

Malaria, A Moving Target

By Joel E. Cohen

Malaria is coming back. In the five years before 1978, according to the director general of the World Health Organization, there was "on average, taken globally, more than a twofold increase in the number of cases reported."

"In some countries," he added, "the increase has reached dramatic proportions, with the figures showing a thirtyfold to fortyfold increase compared with 1969-70; thus malaria is again in some instances endangering not only the health of the population but also overall socio-economic development."

The rise in the number of cases confirmed by laboratory examination and reported by malaria services is not the result of larger malaria detection programs. On the contrary, some earlier efforts at eradication have been reduced to efforts at control. "The search for cases has been drastically curtailed since large-scale detection is not usually carried out in control programs."

Global statistics exclude China, Cambodia and Vietnam, for which figures were not available, and all of Africa, for which the figures were unreliable. Even so, the director general reported a rise from 3,251,000 confirmed new cases in 1972 to 7,517,000 confirmed new cases in 1976, an increase of 131 percent.

The World Health Organization estimates that in Africa alone, a million people, mostly children, die every year from malaria.

In the 1950's and the 1960's, W.H.O., with support from many countries including the United States, aspired bravely to eradicate malaria from the globe. Why did the effort fail?

Lack of money is certainly part of the answer. In 1978, the Rockefeller

Foundation estimated that world funding for research in malaria was \$5 million, or less than 2 cents a year for each of the 300 million people affected. In that year, the United States Government alone spent \$815 million for research on cancer, with a world prevalence of roughly 10 million people.

In 1971, in 25 African countries for which the details are available, the average annual per-capita health budget was \$1.20. But the antimalarial campaigns were substantially supported with outside funds, and still they failed. Why?

Darwin's evolution by natural selection is a big part of the answer. The mosquitoes that carry the parasite evolved. So did the parasites themselves.

Before antimalaria programs began, mosquitoes in one species that transmits malaria came to rest on inside walls of a house after taking a blood meal from an occupant. In eradication programs, insecticide was applied to inside walls. The mosquitoes that landed elsewhere survived. Only the survivors had offspring. Since the behavior involved in choosing a place

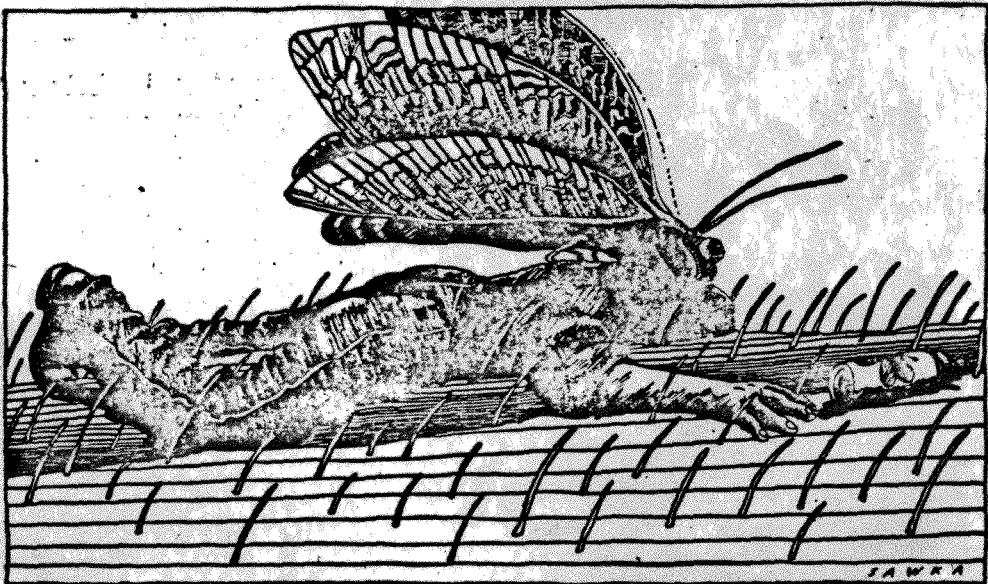
to rest is partly transmitted by genes, the resulting populations of mosquitoes subsequently came to rest outdoors after biting.

Some of the mosquitoes that transmit malaria parasites, rather than adapting their behavior, evolved resistance to the cheap and widely used insecticides. The alternative insecticides were too expensive to use.

The malarial parasites also evolved — to escape control by drugs. In the Americas, Southeast Asia, and the Pacific, *Plasmodium falciparum*, the most virulent of the species that infect humans, became resistant to 4-aminoquinolines, a family of drugs widely used to prevent and treat malarial infections.

The lesson of hindsight is that evolution by natural selection can be a wily foe. There are plausible arguments that malaria has evolved along with its hosts since at least as early in vertebrate evolution as the rise of the reptiles. Malaria is still a moving target.

Now there is new hope. In 1976, two scientists discovered a way to grow sustained cultures of the parasite



Plasmodium falciparum under glass. Previously, it had been possible to obtain only limited quantities of malarial parasites by infecting birds or monkeys in the laboratory.

By eliminating the need to cycle through mammalian or avian hosts, the Trager-Jensen culture technique "has translated malaria vaccination to the realm of practical feasibility since it provides a potential source of antigen for mass vaccination," according to S. Cohen, of Guy's Hospital, London.

But hope should not be naive. The most likely target for vaccines is now believed to be the malarial blood forms, the stage of the parasite's life cycle that lives in a person's red blood cells. If the metabolism of malarial parasites can evolve to escape previously lethal drugs, it is at least possible that the notably variable antigens on the surface of malarial blood forms can also evolve to escape host antibodies stimulated by a vaccine.

The possibility exists that there will never be a single unchanging malaria vaccine but that, as in influenza, the target always will be moving.

Whether this possibility is real depends on the details of malaria genetics. Partly because evolution by natural selection has received inadequate credit for its role in defeating malaria eradication and control programs, there are remarkably few investigators studying the genetics and evolution of malaria. Fortunately, the new technique for cultivating the parasite may be a crucial boon to fundamental studies of its genetics.

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