

THE INTERRELATIONSHIPS OF MALARIA, AGRICULTURE, AND THE USE OF PESTICIDES IN MALARIA CONTROL¹

Guzmán García Martín, M.D.² and José A. Nájera-Morrondo, M.D.³

Insecticides now play a key role in malaria control. As a result, failure to follow through with insecticide house-spraying programs is likely to spark malaria resurgence in zones now almost free of the disease. Also, over-use of insecticides in agriculture can cause vector resistance and lead to similar unfortunate results.

Introduction

Throughout history, vector-borne disease has been one of humanity's heaviest burdens. Malaria, Chagas' disease, plague, epidemic typhus, yellow fever, dengue, encephalitis, filariasis, onchocerciasis, and leishmaniasis, by their endemic or epidemic nature, have seriously affected man's life in the tropics. A prime example among these is malaria, which for years was called the "queen of diseases."

Before 1948 (when effective control measures began to reduce it sharply) malaria was responsible for an estimated 300 million cases and 3 million deaths a year. Because of its wide geographic distribution, the risk of falling sick or dying from malaria was believed to affect at least three-quarters of mankind. At that time 39 per cent of the total area of the Americas, containing 36 per cent of the population, was considered malarious.

Where malaria attacked, it often produced high mortality and morbidity. It impoverished affected areas' inhabitants, often causing depopulation of fertile tropical regions or preventing settlement. Because of malaria, vast sub-tropical and tropical areas were kept from

joining in their countries' economic and social progress.

Even primitive cultures which regarded the disease as a magical or supernatural phenomenon often managed to discover its relationship to the environment, as the location of many primitive communities has shown.

One of the first documented attempts to explore malaria's causal complex appears in Hippocrates' *Airs, Waters, and Places* of the fifth century BC, in which he describes the relation between stagnant water and malaria. That same century, Empedocles of Agrigento protected the town of Selinus in Sicily from malaria by flooding an estuary and draining marshes. In fact, the very name malaria (or *paludismo* in Spanish) derives from *paludis* (marsh) or *mala aria* (bad airs produced by stagnant waters).

A documented history of malaria's effects on agriculture was given in the work of Celli (1925), who indicated that the periods of greatest malaria incidence in the Roman farmlands coincided with periods of agricultural depression for over two thousand years (1). By causing many inhabitants to leave and reducing the energy of those that remained, the vicious circle of disease and poverty was complete: "Men and women were sick because they were poor; they became poorer because they were sick and sicker because they were poorer." (2)

This vicious circle has also operated in large portions of the Americas. Of the Region's 47 political units, originally malarious areas occurred in 34. These areas, taking in roughly 6

¹Paper presented at the V Inter-American Meeting on Foot-and-Mouth Disease and Zoonoses Control (Mexico City, 10-13 April 1972), agenda item 4, Pesticides. Also appearing in Spanish in *Boletín de la Oficina Sanitaria Panamericana*, Vol LXXIV.

²Chief, Malaria Eradication Department, Pan American Health Organization, Washington, D.C.

³Research Officer, Malaria Eradication Department, Pan American Health Organization, Washington, D.C.



Difficult terrain in a remote area is no obstacle to this member of a malaria eradication spraying team in Bahia, Brazil.

million square miles, are now inhabited by 185 million persons.

All epidemiologists who have analyzed the problem in retrospect agree that malaria has been the most effective of all diseases in preventing man's mastery of the land, and that the regions it attacks cannot compete economically with disease-free areas owing to loss of productive capacity during periods of sickness and the aftereffects of anemia, weakness, and mental apathy.

Many countries have estimated what malaria means to their economy, and in some of them the reduction in work output has been placed as high as 25 per cent. In addition, the problem indirectly affects non-malarious nations or ones that are only slightly infected. Russell (1952) calculated that "imports from malarious countries carry a 'malaria tax,' of probably not less than 5 per cent, due to the fact that malaria among laborers always increases the cost of what these workers are trying to manufacture or produce." (3) For the United States of America in 1962, 60 per cent of whose imports were coming from malarious countries, the

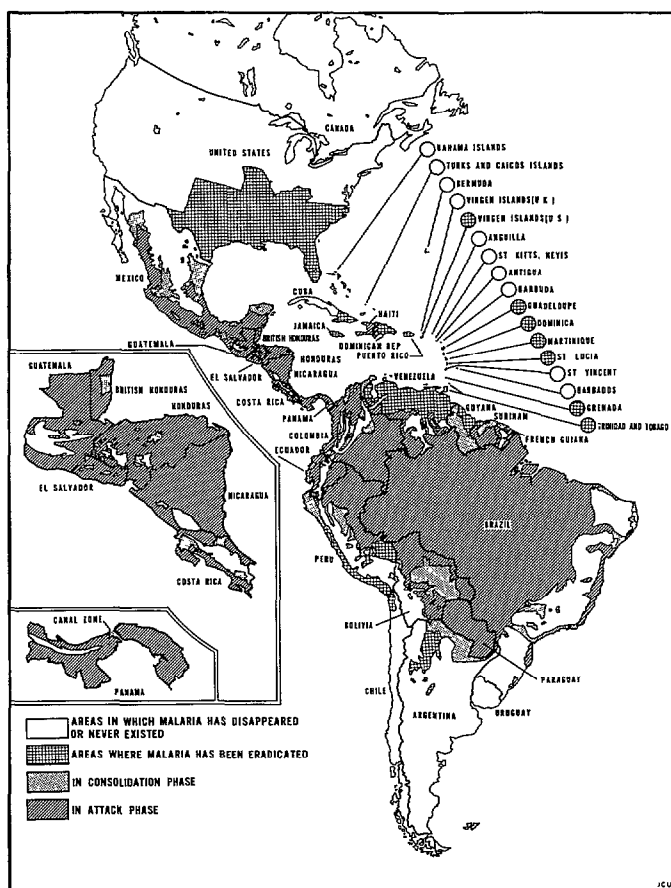
World Health Organization estimated this tax at 300 million dollars per year (4).

In this regard Pampana (1966) said: "In the present era of malaria eradication a number of countries which never had malaria in their territories, or which have now eradicated malaria, are giving substantial assistance to malaria eradication programs abroad. This assistance can certainly be motivated by humanitarian or political reasons, but it might partly be explained also as a profitable long-term investment, because malaria is also an expense for non-malarious nations." (5)

Agricultural Development

The epidemiology of malaria is so closely related to the environment that it can be studied as a "landscape epidemiology." Some areas, because of their ecology, have a high natural malaria potential. The disease is usually eradicated by periodically spraying houses with DDT (thus interrupting disease transmission) and continuing this treatment until human infections die out through aging of the infec-

FIGURE 1—Status of the malaria eradication program in the Americas, December 1971.



tion. In most regions where malaria has been eradicated, however, the vector is still active; and if infected persons enter such areas conditions favor reintroduction of the disease. Such a malaria potential can be favorably modified by agricultural development involving regulation of water courses, drainage, ground levelling, filling in of lagoons and marshes, and removing vegetation that favors vector mosquitoes near dwellings. Frequently, however, man's activities increase a region's malaria potential by increasing the water area and hence the number of breeding places for malaria vectors. Thus, in addition to the basic malaria potential under natural circumstances, man-made conditions can increase the incidence of the disease, should we forget that it is bad engineering that leaves health problems behind.

Once canals meeting indicated health requirements are constructed, problems still remain concerning irrigation systems required for specific crops such as bananas, sugar cane, and especially rice. (These three products are of particular interest, since their importance in domestic consumption is augmented by their contribution to foreign trade.) Rice crops irrigated by flooding have been the cause of serious malaria focal problems, but often the difficulties have been solved, without reducing production, by using a system of intermittent irrigation.

When projects carried out in malarious or potentially malarious areas modify the environment, construction engineers and malariologists must work together to prevent additional malaria and do all possible to eliminate that

which already exists. These actions will protect health, increase the construction workers' output, and increase the projects' benefits by improving the health of the resident population.

The Italians called malaria control by means of small-scale hydraulic works *parziale bonifica* (partial improvement). On the other hand, technically planned agricultural development leads to *bonifica integrale* (total improvement), which was defined by the International Conference on Hygiene of 1931 as the total sanitation of land where malaria and other endemic diseases reduce the inhabitants' vitality. This includes land drainage and preparation for cultivation, construction of roads and sanitary housing, and provision of potable water and hygienic sewage disposal.

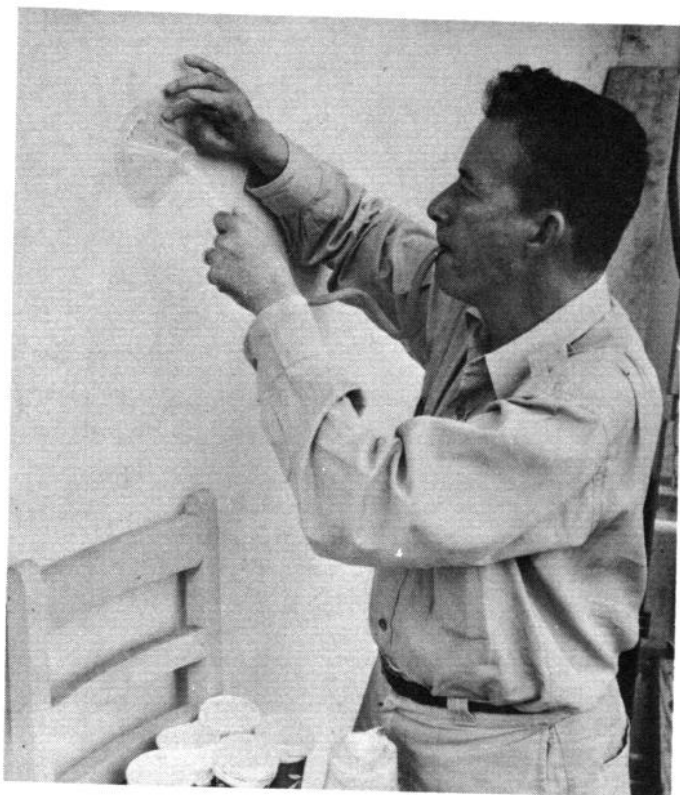
Besides favorably modifying the environment, such actions yield socioeconomic improvements by transforming poor regions with unstable populations into productive areas with stable populations, in which health protection services can be more effective. It should be borne in mind that "as a source of employment, agriculture remains the principal activity in Latin America," and "almost all the countries regularly obtain more than half their foreign exchange earnings from exports of agricultural commodities." (6)

Extensive investments are now being planned for agricultural development projects, most of them in malarious or potentially malarious areas. Also, the general need to include the health sector in economic development plans is currently recognized. Therefore, these projects should include health costs for protecting workers and the resident population by means of a modernized version of the *bonifica integrale*.

The Role of Insecticides

A strong link between agricultural and health activities is their common use of insecticides—on one hand to eradicate or control communicable diseases by attacking their vectors, and on the other to control arthropods that cause major crop losses. Before the arrival

of DDT, available control measures could only attack malaria and other vector-borne diseases in very populous or economically important communities representing small islands in those diseases' zones of distribution. The new weapon made possible intradomiciliary spraying, effectively extending malaria control activities to the rural areas, which were the most gravely affected.



An entomologist collects *Anopheles* mosquitoes, left exposed on a wall sprayed with DDT, to check on the effectiveness of the insecticide.

The advent of malaria control and eradication campaigns on a world scale, based on house-spraying with DDT, reduced the estimated number of cases and fatalities from 250 million cases and 2.5 million deaths per annum in the decade 1950-1960 to roughly 100 million cases and 900,000 deaths per annum ten years later.

If the 1950-1960 incidence had continued during the following decade, there would have been 25 million deaths instead of the 15 million that probably occurred; this means there was a reduction of some 10 million deaths during 1960-1970 owing to the use of DDT in anti-malaria campaigns throughout the world (7). If the pre-DDT incidence of malaria were applied

TABLE 1—Status of malaria eradication in the Americas by region, 1971.

(Thousands of persons)

Region	Total population	Population of originally malarious areas									
		Total		Malaria eradication claimed (maintenance phase)		Consolidation phase		Attack phase		Preparatory phase or program not yet started	
		Total	%	Total	%	Total	%	Total	%	Total	%
Northern America	226,890	56,471	24.8	56,471	100.0	—	—	—	—	—	—
Middle America	91,366	53,193	58.2	12,962	24.4	12,273	23.1	27,958	52.5	—	—
South America	195,288	75,828	38.8	11,873	15.6	31,371	41.4	32,438	42.8	146	0.2
Total	513,544	185,492	36.1	81,306	43.8	43,644	23.5	60,396	32.6	146	0.1

to the total population of malarious areas in the Americas there would currently be about 22 million cases and 220,000 deaths each year. The number of cases reported in 1971 was actually 338,296, and the disease can be estimated to have been the direct or indirect cause of about 3,000 deaths.

Malaria is no longer one of the main causes of death in any country in the Americas. We have been able to take possession of fertile lands of the tropics, because even where malaria still exists, protective use of insecticides keeps the incidence at a level which does not greatly affect economic development.

At the present time the world-wide eradication campaign coordinated by WHO, and by PAHO in the Americas, has freed more than one billion persons from the risk of falling sick or dying from the disease. In the Americas, out of 185 million people living in originally malarious areas, 125 million are practically free of malaria risk and the remaining 60 million are protected to some extent by malaria control measures.

Today it is recognized that insecticides cannot be dispensed with either in health work or in agriculture. They contribute to eliminating or reducing parasites that attack man; they increase food production; and they create economic well-being, which can be translated into better health.

Vector Resistance to Insecticides

Insecticides are not a universal panacea in the struggle against insects, and although much has been achieved, more remains to be done. The adaptive power of insects is so great that all the insect orders present in the Triassic period, 230 million years ago, are still with us, a survival phenomenon not equalled by any higher animals.

Insects are so adaptable to environmental change as to be the only organisms contending with man for mastery of the planet. One author has dramatized this fact, asserting that

When the moon shall have faded out from the sky... and the ice-cap shall have crept downward to the equator from either pole...; then, on a bit of lichen, growing on the bald rocks beside the eternal snows of Panama, shall be seated a tiny insect preening its antennae in the glow of the worn-out sun, representing the sole survival of animal life on this our earth... (8)

This adaptive power vis-à-vis insecticides was first observed in 1908, when the San José scale insect became resistant to lime sulphur in the State of Washington, U.S.A. As of 1970, a total of 224 insect and acarid species had developed resistance to some insecticides. Of these, 105 had an important bearing on human or animal health; for example, 38 species of anopheline

mosquitoes had acquired such resistance (36 to dieldrin, 15 to DDT, and one to malathion and propoxur). (9)

Resistance is an inherited characteristic, so insecticides applied to a susceptible insect population containing resistant genes may select a resistant population by destroying the susceptible members. Resistance to the insecticides used in antimalaria work may be divided into four main types: (1) resistance to benzene hexachloride and to cyclodiene compounds (chlordane, dieldrin, etc.); (2) resistance to DDT; (3) resistance to organophosphates; and (4) resistance to carbamates.

The speed and extent of this selection for resistance is due to several factors, perhaps the most important being the resistant character's degree of genetic dominance and the amount of selection pressure (as determined by the amount and penetrating power of the insecticide applied and the frequency and extent of the applications).

DDT resistance studied in five anopheline species was found to be a recessive character, that is to say, hybrids were found to be susceptible. In the case of dieldrin, however, resistance is intermediate in nature, being neither completely recessive nor completely dominant (10). Because of the limited use of organophosphate and carbamate insecticides in antimalarial work, anopheline resistance to them has not yet been thoroughly studied.

The existence of cross-resistance is also important. This usually involves insecticides of the same chemical series, but apparently may also occur between organophosphates and carbamates.

Of the 10 anopheline species regarded as important malaria vectors in the Americas, only three show physiological resistance to DDT in some places: *A. quadrimaculatus* in the United States of America, *A. pseudopunctipennis* in Mexico, and *A. albimanus* in part of the Pacific Coasts of Mexico, Guatemala, Honduras, El Salvador, Nicaragua, Costa Rica, and Panama, and in limited areas of Haiti and the Dominican Republic. People living in areas where the vector is resistant to DDT represent 9.5 per cent of the total population in still-malarious

zones in the Americas. In the Central American countries, there are zones where *A. albimanus* is resistant to DDT, dieldrin, benzene hexachloride, and malathion; there are also foci of resistance to propoxur, first detected in rice fields where carbamates had been used for crop protection. Dr. Georghiou of the University of California is now making a study, in collaboration with PAHO/WHO, of the mechanisms causing resistance to organophosphates and carbamates in anopheline mosquitoes—and of the extent and importance of cross-resistance.

Longitudinal studies of resistance to organophosphate and carbamate insecticides in an area of El Salvador have shown that the frequency of resistant individuals in an *A. albimanus* population fell sharply between February and June 1971, when no agricultural sprays were used, although the June 1970 population levels had not been reached by the end of the period. This appears to indicate that the selection pressure has a cumulative effect and is intimately associated with use of insecticides in agriculture (11).

Research undertaken by national malaria eradication programs, with the technical assistance of PAHO/WHO, shows that areas where specific insecticides are widely used in agriculture generally overlap the areas where the malaria vector is resistant to those insecticides. This is because agricultural use produces great selective pressure by acting on virtually the whole anopheline population in the area (males, females, larvae, and adults). In contrast, the intradomiciliary sprayings of antimalaria campaigns act solely on the females that reach dwellings, which represent only a small part of the existing anopheline population. This is especially true for those species with no great preference for human blood, such as *A. albimanus*.

Some observations appear to indicate that if agricultural sprayings with DDT were discontinued for sufficient time in some areas, the currently resistant vector might regain its susceptibility. A 1971 report states that *A. albimanus* DDT resistance appeared in an area of Chiapas, Mexico in 1963 and caused a sharp increase in malaria. The resistance appeared

FIGURE 2—Areas of *A. albimanus* resistance to DDT in Middle America, 1971.



after DDT was used on cotton crops. When the crop was changed, suspension of DDT use was followed by reappearance of vector susceptibility, and malaria diminished appreciably (12).

Malaria vector resistance to DDT seriously complicates antimalaria campaigns in affected areas, since DDT continues to be the basic attack weapon. Of more than 1,400 insecticides tested since 1960, WHO recommends only two as possible substitutes for DDT—malathion and propoxur; and in the affected portions of Central America, only propoxur seems likely to succeed in protecting the 2,173,000 inhabitants of areas producing approximately 80,000 cases of malaria each year.

Environmental Issues

There is a growing feeling that use of insecticides, especially DDT and other chlorinated insecticides, contributes to environmental pollution and should be replaced by other methods. Yet despite increased research in this area, WHO recently stated, after in-depth study of the situation, that: "A guess as to the nature of vector control 10 years from now might be that chemical insecticides will still be the principal instrument." (13)

From the standpoint of environmental pollution a distinction must be made between use of insecticides inside dwellings to control malaria, Chagas' disease, plague, and epidemic typhus; outside use for control of other dis-

eases; and agricultural applications designed to protect crops.

Because most living creatures have overlapping habitats, application of insecticides will unavoidably affect non-target organisms. How much they are affected will depend on the size of the areas treated, the dosage applied, the frequency of application, the mobility and dispersibility of the materials sprayed, and the abundance of animal life in the places treated. Dr. Abraham Horwitz, Director of the Pan American Sanitary Bureau, recently noted that

Another dimension was added to the problem in recent years by the outcry against the impairment of natural beauty, the destruction of animal species we wish to preserve, the indiscriminate pollution of water, air and soil, and the consequent effects on the health and welfare of individuals and communities. A veritable syndrome of collective anxiety has developed, accompanied by visions of the future which science has not always been able to substantiate. This is the natural reaction of men in our time who often create crises in order to change given conditions without first pondering other simultaneous or subsequent consequences that may well be even more serious. This kind of thinking applies to malaria eradication and its immediate future. (14)

A report of the Director-General of WHO concludes that indoor house-spraying with DDT in antimalaria work does not constitute a significant risk to man or wildlife, and that the withdrawal of this insecticide would be a major tragedy for human health (15).

A recent survey (Brown, 1971) estimated that the contamination caused by insecticide in giving a typical antimalaria treatment to a heavily populated area (500 inhabitants per square mile) is about 1,000 times less than the contamination due to a normal insecticide application in the tropics to protect a cotton crop (16). Despite the impact that man necessarily must make on the environment, means of protecting both human health and the environment must be sought.

Conclusions

DDT has been the most widely used insecti-

cide for control of vector-borne human diseases, but this use has represented only 15 to 20 per cent of world production. Effective alternative insecticides which are more biodegradable than DDT are available for controlling vectors of most human diseases, two notable exceptions being African trypanosomiasis and malaria. For the latter, there is no sufficiently economical means of replacement on a large scale, though during the last decade consumption has fallen from 60,000 to 35,000 tons of DDT a year.

Using insecticides to increase agricultural production is fully justified, but they should be used in such a way as to prevent risk to the workers who apply them, contamination of human and animal food, accidental poisonings, or production of resistance in vectors leading to resurgence of disease.

According to the recommendations of the Directing Council of PAHO and the Meeting of the Ministers of Health of Central America and Panama (1971), it is necessary to establish efficient mechanisms for cooperation between the ministries of health and the ministries of agriculture in order to determine the specific indications for each insecticide regarding dosage, methods of application, etc.—and to effectively regulate the use of insecticides for agriculture and health so as to obtain the maximum benefits from these chemicals (17, 18).

This inter-ministry coordination should be supported by legislation giving both ministries sufficient authority to prescribe and enforce the rational use of insecticides as well as proper protective measures against any risks they may produce.

In 1971 a survey was made of existing

legislation for the control of pesticides in the Hemisphere. Sixteen countries replied to the questionnaire; six of them had no such legislation; four had some control over pesticide registration, sale, and use, through the ministry of agriculture; the remaining six made some division of responsibility between the ministries of agriculture and health for determining the tolerance levels of pesticide residues and establishing standards for pesticide sale and use. One country had restricted the use of DDT solely to antimalaria activities in certain areas where transmission persists. Seven of the 16 countries were in the process of revising and amending their legislation, actions which indicate the growing concern this problem merits.

The coordination recommended could also produce other benefits, especially in the search for genetic and biologic insect control methods and the application of classical engineering techniques to agricultural and health needs. Keeping in mind the definition of health as “a state of complete physical, mental, and social well-being, not merely the absence of disease or infirmity” (19) such coordination would thus serve both to improve health and to increase agricultural production.

As noted by the World Health Organization, “Where malaria dies the good earth revives. For the individual, eradication makes savings possible, it improves his output and the quality of his work, it urges him along the path of progress. For the nation, malaria eradication means a healthier and happier people, who can make a greater contribution to the national budget. For the Hemisphere, eradication is not an end in itself but has to be coordinated with all the activities leading to improvement of the well-being of the population” (4).

SUMMARY

It has been estimated that antimalaria campaigns saved some ten million lives during the period 1950-1960. This great success is attributed mainly to periodic indoor house-spraying with DDT. It is considered that this method of DDT application does not cause any serious

environmental pollution, nor does it exert enough selection pressure to produce resistance in malaria vectors.

On the other hand, extensive use of DDT for agricultural purposes has been primarily responsible for the emergence of DDT-resistant

anopheline strains. There is some evidence that this resistance wanes if agricultural use of DDT is suspended for a time.

Today there is growing opinion against all uses of DDT. Nevertheless, DDT is still the only effective malaria control weapon in many areas. Of the 1,400 insecticides tested since 1960, the World Health Organization recommends only malathion and propoxur as possible substitutes in limited areas, though neither of the two compares favorably to DDT with respect to safety for those exposed, cost-effectiveness, or ease of application. There is, in short, no possibility to substituting some other insecticide on a large scale.

The growing problem of multiple insecticide resistance, the phenomenon of cross-resistance to various insecticides, and the need to prevent harmful environmental contamination requires creation of effective means of control, by joint action of the Ministries of Health and Agriculture, so as to achieve the best possible use of insecticides for crop protection and health campaigns. Increased cooperation between the Ministries of Agriculture and Health could also lead to development and implementation of more ambitious projects aimed at permanent vector control, on the lines of the classical *bonifica integrale*.

REFERENCES

- (1) Celli, A. (1925) in M. F. Boyd (ed.), *Malariaology*. W. B. Saunders Company, Philadelphia, 1949, p. 7.
- (2) Winslow, C. E. A. *The Cost of Sickness and the Price of Health*. World Health Organization, Monograph Series No. 7, Geneva, 1951, p. 9.
- (3) Russell, P. F. *Malaria: Basic Principles Briefly Stated*. Oxford, England, 1952 (see preface, p. iv).
- (4) World Health Organization. "The World United Against Malaria." *World Health*, Extra Issue, 1962, p. 33.
- (5) Pampana, E. J. *A Textbook of Malaria Eradication*. Oxford University Press, London, 1969, pp. 485-486.
- (6) Inter-American Development Bank. *Socio-Economic Progress in Latin America. Social Progress Trust Fund, X Annual Report, 1970*. Washington, D.C., 1971, pp. 5 and 7.
- (7) Bruce-Chwatt, L. J. "Malaria Eradication at the Crossroads." *Bull NY Acad Med* 45: 999-1012, 1969.
- (8) Holland, W. J. *The Moth Book*. Doubleday, 1905, p. 445.
- (9) World Health Organization. "Insecticide Resistance: The Problem and Its Solution." *WHO Chron* 25: 214-218, 1971.
- (10) Brown, A. W. A. and R. Pal. *Insecticide Resistance in Arthropods*. World Health Organization, Monograph Series, No. 38, Geneva, 1971.
- (11) Georgiou, G. P. "Studies on Resistance to Carbamate and Organophosphorous Insecticides in *Anopheles albimanus*." *J Trop Med Hyg* 21: 797-806, 1972.
- (12) Suárez Torres, G. "Plaguicidas, Medicina y Legislación Sanitaria Mexicana." Paper presented at the I Argentine and Latin American Congress on Pesticides, Buenos Aires, September 1971 (Personal Communication).
- (13) World Health Organization. "The Future of Vector Control." *WHO Chron* 25: 240-242, 1971.
- (14) Horwitz, A. "Malaria Control in the Americas: Introductory Remarks Delivered at the Inter-American Symposium on Malaria Research." Published in this issue, pp. 87-90.
- (15) World Health Organization. "The Place of DDT in Vector Control." *WHO Chron* 25: 201-205, 1971 (See p. 205).
- (16) Brown, A. W. A. "The Ecological Implications of Insecticide Usage in Malaria Programs." *Am J Trop Med Hyg* 21: 829-834, 1972.
- (17) Pan American Health Organization. *XX Meeting, Directing Council of the PAHO; XXIII Meeting, Regional Committee of WHO for the Americas*, (27 September-7 October 1971). Washington, D.C., 1972., p. 124.
- (18) Consejo Centroamericano de Salud Pública. *Informe Final, V Reunión Ordinaria, XVI Reunión de Ministros de Salud de Centroamérica y Panamá*. Secretaría-General de la ODECA, San Salvador, 1971, pp. 34-35.
- (19) World Health Organization. *Constitution of the World Health Organization*. Geneva, 1967, p. 1.