# ARTICLES

## WHAT HAVE INSECTICIDES DONE FOR US? Second AMCA Memorial Lecture, April 1980[1]

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It is fitting that this Memorial Lecture should honor Maurice W. Provost, who as Director of the Florida Medical Entomology Laboratory at Vero Beach carried the torch for mosquito bionomics and ecology during the decade of the 1960's when insecticides were riding high, and had the satisfaction of seeing his ecology studies come into their own when insecticides fell into disfavor. Yet Maury was eminently fair in acknowledging the contribution of chemicals, as expressed in the masterly section he wrote on organized mosquito control in the U.S.A. for the National Academy of Sciences' report on Pest Control and Public Health released in 1976.

Thus today we will address ourselves to what insecticides have done for us. It being a Memorial Lecture, we will look more to the past then to the future. The impact of the introduction of DDT at the end of World War II, I remember, hit us in 1947 on the tundra at Churchill on the shores of Hudson's Bay, where people had to remain muffled to the ears even in the short summer, because of the hordes of mosquitoes. After an aerial application of DDT at 0.25 lb/acre from a C47 military transport, there was Brian Hocking stripped to the waist and sunbathing, to the amazement of Cecil Twinn and Bill McDuffie, the Canadian and American leaders of the study group there. This unprecedented success for an age-old problem led to a regular procedure of DDT airspray for all the northern defense bases which was repeated annually for the next 20 years. No DDT-resistance developed in these northern *Aedes* mosquitoes, and the food-chain residues had not quite reached a level of danger for peregrine falcons by the time that DDT was replaced by malathion in 1970.

In the lower latitudes of the U.S.A., where biological developments happen faster, resistance to control by DDT was noted in the salt-marsh *Aedes* of Cocoa Beach, Florida as soon as 1948, after treatments for the previous 3 years. A year later the development of DDT-resistance in *Aedes nigromaculis* was proved in tests made by R. M. Bohart and Don Murray in Tulare County, California. Extensive testing by C. M. Gjullin and Dick Peters throughout the San Joaquin valley in 1951 revealed resistance not only to DDT but also to toxaphene and cyclodiene-type organochlorines. Since it appeared in all the agricultural areas but not in the uncultivated hinterlands, the resistance evidently was mainly due to insecticides applied to the crops.

In consequence, parathion and malathion were substituted as larvicides in California, and malathion adulticide (sometimes supplemented by Paris green larvicide) in Florida. During the 1950's the organochlorines DDT and HCH were still effective in New Jersey, while in Minnesota DDT could be applied as preemergent dust or granule treatments before the spring thaw. By the early 1960's, more than three-quarters of the total amount of insecticide applied in the

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U.S.A. against mosquitoes were organophosphorus compounds, principally malathion.

Meanwhile on the world stage DDT had been proving its power of controlling the insects that transmit the most formidable parasitic diseases of man, namely malaria with originally 300 million new cases each year, filariasis with some 250 million persisting cases, and onchocerciasis with some 50 million cases in tropical Africa and Central America. It was especially effective against the *Anopheles* vectors of malaria and the *Simulium* vectors of onchocerciasis, although not so effective against *Culex* vectors of filariasis. DDT also controlled the body lice that transmit typhus, and the flea vectors of plague. In 1948, the Nobel prize in medicine was awarded to Paul Müller of Basle, Switzerland, the discoverer of DDT as an insecticide, because of the exceptional promise of this compound to protect human health.

The Mediterranean island of Sardinia, where 9 out of 10 inhabitants contracted malaria, was selected in 1947 by the Rockefeller Foundation for an attempt to eradicate the *Anopheles* vectors by means of DDT (and certain other organochlorines) applied as larvicides and residual adulticides. By 1950 the eradication of the vectors had failed, but the eradication of malaria transmission had succeeded, due essentially to the residual sprays applied to the interior walls and ceilings of the houses. The DDT deposits had ensured that no *Anopheles* female could escape being killed during the 10-day period necessary for an initially infected mosquito to become infective for another human.

In more than a dozen countries in the tropics and subtropics, annual house spraying for 3–4 consecutive years proved its ability to stop the transmission of malaria. With DDT or dieldrin the dosage was 2 grams per square meter of wall surface. A 5% suspension of the insecticide in wettable powder form is applied from a 5-gallon pressurized backpack sprayer, the flat-fan nozzle producing a 75-cm swath from 45 cm away; if the nozzle is moved up the wall, across and down again at 0.5 m/sec, the deposit is expected to be 2 g/m$^2$. Based on such a simple standard procedure, the World Malaria Eradication Campaign got under way in 1957 coordinated by WHO. With more and more countries joining the campaign, by 1961 the 4-year attack phase of total coverage of all dwellings had progressed to cover an aggregate population of 575 million people in more than 100 million houses. In that year, for example, 190,000 spraymen applied a total of 64,000 metric tons of DDT, besides 4,000 tons of dieldrin and 500 tons of gamma-HCH.

The results achieved by the world campaign over the decade 1959–68 are expressed in terms of the total human populations of all the land areas (countries or states) in which the transmission of malaria had completely ceased. In 1959 this figure already stood at 259 million people, but in 1968 it attained a total of 651 million. Thus the eradication campaign during those 10 years had completely stopped the transmission of malaria among a population of nearly 400 million, which is about one-fifth of the global population of 2 billion people living in originally malarious areas.[3]

Residual insecticides had been the essential weapon of attack in the world malaria eradication campaign; indeed the position already attained before it commenced had been mainly due to insecticides. The figure of 651 million reached by 1968 represents almost one-third of the world population in the areas originally subject to malaria transmission. By this date malaria was completely eradicated from all of Europe except Thrace in the far southeast, from the southern U.S.A. and all the West Indian islands except Haiti, from southern Japan, Taiwan and northern Australia, and from Israel and Lebanon. By 1973 the esti-

[3] These figures did not include China (mainland), North Korea, and North Viet Nam.

mated number of cases in the world, exclusive of Africa south of the Sahara, was down to 3.4 million per annum. If we add tropical Africa, however, the global figure becomes nearly 100 million, to be compared with the 300 million at the end of World War II when the population was only half as great. The number of deaths in the world from malaria has been estimated by Leonard Bruce-Chwatt to have dropped from about 2.5 million per annum down to less than 1 million in 1968. The saving each year of more than a million lives, mainly those of children in Asia and Latin America, is no small humanitarian achievement to be credited to the use of insecticides.

It was the inexpensive price of DDT and the other organochlorines that made the global campaign economically possible, the annual cost of insecticide and its application being only 10–40 cents per head of population protected, and most of the countries involved received financial aid, mainly from the U.S.A. But by 1968 the development of DDT-resistance had been detected in 15 of the *Anopheles* species; nearly all had acquired dieldrin-resistance as well, which had developed in 36 species. To counter the double resistance in *An. culicifacies* in western India it became necessary in 1968 to switch to the organophosphorus insecticide malathion, which increased the per capita cost of insecticide plus application by 3 times. Further difficulties became apparent in 1968; in Sri Lanka (formerly Ceylon), where eradication had not quite yet been achieved and spraying had been cut down to residual foci only, there was a sudden epidemic of some 2 million cases, fortunately of the benign tertian *vivax* malaria. During the next 5 years in India, the spread and intensification of DDT-resistance in *An. culicifacies* imposed the Hobson's choice of either continuing with decreased effectiveness or incurring the increased cost of a substitute insecticide; this, coupled with increasing labor costs and decreasing funds available, resulted in the annual number of Indian cases reaching 270,000 in 1974, of which 20,000 were the virulent *falciparum* malaria. By 1979, DDT-resistance had become so prevalent in *An. culicifacies*, and in *An. stephensi* and *An. sacharovi* as well, that malathion simply had to be substituted for DDT over the great stretch of territory extending westwards from India through the Middle East countries as far as Turkey.

In Central America, the resistance problem by 1968 was even more severe, necessitating a switch to the carbamate insecticide propoxur (Baygon). This was because in the agricultural areas of El Salvador and Nicaragua the vector *An. albimanus* had become resistant to malathion (and fenitrothion) as well as to DDT and other organochlorines. But this anopheline quickly proceeded to develop propoxur-resistance in these agricultural areas by 1970 and subsequently in other Central American countries. Of the residual adulticides suitable for house spraying, only fenthion (Baytex) and the carbamate Landrin remain unaffected by this multi-resistance in *An. albimanus*. Meanwhile malathion-resistance has been developing in *An. culicifacies* in India, and in *An. stephensi* in the Middle East, but it is usually not yet strong enough to dictate a switch to propoxur; here again there is no cross-resistance to fenthion. In southern Turkey there is a curious organophosphorous-resistance in *An. sacharovi* that involves fenthion and fenitrothion (also propoxur) but not malathion.

It is possible that the pyrethroids permethrin and decamethrin will prove effective residual adulticides, but pyrethroid-resistance has been induced by laboratory selection experiments in adults of 2 anopheline species. The OP compound temephos (ABATE) has now been quite widely used as a larvicide for anophelines not only in El Salvador, Nigeria and Iran, but also in Jordan and the Arabian peninsula, where there are now indications of growing resistance to temephos. The only biological control agent being employed to any extent against anophelines is the mosquito-fish *Gambusia affinis*, notably in Iran; however, a number of pathogenic microorganisms are under development through a WHO scheme. Genetical control by the sterile-male technique of *An. albimanus* in El Salvador continues to be promising. Greater stress is being placed on reduction of anopheline breeding by a variety of methods. Further breakthrough possibilities to overcome the present obstacles to malaria eradication, e.g. drugs, vaccines, depend on a knowledge of the disease and the causative organism as well as the vector, and these can best be assessed by a malariologist such as Dr. Bruce-Chwatt.

The second great mosquito-borne parasitic disease, filariasis, proved to be much less susceptible to insecticidal control than malaria. Urban rather than rural, the principal vector *Culex quinquefasciatus* (= *fatigans*) was not so dramatically affected by the house-spraying with DDT; its larvae were more tolerant, and quite soon developed resistance to DDT and to dieldrin and gamma-HCH as well. The Indian filariasis control program had to fall back on larvicidal oils, and was discontinued by the early 1960's. Now the organophosphorus compounds fenthion and chlorpyrifos (Dursban) have proved effective weapons against *Culex*, even in heavily polluted water. In the city of Rangoon, Burma, where filariasis had become prevalent due to the post-war influx of population outrunning its sewage facilities, weekly applications of fenthion at 1 ppm to a city quarter where the incidence of the disease had reached 35% by 1960 succeeded in cutting the *Culex* density enough to prevent new infections without encountering resistance problems. However, since such insecticidal control methods are expensive for developing countries, stress has been laid on the introduction of biological control agents, such as the guppy-fish *Poecilia reticulata* which can tolerate water pollution, and the nematode *Romanomermis culicivorax* being more suitable for anopheline control in unpolluted waters. A variety of micro-organisms are under development for larval control, for example the bacteria *Bacillus thuringiensis* var. *israelensis* and *B. sphaericus*, the protozoan *Nosema algerae*, and several species of the fungus *Coelomomyces*, but their effectiveness lies more in the future. Meanwhile genetical control of *Culex* by the sterile-male technique in India has been discontinued.

The third great insect-borne parasitic disease, onchocerciasis, is a filarian infection which eventually harms the eyes, transmitted not by mosquitoes but by black flies. Sometimes called river-blindness, it is particularly vulnerable to control by treating with insecticides the streams in which the *Simulium* larvae breed. A quarter-century ago, DDT applications over a period of years against *S. neavei* succeeded in eradicating this vector and onchocerciasis transmission from western Kenya. In 1973 the Onchocerciasis Control Program in the Volta River Basin was set up to cover an area in inland West Africa measuring 600 km by 1200 km (slightly larger than Texas) shared between 7 nations, in which there were about 1 million human cases including some 100,000 blind. Applications of temephos (ABATE) were made from helicopters and fixed-wing aircraft to the rapids in which the larvae of the *S. damnosum* complex breed, at a dosage of 0.1 ppm per 10 minutes' water-flow. The weekly treatments were commenced in 1975, and by 1977 had been extended to all the 14,000 km of streams and rivers in the area. The result was that by March 1979 the black fly vector population had become virtually zero in all parts of the Program area. No new infections of *Onchocerca* could be found in infants born since the applications had started, and the threatened immigration of new black flies from the southwest had not changed the picture of success. As the control program continues, populations of Africans are now moving into the well-watered riverine lands which they had formerly avoided because of onchocerciasis.

Returning to mosquito-borne diseases, we can now briefly consider *Aedes aegypti* and the highly domestic strain which came to the Western Hemisphere from Africa along with yellow fever virus. Although outbreaks of urban yellow fever in the Americas had ceased by the mid-1930's, the introduction of DDT 15 years later facilitated the eradication of the mosquito vector from Central America by 1957 and from most of South America by 1959. But the species has persisted in Colombia, Venezuela, the Guianas, and in most of the Caribbean islands, where DDT-resistance first became evident in Trinidad in 1955, following an outbreak of jungle yellow fever the year before. Malathion and later fenthion were substituted for use in the perifocal method of spraying on and around the breeding places, but by 1974 malathion-resistance was present in 6 of the island states and fenthion-resistance in 8 of them. Temephos also, introduced as a larvicide, was beginning to encounter increasing tolerance in the Bahamas and Virgin Islands. For the past 17 years the *Ae. aegypti* surviving in the Caribbean islands and Colombia has been transmitting the viruses of dengue fever and causing extensive epidemics. Insecticidal control would still be effective to the extent that money and effort could be put into it, witness the successful elimination of spot reinfestations in the eradication areas in Central and South America. For the much more serious dengue hemorrhagic fever transmitted by *Ae. aegypti* and *Ae. albopictus* in Southeast Asia, 1% temephos on sand granules can eliminate their larvae in the domestic water jars.

With the encephalitis diseases, the role of public health insecticides is often overpowered by the much heavier applications of the same compounds in agriculture. Such is the case with Japanese B encephalitis transmitted by *Cx. tritaeniorhynchus* in the rice-growing areas of eastern Asia. It also applies to the control of western equine encephalitis transmitted by *Cx. tarsalis* in the multiple-crop areas of California, where the public demand for mosquito control is mainly prompted by the prolific breeding of *Ae. nigromaculis* in irrigated pastures. But despite the growth of larval resistance to malathion, parathion, methyl-parathion, fenthion, chlorpyrifos and temephos in these mosquitos, human cases of western encephalitis have been reduced to rarities, except after disasters such as floods and earthquakes. MADs in the western mountain states have been similarly successful. New control commissions have been formed in the North-Central states and Canada, due partly to the threat of *Aedes*-transmitted viruses in the California encephalitis (CE) group. On the eastern seaboard, chemical adulticiding in Florida and larviciding farther north have kept the total cases of *Aedes*-transmitted eastern equine encephalitis below 40 per decade. For sudden epidemics of St. Louis encephalitis, which are characteristically unanticipated, the only possible decisive response is chemical control, such as the malathion airspray which terminated the Dallas outbreak in 1966; the same applies to invasions of Venezuelan equine encephalitis, such as that of 1971.

Now that insecticides have passed their heyday, largely due to resistance problems, we must learn what we can from the past to cope with the future. We can expect resistance to come sooner or later to any larvicide we use; laboratory selection experiments have produced strains of *Culex* highly resistant to the pyrethroid permethrin and the juvenile-hormone mimic methoprene (Altosid). We must exploit the full variety of suitable organophosphorus compounds for as long as we can. Periodic susceptibility tests with the methods and kits available can not only detect the development of resistance in a target population but can also investigate its cross-resistance spectrum to see what OP compounds are still effective. Sometimes the OP-resistance does not extend to malathion, and sometimes it is conversely restricted to malathion. Some OP-resistant strains of *Anopheles*, as we have seen, remain susceptible to fenthion. Where adulticides are used, it is important to know whether OP-resistance is accompanied by carbamate-resistance or not. But propoxur adulticide has induced resistance in *Culex* in Tulare County, California as well as in *Anopheles* in Central America. From the standpoint of insecticide management, it is important to know which compound to use first and which one to have in reserve; laboratory selection experiments on culicine larvae have shown that chlorpyrifos is slower to induce resistance to itself and cross-resistance to temephos than vice versa, which would indicate that for larviciding chlorpyrifos should be used before temephos.

Insecticides have enabled MAD's and control commissions to continue meriting and receiving local public funds, any criticisms having been on environmental grounds rather than for lack of overall effectiveness. Decisive control of nuisance populations of mosquitoes has improved the quality of living and protected real-estate values especially in resort areas. Although thousands of tourists return each year from the dengue-infected Caribbean islands, there has been no dengue outbreak in the U.S.A. since 1945, due partly to the Federal insecticidal campaign against *Ae. aegypti* from 1964 to 1968. The high level of protection of public health and well-being already achieved makes it difficult for people to accept anything less. In this sense we are hooked on insecticides, despite their resistance problems. Moreover, insecticides are self-perpetuating to the extent that they upset the existing but rather inadequate natural control exerted by the arthropod predators of mosquitoes. Meanwhile, whatever the future may bring, for the present we may take pride in what insecticides have done for us.

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