day. That

method of protection was also used by British workers in malarious countries, and they discovered that drinking gin and tonic to wash the pill down made the quinine less repulsive.

An epidemic in Brazil, in 1938, was spread by imported *Anopheles gambiae*. There were more than 100,000 malaria cases, and 14,000 of the victims died within six months

Malnourished feverish malaria victims simply can not perform the necessary labor in the fields. Before the 1940s India produced less than 25 million tons of wheat per year, and starvation was widespread. Protein deficiencies also caused conditions such as marasmus and kwashiorkor. After DDT reduced malaria rates, India's farmers produced more than 100 million tons of wheat annually, and the nation's health was vastly improved.

Prior to their National Malaria Campaign, India had more than a million cases annually. The DDT anti-malaria campaign resulted in the number of deaths dropping from 750,000 annually to just 1,500 deaths per year. Also, their average longevity of 32 years increased to 45 years.

During WWII the South Pacific was a great center of malaria. On Guadalcanal the annual malaria rate among our troops was 1,800 cases per 1,000 men. (Meaning that most of them had malaria twice during that year.) After DDT became available the malaria rate there fell to about 40 cases per 1,000 men.

The Mediterranean island of Sardinia suffered 40,000 to 70,000 cases of malaria per year in the early 1940s. After DDT was applied, the infestation dropped to just 44 cases, in 1950.

In Ceylon (Sri Lanka), in the 1950s, there were 3 million malaria cases a year, with over 12,000 deaths. DDT reduced the number of cases to only 31 in 1962 and a total of 17 in 1963 (with no deaths). Unfortunately DDT use was stopped there and malaria rates soared to 1700 in January 1968, 42,000 in February 1968, and nearly two million cases in l969.

TDR News, June 1996. In Africa, before DDT, 1.5 to 2.7 million people died from malaria every year. Malaria still kills half of all children there before they are five years old. Bed nets cost $5.00 and it costs 50 cents a year to treat a net with permethrin (a synthetic pyrethroid insecticide). Nets that are thus treated will repel or kill all mosquitoes for at least a month. Those nets are saving the lives of 500,000 African children from malaria, every year.

Kevin Baird (U.S. Navy Commander) says that in malarious regions "Even if a person sleeps in a screened room under a bednet he or she will still receive roughly one infectious bite a week" and "There are parts of Africa where persons will get infectious bites every day."

Malaria Plasmodia Are Not All Alike

Four species of *Plasmodium* can cause malaria in humans. They are *P. vivax, P. falciparum, P. ovale* and *P. malariae.* The members of those species differ morphologically,

behaviorally, and physiologically. Their plasmodia pass through three major developmental stages (sporozoites, merozoites, and gametozoites). The blood of a person suffering with malaria has blood containing all of those stages. When a female *Anopheles* sucks up that blood, all of those stages enter the mosquito stomach. (*Anopheles* males do not eat vertebrate blood.) The gametocytes mature in the mosquito stomach and engage in sexual reproduction there. The resulting zygote penetrates the stomach wall and becomes an oocyst attached to the outside of the stomach, bathed in the blood of the mosquito hemocoele. More divisions occur in the oocyst, releasing hundreds of young plasmodia (called sporozoites) into the mosquito blood. A large number of them enter the mosquito salivary glands, and when the mosquito feeds, thousands of sporozoites are injected with the saliva. They travel very quickly to the human liver, where they multiply asexually for 6 to 12 days, producing hundreds of thousands of "merozoites" which then enter the bloodstream. Each one can invade an erythrocyte and reproduce asexually there, producing 6 to 26 new erythrocytes. In tertian malaria, that only takes 48 hours, but in quartan malaria it takes 72 hours. At the end of that time the new generation of merozoites bursts out of all the invaded erythrocytes and quickly burrow into new ones. After another 48 or 72 hours they synchronically burst out of the blood cells and repeat the process. When merozoite numbers exceed 50 per cubic milliliter of blood (more than 150 million merozoites in a 140 pound person) the victim suffers a chill because of the shortage of functional red blood cells. As the erythrocytes are ruptured, toxins are released, resulting in fevers of 96 to 104 degrees. Frequently victims also suffer with hallucinations and extreme anxiety. The human spleen removes sporozoites and merozoites from the blood, and becomes enlarged as a result. The swollen spleen is one symptom

relied on to diagnose malaria. Kidney failure may also result in "blackwater fever," so-called because dead blood cells in the urine causes it to become a dark mahogany color. Cerebral malaria occurs if abundant parasites plug capillaries in the brain, and death may then result very quickly.

Falciparum malaria accounts for over 90% of all malaria fatalities. Thirteen percent of its total genetic material is in variable genes that can switch on and off, fooling the immune response. The mortality rate of untreated falciparum malaria is 30 to 40% (about the same as for plague)

In quartan malaria, caused by *Plasmodium malariae*, the life cycle takes 72 hours, so the attacks of chills and fever occur every fourth day. The entire life cycle of the other three species of *Plasmodium* takes only 48 hours, so the chills and fever recur every third day, and the disease is called "tertian malaria." *Plasmodium vivax* and *P. ovale* cause a relatively mild "benign tertian malaria," but *Plasmodium falciparum* causes potentially deadly "malignant tertian malaria." If the victim has paroxysms more often than every 48 hours, it indicates that multiple infections have occurred, and the ailment is called "quotidian malaria."

How Malaria Plasmodia Are Protected

The malarial parasite has 14 chromosomes and perhaps 7000 genes. Researchers have predicted that "within five or ten years they will have a vaccine that will actually save lives." (They have been predicting that for 25 years, but no effective vaccines are yet available!) Difficulties include the plasmodia being able to avoid human antibodies in the blood, and the plasmodia not staying long enough in the human liver to be attacked by cytotoxic T cells there. When the merozoites are inside the human erythrocytes they are safe from the immune system, and they multiply so furiously that "even if an immune response kills 99% of them, there are likely to be enough parasites left to multiply and cause disease to continue to develop." The primary antibody target on the sporozoites is a protein in the parasite's surface, but sporozoites are proficient at evading the immune system of human blood systems. When an infected mosquito bites, thousands of sporozoites enter the human blood, however they quickly enter the liver (in less than 10 minutes) before the antibody response can be effective. There they are safe from the antibodies. In the liver it takes 10 or 12 days for killer T cells to develop, and the parasites do not stay there that long. Each sporozoite in the liver forms a reproductive stage that produces about 30,000 merozoites, which quickly enter erythrocytes, where they are thus safe from both the antibodies and the T cells. Each developmental stage (sporozoites, gametocytes and merozoites) may mutate independently **and** frequently, so within each population there develop slightly different "strains" whose members may differ significantly.

Immunity to vivax malaria sometimes develops naturally. Fetal hemoglobin is evidently not favored by mosquitoes, so babies

may have a degree of resistance to malaria. It takes about five years for adult humans to develop partial immunity to vivax plasmodia (*Natural History* July 1991), and if the person moves to another location the immunity may be lost because of local differences in the plasmodia.

A different kind of immunity to malaria occurs in people who suffer from sickle-cell anemia. They have erythrocytes that are hard and somehat curved, and are not good hosts for the malaria plasmodia. Children who inherit the gene for sickle cell from both parents usually die early, of anemia. If they inherit the sickle cell trait from only one parent they are likely to live, and they will not suffer as much from malaria because the plasmodia do not prosper in sickled cells. A "balance" therefore exists between homozygous sickle cell victims (who may die of anemia), homozygous non-sickle-cell victims (who may die of malaria), and heterozygous individuals who may suffer slightly from both the anemia and the malaria but are not killed by either.

When a DDT malaria control operation is under way, the inhabitants are simultaneously protected from other insect-transmitted diseases, including plague, typhus, yellow fever, dengue fever, hemorrhagic fever, leishmaniasis, elephantiasis, river blindness, and sleeping sickness.

Frances B. Smith, executive director of Consumer Alert, stated that the DDT and malaria issue reveals greater human

risks, including the tragic deaths of millions of people, mainly children, in developing countries. "DDT, as used for local mosquito control, poses little risk to human health or the environment, yet it is one of the most affordable and effective tools for controlling malaria."

Because environmental extremists raised unwarranted fears about DDT, the spray programs were reduced and there was a resurgence of malaria that is still continuing. There are now over 300 million cases of malaria, and the number in South Africa has risen by over 1,000 percent in the past five years.

Today, more than 2 billion people – 40% of the earth's population -- live in malarious countries. About 270 million of them are infected with malaria, and there are nearly 300,000 new cases every day. More than 30% of childhood deaths in Africa are due directly to malaria.

Mosquitoes Are Not All Alike

Adult female *Anopheles* have palpi about as long as their proboscis, while all other female mosquitoes in the United States have very short palpi.

In both sexes of *Anopheles* the top of the abdomen bears slender hairs instead of the flat scales that occur on the abdomen of our other mosquitoes.

Adults of genera *Culex* and *Culiseta* have the abdominal apex blunt, or rounded, but in the genus *Aedes* adults have the tip of the abdomen slender and pointed.

Mosquitoes develop in four larval stages, followed by the pupal stage. The time from egg to adult may be as short as 4 days, but usually is a week or two, depending on temperature and food.

The larvae (wrigglers) of most mosquitoes have a slender breathing tube at the end of the abdomen, and the body hangs downward from the breathing tube (the tip of which is at the water surface). *Anopheles* larvae have no such breathing tube, and their body floats parallel below the water surface.

Anopheles eggs have a buoyant "float" on each side, and they float individually on the water surface.
Culex and *Culiseta* eggs are deposited in "rafts" that float atop the water, while *Aedes* eggs are deposited individually in the sand or mud by the water's edge.

The behavior and habitat preferred by members of the different species are very specific. Some larvae live only in fresh water, others only in stagnant water, brackish water, or saline water. Some prefer sunny water, others only live only in shaded areas. A few kinds live only in the water in "tree-holes."

Blood meals are usually required before parasitic insects can produce offspring, however some species of mosquitoes are "autogenous" and can produce eggs without having a blood meal.

Entomologists employed to control mosquitoes must be able to identify each adult mosquito seen, and know exactly where their larvae will be found. If those larvae can then be killed, the emergence of adults that would otherwise be feeding on blood (and perhaps transmitting diseases), will be prevented. Unfortunately, even after the habitats are located it may now be impossible to control the blood-sucking pests, because environmental regulations restrict all water management procedures, and prohibit the addition of effective chemicals to the water or air. The introduction of minnows to destroy the mosquito larvae may also be prohibited, because those minnows also eat other small aquatic invertebrates, some of which have been listed by the EPA as "endangered" or "threatened" species. Any alteration of their "critical habitat" is also illegal under the EPA's Endangered Species Act.

Chemicals to Prevent Malaria

TDR News, Feb 2000 Antimalarial chemical medication might either (1) destroy the sporozoites or merozoites in human blood, or (2) destroy some of the plasmodia in human liver cells.

Natural History (October 1989) reported that in the 1630s Incas told missionaries in Peru about tree bark that cures malaria. Bark from the Cinchona tree was taken from Peru to Europe in 1652, and cured malaria. 200 years later, quinine was discovered to be the chemical in Cinchona bark that was so effective in relieving malaria symptoms. Natives in Peru and Bolivia engaged in the bark trade, getting about $15 for a hundred pounds of bark. Some seeds were smuggled out and planted in Java, where selective breeding developed trees with bark

containing 15% quinine. Eventually they produced over 95% of the world's quinine, but early in World War II Japan occupied Java, and the quinine was no longer available to other countries. (*Natural History*, January 1948) Quinine is now readily available, but the bitter 0.6 gram quinine pills must be swallowed three times a day, and they cause ringing of the ears, kidney damage, and (sometimes) blackwater fever. They kill merozoites, but only some sporozoites.

For hundreds of years Qinghaosu (Artemisinin) was a popular medication in China but not elsewhere. It is derived from the leaves of a common composite weed named Sweet Wormwood, *Artemisia annua* (L.) and was described in a 1527 treatise on Chinese herbs by doctor Li Shi-ze. (*Natural History,* October 1989) There are about 400 species of *Artemisia*, but of the 100 species tested, only *annua* was found to produce the curative chemical, artemisinin. Artemisinin has been synthesized by chemists in Switzerland, United States, and China, but the price is too expensive for mass production.

Clinical trials in China suggested that injectable artemisinin could cure as many as 90% of cerebral malaria cases. Safety data are not yet complete, and the World Health Organization expressed concerns about possible neurotoxicity in animals. Donald E. Davidson (of the TDE staff) says qinghaosu has the structure of a sesquiterpene lactone, with an internal peroxide linkage. It may be recommended, either by tablet or injection, for malaria victims who can not tolerate quinine. Tests indicate foetotoxicity in rodents, so use is discouraged in pregnant women. Two derivatives, Artemether and Artesunate, are more water soluble than the parent compound but the developer of artesunate, Nicholas White, warns that it may have neurotoxic effects at high doses (injury to the brainstem).

Science 20 October 2000, pages 437-439. "Reinventing an Ancient Cure for Malaria." Resistance is making every antimalarial drug useless. Nicholas White, in Bangkok, expresses hope for artemisinin, extracted from *Artemisia annua,* that has been used a malaria remedy in China for nearly 2,000 years." A report in *The Lancet*, 22 July 1994, stated that artesumate was nearly 100% effective, when combined with mefloquine.

To replace quinine, the Germans manufactured Atabrine in 1936. It caused no ringing ears and no kidney damage, but caused skin to turn yellow for months afterward. The big pills were only taken once a day. It killed the merozoites in red blood cells.

Primaquine (1940's) kills gametocytes in human blood, as well as destroying merozoites before they get from the liver into the blood.

Chloroquine and amodiaquine kill the plasmodia in the red blood cells. In the early 1950's Americans developed chloroquine compounds: hydroxychloroquine (= plaquenil) and chloroquine phosphate (= Aralen). In Cambodia and in Brazil chloroquine was sometimes added to salt, which was given free to natives and protected them from malaria. Both chloroquine and quinine block the removal of heme, which is a byproduct of hemoglobin degradation, and is toxic to plasmodia.

Chloroquine phosphate (Aralen) was the preferred antimalaria protection for decades. The small pill was taken once a week, beginning two weeks before entering the jungles and continuing for 6 weeks after returning. It was widely used, until it lost its effectiveness in the late 1990's. Aralen suppressed *vivax, ovale* and *malariae*

plasmodia, and entirely cured *falciparum* malaria UNTIL a resistent strain appeared in Viet Nam in 1955.

If *falciparum* malaria becomes resistant to chloroquine, go immediately to quinine therapy (2 grams a day for at least four days. (BUT some *falciparum* are also resistant to quinine.)

In 1967 the government was screening 60 to 70 new chemicals and spending over $11 million seeking drugs that might prevent or cure resistant *falciparum* malaria.

Fansidar is a 1970's combination of pyrimethamine and sulfadoxine. These antimetabolites kill the sporozoites before they reach the liver. Until recently Fansidar was recommended for protection, but severe allergic rashes have been caused in a few people.

Mefloquine (Lariam) was approved by U. S. in 1989 for malaria control. Taken once a week, it is a potent killer of merozoites, but about 20% of takers may suffer unpleasant symptoms such as nausea, dizziness, vivid dreams, hallucinations, and severe attacks of anxiety. It has a half life of about 21 days in the human body.

Altocid - This is an insect growth regulator produced in 1978 by Zoecon Industries in Palo Alto, at a developmental cost of $11 million. It inhibits the growth of larvae into adult mosquitoes. It mimics a mosquito hormone that regulates growth and pupation. The larvae develop normally, but the pupae fail to become adults.

On the first page of *the CDC Morbidity and Mortality Weekly Report* for 12 April 1986 it states: "Travelers must be informed that regardless of the malaria prophylactic regimen employed, it is still possible to contract malaria."

TDR News, Feb 2000 and *Science*, 17 March 2000, reported that in 1999 a WHO-funded agency, "Medicines for Malaria Venture" (MMV) was established. They had a budget of $4 million (in 2000) and their goal was $30 million a year, which the director said "is enough to produce one new antimalaria drug every five years." If adequately funded, they intend to decode mosquito genomes and pathogenomics and seek new approaches for drug discovery.

The Communicable Disease Center in Atlanta reported that they receive 1,000 to 1,500 reports a year of travelers accidentally bringing malaria into the United States. This may result in malaria surprising victims who have never left the United States.

In 1952 a Korean war veteran had a relapse while camped for a weekend near a girl scout camp in Nevada County, California. As a result, 35 of the girls got vivax malaria. (9 cases that fall, and 26 cases in the following spring.)

Pesticides to Control Mosquitoes

To control *Anopheles* mosquitoes, DDT was sprayed on inside walls once or twice a year. In 1959, spraymen applied 60,000 tons of DDT to the inside walls of 100 million houses. The cost was

$205,000, but if substitutes were used, malathion would have cost $637,000 and propoxur would have cost $1,762,000 for the same control. A 1.5 oz. whisky jigger full of 70% wettable DDT covers 144 square feet of wall surface, killing all mosquitoes that land there during the next six months. There was never any need to wear masks or protective clothing. No adverse effects were ever experienced by the 130,000 spraymen or the millions of people living in the sprayed houses. *(The Lancet,* 15 July 1972) There is a strong correlation between reduced wall spraying and the tremendous increase in malaria cases.

WHO Press Release 16 July 1969. The World Health Organization tested more than 1,300 pesticides, seeking effective substitutes for DDT in mosquito control. Only four approached DDT's effectiveness. They were: Malathion, Aprocarb (Baygon), fenthion, and fenitrothion. All were more hazardous to humans than DDT and were four to twenty times more expensive than DDT.

Non-Toxicity of DDT to Non-Insects

Because I kept hearing propagandist claims that DDT is toxic to people, I studied all of the relevant scientific and medical literature. Some details are mentioned below.

In 1969 the World Health Organization Director pointed out that DDT was so safe that no symptoms developed among the 130,000 spraymen or the 535 million inhabitants of sprayed houses. In house spraying, the amount applied was 2 grams of DDT per square meter of wall, every 6 months *The Lancet* 22 July 2000. Also, no wildlife was injured by DDT those areas. The Director concluded that "The

discontinuation of the use of DDT would be a disaster to world health."
Montrose Chemical Company workers, who wore no masks or goggles, were never harmed by their constant exposure to DDT. When their fatty tissues were analyzed, they were found to contain up to 647 ppm of DDT residues. The general population at that time contained only 5 or 6 ppm of DDT in their fat tissue. *Arch. Environmental Health* 15: 768-75 (1967). There were no cancer cases in those workers, even after 1300 man years of heavy daily exposure to DDT. Dr. Edward R. Laws (USPHS), found that those workers still were healthy after 10 to 20 years of that exposure.

Dr. Wayland Hayes performed tests for the U. S. Public Health Service, feeding human volunteers up to 35 mgs of DDT in their food every day for 18 months. No adverse effects resulted, either at the time or during the next 10 years. (*J. Amer. Medical Assn* 162: 890-97, 1956)

Dr. Laws experimentally transplanted malignant tumors directly into rodent brains to determine the effects of DDT in their diet. Rodents without DDT in their diet all died, but nearly half of the DDT-dosed rodents survived and the cancers disappeared from their brains. (*Arch. Environmental Health* 23: 181-84, 1971)

Drs Charles Salinskas and Allan E. Okey reported that DDT in rodent diets inhibited development of induced mammary cancers and leukemia. *J. National Cancer Institute* 55: 653-57 (1975)

A.E. and E.K. McLean determined that after animals had ingested DDT the highly toxic aflatoxins they had been fed were not fatal, perhaps because they were converted to non-toxic metabolites by the

liver. *British Med. J.* 25: 278-81 (1969) DDT was also known to induce the formation of hepatic microsomal enzymes which, in turn, inhibited the growth of tumors and cancers.)

As a result of such studies, I felt it was safe to ingest DDT, myself. I was delivering addresses to audiences almost every week. I carried a commercial box of DDT onto the stage, dug out a tablespoon of DDT (about 12 mgs), swallowed it, and washed it down with water before beginning my talk about DDT's lack of toxicity to vertebrate animals. The average human intake of DDT in the United States at that time was about 0.03 mgs/day, or 0.36 mgs per year. (*Science News*, 25 October 1969) Wayland Hayes wrote in *Hospital Practice*, October 1969, that "0.03 mgs for a 68 kg man (150 lbs) is the present daily intake." *Esquire Magazine* (September 1971) pictured me ingesting a tablespoon of DDT. Their title explained that I had "eaten two-hundred times the normal human intake of DDT, to show it's not as bad as people think."

Clifton Curtis, however, of the World Wildlife Fund, was evidently totally unaware of reality! He wrote that "DDT is so potent that as long as it is used anywhere in the world, nobody is safe." (He provided **no** data.) Curtis' allegation is thoroughly refuted by Claus and Bolander, on pages 288 to 550 of their carefully-researched book titled *Ecological Sanity* (David McKay Company, 1977)

Dr. Gilbert L. Ross (at the American Council on Science and Health) said such assaults are "typical of the dangerous environmental disinformation masquerading as science that has been stirring DDT hysteria ever since the 1960s. He pointed out that "Extensive scientific studies have not found any harm to humans, even during the massive overuse of DDT in agriculture in the 1950s and 60s."

Also, most science reports now agree that there is NO indication of DDT use harming people, birds, bird eggshells, or other vertebrate animals.

The World Health Organization proposed the possible eradication of malaria, world-wide, and malaria control was achieved in areas with a population of 279 million people. Thirty-six formerly malarious countries totally eradicated the disease. The National Academy of Sciences stated in 1970: "To only a few chemicals does man owe as great a debt as to DDT. In little more than two decades DDT has prevented 500 million human deaths, due to malaria, that would otherwise have been inevitable." (In *The Life Sciences*)

Then Along Came Rachel Carson And Her Book, *Silent Spring*. She advocated a halt to most uses of pesticides, especially DDT. She stated: "Only yesterday mankind lived in fear of scourges of smallpox, cholera and plague. Now our major concern is no longer with the disease organisms; better living conditions and new drugs have given us control over infectious disease." Some of the infectious diseases that she ignored, which were NOT controlled, were malaria, typhus, yellow fever, plague, dengue, encephalitis, sleeping sickness, river blindness, leishmaniasis and elephantiasis!! (All of those **had** been locally controlled by DDT)

The president of a leading British scientific organization stated that "If there had been a world ban of DDT, as many sought, then Rachel Carson and her book, *Silent Spring*, would now be killing more people every year than Adolf Hitler killed during his entire

holocaust." (Unfortunately, a world ban on DDT is still the goal of many pseudoenvironmentalists.)

On the first page of her book Rachel Carson dedicated *Silent Spring* as follows: "To Albert Schweitzer, who said 'Man has lost the capacity to foresee and to forestall. He will end by destroying the earth.' " Since the major theme of her book was anti-pesticide (especially anti-DDT) this seemed to indicate that the great man opposed the use of DDT. However in his autobiography Schweitzer wrote: "How much labor and waste of time these wicked insects do cause to us . . . but a ray of hope, in the use of DDT, is now held out to us." (Schweitzer was worried about nuclear warfare, rather than DDT!)

The Environmental Protection Agency supported Rachel Carson, and appeared to be determined to ban DDT. In 197I-72 they supervised seven months of hearings, which they hoped would have that result. Testimony by scientists before Hearings Judge Edmund Sweeney filled more than 9,000 pages In his final official decision, issued on 26 April 1972, Judge Sweeney stated that: "DDT is not a carcinogenic, mutagenic, or teratogenic hazard to man. The uses of DDT (under the regulations involved here) do not have a deleterious effect on freshwater fish, estuarine organisms, wild birds, or other wildlife. The evidence in this proceeding supports the conclusion that there is a present need for the essential uses of DDT."

EPA administrator William Ruckelshaus never attended a single day of those seven months of expensive EPA hearings, and his aide, Marshall Miller, reported that he did not even read the transcript (*Santa Ana Register* 25 April 1972). Nevertheless, he overruled his own judge's decision and single-handedly banned DDT.

In his "Final Opinion and Decision" on DDT, Ruckelshaus not only omitted the scientific data which had so deeply impressed the EPA judge, but his "decision" was padded with propaganda from Environmental Defense Fund literature that appeared nowhere in the entire transcript of the hearings. (Ruckelshaus was a member of the Environmental Defense Fund and solicited donations for that group on his personal stationery.)

I summarized a few of the obvious misstatements in Ruckelshaus' "Final Opinion and Decision" on DDT, and Senator Barry Goldwater entered that summary in the *Congressional Record* (pp. S11545-47, 24 July 1972) On page 1 Ruckelshaus wrote: "DDT is the familiar abbreviation of the chemical (1,1,1-trichlorophenyl ethane)." That should be: 1,1,1-trichloro-2,2, bis(p-chlorophenyl) ethane. On page 4 he stated: "DDT has three major breakdown products: DDA, DDE, and DDD; separate registrations exist for TDE (DDE)." The truth is that TDE is another name for DDD, not DDE, and that DDE is not insecticidal at all, thus there were no registrations for it. Those errors are significant only as an indication of slovenly attention to details. On page 37 he stated that farmers should use "the less acutely toxic organophosphates, like carbaryl." Even Ruckelshaus should have known that carbaryl is not an organophosphate pesticide, and that carbaryl and organophosphates are NOT less toxic than DDT! Remember Ruckelshaus' response when the Secret Service exposed his lies about arm-wrestling with them to get papers from Ehrlichman's file cabinet? His defense was: "My allusion to arm wrestling was an effort at hyperbole at a time when reality could not absorb exaggeration. The gloves were never donned and the bell never sounded. . . in short, the bout never occurred." (EPA Radio Broadcast, 15 May 1975)

On 7 March 1994 a letter from Dr. Fredrick M. Steinberg was published in the *Wall Street Journal.* The title was: "Millions Must Perish Because of DDT Ban." After reviewing the statistics, Dr. Steinberg said "None of the charges against DDT -- namely, as an agent of widespread bird deaths, as a nonbiodegradable material, or as an agent of human carcinogenicity -- have ever been substantiated." (Dr. Steinberg is Chairman of the Board of Directors of the American Council on Science and Health.)

In *The Lancet* (15 July 1972) Dr. L. J. Bruce-Chwatt (of the London School of Tropical Medicine) wrote: "The Environmental Protection Agency of the USA has imposed almost a total ban on the use of DDT, which increases the difficulty of controlling several tropical arthropod-borne diseases. This may have an unexpected rebound effect and jeopardize the health gains achieved over many years. "

EPA officials vigorously denied that the ban was political, but on 26 April 1979 Ruckelshaus himself wrote a letter to Allan Grant (American Farm Bureau Federation president) in which he stated: "Decisions by the government involving the use of toxic substances are political with a small 'p'...Science, along with other disciplines such as economics, has a role to play, but the ultimate judgement remains political." (Emphasis added)

Other apologists for Rachel Carson and the Environmental Protection Agency have contributed remarkable statements, including the following.

In *Science* 8 February 1992, the author stated that "The significance of Rachel Carson's book was not its scientific accuracy, and not the

position it took on DDT. Its significance was that it helped to turn national, even global, consciousness in a different direction." He recommended "taking a value-laden leap of faith beyond the present state of knowledge." That doesn't sound very scientific, but another discussion was even less rational. In *Science,* 10 October 1997, page 223, Koella and Mackinn wrote: "Most mosquitoes die when they bite someone, and get squashed. It thus makes sense for a mosquito to keep its biting to a minimum. It might also make sense for the malaria parasite to want its insect host to behave with some restraint, as the longer the insect is alive the more opportunities the parasite has to be transmitted." In fact (Koella says) "the malaria plasmodium wants the mosquito to bite as often as possible." (emphasis added) Perhaps other such writers can conduct more personal interviews with protozoans and mosquitoes, and pass their opinions along to scientists in future issues of "Science" magazine?

The U. S. Export/Import Bank financed over $3 billion worth of pesticide exports in 1974-76, saving millions of human lives. In 1976 the Audubon Society and the Natural Resources Defense Council sued in federal court to prevent more pesticides from being shipped to undeveloped countries. The National Legal Center for Public Interest opposed that suit, and four years later the court finally ruled against the environmental extremists.

In 1977 pseudoenvironmentalists sued to force the Agency for International Development to submit Environmental Impact Studies before pesticides could be sent to save lives in poor countries. They were partially successful, and in 1986 the Agency for International Development responded by issuing "Regulation 16 Guidelines." Based on those Guidelines, Secretary of State George Schultz telegraphed orders to U. S. embassies in poor countries, stating that:

"The U.S. cannot – repeat cannot – participate in programs using any of the following pesticides: (1) lindane; (2) BHC; (3) DDT; and (4) dieldrin." The poor countries thus either had to survive without U. S. aid OR try to get along without the pesticides needed to protect the health of their inhabitants. Hundreds of thousands may have starved or died, as a result.

The Communicable Disease Center in Atlanta warned that: "A decision to ban the production of DDT in the U. S. would result in a denial of the use of DDT to most of the malarious areas of the world. The available evidence on the very slight risks, if any, does not justify the U. S. making a unilateral decision that would so adversely affect the future economic and social well-being of so many other nations of the world. The mere banning of the use of DDT within the U.S. may raise unwarranted fears in the minds of those responsible for decision making in other governments who will not be fully informed of the known facts about the benefits and risks involved in the continued use of DDT in malaria eradication."

Some donor countries frowned on DDT use in poor countries and withheld financial aid if the countries use DDT. If aid is really intended to save human lives, the recipients should be allowed to decide what is best for themselves.

Dr. Roger Bate, chairman of the Save Children from Malaria campaign, warns that "Problems will arise from restrictions on DDT use, but it is of far greater importance that countries can continue to use DDT without fear of reprisals – at least official reprisals. Aid agencies and environmental groups pressuring countries to abandon DDT for public uses could kill thousands of people and cost millions of dollars." (*Environment and Climate News,* April 2000).

In Mozambique DDT use was stopped "because 80% of the health budget came from donors who refused to allow the use of DDT" (*British Medical Journal*, March 2000)

Belize and Bolivia stopped using DDT in their public health programs because they feared the loss of aid from international agencies.

International agencies that block aid to countries that use DDT for malaria control should be held responsible for the deaths that result.

South Africa also halted their DDT spraying in 1995, after which malaria cases in the country quadrupled to over 50,000 and malaria incidence there has risen by over 1000 percent in the last five years.

In *Excite News* (news.excite.com), 21 Nov 2000, Dr. Donald Roberts (professor at Uniformed Services University of Health Sciences, at Bethesda, Maryland) reported: "Malaria rates are climbing in poor countries that stopped using DDT." Rates increased by 12 times in Guyana after DDT spraying was reduced."

Countries that have continued to use DDT have halted their malaria epidemics. In Africa, Swaziland still benefits from DDT spraying (with less than 4 per cent of the residents infected), but just across the border about half of the people in unsprayed South Africa have malaria infections.

In Madagascar, malaria killed more than 100,000 people in 1986-88.. Authorities belatedly began spraying DDT again, and stopped the

epidemic. *J. Amer. Mosquito Control Association* 1998: 1114, pp 121-130

Malaria cases in South America have risen by over 1,000 percent in the past five years. Only Ecuador and Venezuela have contained or reduced malaria in the past few years. (See graph prepared by Dr. Donald R. Roberts, in *Emerging Infectious Diseases*, 1997, page 300, and more details regarding the results of malaria spray programs in South America.)

We recently visited Ecuador, to study conditions along Rio Napo. People are responding well to the 61% reduction in malaria cases that resulted from three years of DDT programs there. (The surrounding countries stopped their DDT programs three years earlier, and are now suffering up to 91% more malaria, as a result.

Before DDT appeared about 10% of the people in the world had malaria attacks, and someone died of the disease every 10 seconds.

The National Academy of Sciences said, in 1996, that "malaria is affecting 2,400 million people, or 40% of the world's population. A child dies of malaria, somewhere, every 30 seconds, and most of these deaths are unnecessary."

Without DDT, malaria rates around the world are returning to those in the 1940s, affecting additional millions of children and adults." Where are the promoters of the international genocide treaty?

Paul Driessen wondered "Is the DDT ban intended to control global populations?" (*Environment and Climate News,* April 2001) "In 1972 the EPA banned the use of DDT in any nation receiving U. S. aid.

Within just six years, 800 million cases of malaria developed and 8.2 million malaria deaths were reported in countries affected by EPA's ban." In response, many countries wish to turn again to DDT, prompting the World Wildlife Fund and other environmental groups to demand a permanent, inflexible, global ban on this life-saving pesticide. At best, their campaign suggests a painfully callous indifference to the devastating impact the ban would have on the world's most destitute and disease-ridden peoples."

Many Anti-DDT Activists seem to believe that the answer to the world population problem is to permit up to half of the people in poor nations to die of malaria. Such a view apparently was shared by Edwin J. Cohn, **of** the Agency for International Development's Office of Policy Development and Analysis. Referring to the fecundity of many women in poor tropical countries, he said: **"Better dead than alive and riotously reproducing."**

In *Earthbound* it was written that "Massive human diebacks would be good. It is our duty to cause them. It is our duty to eliminate 90 percent of our numbers." But how might that be accomplished? Ethiopia was experiencing a severe famine, and David Foreman, of the Sierra Club, said: "The worst thing we could do is to give aid . . . the best thing would be to just let nature seek its own balance, to let the people there just starve."

In 1970 the National Audubon Society distributed 17,000 yellow leaflets bearing the message: "DDT should be banned throughout the land, and banned from export."

Sierra Club Executive-Director Michael McClosky told UPI (25 February 1971) that "The Sierra Club wants a ban, not just a curb, on

persistent pesticides**, even in the tropical countries where DDT has kept malaria under control."**

Britain's Prince Philip (in *People* magazine, December 1981): "I was in Sri Lanka, where malaria was controlled by DDT. What people didn't realize was that **malaria was actually controlling population growth. The consequence was that within about 20 years the population doubled."**

Alexander King The president of the Club of Rome, which is active in more than 40 countries, saw the DDT spray program succeed in Guyana, where within two years it had almost eliminated malaria. He wrote in his 1990 book, *The Discipline of Curiosity,* that **"my chief quarrel with DDT in hindsight is that it has greatly added to the population problem."**

Jacques Cousteau stated in the *UNESCO Courier*, November 1991: **"In order to stabilize world population, we need to eliminate 350,000 people per day. It is a terrible thing to say, but it is just as bad not to say it."**

Mosquito Control Is Now Very Difficult

Before the development of powerful pseudoenvironmental businesses mosquito larvae could be easily controlled by filling puddles, draining swampy breeding sites, and adding appropriate chemicals to the water. Effective control by water management operations have been made illegal by the so-called environmentalists We cannot legally alter mosquito larva habitats, because of the Clean Water Act, the Wetlands

Protection Rules, and the Endangered Species Act. We cannot put oil or chemicals in ditches or puddles, because of the Clean Water Act. We can't spray anything into the air, because of the Clean Air Act and the Endangered Species Act. Most insecticides have been banned, or criticized so violently that their application is impossible. Environmentalists even oppose the introduction of surface-feeding minnows (because they may also eat other forms of aquatic life, some of which are protected as "endangered species." Even their potential habitats are now untouchable because they are listed as "critical habitats for endangered species" and cannot legally be disturbed. In seeking possible ways to protect public health by reducing mosquito attacks, abatement personnel have also experimented with nematodes, hydra, planaria, gregarine protozoa, fungi, and bacteria. None of those show much promise for practical reductions of mosquito numbers, and every one of them can be outlawed by environmental extremists because they may threaten aquatic life forms other than mosquitoes. Obviously it is not possible to prevent mosquito outbreaks after all of the effective defense measures are banned. The only protections that people can be sure of being permitted to use are mosquito netting, insect-proof buildings, and perhaps using mosquito repellents. Even those repellents are now likely to be banned, because of adverse or potential effects on endangered or threatened species or their "critical habitats."

Roll Back Malaria

The "Roll Back Malaria" program began in winter of 1989. *(TDR News* June 2000) Twenty four African countries participated, but 26 did not. The planners stated "the emphasis is on dialogue and flexibility."

Countries are called upon to "stimulate development of vaccines," and to "foster collaboration between institutions to ensure full utilization of research knowledge and programme experience." No interest was shown in actually suppressing mosquito numbers

Vaccine Research

Science 26 Sept 97 observed: "Last spring, 134 potential vaccine research groups were seeking $130 million." "Since only $2 million was available, not much resulted."

Brigham Young's James Jenson, regarding vaccine research: "Malaria is thousands of times more complex than anything else we've ever tried to make a vaccine for." Unfortunately, malaria plasmodia mutate rapidly, which would probably limit the usefulness of any vaccine that is developed.

Science News 3 February 1990. Genetic alterations. The Institute for Genomic Research is currently trying to crack the entire 30-million-base-genome of *Plasmodium falciparum.* A $1.1 million dollar program financed by the MacArthur Foundation seeks "to forge a marriage between modern genetics and vector biology, at five U. S. Research Centers." They hope to develop vector incompetence, and stated: "We may enhance populations that are not good disease transmitters, without removing a significant piece of the ecological puzzle."

Science 9 March 2001. Meeting at the Pasteur Institute on 3 March, representatives from 20 research centers in 12 countries started laying plans for sequencing the genome of *Anopheles gambiae.* Revealing the mosquito's 260 million DNA base pair sequence, together with those of *Plasmodium falciparum* (now nearing completion) should open up new strategies for controlling malaria. The cost should run less than $10 million, say the chief participants. Additional funds will be needed to fine-tune the sequences and begin detailed analyses of the genes and their functions.

A vaccine must attack each of the very different stages in the *Plasmodium* life cycle, to be effective. Furthermore, the four species of *Plasmodium* that can cause human malaria differ in many ways. *Plasmodium vivax* and *P. ovale* are relatively mild forms, but *P. falciparum* is a violent killer, with attacks every 48 hours, and *P. malariae* causes attacks only every 72 hours. Any single vaccine obviously can not protect humans from all malarias. Stephen Hoffman also says that a 6-year old boy in Africa "may have as many as five different strains of malaria existing at once within him, and you must have a vaccine that attacks all five."

Doctors for Disaster Preparedness Newsletter, May 1997. Vaccines may be of such short duration that they will be useful primarily to protect travelers. In countries where people cannot even afford mosquito nets, expensive vaccines will obviously be useless."

In *Science*, 20 October 2000, pages 437-439, Ruth and Victor Nussenzweig identified the primary antibody "target" on attenuated sporozoites, and called it a "circumsporozoite protein (CSP)." They synthesized a portion of that protein and used it as their vaccine.

They said a problem is that if just one sporozoite escapes it produces 30,000 merozoites in a week, and they are not affected. There is no known "target" on merozoites.

Researchers seeking vaccines for disease control routinely inject a killed form of the pathogen into the victim's blood. That sometimes causes the body to stimulate the production of chemical defenses. Injecting the killed plasmodia of malaria did not bring about the desired effect. In 1945 Jules Freund discovered that Rhesus monkeys could be immunized with a vaccine protecting them from *P. knowlesi*, but only when it was used with an adjuvant. Freund's adjuvant is an emulsified suspension of a killed tuberculosis *Mycobacterium*, in mineral oil. The mineral oil is largely responsible for the adjuvant's toxicity, since it is metabolically inert and cannot be metabolized. The addition of such an adjuvant seemed to stimulate the body's defense system and prevent the malaria from becoming fatal. For 30 years, Freund's adjuvant was used in malaria vaccine research, however it was found to cause tumors, abscesses, and other side-effects that were often fatal. In monkeys it produced auto-imune damage to nervous tissues, and half of the monkeys died. It could never be routinely used in humans and was in fact too harmful to even be tested on humans. As a result, vaccines to protect humans from malaria have been difficult to develop.

In 1983 Miodrag Ristic, of University of Illinois, submitted a proposal to A.I.D. for three years funding of his malaria vaccine research. His budget proposal was for $2.38 million. The A.I.D. expert panel of consultants recommended that it not be funded. However, A.I.D.'s malaria vaccine project director, James Erickson, approved it, so Ristic got his millions . During the next three years he transferred $24,000 to a personal account, and in 1987 investigators

found enough fiscal improprieties to warrant criminal investigation by the Attorney General of Illinois. No vaccine was developed, and in 1990 Ristic was indicted on four counts of theft. Erickson was indicted by the grand jury and charged with conflict of interest, conspiracy, illegally accepting gratuities, making false claims, and submitting false income tax returns. He could have been jailed for five years and fined $250,000.00, but a lenient court fined him just $20,000.00

Wasim Siddiqui, at University of Hawaii, exploited 1966 research by Martin Young (of the National Institutes of Health), who had reported that the South American Owl Monkey could be experimentally infected with human falciparum malaria. and 1977 research by William Trager and James Jensen of the Rockefeller University, who found that *P. falciparum* could be grown in a media culture if oxygen was diminished and CO2 was increased in the incubator. Siddiqui immunized Owl Monkeys with *P. falciparum* cultured in the Trager/Jensen method, and mixed with Freund's adjuvant. (The vaccine could never be available for clinical trials because that adjuvant has such severe effects.) Siddiqui was later indicted for appropriating $130,000 through "accounting tricks."

Siddiqui reported that muramyl dipeptide had some of the properties of Freund's adjuvant, but when he tested it on four monkeys, only one monkey survived.

In 1985 he requested another $1.65 million. A.I.D reviewers, rejected it as "mediocre, unrealistic, outlandish, and outrageous," with an "excessive budget." James Erickson again ignored their evaluation and awarded Siddiqui the total amount requested. Siddiqui then falsely claimed that his vaccine was "almost ready for human use." In

1988 the A.I.D. asked the Inspector-General to investigate, and those investigators soon stated that there was "an apparent diversion and theft of funds, submission of false claims, and intent to cover up the actual use of the funds." On 14 September 1989 the Grand Jury of Hawaii indicted Siddiqui with theft, criminal conspiracy, and criminal solicitation. On the very day he was arrested by the Honolulu police the A.I.D. Vaccine Research Office announced that it was giving Siddiqui $1.65 million to continue his research. Senator Inouye went on TV and said that if Siddiqui was handed any more federal funds he personally would see to it that the University of Hawaii would never get another cent of federal research money. The University therefore replaced Siddiqui with a psychologist and a young bacteriologist, and A.I.D. found them to be acceptable to carry out the $1.65 million research program. *Science* (4 June 1993) reported that in February 1993 Hawaii's deputy attorney general had closed the case against Siddiqui for misappropriating another $114,000 in A.I.D. research funds. He was sentenced to just six months of house detention, and the University relieved him of teaching duties. University lawyers were attempting to recover an additional $250,000 which they said he had diverted from University accounts. The university newspaper reported that he was still drawing his salary of $92,340 a year.

Paul Silverman (of the Liverpool School of Tropical Medicine) moved to the University of Illinois as a biologist. He requested a million dollars from the Agency for International Development to finance the development of a malaria vaccine. In 1965 he proposed a vaccine composed of antigens from two stages of the malaria parasite life cycle, the sporozoite antigen (to destroy those injected with mosquito saliva) and the merozoite antigen to stop erythrocyte destruction. A panel of malaria researchers said the proposal was not

feasible, but A.I.D. gave him the requested million dollars anyway. Silverman replaced Freund's *Mycobacterium* with a different *Mycobacterium* (that had been used to vaccinate humans against tuberculosis), He also replaced the mineral oil with peanut oil (which is biodegradable). Silverman couldn't get permission to experiment on human malaria plasmodia, so he worked on a monkey *Plasmodium* instead. Unfortunately, after testing was completed, only about half of his experimental monkeys lived. After five years, he had made no hopeful progress. His vaccine would only protect the monkeys when it was aided by Freund's adjuvant, and nobody could find an effective substitute for it. After another two years, Silverman finally gave up and became an administrator.

Dr. Manuel Patarroyo, Director of Bogota's Institute of Immunology, developed a vaccine that is "a combination of four synthetic peptides mimicking surface proteins from both the merozoite and sporozoite stages of *Plasmodium falciparum.*" Many scientists were skeptical, and the British Medical Research Council concluded that "the available data are not adequate to justify their support for experiments on humans." Patarroyo did not report any double-blind studies or any experiment in which his treated patients were compared with "controls" receiving placebos.

TDR News, July 1993, stated that Dr. Patarroyo had worked for the last 13 years on the production of a vaccine to protect humans from malaria. He recently declined to accept $8 million from a U. S. Firm and instead donated all rights to his vaccine to WHO, saying "All I wanted to do was to solve a complicated problem and help the poor people of the world." His vaccine, if effective, would only cost about 50 cents (US) for a three-dose regimen. Bogota government officials were ready to begin construction of a $4 million facility to produce

the vaccine. (*Science* 10 September 1993) reported that after six years of skepticism, the United Kingdom Medical Research Council (MRC) endorsed plans for a vaccine trial in Gambia, involving 600 infants less than a year old. The vaccine was not as effective as hoped. The study found that it did not prevent malaria among the vast majority of the 630 Gambian children (6 to 11 months of age) who took part in the study. Only 3 percent of them were protected.

Dr. Stephen Hoffman at the Naval Medical Research Center in Maryland says he is working on a DNA-based vaccine that will attack the parasite before any symptoms emerge. (*Smithsonian,* 2001) Hoffman says the malaria plasmodia have about 6,000 genes in their DNA, compared to common viruses which have less than 30. He is hopeful that his and other vaccines "will be ready in 7 to 15 years." [It might be remembered that during 7 years, 21 million more humans will die of malaria, and in 15 years the total will be 45 million more deaths that could have been saved if adequate mosquito control programs had been carried out during those years of vaccine research.]

In 1983 the Agency for International Development (AID) stated that many malaria vaccines would soon be ready for testing. They were obviously wrong, since NONE have been developed, by the year 2001!

Malaria Capers (a book by Robert Desowitz) reported (page 275) that "After 25 years, the AID malaria vaccine research project has proven to be a disaster. The failure was primarily due to mediocre science, irresponsible experimental procedures, and corruption."

Another reason may be that the human constitution is such that no vaccine can confer a protective immunity to human malaria."

Expensive Malaria Research Requests

Science 20 October 2000, pages 428 – 431. "A Renewed Assault on an Old and Deadly Foe." The World Bank is pledging $300 million in interest-free loans to fight malaria, the Bill & Melinda Gates Foundation is donating $115 million, and the National Institute of Allergy and Infectious Diseases budget is expected to raise more than $52 million in 2001."

The World Health Organization allocated $10 million "to help countries develop plans for tackling malaria, training staff, and initiating more effective action." They said "it is not going to be easy, however the potential is there, and if the scientific and technical inputs can be channeled through effective health systems and supported by adequate finances and political commitment, the benefits for the poor of the world will be enormous." *Science* 26 June 1998 They did not allocate any funds to help the countries control the numbers of larvae and adult mosquitoes in those suffering countries!

Gro Harlem Brundtland took office as director of the World Health Organization and announced a crusade to "reduce malaria over the next 10 to 15 years." She announced in 1998 that her goal was not the eradication of malaria anywhere, but "just to halt half of the malarial mortality by 2010 and half again by 2015." (From *Emerging Infectious Diseases*, July 1997.) Apparently she will be content if only two children die of malaria every minute (instead of four), and if

one person dies every 24 seconds (instead of one every 12 seconds)! And what of the 500 million cases of malarial sickness? Will she continue to ignore those millions of deaths, with no intention of saving them?

At a meeting sponsored by the National Institutes of Health, the Fogarty International Center, the Gates Foundation, Tropical Disease Research and the WHO it was stated that "with adequate support, the necessary field testing of candidate vaccines could be achieved in five to ten years," at which point "industry might be induced to come on board, provided the required milestones are met." Participants said that "within 10 to 15 years licensing and deployment of vaccines could be feasible, given sufficient backing." (SO, they also favor another 10 to 15 years with no relief from mosquito-borne diseases.)

Aotus (Owl Monkeys) and *Saimiri* (Squirrel Monkeys) from Central America can be infected with human malaria protozoans. Researchers therefore bought hundreds of those monkeys (for $245,000) and also the Agency for International Development (AID) gave Columbia's National Institutes of Health a grant of $1,530,000 to make it easier to get more owl monkeys trapped and shipped to Florida for research. They also gave $1.1 million to Peru for a monkey conservation program, then had Peru ship 600 more owl monkeys to Florida. AID has already paid about $2 million for maintaining those hundreds of monkeys in the Florida research facilities.

"As science advances, pessimism arises from the financial constraints of developing a malaria vaccine." According to a recent NIH report, it would take more than $250,000,000 and a dozen years to develop a vaccine and get it licensed. They stated "large-scale clinical trials are still a distant dream of malaria vaccine researchers." Those

millions of dollars already appear to be inadequate! It is hard to believe, but the *TDR News* (Feb 2000) stated that "Malaria vaccines represent one of the most cost-effective interventions for reducing the burden of malaria." That view on the cost-effectiveness of producing vaccines borders on silliness! The costs have been exorbitant and there is no imminent help for the millions of humans who so desperately need protection! The World Health Organization (TDR) admitted that "Transmission Blocking Vaccines have not as yet attracted any industrial interest."

In *Science,* 20 October 2000, an article appeared, titled "Against All Odds" (pages 431-433). The authors describe their activities, which consisted of "monitoring malaria since 1997, laying the groundwork for future trials of a hoped-for vaccine, and providing treatment for feverish children." They also collaborated with native healers, who referred children to the researchers for treatment with quinine and Fansidar.

Science, 20 October 2000, pages 440-441. "Building a Disease-fighting Mosquito." "Several labs have embarked on the most futuristic of all approaches to combat malaria," say the authors. They hope "to replace billions and billions of mosquitoes in the world's endemic areas with new strains of mosquitoes, created in the lab, that would be 'refractive,' or unable to transmit the parasites." They based their research on the transmission of a chicken parasite, by *Aedes aegypti.* They tried to transpose new genes in *Drosophila* into genetically engineered mosquitoes, but couldn't get <u>any</u> genes delivered from *Drosophila* into a mosquito! "It put a cloud over the whole research area," said Anthony James, and "At meetings we were always talking about things that didn't work."

Persistent Organic Pollutants

Science, 15 December 2000, page 2053. A Treaty on POPs (Persistent Organic Pollutants), was organized by the United Nations Environment Program to address the so-called "Dirty Dozen Chemicals." They proposed an international treaty to ban or phase out 12 chemicals, including 8 insecticides. The insecticides are: aldrin, chlordane, DDT, dieldrin, endrin, heptachlor, mirex, and toxaphene. All are categorized as chlorinated hydrocarbons. Also targetted are PCBs, hexachlorobenzene, dioxins, and furans.

At the United Nations Convention on Persistent Organic Pollutants (POPs), 600 activists assembled in Johannesburg, South Africa to urge banning the "Dirty Dozen" chemicals. The POP treaty grew out of earlier agreements spawned at the 1992 Earth Summit in Rio de Janeiro, particularly the United Nations' manifesto known as *Agenda 21*.

The Treaty was formally adopted at a Conference in Stockholm on 23 May 2001. After 50 governments have ratified it the treaty will enter into force. DDT (the most famous of the banned chemicals) still saves millions of human lives every year. At least 23 countries voted against banning it, and requested exemptions for usage of DDT for public health purposes.

A marvelously-detailed cover story by William Jasper in *The New American,* 2 July 2001, was appropriately titled "Environmental Genocide." He wrote: "The POPs Convention, signed in Stockholm on May 23rd, is heralded by the media as a boon for humankind. But

the POPs treaty is, in truth, a global death warrant for millions, and potentially hundreds of millions, of human beings."

The Treaty sought to ban eight chlorinated pesticides, but to the relief of some public health experts, it permits the limited use of DDT where it is needed for malaria control. Dr. Donald Roberts, as spokesman for the "Save Children from Malaria Campaign" reported that an international coalition of health and advocacy groups applauded the UN vote against banning DDT worldwide. That intelligent vote could save the lives of millions of people.

Dr. Jane M. Orient reports that "Physicians for Social Responsibility (although billed as a group concerned with environmental health) is working for the disarmament of malaria fighters, through a comprehensive ban on their most effective weapon, DDT." Dr. Orient reveals the activities of many groups and individuals involved in this world-wide public health conflict. She has been a very effective defender of public health, both in the United States and around the world, with her great humanitarian organization, Doctors For Disaster Preparedness.

Dr. Jay Lehr, Managing Editor of *Environment and Climate News,* reports that an international coalition of public health groups applauded the United Nation's recent vote against erecting a global ban on the pesticide DDT. "Most of the delegates and observers arrived with the goal of enacting a global ban on organic chemicals, most notably DDT, which is used to control malaria and other insect-transmitted diseases in 23 countries in Africa, Asia and South America. Delegates added DDT to a list of restricted–use chemicals, but voted against an immediate worldwide ban." (April 2001) Dr. Lehr has produced two great books that also urge rational approaches

to pesticide use, especially where DDT and malaria are involved. Those books are: *Rational Readings on Environmental Concerns* (Van Nostrand Reinhold 1992) (841 pages), and *Standard Handbook of Environmental Science, Health, and Technology* (McGraw-Hill 2000) (1650 pages)

General References

California Agriculture, March 1980. Mosquito Research, Special Report, 43 pages.

Cushing, E. C. 1957. History of Entomology in World War II. *Smithsonian Institution Publ.* 4294, 117 pages.

Desowitz, R. 1992. *The Malaria Capers.* H. H. Norton, Publisher.

Edwards, J. G. 1993. Malaria, the Killer That Could Have Been Conquered. *21st Century Science and Technology*

Eldridge, B. F. & J. D. Edman 2001 . *Medical Entomology*, Kluwer Academic Publishers, 659 pp

Natural History magazine, July 1991. Mosquitoes and Human Diseases, 69 pages.

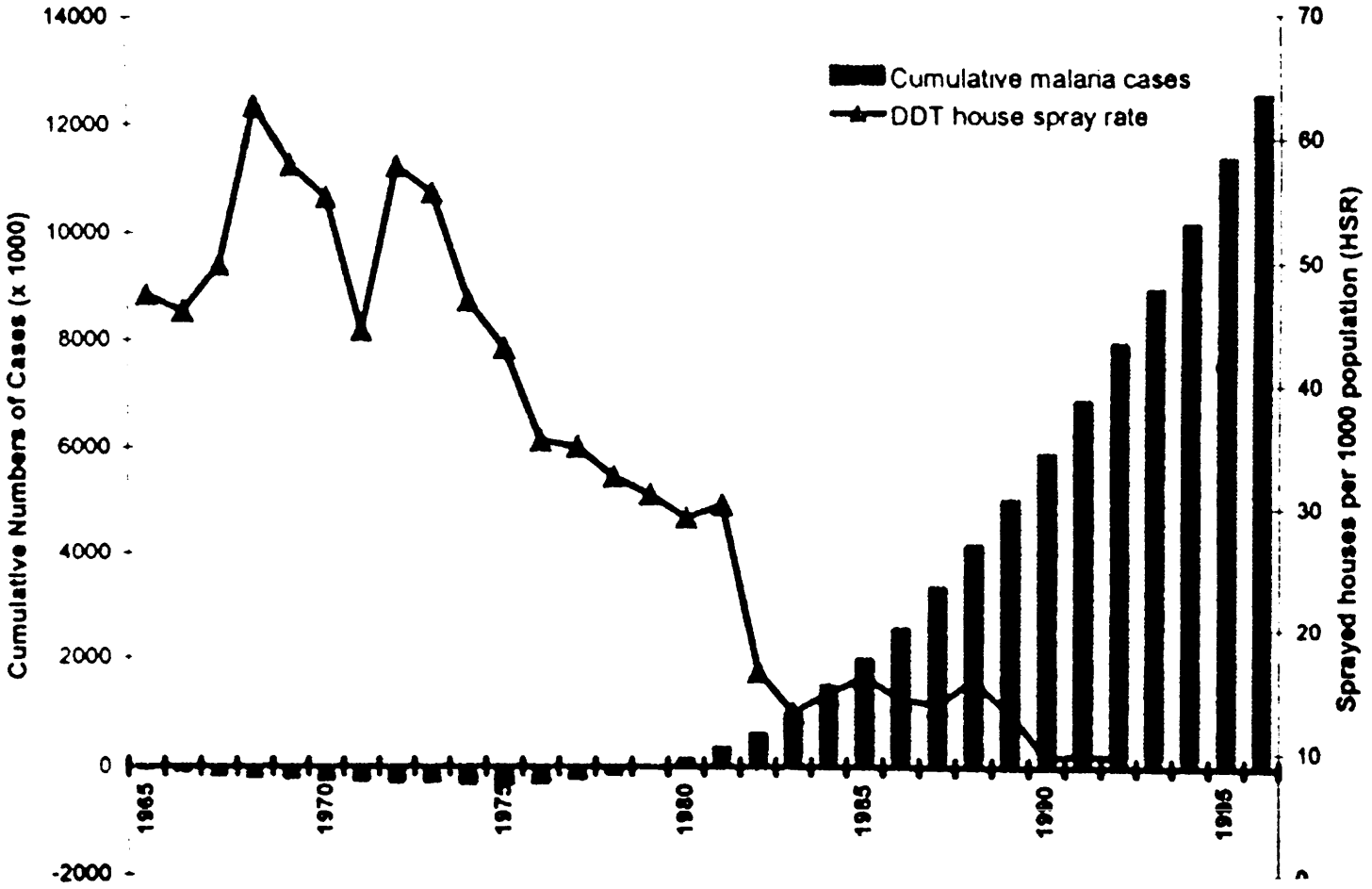
Navy Environmental Health Center. 1984. Guide to Malaria Prevention and Control. *U. S. Navy Medical Department,* 90 pages.

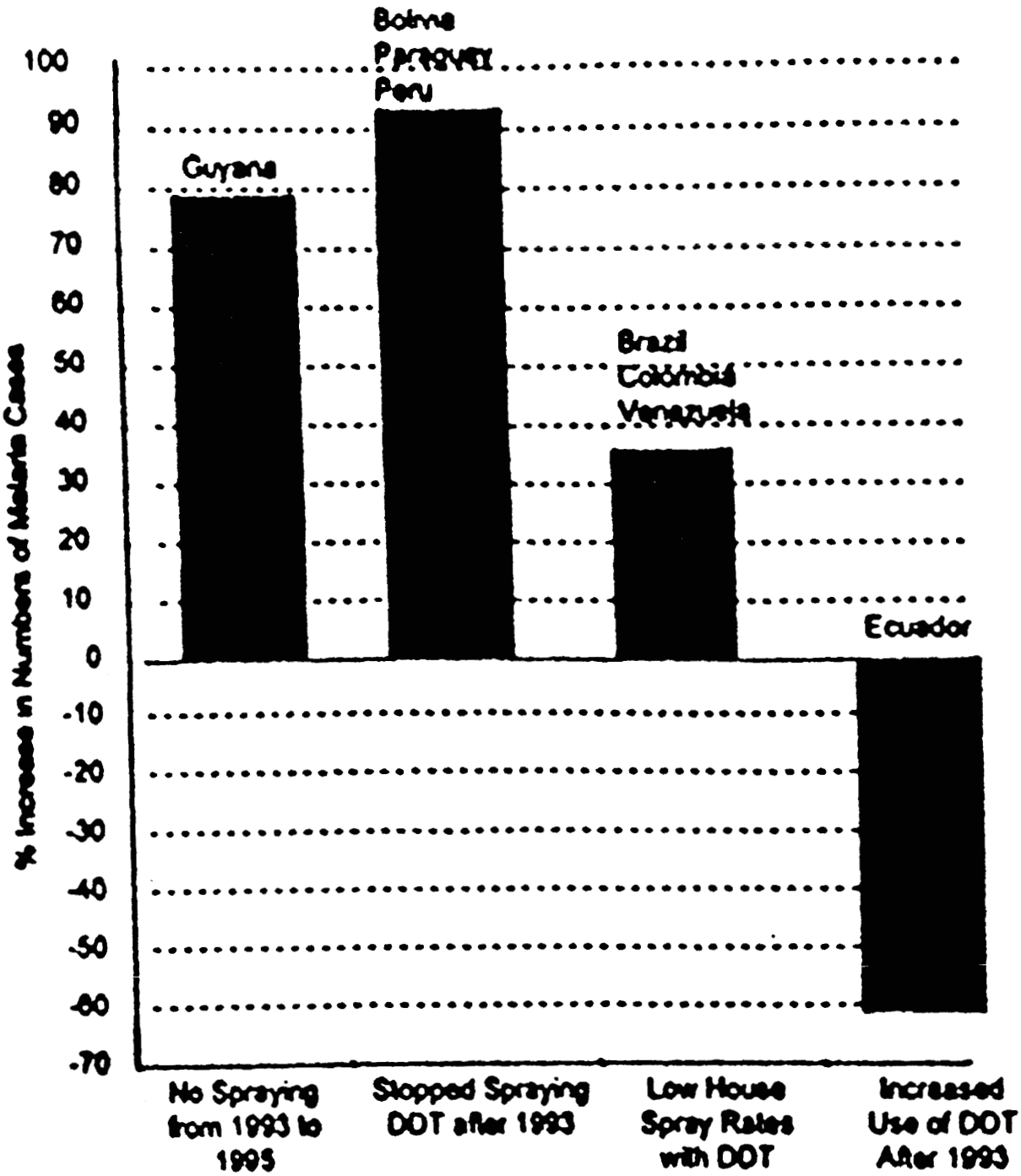
Roberts, D. R. *et al.* 1997. DDT, Global Strategies, and a Malaria Control Crisis in South America. *Emerging Infectious Diseases*, pages 295-302.

Tren, R. & R. Bate 2000. When Politics Kills: Malaria and the DDT Story. *Africa Fighting Malaria,* 70 pages

Index For Mosquito Speech

House Spray Rates, 1965-92, and Cumulative Malaria Cases, pre- vs. post-1979
(Brazil, Colombia, Ecuador, Peru, Venezuela)




Bolivia
Paraguay
Peru
Guyana
Brazil
Colombia
Venezuela
Ecuador
100
90
80
70
60
50
40
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
% Increase in Numbers of Malaria Cases
No Spraying from 1993 to 1995
Stopped Spraying DDT after 1993
Low House Spray Rates with DDT
Increased Use of DDT After 1993