Epidemiological Bulletin

PAN AMERICAN HEALTH ORGANIZATION

Vol. 5, No. 6, 1984

Plague: Epidemiology and Control

Introduction

Despite earlier hopes that plague would no longer present a public health problem, the disease continues to persist in natural foci which seed recurrent outbreaks in many parts of the world (all continents except Australia) with apparently increasing frequency. These persistent natural foci are situated in a broad belt in the tropical and subtropical latitudes and the warmer parts of the temperate latitudes; the irregular boundaries of this belt extend between 50°N to 40°S latitude. However, within these limits many areas are free of plague. Persistent endemic plague foci, identified by the occurrence of sporadic human cases over the past ten years, are reportedly firmly established in 21 countries of the world; 5 of these are in the Americas.

There have been many recent advances in diagnosis, therapy, surveillance and control of plague, but most of these advances have not yet been put into practice. The need for implementing these new strategies is particularly great in developing countries, where persistent plague is evident. Nevertheless, with general sanitation improvements developed over the last 50 years, and the introduction of antibiotics in the late 1930s and 1940s, the threat of large urban outbreaks with concommitant high case fatality rates has been greatly diminished.

History

Plague is an ancient disease believed to have originated in the Central Asiatic Plateau. Throughout the centuries several devastating pandemics have been recorded:

- Plague that infected the Philistines about 1320 B.C. (recorded in the Bible, 1 Sam. V-VI).
- Plague in Egypt in 100 A.D. (recorded in the writings of the physician Rufus).
- The first recorded world pandemic, in Justinian's time (542-602 A.D.) with the pneumonic form of the disease prominent and with very high mortality.
- The second recorded world pandemic (14th to 16th centuries), which covered Central Asia, Africa and Europe where it was known as the "Black Death," also with very high mortality.
- The third and most recent pandemic (beginning in 1855) probably originated in Central Asia, reached Hong Kong in 1894 and was transmitted by ship to the United States in 1898.

It was during this last pandemic that plague first occurred in the Region of the Americas, initially in port cities, probably introduced by sea or riverboat traffic. Table 1 lists the dates plague first appeared in

IN THIS ISSUE . . .

Table 1. Plague in the Americas, by year of first and last reported cases.

Year of first reported case	Countries infected	Year of last reported case
1898	United States of America	Persistent
1899	Paraguay	1928
1899	Argentina	1944 (1958, 1 case)
1899	Brazil	Persistent
1900	Uruguay	1931
1902	Mexico	1923 (1963, 1 possible case)
1903	Peru	Persistent
1903	Chile	1942
1905 (2 cases in dock workers)	Panama	...
1907	Trinidad	1912
1908	Ecuador	Persistent
1908	Venezuela	1962
1912	Cuba	1915
1912	Puerto Rico	1921
1912 (1 case imported from Trinidad)	Grenada	...
1921	Bolivia	Persistent
1939	Canada	Persistent (in animals only)

Sources: Moll, A. A. *Plague in the Americas*. Publication 225. Washington, D.C., Pan American Sanitary Bureau, 1945.

countries of the Region as well as the dates of the last reported cases. It is interesting to note that the disease persists today in only five of the originally infected countries.

Immediately following the introduction of plague to the port cities of the Region, the large human outbreaks that occurred were initially confined to the more densely populated urban centers. Gradually, however, the infection spread inland, usually along the common routes of transportation. As this geographic dissemination of the disease progressed and the domestic rats intermingled with wild sylvan animals in the more rural areas, the infection was transferred to these sylvatic hosts which today serve as the principal reservoir in areas where plague remains a persistent problem. Extensive, prompt control measures instituted in Panama, Trinidad and Tobago, Cuba and Puerto Rico may have prevented the establishment of persistent sylvan foci of plague in these countries.

Epidemiological Situation

A review of reported cases of plague occurring in the Region of the Americas during the last 48 years is presented in Table 2. It is believed that these reported cases represent only a fraction of the real number of cases that have occurred throughout the years, although as health services are gradually becoming more available in the rural areas where plague is endemic, notification and reporting are steadily improving. Although mortality figures are incomplete, there is also an indication, based on a few well investigated outbreaks, that the case fatality rates which had reached 40 to 50 per cent in earlier years have been steadily decreasing, to 15 to 25 per cent. This also tends to suggest an improvement in surveillance and increased accessibility of health services.

Another global problem in reporting reflects standardization difficulties in case identification. Some countries report only laboratory-confirmed cases, others report both suspected and confirmed cases and still others report only deaths.

Table 2. Plague cases reported from some countries of the Americas since 1950.[a]

Country	1950-1954	1955-1959	1960-1964	1965-1969	1970-1974	1975-1979	1980-1984[b]
Argentina	3	1	–	–	–	–	–
Bolivia	96	48	134	285	87	134	81
Brazil	156	109	494	902	858	594	407
Ecuador	276	306	960	606	69	8	79
Peru	448[c]	151	568	963	306	10	344
U.S.A.	–	6	6	25	26	79	120
Venezuela	14	3	7	–	–	–	–

[a]Total cases for each five-year period.
[b]Reports through August 1984.
[c]Fatalities only for 1950-1952.

Observations made in several areas of the world suggest that there is a cyclic periodicity of rodent plague which is generally reflected by the number of human cases peaking every 5 or 10 years. These years of increased numbers of human cases usually reflect an increase in the geographic areas infected, which relates to movement of rodent populations due to pressures of increased population densities. Since the severity of zootic plague outbreaks is associated with the density of susceptible rodents available, one would expect that following a severe epizootic in which a major proportion of susceptible rodents die from the infection, a period of plague quiescence would follow until the population of susceptible animals is sufficiently high to support a new epizootic.

Further analysis of the available data from South America shows a definitive seasonality which has been related to meteorological conditions which in turn cause population fluctuations in both the rodent hosts and vector fleas. In the United States, sporadic human plague cases generally increase in frequency in early spring (April, May), reach a peak during the summer months (June, July, August) and markedly decrease in autumn (September, October). Similarly, in the Andean countries of South America, the majority of plague cases usually occur during the summer months (November, December, January).

The Role of Rodents in the Epidemiology of Plague

Current concern is directed to certain areas of the world where plague persists. These permanent enzootic foci of the infection serve as the starting point for human outbreaks. The maintenance of infection in these areas appears to be dependent on the wild rodent or small wild animal populations. Periodically, epizootics of plague break out among these animals, exterminating a large portion of them. For some, the infection lies dormant, manifesting itself only by isolated deaths, then later, as the animals breed and a fresh susceptible population arises, another wave occurs leading again to the decimation of the rodent population.

Since about 1910, more and more emphasis has been given to wild rodents as true reservoirs of plague. It was realized that, as a side reaction in the plague cycle, widespread epizootics occurring among wild rodents in natural plague foci may, on occasion, also involve commensal (domestic) rats and mice due to their sporadic contact with the wild rodents. It has been clearly shown that there are ecological differences between wild or sylvatic plague and urban rat plague with respect to host and vector and in the relations of the host and vector to the etiological agent, *Yersinia pestis*, a gram-negative bacterium with wide geographic distribution.

Many attempts have been made to demonstrate the role of various wild or domestic rats and mice in the maintenance of the infection during quiescent periods. From these studies one can only infer that the situation is extremely complex and that extrapolating from one geographical area to another must be done with caution.

It is important to note that some of these small wild mammal species (peridomestic) are more closely associated with domestic rats in the immediate environs of human habitation than are other sylvan colonial species. Thus, the potential danger of transmission of the infection to the urban domestic rats, and hence to man, is obvious.

While the transfer of the infection from wild to domestic rats constitutes a most serious potential for large urban human outbreaks, infection of humans directly from wild rodent sources is a continuous threat.

Although rodents have been shown to be a major reservoir of plague in nature, lagomorphs (rabbits) and insectivores (shrews) have also been incriminated in some areas. To date, over 200 species of mammals have been shown to be naturally infected or directly involved in the plague cycle.

Domestic Animals in the Transmission of Plague

In recent years it has become evident that domestic animals can also play a role in the transmission of plague to man. Both dogs and cats have been shown to be infected by consuming infected rodents. In dogs the infection does not lead to overt clinical disease and is demonstrated only by the appearance of specific plague antibodies. Cats, on the other hand, suffer high mortality, frequently demonstrating clinical symptoms of bubonic plague with suppurating bubos and on occasion, pneumonia, and thus are highly infective to man. Cats that survive the infection also demonstrate high levels of plague antibody. Current investigations are in progress to identify infected areas and to predict increased rodent plague activity by monitoring levels of plague antibody in sera of dogs residing in suspected plague areas.

The Vector

Plague is most commonly transmitted from one rodent to another or to humans through the bite of an infected flea. The plague bacilli develop in a flea which has bitten and fed on an infected, septicemic rat. The ingested organisms multiply in the flea's esophagus at the level of the proventriculus, causing its blockage. This may result in starvation of the flea and subsequent repeated attempts to feed result only in regurgitation of bacteria into the wound of the bite. "Blocked fleas" may live from three to five days and are extremely efficient vectors of plague during this time. Some species of fleas do not have the capability to "block" but nevertheless can cause infection by regurgitation of stomach contents into the bite wound when feeding; these fleas are much less efficient vectors of plague.

Natural transmission of plague from animal to man can also occur directly by contamination of breaks in the skin during handling of tissue or blood from infected animals.

Throughout the years, the oriental rat flea *Xenopsylla cheopis*, the most common flea infesting domestic rodents and perhaps the most efficient flea for plague transmission, has been classically associated with the majority of large urban plague outbreaks. The smaller outbreaks or singly occurring cases of current times are more commonly associated with wild rodent fleas, of which over 100 species have been found naturally infected or passively incriminated as plague vectors.

It is particularly interesting to note that many recent small plague outbreaks in the rural Andean region of South America, and possibly in Nepal, appear, epidemiologically, to involve the human flea *Pulex irritans*. Observations tend to suggest that the index or primary case is infected through the bite of an infected wild rodent flea. Identification and treatment of this index case is frequently delayed and the patient develops a septicemia, often with fatal results. Several days following this initial fatal case, a small outbreak of plague occurs among family members or in members of the community who have attended the wake or funeral of the deceased plague patient. This epidemiological pattern frequently occurs in areas where domestic rodents do not exist, where overt evidence of wild rodent plague cannot be demonstrated and where the human population is heavily infested with *Pulex irritans*. On occasion *Pulex* fleas obtained from the house of deceased plague victims have been shown to be infected with *Y. pestis* and one must deduce that this is truly a human to human transmission cycle with *Pulex irritans* the probable vector.

Some Clinical Aspects of the Disease

The disease in man may appear in three distinct forms. The most common form, bubonic plague, presents as lymphadenopathy with fever. The lymph nodes involved are invariably the nodes draining the site of the infected flea bite. Thus, if the site of the infection (flea bite) occurs in the lower extremities, inguinal or femoral lymph nodes are involved; an infected flea bite on the upper extremities gives rise to axillary lymph node involvement. The incubation period for bubonic plague is usually two to six days; the fatality rate is 40 to 60 per cent if treatment is not prompt. On occasion, in some bubonic patients, the disease may disseminate with lung involvement, thus giving rise to secondary pneumonic plague. Plague pneumonia is a particularly dangerous form of the disease since it is invariably fatal when untreated, and patients with pneumonic plague can transmit the disease directly through aerosolized droplets to contacts who develop a primary pneumonia. The incubation period of primary pneumonic plague is one to two days.

In some infected individuals bubos are not evident and the disease presents with systemic manifestations caused by a septicemia (septicemic plague) which, if untreated, is invariably fatal. On rare occasions bubonic plague may develop into meningeal plague, and is characterized by typical symptoms of meningitis.

Modern therapy with appropriate antibiotics significantly reduces mortality from bubonic plague. Pneumonic and septicemic plague also respond to antibiotic therapy if patients are treated very early in the course of the disease.

Drugs of choice for treatment of plague patients are streptomycin, chloramphenicol and tetracycline. Sulfadiazine is also useful. It should be mentioned that, although in *in vitro* laboratory tests *Y. pestis* demonstrates sensitivity to penicillin, this drug is completely ineffective *in vivo* and should never be considered in the management of plague patients.

Control

The plague transmission cycle in nature can be described as animal-flea-animal with infections to man being more or less an accidental event. Thus, for human

plague to occur it is necessary to have the natural host (small mammals), the vector (fleas), the organism *(Y. pestis)* and the abnormal host (man) temporally and spatially congruent.

Control measures are directed towards interrupting this chain of transmission. The simplest and most economically feasible element to attack in the short term is the flea vector. This can be accomplished by the utilization of an appropriate insecticide dust, to which the fleas are susceptible, carefully applied so that the fleas come in contact with it.

Long term control measures may be directed to reduction of rodent reservoirs, especially in areas of human habitation through improving the environmental sanitation by elimination of rodent harborage and rodent food supply. Rodenticides are of limited use in achieving short term control and should be used with extreme caution. Not only are the majority of rodenticides highly toxic for man and domestic animals, but the rapid destruction of the rodent populations creates a large population of fleas that must seek a warm blooded host—frequently man—to satisfy their nutritional needs. *Therefore, any use of rodenticides in plague areas must be preceded by a thorough and complete flea destruction campaign.*

An additional control activity—especially in areas where human fleas abound—is the prompt prophylactic treatment of all individuals who have had close contact with any septicemic plague patient. Sulfadiazine has been shown to be an excellent drug for prophylactic treatment; however, tetracycline and chloramphenicol are also effective. This treatment, of course, should be combined with the elimination of the human fleas in houses, with special attention to the infested bedding and clothing of the inhabitants.

Evidence provided through a succession of recent outbreaks suggests that the technological advances made to date are inadequate to eradicate the disease in sylvatic foci. The long periods of quiescence in some foci can not be explained nor can the natural disappearance of the disease from other foci. Ecological conditions in each natural focus can be expected to vary and require study to determine the local characteristics of the disease. At the same time, these studies will provide baseline data for improved surveillance and integrated control measures.

Plague in man can be prevented, but only through an ongoing, intensive surveillance system with prompt implementation of appropriate control measures when indicated.

(Source: Dr. James H. Rust, Regional Advisor, PAHO.)

The Social Epidemiology of Malaria

Introduction

The need to understand the social epidemiology of malaria is no longer an issue of debate in PAHO or in WHO. There is now explicit recognition that social and economic factors are significant influences in the transmission and control of malaria.

The stagnation of progress towards the eradication of the disease, which led the Twenty-second World Health Assembly to abandon the global policy for eradication of malaria within a programmable time-limit, also led to the multidisciplinary review of most malaria eradication programs and the recognition that malaria control has to be pursued in the context of health development; in 1978, the Thirty-first World Health Assembly formulated a strategy for malaria control following the principles of primary health care which were to be adopted at Alma-Ata as the overall strategy for health development. The PAHO Advisory Committee on Medical Research (ACMR),[1] which had promoted and stimulated social sciences research in health, recognized malaria as a priority area in 1980 *(1)*. Since then several meetings and at least six research projects have been supported by PAHO in the

[1] At its 23rd meeting, 4-7 September 1984, this Committee changed its name to Advisory Committee on Health Research (ACHR).

Americas, in collaboration with WHO and the UNDP/World Bank/WHO Special Program for Research and Training in Tropical Diseases (TDR).

The term "social epidemiology" may sound redundant since "epidemiology," the study of diseases in human populations, implies a social framework. The adjective "social" is used to focus attention on those social factors which influence the occurrence, distribution and control of disease, as distinct from the biological, geographical and ecological factors which have received more attention.

There is no doubt that epidemiological studies have played a major role in the discovery of the etiology of diseases and will continue to do so. Also it is clear that epidemiological information will greatly assist the physician in the diagnosis and treatment of disease. However, the main purpose for studying the distribution and dynamics of disease in a population is to provide the basis for development of an appropriate control strategy. Epidemiology provides the guidance for public health activities, which are social activities, and therefore, epidemiology must become more closely associated with the social sciences. Social epidemiology must draw on research methodologies and the collaboration of research workers from the social sciences.

Social and Economic Impact of Malaria

Malaria has long been recognized as a disease having social and economic determinants and impact. Most epidemiological descriptions, however, considered social factors, together with the genetic constitution of the population and the physical geography of the area, to be a fixed framework for the interplay of the basic biological factors—man, parasite, vector—which determined the dynamics of the epidemiological phenomena.

Few other diseases have led to the mobilization of such large expenditures in public works and public resources. There are numerous examples of large-scale environmental modifications for the purpose of controlling malaria as early as the draining of the marshes of Selinos by Empedocles of Agrigentum in the VI century B.C. Scientific malaria control was developed after the discovery of the transmission cycle and after the success of economic development projects in malarious areas where malaria control measures had been applied, e.g., the "bonificia integrale" of the Pontine marshes near Rome and the works of the Tennessee Valley Authority *(2)*. Malaria control was recognized as an integral part of the investment for economic development in malarious areas. After the introduction of residual insecticides for malaria control, several areas succeeded in the actual eradication of the disease, and in 1955 the world embarked on an effort to eradicate malaria, the total cost of which in the Americas alone has been of the order of US$1,500 million *(3)*, up to now the largest health campaign ever undertaken.

The Effect of Social Developments on Malaria

Malaria has had a significant impact on society and, in turn, social developments have greatly affected malaria. Processes such as intensive cultivation, leveling and adequate drainage of the land, appropriate construction and maintenance of irrigation canals to prevent wastage of water, improvement of housing, urbanization and proper construction and maintenance of potable water and sanitary systems, particularly when they were part of a balanced socioeconomic development, resulted in the elimination of mosquito breeding places and in reducing man-vector contact. These changes caused malaria to disappear from most of Europe and North America even before specific measures were taken towards its eradication. Whenever these works are improperly built or maintained or are done in disregard of the local population, e.g., irrigation without proper drainage, they will exacerbate the malaria problem, creating the conditions described as "man-made malaria."

Several attempts have been made to relate the favorable evolution of malaria control and the eventual achievement of eradication to the degree of economic development. Although such correlation can be demonstrated in general, it cannot be taken as a scientific law. There are many counter examples—in Northern Germany and Holland in the first half of this century, in Southern Turkey and in many areas of Latin America today—where economic development alone did not lead to elimination of malaria and in many instances resulted in intensification of transmission, until specific antimalarial measures were introduced *(4)*.

Social Epidemiology in Malaria Control

It must be emphasized that social epidemiology should be considered foremost a branch or an aspect of epidemiology. There is no doubt that the impact of malaria on society and social development should in-

terest the sociologist. However, it is likely that the sociologist would consider malaria only in terms of the social impact of illness and of healing, or perhaps in terms of the problems of priority selection in policy making or health policy implementation.

The malariologist sees in the contribution of social epidemiology the possibilities of understanding better the real dynamics of the disease in the population and of being able to design better control measures, adapted to local conditions, and thus to use scarce resources far more efficiently.

The failure of malaria control has been due not so much to the lack of effectiveness of the measures to be applied as to a set of mainly socioeconomic barriers which has affected implementation. Social research may not help to remove these barriers but should help in the understanding of what they are so that a way through can be found or another path selected. In certain perhaps exceptional cases the barriers may be removed.

An appropriate knowledge of the social epidemiology of malaria must be included in the process of designing and implementing malaria control plans. A program for acquiring and improving such knowledge should be developed by those responsible for malaria control, who must be part of the health planning team. Whether the team should include social science specialists as full members or as consultants or whether the malariologist should receive adequate training in social sciences methodologies will depend on the complexity of the social problems involved and the magnitude of their impact, expected or observed, on the epidemiology and control of malaria. How much effort should be devoted to research on the social epidemiology of malaria will depend on local circumstances. In many instances important issues, such as migration, forms of production, working relations, housing and human settlements, will be studied from a broader perspective than that of malaria epidemiology and control; in other cases, studies initiated for the purpose of reorienting antimalaria activities may provide important epidemiological and sociological information of more general applicability.

Traditional Methods of Epidemiological Research

Epidemiology at its beginning, between the 16th and the 18th centuries, was a descriptive science of epidemics and their control. In the second part of the 19th century, epidemiology was part of the great enterprise of elucidating the specific etiology of diseases, to which it has made outstanding contributions. The parallel development of statistics both as an offshoot of mathematics and as a tool for the design and conduct of surveys provided a scientific method for data collection and analysis. The epidemiological method, when it included statistics, proved useful for: a) identification of causes of epidemic phenomena and b) development and evaluation of control measures and their implementation as public health interventions. The inclusion of epidemiology in medical science and its practice mainly by physicians contributed to the emphasis on the natural science research methodologies. This further removed epidemiology from the realm of social studies.

As far as malaria control was concerned, the global malaria eradication program was developed scientifically, following the processes of observation, hypothesis formulation, experimental verification, model building, pilot testing, planning, implementation and evaluation required by the scientific method.

Evaluation, using the epidemiological method, soon showed that progress in malaria control was uneven. Failure was associated with a variety of biological and social problems, and the biological problems were often associated with social problems. For example, parasite resistance to drugs first occurred where socially marginal populations in border areas engaged in certain occupations either illegal (smuggling, marijuana or opium cultivation) or characterized by a great mobility (e.g., rubber collection and gem searching and digging), and vector resistance to insecticides developed and is still most intense in areas of extensive cotton production, which depends on high use of pesticides and temporary migrant labor *(5)*. The investigation of these associations by traditional quantitative epidemiological methods was too slow and costly, and produced only vague or contradictory results.

Social Epidemiological Research Methods

It is now proving necessary to revive appreciation of the interrelationship of social structure, culture, economics, agricultural and other economic practices, ecology, migration and housing in order to select the more pertinent control activities, determine their timing and population targets and improve their acceptability. Social research, particularly using anthropological methods of study, is proving to be the most suitable

approach for providing explanations of many issues involved. Among the qualitative methods generally used in social anthropological research, the following should be mentioned: participant observation, life stories, interviews, mapping, the use of children as collectors of information and essays by older schoolchildren. As Buzzard notes, "older schoolchildren are often the repositories of their societies' highest aspirations and values, as yet undimmed by reality" *(6)*.

Once a tentative explanation for a problem has been obtained, more quantitative methods can be introduced, such as case studies using questionnaires, quasi-experimental designs and epidemiological causal methods, although the use of quantitative methods in social research often presents problems. As Strong and McPherson explain, there are four main dangers to be avoided: 1) to believe that social research should be qualitative only; 2) to force the imposition of measurement to the extent that "relevant data become purely artefactual results"; 3) to build premature models where the mathematical assumptions are "so far removed of the real world that the model is merely a toy without practical use"; and 4) to forget "just how vast the gap is that separates" the achievements of the social and natural sciences *(7)*. It must be recognized, as indicated in this last point, that social epidemiological studies will not provide widely applicable standard solutions.

Social epidemiological research will not in itself give the solution to the general problem of malaria control; rather, it should provide a better understanding of particular problems in malaria control programs so that more effective solutions can be developed.

The Researcher

A critical factor in social research, and as a result in social epidemiological research, is the researcher. It is the researcher who plays the key role in observation, comprehension and analysis of the community and its problems. Moreover, most social research in the field of malaria will involve a type of cross-cultural research. Even if the investigators are working in their own country, they will often find cultural barriers to communication with the study populations. The problem of communication could be formidable; answering patterns, local terminology and culturally determined systems of understanding disease must all be clearly understood by the researcher.

Development of Research Priorities

Research priorities on the social epidemiology of malaria were first discussed under the aegis of the PAHO ACMR at their 1981 meeting *(8)*. At that meeting, work in this area was endorsed, particularly work to refine the conceptual framework for the research, which was developed by PAHO and adopted by the ACMR in 1982.

Since 1979, the Social and Economic Research (SER) Scientific Working Group of TDR has been supporting social science research in tropical diseases *(9)*. The research has as its overall aim to contribute to improving disease control through the inclusion of social, economic and cultural factors in the planning and implementation of control activities. There are two intermediate objectives which guide the promotion of this research:

- Determination of the impact of social, cultural, demographic and economic conditions on disease transmission and control.
- Promotion of the design and use of cost-effective, acceptable disease control programs and policies.

Of the 44 ongoing or completed projects, 22 have focused on malaria, either alone or in combination with other diseases. Six of the projects are in the Region of the Americas and are discussed below. These projects, launched in collaboration between the ACMR's Working Group on Social Science Health Research, the Malaria Action Program and TDR's Scientific Working Group on Social and Economic Research, cover issues in migration, housing and the economic and social factors associated with transmission and control. In addition, one meeting on the general area of migration and tropical diseases has been held in Brazil in collaboration with PAHO *(10)*.

Three of the six projects *(11)* are focusing on the issues of migration and associated social and economic factors in relation to malaria transmission and control. One project in the Dominican Republic intends to use this information to restratify control program efforts. Detailed information has been collected on modes of production, especially the agrarian structure of the country, economic changes and the influx of migratory workers. The restratification of malarious areas will help to concentrate attention where malaria risk is likely to be higher.

Another project, in Peru, will analyze how different ethnic groups and social strata of native communities, seasonal workers and settlers in the jungle react to

malaria transmission. Based on this information, the national control programs will develop control activities for the jungle area. Another team will be working in Rondônia State, Brazil, to assist the national and state health authorities to evaluate economic and social aspects of malaria *(12)*.

In Colombia, one project is analyzing the relationship of malaria to socioeconomic conditions of the families affected by the disease. It is also developing and evaluating methods to analyze the social and economic effects of malaria eradication. Using these results, a methodology is being designed for the control program to use in planning and evaluating control strategies *(13,14)*.

The sixth project underway is a retrospective analysis of the factors leading to successful malaria control in Costa Rica.

While it is too early to speak of results, these projects all aim towards better understanding of the problems confronting malaria control, and particularly towards assisting control program planners in reorienting their strategies. In addition, the methods used in carrying out this research may provide new approaches to the evaluation of control activities.

The 1982 report of the Working Group on Social Science Health Research of the ACMR, noting this research already underway, developed a conceptual framework covering the biological factors, the social variables directly related to them and other social factors affecting the transmission and control of malaria *(15)*.

The Fourth Meeting of Directors of Malaria Programs in the Americas, held in Brasilia in July 1983, recognized the need for investigating the social and economic processes influencing malaria and its control, and recommended as a plan of action for this research *(16)*:

- Development of continental and national research policies.
- Selection of relevant issues for research.
- Development of the research capabilities in antimalarial programs.
- Development by PAHO of conceptual, methodological and operational guidelines.
- Advancement of research on already recognized priority issues, such as migration, modes of production and housing.

These recommendations constitute the framework of a plan of action, developed by the national authorities responsible for malaria control, after assessing the status of the malaria problem in the Region and its trends. This plan reflects, therefore, their joint aspirations concerning the results of this research. The general issues of social epidemiology were addressed at the PAHO meeting on the Uses and Perspectives of Epidemiology held in Buenos Aires in late 1983, whose recommendations are in full concordance with the plan *(17)*. The PAHO Programs of Tropical Diseases, Epidemiology and Research have joined forces in order to provide the best possible support for development and implementation.

Development of Research Policies

There is no doubt that the development of research policies relevant to local needs is a *conditio sine qua non* for ensuring the necessary commitment to appropriate research activities. It is expected that, with the advice of the ACHR and the advocacy and collaboration of PAHO, the countries themselves will succeed in this development.

Relevant Issues for Research

The selection of relevant issues for research will also be done by countries and local authorities in response to the particular problems and constraints which they have identified in attempting to control malaria or in their reorientation of existing vertical antimalarial programs towards the strategy of primary health care. Priorities should be selected according to the key problems facing malaria control and should conform to the specific national research policies.

The evaluation of the malaria situation, the review of past eradication and control efforts and the attempts to reorient the approaches to control have suggested important areas where social epidemiological research should start. Possible approaches to research which can be considered in setting research priorities include: 1) following the objectives and targets of the malaria program such as a) build-up of diagnostic and treatment facilities, b) reduction or prevention of malaria transmission or c) surveillance and reaction to abnormal situations; 2) focusing on the major approaches to primary health care, such as community participation, intersectoral cooperation or selection of appropriate technologies; and 3) studying the problem of malaria control at one level of action—the household, the com-

munity, the lowest peripheral level of the health service, the intermediate level or the center.

A few examples of the types of problems which could be addressed using a combination of the above approaches are described as follows *(18)*:

a) Providing services to the community so that basic facilities for timely treatment of malaria function properly.

- What is the role of the community health worker (CHW) in malaria control?
- How can high risk groups, e.g., pregnant mothers, infants and children, best be protected?
- Who are the traditional providers of antimalarial treatment? Can or should some or all of them be incorporated into the primary health care system? Under which circumstances? How?

b) Evaluating the feasibility of promoting participation of the community in malaria control.

- What are the true costs and benefits to the community and how can they be evaluated, taking into consideration their social weights for each activity?
- What is the role of malaria voluntary collaborators? Should they or can they become CHWs? How should they relate to CHWs and the health services?
- How can the use of personal protective measures be encouraged and supported? Is there a need for any specific malaria message to be developed separately from the general education activities for health?
- What is the level of control program acceptance by different population groups, e.g., new settlers in colonization projects or residents in endemic areas?
- Can the community assist with surveillance and monitoring by reporting treatment failures or new mosquito breeding places or through some other activities?

c) Drawing on the historical lessons of antimalarial work, exploring ways to promote intersectoral cooperation in malaria control.

- What are the priority problems for intersectoral cooperation? Do they include water resources development projects, use of pesticides in agriculture and health resettlement schemes or road building schemes?
- How can use of operational measures for malaria control in economic development projects and other intersectoral activities be ensured?
- How can an appropriate malaria component be incorporated into school and adult educational programs?
- What are the mechanisms for stimulating and supporting collaboration at village and district levels and at the center?

Development of Research Capabilities

A logical complement to PAHO's efforts for the development of national research policies is collaboration with countries in the development of human resources. In the specific field of malaria, training constitutes one of the basic elements of the hemispheric plan for malaria control. Technical collaboration among developing and between developing and developed countries represents the best approach to these activities. PAHO has a key role in promoting and supporting these collaborative efforts and the mobilization of required financial support within the Region or outside, including the TDR Research Strengthening Program.

Conceptual Guidelines

Mention has already been made of the conceptual framework developed by PAHO and adopted by the ACMR at its 1982 meeting. Methodological and operational guidelines, as we mentioned above when discussing general concepts of sociological methodologies, should evolve from attempts to address specific problems.

Applicability of research, as was mentioned before, can only come from comparison of social research carried out under different local conditions. At the moment most research efforts in social epidemiology are being carried out in isolation. In order to assess the wider applicability of the results and of the methods being used, it will be necessary to compare, assess and evaluate these projects. Development of guidelines is a continuing process of comparison, revision and accumulation of experiences, not only by those who are doing the research but by those who use the research.

It is therefore essential that mechanisms for collaboration and interchange of experience and research approaches should be developed. Workshops to compare approaches and situations constitute one useful mechanism for initiating and maintaining this type of collaboration. They should, however, be complemented by joint evaluation of projects, exchanges of research workers and consultations.

Through the use of these mechanisms, PAHO could formulate, review and update guidelines for research and for the conditions of the applicability of results.

Advancement of Research

Finally, current research projects will require continued support. The collaborative study on migration, presented to the ACMR in 1983 and in the process of

development in eight countries of the Region, will address the impact of migration on malaria epidemiology and control. Continued efforts need to be made to stimulate research in the priority areas identified at the country, regional and global levels.

By continuing to encourage and support the application of research to the needs of control programs, the PAHO ACHR can contribute to establishing the field of social epidemiology of malaria and, ultimately, to ensuring that control of malaria can be sustained by countries and communities.

Dedication

The authors dedicated this work to the memory of Dr. Juan César García, whose wisdom, enthusiasm, and determination in support of these issues continue to inspire and guide us.

(Source: J. A. Nájera, Director, Malaria Action Program, WHO, Geneva, and P. L. Rosenfield, UNDP/World Bank/WHO Special Program for Research and Training in Tropical Diseases. Presentation to the PAHO Advisory Committee on Health Research, 4-7 September 1984.)

References

(1) Pan American Health Organization. Report of the Advisory Committee on Medical Research. Working Group on Social Science Health Research, from the Twenty-first meeting. Caracas, Venezuela, April 1982. (PAHO/ACMR/2115).

(2) Harrison, G. *Mosquitoes, Malaria and Man: A History of the Hostilities Since 1880.* New York, E. P. Dutton, 1978.

(3) Pan American Health Organization. Status of Malaria Programs in the Americas. XXXII report. PAHO mimeographed document CD30/INF/1. 1984.

(4) Bruce-Chwatt, L. J. and J. de Zuleta. *The Rise and Fall of Malaria in Europe: A Historico-Epidemiological Study.* Oxford, Oxford University Press, 1980.

(5) Nájera Morrondo, J. A. Malaria as a World Problem. Paper for Study Group on Malaria Control as part of Primary Health Care. Unpublished WHO document MAP/SHS/SG/WP/83.24. Geneva, November 1983.

(6) Buzzard, S. Appropriate Research for Primary Health Care: An Anthropologist's View. *Soc Sci Med* 19(3):273, 1984.

(7) Strong, P. M. and K. McPherson. Natural Science and Medicine: Social Science and Medicine; Some Methodological Controversies. *Soc Sci Med* 16:643, 1982.

(8) Pan American Health Organization, op.cit., Reference *(1), pp. 1-16.*

(9) UNDP/World Bank/WHO. Special Programme for Research and Training in Tropical Diseases. Social and Economic Research. Chapter 12. In *Sixth Programme Report.* pp. 343-376. Geneva, 1983.

(10) Ministerio da Saúde e Superintendencia de Campanhas de Saúde Pública. *Doenças e Migração Humana.* Serie D, Reuniãos e conferencias. Brasília, 1982.

(11) UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases. (Facts and Figures No. 7, 1983.)

(12) Sawyer, D. et al. Malaria on the Amazon Frontier: Economic and Social Aspects of Transmission and Control. (TDR Project ID 840137).

(13) Bonilla de Ramos, E. et al. Development of Research Training Project on Socio-Economics of Malaria Eradication in Colombia. (TDR Project ID 810366).

(14) Franco, S. et al. Malaria and Economic, Social and Cultural Factors: Its Expression in Housing. Necoclí, Colombia, 1982. (TDR Project ID 810082).

(15) Pan American Health Organization, op.cit., Reference *(1),* pp. 21-37.

(16) Pan American Health Organization. Informe Final. Reunião de Diretores dos Servico de Malária das Américas. Junio, 1983. pp. 37-38.

(17) Pan American Health Organization. Informe Final. Seminario sobre Usos y Perspectivas de la Epidemiología. Buenos Aires, 7-10 de noviembre 1983.

(18) These examples are drawn from several reports and discussions held on research priorities in malaria in the different WHO Regions.

Leprosy Update

The number of leprosy cases in the world is now estimated to be at least 10.6 million, and in some tropical areas the frequency of disease exceeds 10 per 1,000 inhabitants. Leprosy can cause severe incapacitating deformities, especially of the hands and feet, and deformed people frequently have to endure the traditional

social abhorrence of this disease. There are two main areas of study, immunology and therapy, each handled by a WHO Scientific Working Group.

Immunology of Leprosy

The lack of any method for in vitro cultivation of *Mycobacterium leprae* is a serious obstacle to progress in research. The discovery that *M. leprae* could be obtained in large quantities from infected armadillos made possible for the first time the systematic development of immunological test reagents and vaccines. In 1974 the Scientific Working Group on the Immunology of Leprosy (IMMLEP) prepared a plan to develop a leprosy vaccine and tests of the immune response to *M. leprae* in man, and to increase understanding of immunopathological mechanisms of disease. This plan has been followed in its main features since that time, although some changes have been made. For example, work on the transfer factor is no longer included, and work on the development of vaccines based on cross-reactive mycobacteria is given a much lower priority. IMMLEP has made a major investment in the production of *M. leprae* in armadillos, and a stock of some 8 kilograms of infected armadillo tissues, chiefly liver, is held at the present time. Methods for the separation of *M. leprae* have been carefully devised to obtain good yields of antigenically intact material, free from contamination with armadillo tissue components. A batch of purified killed *M. leprae* has been produced for human use, and protocols for standardization, potency, and toxicity have been established.

Lepromatous leprosy is the severe disfiguring form of disease, associated with many bacilli in the tissues, and is the main source of transmission of infection. In this form of leprosy, there is a specific deficiency of the cell-mediated immune response to *M. leprae*. Measures to prevent this defect might prevent lepromatous disease, and measures to restore it might cure or prevent the progression of established disease. The immunological basis of vaccine development has been the assessment of *M. leprae* preparations for their ability to induce a specific cell-mediated immune response, and as far as possible, to ensure that all antigens of *M. leprae* are represented in the vaccine preparation. A most encouraging finding has been that killed *M. leprae* without adjuvant induce strong cell-mediated responses and immunity to subsequent challenge with live organisms in animal models. Preparations are now being made for trials of killed *M. leprae* in man. The first step, now beginning, is to conduct sensitization studies in volunteers in nonendemic areas, to determine whether the preparation can induce a significant delayed hypersensitivity response. Studies on protection in endemic populations will necessarily be long term, and a number of epidemiological requirements are being considered in their design. A recent claim has been made, based on research outside the Program, that immunotherapy with killed *M. leprae* and BCG causes skin test conversion and promotes healing in lepromatous leprosy, and studies will be made to confirm this very encouraging and important finding.

Chemotherapy of Leprosy

The objective is to improve leprosy control by chemotherapeutic means. At present, long-term treatment with dapsone is the most frequently used measure, although other drugs are available. There are three main directions of research.

- *The assessment of the needs for improved chemotherapy.* Surveys of dapsone resistance subsequent to therapy have been conducted in many countries and resistance has always been found. This secondary form of resistance appears to be worldwide, and prevalence rates in treated cases may be as high as 10%. Resistant organisms which persist in treated patients are clearly a likely source of infection for others, so that it is not surprising that primary resistance, before treatment with dapsone, has been found in high prevalence in some areas.
- *The better use of existing drugs.* Controlled clinical trials are in progress on the effectiveness of different regimens of combined therapy in sterilizing infections. Dapsone, rifampicin, clofazimine, and prothionamide are included in these studies. The persistence of viable *M. leprae* in tissues is detected by injection into immune-suppressed T-cell deficient rodents, and several laboratories are now capable of undertaking this test. There is now good evidence that chemotherapy need not be continued through the lifetime of the patient, and combined regimens which include rifampicin may shorten the time required for cure. Field trials of combined chemotherapy for a limited period followed by a prolonged period of observation are in progress.
- *The development of new drugs.* Analogues of existing drugs have been screened for activity, and dapsone analogues have been identified which are considerably more active than the parent compound in an in vitro system. Patients often take dapsone irregulary, and a search is being made for long-acting formulations; dapsone prepared as crystals of appropriate size is promising.

The development of new compounds is hampered

by inability to cultivate *M. leprae* in vitro. Present screening methods are slow and require large amounts of the material under test. A slow-growing cultivable mycobacteria *(M. lufu)* found on the banks of a river in Zaire is now being used as a model for screening activity against *M. leprae*.

(Source: Science at Work, UNDP/World Bank/WHO Special Program for Research and Training in Tropical Diseases, 1984.)

The Takemi Program in International Health

The Takemi Program in International Health at the Harvard School of Public Health offers a limited number of fellowships for research and advanced training on critical issues of international health, especially those relating to developing countries. This interdisciplinary program focuses primarily on mobilizing, allocating and managing scarce resources to improve health and on creating sound strategies for disease control and health promotion. To address these issues, it seeks to attract mid-career and young professionals from around the world and from diverse disciplines. Through its fellowships for highly qualified individuals, the Takemi Program seeks to contribute to institutional development and to improvement of national health policy as well as to the advancement of knowledge.

The program is named for Dr. Taro Takemi, the distinguished physician-scientist who served for more than 25 years as President of the Japan Medical Association. Dr. Takemi also served as President of the World Medical Association, through which he worked energetically to bring together people from many nations to address common issues, particularly the development and allocation of resources for health improvement. Dr. Takemi was an early advocate of multi-disciplinary approaches to such complex problems.

The Takemi Program has four major objectives:

1. To create better methods for mobilizing and using health resources in both rich and poor countries.
2. To promote cooperative research and comparative analysis of health policies and programs in different countries.
3. To study transnational causes of ill health, such as population migration and disease transmission, and air and water pollution.
4. To bring together leading health professionals and scholars from many nations for research and training.

The primary goals of research under the Takemi Program are to investigate how resources are allocated and used for health purposes and to develop methods for making such choices more rational and equitable. Initially, the program will focus its research on a few of the world's most urgent health needs, especially in the developing countries, and the most effective ways to meet them. A number of areas of research will be explored, including:

1. The assessment, choice and application of health technology.
2. The structure, organization and financing of health care.
3. The relationships among rapid population growth, increasing pressures on the environment and health status.

In all areas of research, the program will emphasize the social and cultural factors that shape each country's efforts to improve health.

Within this general framework, specific research activities will be selected by the faculty and fellows associated with the program. Fellows will carry out their research projects at Harvard, generally using data they bring with them, but the projects are expected to be closely linked to action programs and to the fellows' subsequent work after returning home. Each Takemi

Fellow will be responsible for a specific research project and will participate in the program's weekly seminar, where the question of how to set priorities under conditions of limited resources and evolving technology will be examined. In addition, fellows are encouraged to participate in courses and other activities, including seminars, relevant to their interests.

The program is not degree-oriented, as course requirements would substantially reduce the time for research and writing. Upon completion of the program, however, Takemi Fellows receive a certificate and a record of their accomplishments as participants. Takemi Fellowships are generally awarded for ten months.

Applicants must have completed graduate degrees and/or had some years of experience. They are expected to demonstrate strong interests in the issues central to the program; potential leadership capacity in their home countries and appropriate preparation (including facility in English) to enable them to benefit from a period at Harvard. Further, they are expected to have made, or to intend to make, a commitment to a career in health for which participation in the program will be of significant value. Applicants may come from any relevant discipline or profession. For additional information contact: Professor David E. Bell, Acting Director, Takemi Program in International Health, Harvard School of Public Health, 665 Huntington Avenue, Building 1, Boston, Massachusetts 02115, U.S.A.

Reports on Meetings and Seminars

Resolution of the Directing Council on Epidemiology in the Americas

On 28 September 1984, at the ninth plenary session of its XXX Meeting, the Directing Council of the Pan American Health Organization resolved to accept the recommendations of the Seminar on Uses and Perspectives in Epidemiology, held in Buenos Aires, Argentina, 7-10 November 1983 (see *Epidemiological Bulletin* Vol. 5, No. 1, 1984). In Resolution XVI, the Directing Council resolved to urge the Member Governments of the Organization:

"a) to reinforce, at all levels, the practice of epidemiology, expanding its scope application to all areas of the sector, including health planning and evaluation;

b) to mobilize and promote the coordination of epidemiological services, research and teaching accordance with the needs of their countries."

It also requested that the Director of PAHO "develop, within the Organization's regular budget, a program of activities to assist the Member Countries in implementing the recommendations of the report," and that he "...seek extrabudgetary funds to enhance assistance in epidemiologic activities in the Region."

Calendar of Courses and Meetings

Courses on Methods in Epidemiology

In collaboration with the University of Montreal, Canada, Claude Bernard University of Lyon, France, is conducting a program of instruction on methods in epidemiology leading to a certificate of university studies.

From 24 June to 12 July 1985 a course will be offered that is open to members of the clinical and public health professions and to all health professionals interested in acquiring an understanding of the methodological bases of epidemiology. The course will draw on the practical problems presented by participants and will require the design of a research project.

The program of study covers aspects of modern epidemiology and the interaction between man and his environment, health indicators, descriptive methods in epidemiology, methods of analytical epidemiology, the foundations of clinical and experimental epidemiology, the epidemiology of the infectious and chronic diseases, the planning of an epidemiological survey and the epidemiology of some pathologies (chosen for their interest to the participants).

For more information write to: Laboratoire de Médecine Préventive, Santé Publique et Hygiene, 8, avenue Rockefeller, 69008 Lyon, France.

International Congress for Infectious Diseases

This Congress will take place in Cairo, Egypt, from April 20 to 25, 1985. One of its objectives is to provide a forum for critical analysis of recent advances in infectious diseases and for analysis of the means whereby such advances can be translated into practical application to meet the needs of all populations of the world. The Congress will discuss the problems of pathogenesis, natural history and control of infectious diseases, and will include in its scope advances in clinical infectious diseases, epidemiology, medical microbiology, protozoology, helminthology, virology and immunology of infectious diseases.

The scientific meetings will consist of an initial two-day colloquium on strategies for control of infectious diseases in developing countries, after which the program will, on each day, consist of one-half day of plenary session and one-half day of open papers. The official language of the Congress will be English. For further information write to: International Congress for Infectious Diseases, c/o Stewart International Ltd., 37 Harvard Street, Brookline, Massachusetts 02146, U.S.A.

Second World Congress on Sexually Transmitted Diseases (STD)

Under the auspices of the World Health Organization and the International Union against Venereal Diseases and the Treponematoses, this Congress will take place in Paris, France, 25-29 June 1986.

The general theme of the second world congress will be "STD and their Social and Economic Consequences." The scientific program will include in particular the following subjects: complications of STD—perinatal and congenital diseases, genital ulcerations, genito-urinary infections with double etiology, AIDS, nonvenereal treponematosis; epidemiological aspects, control programs, and treatments—new approaches to antiviral therapy on STD, resistance to antibiotics used against STD, treatment trials, research into antigenic components of STD factors, methods of rapid diagnosis, vaccines, including hepatitis B vaccine, contraception and STD, health education, high risk groups and how to approach them, and prevention programs and how their components are adapted to different socioeconomic and cultural conditions.

Official languages of the Congress will be French and English, and registrations are open from 1 October 1984. For more information write to: Docteur André Siboulet, 2nd STD World Congress, Institut Alfred Fournier, 25, boulevard Saint-Jacques, 75680 Paris - Cedex 14, France.

First International Course on the Epidemiology of Aging

The London School of Hygiene and Tropical Medicine, in collaboration with the World Health Organization, will conduct a short course on the epidemiology of aging, to be held in London, from 2 to 27 September 1985.

The course is intended for persons who will have the responsibility for planning and running existing services for the elderly or developing new services, or for staff in academic departments with similar commitments to programs for the elderly. It will be limited to 15 participants, who must be fluent in English. The participants will be sponsored by their own governments and, where possible, supported by World Health Organization fellowships.

Topics included are: the demographic transition and its consequences; epidemiological approaches to the study of aging; health and social impacts of aging; the principles of planning and evaluation of health and social services for the elderly; and the definition and measurement of local problems, survey design, sources of information, analysis and utilization of survey data. All inquiries should be addressed to: Professor P. Hamilton, Head, Department of Community Health, London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT, England.

Diseases Subject to the International Health Regulations

Cholera, yellow fever and plague cases and deaths reported in the Region of the Americas up to 31 December 1984.

Country and administrative subdivision	Cholera Cases	Yellow fever		Plague Cases
		Cases	Deaths	
BOLIVIA	–	*5*	*5*	*12*
La Paz	–	5	5	12
BRAZIL	–	*45*	*28*	*26*
Amapá	–	2	2	–
Amazonas	–	9	8	–
Bahía	–	–	–	10
Ceará	–	–	–	14
Minas Gerais	–	–	–	2
Pará	–	31	15	–
Rondônia	–	1	1	–
Roraima	–	2	2	–
COLOMBIA	–	*14*	*14*	–
Arauca	–	1	1	–
Boyacá	–	1	1	–
Caquetá	–	1	1	–
Casanare	–	4	4	–
Cesar	–	1	1	–
Cundinamarca	–	1	1	–
Meta	–	3	3	–
Santander del Norte	–	1	1	–
Santander del Sur	–	1	1	–
ECUADOR	–	*1*	*1*	*6*
Chimborazo	–	–	–	6
Pastaza	–	1	1	–
PERU	–	*23*	*18*	*389*
Ayacucho	–	1	1	–
Cajamarca	–	–	–	269
Huánuco	–	12	9	–
Junín	–	6	5	–
Loreto	–	1	1	–
Madre de Dios	–	1	1	–
San Martín	–	2	1	–
Piura	–	–	–	120
UNITED STATES OF AMERICA	*1*	–	–	*31*
Arizona	–	–	–	2
California	–	–	–	5
Colorado	–	–	–	4
Maryland	1	–	–	–
New Mexico	–	–	–	16
Texas	–	–	–	1
Utah	–	–	–	2
Washington	–	–	–	1

PAN AMERICAN HEALTH ORGANIZATION
Pan American Sanitary Bureau, Regional Office of the
WORLD HEALTH ORGANIZATION
525 Twenty-third Street, N.W.
Washington, D.C. 20037, U.S.A.