# EPIDEMIOLOGY AND CONTROL OF MALARIA AND OTHER ARTHROPOD BORN DISEASES

### F. J. LÓPEZ-ANTUÑANO

Pan American Health Organization, 525 Twenty-third Street, NW, Washington, DC 20037, U.S.A.

Malaria and other arthropod born diseases remain a serious public health problem affecting the lives and health of certain social groups when the two basic strategies to control fail due to: (1) the lack of effective chemoprophylaxis/chemotherapy or the rapid development of drug resistance of the infectious agents and (2) the ineffectiveness of pesticides or the arthropod vectors develop resistance to them. These situations enhances the need for the design and implementation of other alternatives for sustainable health programmes.

The application of the epidemiological methods is essential not only for analyzing the relevant data for the understanding of the biological characteristics of the infectious agents, their reservoirs and vectors and the methods for their control, but also for the assessment of the human behaviour, the environmental, social and economic factors involved in disease transmission and the capacity of the health systems to implement interventions for both changes in human behaviour and environmental management to purpose guaranteed prevention and control of malaria and other arthropod born diseases with efficiency, efficacy and equity.

This paper discuss the evolution of the malaria and arthropod diseases programmes in the American Region and the perspectives for their integration into health promotion programs and emphasis is made in the need to establish solid basis in the decision-making process for the selection of intervention strategies to remove the risk factors determining the probability to get sick or die from ABDs. The implications of the general planning and the polices to be adopted in an area should be analyzed in the light of programme feasibility at the local level, in the multisectoral context of specific social groups and taking in consideration the principles of stratification and equity.

Key words: malaria epidemiology and control – vector/arthropod born diseases epidemiology and control

The analysis of the health policies and the identification, hierarchization and stratification of the risk factors of being sick or dying from malaria or other arthropod born diseases (ABDs), have been incorporated in the mystic of the public health workers.

Kuller (1978), pragmatically defines health policy as a systematic process for the evaluation and management of the quality and quantity of health care services, including prevention, control and health care services.

In general, the quality of health care is measured by the structure, process and impact of the interventions and the quantity is related to the availability, assessment, cost and utilization of the health services.

One of the greatest challenges for the epidemiologist is the analysis of the health policies and probably their major difficulty is represented by the health economics. The reliable epidemiological information is characterized by the adequate design of protocols (including objectives, hypothesis, methods and means, targets and expected results), the precise definition of numerator and denominator, the quality of data collection and the definition of methodology used of the careful interpretation of the analysis of expected results.

The epidemiologists are not satisfied with a punctual observation, so they prefer multivariate studies in order to determine the value of the dependent and independent variables as well as the weight of destructor elements and to measure the confidence limit of the estimated points.

Ibrahim (1985) relates the application of epidemiological methods for the evaluation of the

F. J. López-Antuñano

health care services in relation to specific problems such as coronary diseases, hypertension, pre and perinatal care but he does not make a deep study of the methodology used for generating health policies that could result in changes to the life-styles of the people at risk of getting sick or dying by these particular health outcomes.

Holland & Wainwright (1979), are sure that the increased utilization of epidemiology contributes to the development of health care services and to the improvement of health. The authors mention specific examples of these contributions; e.g., the relationship between smoking cigarettes and pulmonary cancer, the children's acute respiratory diseases and air pollution control. The emphasis is given to the value of the studies and not to the utilization of generated knowledge in these studies, for the implementation of health policies.

Terries (1980), describes the success of the epidemiological studies to determine the risk factors as well as to design the disease control methods.

Unfortunately, none of these reviews analyzes the risk factors in relation to the activities and life-style of the individuals or social groups, neither the environment risk factors and the characteristics of social and health services for the development of health policies, that will construct favorable conditions for planning and implementing effective investments and interventions based on scientific, political, managerial, operational and financial feasibility studies.

## PERSPECTIVES FOR INTEGRATION OF HEALTH PROGRAMS

"Per capita" indicators should be settled if the existing health policies are to be changed. The degree of social and economic development must be considered, and to determine such level, the study could be concentrated in a limit number of production and consumption of food and nutrients, and other articles for basic needs. Regarding economic development, similar correlation has been documented in relation to different indicators of poverty: for instance, low productivity and low capitalization; high level of illiteracy and high natality and mortality infant rate together with an inadequate consumption of calories and proteins in all ages (Mac Kenzie, 1972). In all industrialized coun-

tries, this correlation is direct within some areas, some social groups and some families; however the global distribution of arthropod born diseases, such as malaria, is a serious health care and public health problem and represents a challenge for the development of health infrastructures in certain developing areas for agriculture, live-stock and exploration of natural resources.

Russett (1974) considers the economical indicators together with political ones and constructs several stages or levels of political and economical development. Easton (1966) and Persons (1976) concept's about the State, search for the reality behind the forms, but no one accepts that, without forms, there is no reality and in the complete organization of a society, collective decisions only may be recognized when the norms are adequate to their procedures.

For Easton (1966) each society has its own political system that takes care of its general disposition and assign values in an authoritarian manner. The political system is the directional nucleous of the society. Parsons, apparently, persists in using the paradigm A-G-I-L since the society is plural and cooperative and include for attributes: Adaptative that persuade Goals, Integrant and Latent; in other words, the economy, the politics, the volunteer organization and the families are totally articulated in each one of the continuous social activities.

The environmental and live-stock management for malaria and other ABDs prevention and control is a priority in the practice of traditional public health and also constitutes an area of special scientific interest. The epidemiologists should be associated with managers and administrators of human and veterinarian public health services, ecologists, entomologists, sanitary engineers, specialists in environmental sciences, sociologists, anthropologists, economists and politicians, not only to design protocols of epidemiological investigations, but also to generate the indispensable information for making the feasibility studies and implementing the resulting plans of actions.

These studies must include the econometric basis of cost-efficiency, cost-efficacy and cost-benefit for the different options of intervention. The decision-making process at political level with then have available the technical and

scientific knowledge of the situation, and the intervention and investment plans will be supported by the feasibility studies.

The apparent success of some vertical programs organized and financed for the eradication of endemic diseases such as malaria, by means of a single control method, has been attracting the attention of the mangers of the general health services and specialized programs, who tried to promote and reproduce it, without taking into account the social and economical transformation, neither the evolution process of social and health services. Consequently, the change of the population's life conditions would make possible the interruption of the transmission and its maintenance with a positive cost-benefit.

It is recognized by the WHO (1960, 1969, 1978, 1979, 1986) that the failure to eradicate endemic diseases, such as malaria, is related to a lack of development of the health and social services infrastructure. Nevertheless, there were programs that intended to be "completely operative" during the preparatory and attack phases of the eradication programs.

The programs expected to solve the problem with a single intervention measure: the spray of insecticides with residual action, inside of all houses, without taking into account the transmission affecting risk factors or other interventions, including protective factors determining prevention and control of malaria and other ABDs.

During the World Health Assembly in Boston (WHO, 1969) it was recognized that malaria eradication was not feasible at global levels with a single attack measure in a predetermined time, so its control must be extended in some areas of the planet using other strategies.

In 1978 (WHO, 1978) the World Health Assembly approved the control strategies as part of the general principles of primary health care strategies, recognizing the variability of epidemiological situations that could favor malaria transmission, the differences among the development levels in the health services and the availability of human, technological and financial resources (WHO, 1979).

Since 1979, important efforts were carried out for implementing the strategies of primary

health care aiming "health for all by the year 2000." But the actual assimilation and implementation of these strategies in concrete programs for the prevention and control of infectious and parasitic diseases, such as malaria, has shown many problems of interpretation, delay in their implementation and resistance for changing the structural functions already established with different goals. Currently, the malaria control programs would present the following characteristics:

- 1. The vertical specialized programs were abolished as a Central Administration Unit and were linked to the province or state level. They remain specialized and semiautonomous both in their technical and in financial components.
- 2. The control program rises as need of the General Health Services, as an answer to the incompetence of the specialized services and to the real demand of the affected population.
- 3. The specialized service, with strong administrative support, keeps its functions with the objective to identify, characterize and con troll health problems. However, before the impossibility to take care of all the social risk groups this service is forced to be associated with other health organizations and social securities, with more potential action.
- 4. The decentralization of the decision-making process and the technical and financial strengthening of peripheric sanitary units (local health services) where it was possible to organize, implement and evaluate "in locus" the opportunity and efficacy of the interventions. The removal of the risk factors for getting sick or to dying from malaria or from other ABDs generates favorable conditions to prevent transmission, utilizing all available local resources with an authentic social participation.

In developing countries, where Health Sectors have economical and technological limitations, attempts to develop modern health carte services capable to provide sensitive and specific medical technology, are expanding.

Many areas of the developing countries have a weak infrastructure and undefined policies to deal with medical technology and public health as a result of a lack of the use of research and of the analysis of policies and norms as basic lines of action. The absence of development urges the countries to import great quantities of biologic materials, pharmaceutical products, insecticides and medical instruments without a careful selection of the best choice, neither taking into account the national capacity to import technology or to make the products in the country (Banta, 1986).

PROJECT PROFILES FOR THE CONTROL OF MA-LARIA AND OTHER DISEASES TRANSMITTED BY VECTORS IN REGIONS OF AMERICA

As was mentioned during the 103 Executive Committee, 1989, the eradication of malaria and other arthropod born diseases needs an urgent reorganization of prevention and control programs. It is not sufficient to give political priority to combat these diseases by the governments, it retrofires the effective participation of all affected sectors: households, health social security, education, agriculture, live-stock and extractive industry.

The control plans have to be based on epidemiological knowledge, in order to allow the identification: (a) the risk groups and the risks factors for getting sick or dying from these diseases; (b) the hierarchization of the risk factors, and (c) the different social and epidemiological strata where the diseases are transmitted, in order to design a feasible investment plan for the execution of efficient and efficacious interventions with social and economical impact.

For this, the following steps for the elaboration of specific would be appropriate projects:

- 1. Improvement of the project outline proposal taking into account aspects related to a detailed knowledge of: (a) the epidemiology (situations, risk factors and trends); (b) the biology and ecology of vectors and reserves, and the environment management for the vector control; (c) the administration, resolution capacity and evaluation of the general social services and, in particular, health services; (d) the social and economic aspects related to the life and health conditions of human population and the analysis of cost-efficiency, cost-effectiveness and cost-benefit of different alternative measures for the prevention and control of arthropod born diseases.
- 2. Elaboration of investment and intervention plan identifying with precision the objection

tives, targets, strategies, activities, presumptive and expected results, based on previous studies of technical and financial feasibility.

3. Identification of internal and external financial sources for the project negotiation and fitness.

The identification and alteration of the environmental risk factors of communicable diseases becomes an important task for the prevention of epidemics caused by ABDs, such as malaria, american trypanosomiasis, leishmaniasis and dengue in the American Region.

The socioeconomical decline, many people living in one bedroom, changes in the way of living and rapid modifications of microe-pidemiology, favor the breeding places for mosquito vectors, increase the contact man/vector/pathogen, affect the transmission of ABDs and accentuate the worsening of the epidemiological situation in the region.

In recognition of these problems, the Secretariat of the Pan American Health Organization has been supporting the development of the following activities: case studies, courses, seminars and practical professional training, generation and dissemination of information, provision of orientation and delivery of technical cooperation. These activities are directed to evaluate the impact on health of the environmental development projects of cattle-raising, mining, public labor, irrigation and urbanism, aiming to minimize or eliminate health outcomes.

Environmental Health, Veterinary Public Health, and Communicable Diseases Programs, together with the Pan American Center of Human Ecology and Health (ECO) and the Pan American Center of Sanitary Engineering and Environmental Sciences (CEPIS) are preparing guidelines for these evaluations.

Furthermore, a Panel of Experts for Environmental Management (PEEM) of WHO, UNEP and FAO, have been preparing materials and recommendations and are given support to research in this field, and promoting financial support for the elaboration of projects for control and prevention of ABDs by means of environmental management.

The prediction of the impact of the environmental risk factors in health is difficult to establish due to the lack of understanding and to the high level of inaccuracy, in the attempts to measure the transmission process of the communicable diseases. One of the major problems for the risk approach is the lack of appropriate methods to measure the absolute risk or the incidence of ABDs, in which the relative and attributed risk are based.

It is important to determine the changes and causes of a population's health. Equally important is to establish a system for the surveillance and monitoring of the ecosystem modifications that have consequences in the health, and economical and social well-being of the human population.

Usually, the capacity needed to perform this task is found among the productive system and the scientific community of the agricultural, educational and mining sectors rather than within the health workers.

The indispensable information to understand and manage the effects of the environment in human health, helps for the construction of a sensible alarm system capable to protect the environment and to prevent and control the ABDs.

THEORY AND PRACTICE OF THE MODELS FOR THE DEVELOPMENT OF THE PROGRAMS

Beyond the logical aspects among several kinds of study models, there are hierarchical levels of decision that could have a great relevance in the selection of the criteria to judge the success or failure of any modeling activity and also to establish the appropriate analysis of cost-benefit of the interventions supposed to be most efficacious.

The technical models represent a basic level of scientific research in traditional disciplines such as molecular biology, biochemistry and immunology focused to individuals; or demography, ecology, epidemiology or health systems, if the objectives are directed to social phenomena. The main objective in this kind of work is to generate knowledge not only for understanding the phenomenon but also with the hope for utilizing it in the control of natural phenomena. The important disciplines in malariology include the diagnosis and medical treatment, chemotherapy, pathology, immunology, parasitology, entomology and epidemiology. In the great majority

of these areas, mathematical models have not been extensively developed and only elementary statistical methods. The major application of models is for the study of dynamic interaction among human population and mosquitoes (McDonald, 1955).

The operational models are at the level of operational research and system analysis. They are more concerned with practical activities for prevention and control. The related systems consider mainly the man made aspects, but frequently incorporate the natural systems at scientific level. The emphasis of operational level is modeling the problems faced by the administrative and executive authorities, including some aspects related to organization, management and decision-making process. Most of them are relevant for the malaria and other ABDs control, but the emphasis is still the use of antimalarial drugs against Plasmodium and insecticides against the mosquitoes. The operational models have the purpose of elucidating man made complex systems, in which the managerial control of phenomena requires the understanding of both, natural process and social factors. It must be taken account all kind of barriers imposed by psychological, social, economical and political aspects.

Finally, the hierarchical pyramid apex is at political level where the administrating and the designers wanted to deal with great strategic programs. Notoriously, this type of activity is undefined in its operation. The decisions at this level have unavoidable consequences of great scale and it is highly desirable that they are taken, in the most possible sensible and resonable manner. Unfortunately, the decisions are frequently taken in a precipitated manner, under a great psychological and emotional pressures. There are restrictions about the opportunity to do reflections in the basis of scientific analysis, leading to biased impressions and data, subjective thoughts and arbitrary actions.

The decision-making based on political viability of a model has been recognized at local, national or international levels as a difficult but vital process for the health, happiness and well-being of thousands and millions of people. Nevertheless, the discipline for political analysis to design sound proposals for helping those who make the health policies is not as yet well developed.

Until now, a careful analysis of the physical, biological, social, economical and political impediments has been done, but an opportunity of introducing a major scientific orientation is suggested by Majone (1975): "Policies are made by tentative about the nature of the social process and the performance of social institutions..." and the analysis of the policies must be made by an organism capable to make a critical evaluation of the proposed solutions.

The questions related to the demonstration and validation of the tentative theories can be managed by proper models made ex profeso.

In the present context of malaria control any planning at medium or long-term must be constructed under appreciation of the lower hierarchical activity levels, which includes operational modeling. The first task of the policy analysis is the development of appropriated quantitative models to follow-up the possible consequences of alternative strategies. These may be represented in different scenarios in such a way to facilitate the selection of the more resonable and satisfactory option (not necessarily the best in theory).

In the past, the planning and supply of medicaments and insecticides was the central point. The need was assumed to have adequate quantities of effective components at certain time and place, a lot of information of different type was integrated, but this information was not focused for technical and epidemiological monitoring of endemic malaria.

At operational level, the well structured ABDs control programs knew very well the problems related to resources allocation; the logistics for supplying, distribution, administration and evaluation of drugs and insecticides; they knew much less or nothing about the planning, organization and execution of sanitary measures; the household improvement and the personal protection activities of the population at risk. Parameters comprising the social, economical and political conditions that could facilitate or prevent the execution of the program at local level have been ignored or neglected.

The accuracy of the strategies will depend mostly on the development of quantitative models for the political level.

The biomathematics theory is the basis to epidemiologists and public health authorities for

any practical use of quantitative methods that could help them to understand and control the population dynamics of ABDs protagonists.

It is well known that the malariologists, first Ross (1910, 1915, 1916), and then McDonald (1950a,b) were the first ones to utilize mathematical methods. Even though the malaria literature is full of mathematical and statistical arguments that are used by epidemiologists, entomologists, parasitologists and immunologists, the application of these methods are not always well-grounded.

The concepts of probability can be introduced or ignored without justification. The estimation of parameters with uncertain precision may be derived of numeric data without taking into account standardized methods of the highest probability.

The formulas selected for practical application should reflect the hypothesis of the investigator.

In our opinion the types of biomathematic that we should promote and develop are those that support and facilitate the generation of knowledge, as well as the application of this knowledge to the control of public health problems. The clarity of this thought and the production of a general true and coherent general theory is not completed as yet, because of: (1) the scarcity of available data in the field that allows us to explore and to test the existing models; (2) the absence of opportunities for a productive relationship among the health authorities responsable for ABDs control and those that can contribute for the management of the quantitative methodology of control activities.

Before the simulation models of McDonald et al. (1968) the mathematical work was essentially deterministic in its approach, although occasionally interpretation in a probabilistic manner was made. The first mathematical discussion of genuine stochastic formulation appeared in the critical review made by Dietz (1970), particularly the connection with the hyperinfected model that includes the immigrations and deaths, developed by McDonald (1955) and Dietz (1970, 1971, 1975).

Subsequently, Dietz et al. (1974) and Dietz (1976) returned to the deterministic specification in an improved form (Molineaux et al.,

1978). The simulation model of Dutertre (1976) is also deterministic, but the modifications required to provide the stochastic transitions should be easily made.

Recent studies made by Nasell (1980) revived the stochastic approach. The use of deterministic models, as the first approximation for dealing with the mean values in more complicated models, is always doubtful, specially when these processes are not linear. This could be true even if the size of population studied is large.

It is worth to mention the application of modeling host/vector to a different field: "The transmission of ideas" (Gossman & nEWILL, 1964), that includes the continuous introduction in both populations of new susceptible and infective, as well as the direct removal of susceptible populations.

The work of Dietz et al. (1974) and Molineaus et al. (1978) are examples of the need: (a) to enunciate clearly the hypothesis; (b) to estimate the standard error; (c) to measure the parameters with methods of proven validity; (d) to test the hypothesis; (e) to prove the relationship between the models and the observed data base, and (f) to examine the sensibility of the main conclusions in relation to the possible changes in the parametrical values or to the model structure.

In spite of the methodological difficulties, the work realized by Nájera (1974), in Kankiya, suggests that enough epidemiological information is not available to specify the model parameters with precision. He also found important discrepancy among the calculation of the reproduction rate of malaria parasites when obtained by different formulas. Consequently, a complete review of mathematical models is needed, specially in relation to the incorporation of the effects of the immune response.

Notwithstanding the efforts made by Halloran et al. (1989) and Struchiner et al. (1989), it looks like the observations by Nájera (1974) are still valid regarding the gap in the present knowledge for the implementation of models for planning effective interventions for malaria prevention and control.

Nevertheless, Thacker & Millar (1991) recognized the usefulness of McDonald's stochastic mathematical model as a tool for planning

a successful measles eradication program in Gambia, 1969. This is attributed to the clarity of the hypothesis and to the knowledge of the course of infection, as well as that of the immune response. One of the model hypothesis assumes that the probability of daily contact between an infected and a susceptible person, during the infectious period, is constant and does not depend on the time factor.

Generally, the investigations about the sensibility of mathematical models in malaria or other parasitic diseases only used intuitive ideas. However, there is an extensive relevant literature of application in engineering, and the readers could be interested in reading the text about Tomovic & Vukobratovic's theory (1972) or the book edited by Cruz (1973). For the general discussion about the identification of systems, the Mehra & Lainiotis could be consulted (1976). Dickson & Gelinas (1976) emphasize the systematic determination of the sensibility for the solution of differential ordinary and nonlinear equations with the purpose of estimating the uncertainty both of the parameter's rates and the initial condition.

THE DEVELOPMENT OF PUBLIC HEALTH PRO-GRAMS

#### **CONCLUSIONS**

One of the most complex problems to be considered is the presence of a single plasmodial species transmitted by two or more Anopheline vectors. This problem could be approached following the Garrett-Jones model (1964a, b), that combines the vector capacity of individual populations to form a single aggregate vector capacity. But, when there is other plasmodial species new difficulties are present.

Cohen & Singer (1979) demonstrated the difficulties for the development f a model when P. falciparum and P. malariae are involved. The results seem to show that a simple Markovian model, which describes the changes of probability between one and other survey, is inadequate and does not take in consideration the occurrence of false diagnosis among the infected persons.

Perhaps there is even more pressure for the need to know and deal with the coexistence of other infectious and parasitic diseases. The occurrence of polyparasitism has been reported by Buck et al. (1978a, b, c, d). This implies not

only the presence of multiple infections in social groups, but also multiple successive or simultaneous infections in the same individual.

A variety of clinical, parasitological, virological, immunological, entomological, epidemiological and public health programs have been identified that are mobilizing interdisciplinary research groups for generating more knowledge in benefit of ABDs control and prevention. Little is known about the population dynamics of infectious agents and vectors in the case of multiple infections, which constitute one of the major challenges for epidemiologists and biomathematics interested in ABDs control (González-Guzmán, 1980).

The social end economical implications of the epidemiological situation of ETV are considerable. Green & Baker (1988) stated that selected mechanisms have important implications for the type and priorities of a plan and, in particular, with their relationship with the principles of primary health care strategy (PHC). One of the techniques to evaluate priorities is the economical situation.

To support the PHC strategy, the health authorities of the Americas decided to incorporate the activities of ABDs prevention and control in the local health systems (OPS/OMS, 1988, 1989).

The benefits of infrastructure, irrigation, urbanization, agriculture, live-stock and mining projects could be ebnormous in terms of economic growth, but they could cause a high social cost, as the result of substantial increase of ABDs associated with a missive and disseminated increase of other health outcomes related to the work, nutrition and reproductive functions of the population, the hygiene of the households, the basic sanitation and the depredation and inappropriate management of the environment.

The human behavior for the dissemination or prevention and control of infectious or parasitic diseases (Dunn, 1979) is of vital importance, since it is related with the level of commitent, responsibility and social participation to achieve the goals or not.

To establish solid basis in the decisionmaking process for the selection of strategies, the following scheme is suggested:

- 1. The epidemiological realities should be translated in quantitative terms with a minor ambiguity and more accuracy.
- 2. An essential component to establish the required quantitative basis is that they should be validated and widely applied to real life situations.
- 3. The alternatives of intervention to remove the risk factors which determine the probabilities of getting sick or dying from ABDs must be related to relevant forms of cost-efficiency, cost-efficacy, and cost-benefit analysis and, if possible, with other econometric aspects.
- 4. The implications of general planning and the policies to be adopted in a defined country or area should be analyzed in terms of the program feasibility at local level, in the multisectorial context of specific social groups, taking into account the principles of stratifications and a sense of equity.

The increment of ABDs in their several forms and combinations in some areas of our Continent, together with the lack of knowledge of the transmission dynamics makes the development of epidemiological services one of the highest priorities. We agree that the development of theorical mathematics models are an unnecessary luxury, but it is urgent and necessary to develop and validate practical, sensible and specific instruments to analyze, classify, and stratify different situations and evaluate interventions.

Academic teaching will have a great impact in our countries when the capacity to implement research projects are amplified in order to generate the knowledge about local problems and solutions, and also to contribute for development of science and technology in endemic countries. This will result in the construction and implementation of permanent health programs with an authentic social solidarity participation, towards human development in a healthy work environmental and wellbeing for all.

### **REFERENCES**

BANTA, H.D., 1986. Medical technology and developing countries: the case of Brazil. *Internat. J. Hlth. Serv.*, 16: 3.

BUCK, A.A.; ANDERSON, R.I.; A.A. & FAIN, A., 1978a. Epidemiology of poliparasitism. I. Occur-

- rence, frequency and distribution of multiple infections in rural communities in Chad, Perú, Afganistan and Zaire. *Tropenmed. Parasit.*, 29: 61-70.
- BUCK, A.A.; ANDERSON, R.I.; MacRAE, A.A. & FAIN, A., 1978b. Epidemiology of poliparasitism. II. Types of combinations, relative frequency and associations of multiple infections. *Tropenmed. Parasit.*, 29: 137-44.
- BUCK, A.A.; ANDERSON, R.I.; MacRAE, A.A. & FAIN, A., 1978c. Epidemiology of poliparasitism. Ill Efects on the diagnostic capacity of immunological tests. *Tropenmed. Parasit.*, 29: 145-55.
- BUCK, A.A.; ANDERSON, R.I.; MacRAE, A.A. & FAIN, A., 1978d. Epidemiology of poliparasitism. IV Combined effects on the state of health. *Tropenmed. Parasit.*, 29: 253-68.
- COHEN, J.E. & SINGER, B., 1979. Malária un Nigéria: Constrained continuous-time Markov models for discrete-time longitudinal data on human mixed-species infections. Lectures on Mathematics in the Life Sciences, 12: 69-133.
- CRUZ, Jr., J.B., 1973. System Sensitivity Analysis. Stroudsberg, Penn.: Dowden, Hutchinson & Ross.
- DICKINSON, R.P. & GELINAS, R.S., 1976. Sensibility analysis of ordinary differential equations a direct method. J. Comp. Phys., 21: 123-43.
- DIETZ, K., 1970. Mathematical models for malaria in different ecological zones. Presented to the 7th International Biometric Conference, Hannover, 16-21, August 1970.
- DIETZ, K., 1975. Models for parasitic disease control. Bull. I.S.I., 46: 531-544.
- DIETZ, K., 1976. The incidence of infectious disease under the influence of seasonal fluctuations. *Lecture Notes in Biomathematics*, 11: 1-15. New York: Springer.
- DIETZ, K., MOLINEAUX, L. & THOMAS, A., 1974. A malaria model tested in the African Savannha. Bull. Wld. Hlth. Org., 50: 347-357.
- DUNN, F.L., 1979. Behavioural aspects of the control of parasitic diseases. Bull. Wld. Hlth. Org., 57: 499-512.
- DUTERTRE, J., 1976. Etude d'une modele epidemiologique applique au paludisme. Ann. Soc. Belge Med. Trop., 56: 127-141.
- EASTON, D., 1966. A system analysis of political life. Willey, New York. (dir. ed.): Varieties of political theory, Prentice-Hall, Englewood Cliffs.
- GARRETT-JONES, C., 1964a. The human blood index of malaria vectors in relation eo epidemiological assessment. Bull. Wld. Hlth Org., 30: 241-261.
- GARRETT-JONES, C., 1964b. Prognosis for interruption of malaria transmission through assessment of the mosquito's vectorial capacity. Nature, 204: 1173-1175.
- GOFFMAN, W. & NEWILL, V.A., 1964. Generalization of epidemic theory. An application to the transmission of ideas. *Nature*, 204: 225-8.
- GONZÁLEZ-GUZMAN, J., 1980. A mixed program for parasitic disease control. J. Malth. Biol., 10: 53-64.
- GREEN, A. & BAKER, C., 1988. Priority setting and economic appraisal: Whose priorities are the community or the economy? Soc. Sc. Med., 26: 9191-929.

- IBRAIM, M.A., 1985. Epidemiology and Health policy. Rockville, Maryland: Aspen Systems Corporation.
- HALLORAN M.E.; STRUCHINER C.J. & SPIELMAN A., 1989 Modeling malaria vaccines: Population effects of stage-specific malaria vaccines dependent on natural boosting. *Math. MBiosci.*, 94: 115-149.
- HOLLAND, W.W. & WAINWRIGHT, A.H., 1979. Epidemiological and health policy. *Epidemiol. Rev. 1:* 211-232.
- KULLER, J.H., 1988. Epidemiology and health policy. Am. J. Epidemiol., 127: 2-16.
- MacDONALD, G., 1950a. The analysis of the infection rates in diseases in which superinfection occurs. *Trops. Dis. Bull.*, 47: 907-915.
- MacDONALD, G., 1955. The measurement of malaria transmission. Proc. Roy. Soc. Med., 48: 295-301.
- MacDONALD, G.; CUELLAR, C.B. & FOLL, C.V., 1968. The dynamics of malaria. Bull. Wld Hlth. Org., 38: 743-755.
- MacKENZIE, 1972. Politica y Ciência. Traducción del Inglés por J. Casorla Perez. Aguilar SA de ediciones 1972, Juan Bravo 38, Madrid.
- MAJONE, G., 1975. The feasibility of social policies. Policy Science, 6: 49-69.
- MEHRA, R.K. & LAINIOTIS, D.G., 1976, Sistem identistication: Advances and case studies. London: Accademic Press.
- MOLINEAUX, L.; DIETZ, K. & THOMAS, A., 1978. Further epidemiological evaluation of a malaria moidel. Bull. Wld Hlth Org., 56: 565-571.
- NAJERA, J.A., 1974. A critical review of the field application of a mathematical model of malaria eradication. Bull. Wld Hlth Org., 50: 449-457.
- NASELL, I., 1980. On the Macdonald-Inwin treatment of superinfection in malaria. Report No. TRITA-MAT-1980-4, Dept. Math. Royal Inst. Technology, Stockholm.
- PERSONS, T., 1966. The political aspect of social structure and process. In D. Easton dir. ed. Varieties of political theory.
- OPS/OMS, 1988. Malaria en las Américas. Cuaderno Técnico 19.
- OPS/OMS, 1989. Resolución XIII. Control de la Malaria. 102 y 103 Reunión del Comité Ejecutivo de la OPS. XXXIV Reunión! del Consejho Directivo de la OPS. XLI Reunión, Comité Regional de la OMS para las Américas. Documento Oficial No. 232.
- ROSS, R., 1910. The prevention of malaria. London: Murray.
- ROSS, R., 1915. Some a priori pathometric equations. Brit. Med J., 1: 546-7.
- ROSS, R., 1915. Some a priori pathometric equations. Brit. Med J., 1: 546-7.
- ROSS, R., 1916. An application of the theory of probabilities to the study of a priori pathometry, I. Proc. Roy. Soc., A., 92: 204-30.
- RUSSETT, B.M., 1964. World Handbook of Political and Social Indicators. Yale University Press.
- STRUCHINER, C.J.; HALLORAN M.E. SPIELMAN A., 1989. Modeling malaria vaccines. I: New uses for old ideas. *Math. Biosc.*, 94: 148.
- TERRIS, M., 1980. Epidemiology as a guide to health policy. In: L., Breslow, J.E. & Fielding & L.B., Lave (eds.) Annu. Rev. Public Health: 1: 323-344.

F. J. López-Antuñano

THACKER, S.B. & MILLAR, J.D., 1991. Mathematical modeling and attemps to eliminate measles: A tribute to the late Professor George Macdonald. Am. J. Epidemiol., 133: 517-525.

- TOMOVIC, R. & VULKOBRATOVIC, M., 1972. General sensitivity theory. New Yor: American Elsevier.
- WHO, 1960. World Health Assambly Resolution 13.55, May.
- WHO, 1969. World Health Assambly Resolution 22.39, July.
- WHO, 1978. World Health Assambly Resolution 31.45, May.
- WHO, 1979. World Health Assambly Resolution 32.30, May.
- WHO, 1986. WHO Expert Committee on Malaria. XVIII Report. Techn Rep. Ser. 735.