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Yellow Fever in the Americas, 1981-1985

Jungle yellow fever (YF) continues to be a major threat in endemic areas of South America. In the 1981-1985 period, five countries—Bolivia, Brazil, Colombia, Ecuador and Peru—reported a total of 640 cases showing a decrease of 61 cases as compared to the 1976-1980 period (Figure 1). Bolivia (266 cases) and Peru (231 cases) accounted for 77.7% of reported cases. Colonists and temporary workers from non-endemic zones as well as natives from enzootic areas engaged in agricultural and foresting activities were the main targets of the disease.

Typically, most patients are males 15 to 45 years old. Thus, reports concerning the 1981-1982 period revealed that males outnumbered females by a large proportion and that about 90% of the patients were above 15 years of age. No cases were recorded in infants below 1 year of age and, with one exception, all in the 1 to 4 year old age group were documented in the Rincón del Tigre region of Bolivia during the 1981 epidemic. Diagnoses for this outbreak, however, were retrospective and relied mainly on clinical data. During the 1984 YF outbreak in Pará State, northern Brazil, 11 of 31 laboratory-confirmed cases occurred among children under 14 years of age including 3 children (1 death) in the 1 to 4 year old age group (the youngest was 2 years old).[1]

[1] *Bol Epidemiol Minist Saude* (Brazil) 16(15-16), 1984.

The highest number of cases in the Region occurs during the first half of the year, usually peaking in March-April. This is probably due to the higher density

Figure 1. Number of cases of yellow fever in South American countries, 1981-1985.

IN THIS ISSUE . . .

Table 1. Reported cases of yellow fever by country, 1976-1985.

Country	1976	1977	1978	1979	1980	1981	1982	1983	1984	1985
Bolivia	19	2	11	10	46	102	95	11	5	53
Brazil	1	9	27	12	27	22	24	6	45	7
Colombia	22	9	105	51	11	7	2	1	16	4
Ecuador	1	–	1	14	2	2	–	5	1	1
Peru	1	82	93	97	30	98	19	27	28	59
Trinidad and Tobago	–	–	–	18	–	–	–	–	–	–
Venezuela	–	–	3	3	4	–	–	–	–	–
Total	44	102	240	205	120	231	140	50	95	124

Source: Health Situation and Trend Assessment Unit, PAHO.

of *Haemagogus* mosquitoes, main jungle yellow fever vector in the Americas, during the rainy season.

No confirmed cases of urban YF have been documented in South America since 1942. The reestablishment and burgeoning of *Aedes aegypti* populations in extensive areas of South America, including rural areas where YF is endemic, pose once more the threat of urbanization of sylvatic yellow fever. The occurrence in 1981 of YF cases near Santa Cruz, Bolivia, a city infested with *A. aegypti,* and the hospitalization of some cases in that city, illustrates the risk of urbanization of the disease. Similar risk was observed in Brazil early in 1985, when three truck drivers sickened in Presidente Prudente, São Paulo State, after contracting the infection, probably in the forests located several hundred kilometers away. Presidente Prudente was found to be highly infested with *A. aegypti* but the prompt establishment of vector control measures and of a YF vaccination campaign prevented a potentially dangerous situation.

During the period 1981 to 1985, the highest number of reported cases were from Bolivia (266). Of the country's departments, Santa Cruz was the most affected. It is noteworthy that the 1981 outbreak in the locality of Espejos, Andrés Ibáñez Province (Santa Cruz), occurred after more than three decades of apparent absence of the disease. Missionaries established for some 50 years in the locality of Rincón del Tigre, which was also affected by an outbreak in 1981, did not recall the presence of the disease in the hamlet before the 1981 episode. Another significant outbreak of yellow fever was documented early in 1985 among migratory workers in the provinces of Nor Yungas, Sur Yungas, and Larecaja (La Paz). Agricultural work and gold mining are the main economic activities in those provinces. The epidemic occurred between January and May and there were 44 patients, 28 of whom died; the case fatality rate was 63.6%. None of the patients had been vaccinated against yellow fever.

Brazil notified 104 cases during 1981-1985 (Table 1). There was a slight increase over the 1976-1980 period, when 76 cases were reported. Of the 46 cases recorded in the 1981-1982 biennium, the majority (32) occurred in states of central-western Brazil (Goiás, Mato Grosso and Mato Grosso do Sul). The outbreak in this region, which started in 1980, demonstrates the cyclical reappearance of the virus in central-western Brazil as documented since 1935. All 58 cases in the period 1983-1985 occurred in the Amazon Region. The number of cases registered in 1984 (45) exceeded by far those in 1983 (6 cases). The 1984 outbreak hit mainly localities of Pará State situated along the north side of the Amazon River. Studies of this outbreak incriminated *Haemagogus (Hag) janthinomys* and *Haemagogus (Hag) albomaculatus* as the main vectors. The first species is a well known vector in the region; however, this was the first time that *Haemagogus (Hag) albomaculatus* had been recognized in Brazil. Mosquitoes of this species were found biting persons near houses located in the forest outskirts and this fact may explain the occurrence of several cases among children recorded during the outbreak. All persons affected were local residents. Prompt vaccination coverage was instituted soon after the outbreak was detected.

A marked reduction in the number of cases was observed in Colombia during 1981-1985 (30 cases) as compared to the 1976-1980 period (198 cases). A significant decrease in case reporting (from 303 to 231 cases) was also observed in Peru during the periods under consideration (see Table 1).

(*Source:* Health Situation and Trend Assessment Program, PAHO.)

Epidemiological Activities in the Countries

National Workshop on Epidemiology in Cuba

In July 1985 a national workshop on epidemiology was held in Havana, Cuba. The purpose was to identify the actions needed to adjust current practice in the areas of services, research, and training, and to formulate a plan of action for the implementation and coordination of the measures proposed. The meeting was attended by 38 local epidemiologists and 2 from PAHO. Of the local epidemiologists, 15 were employed at the provincial level and 2 at the municipal level of the Institutes of Hygiene, Epidemiology and Microbiology, the Pedro Kourí Tropical Medicine Institute, the Institute of Occupational Medicine, the Institute of Cardiology, the Institute of Oncology and the Institute of Angiology, 10 were from the Institute for Nephrology, 4 from the central level, and 7 were members of the teaching staff of the schools of medicine and graduate courses.

During the workshop, discussions centered on the need to broaden the use of epidemiology on the basis of the following conclusions and recommendations:

- To improve the interpretation of existing information, particularly at the most outlying local levels, there should be, in the medium term, at least one staff epidemiologist in each of the country's 169 municipalities and in each teaching hospital.
- The problems of chronic and degenerative diseases, occupational health conditions, environmental pollution, and accidents must be brought progressively within the sphere of epidemiological surveillance through an approach different from that taken to communicable diseases. Future implementation of the nationwide program of one physician for 120 families requires the performance of operations research before new systems for the reporting of those diseases are put in operation.
- Since the evaluation of programs and technologies is tied to the administrative, scientific, and technological areas, active coordination is essential between the epidemiological services and those of medical care, planning, and technology.
- At the same time, it is important to go on improving the epidemiological surveillance of communicable and parasitic diseases that are prevalent or pose a threat of possible reintroduction into the country. The methodology of the study of outbreaks has been improved on the basis of experience acquired during the epidemics of hemorrhagic dengue and other diseases.
- The recent computerization of the provincial surveillance system with the inclusion of "statistical packages" will make it possible to extend and enrich the analysis of information gathered through the regular surveillance system and in directed research.
- The diagnosis of the health situation is regarded as the primary source of guidance for decisions and actions in the health field, and as a basic task of the epidemiological services. It must be steadily improved by including procedures for the analysis of mortality data such as years of potential life lost due to particular causes, and the grouping of causes of death on the basis of the criteria and lists of the *International Classification of Diseases* (ICE).
- Timely application of the results of research in health services is a critical stage of utmost importance. It is therefore recommended that research be integrated into the services at all levels of the system. It was also noted that there is a need to organize a computerized bibliography of published and unpublished epidemiological studies and surveys done in the country during the last five years for wide dissemination to all health services.
- In order for the program to develop properly, and for epidemiologists to accomodate the expected demand for services, it is important that they be enabled to devote full attention to epidemiological tasks and gradually and efficiently delegate their administrative functions, particularly the management of control programs.
- To give effect to the conclusions and recommendations reached in this workshop, some of the components of the epidemiological training now given to health personnel must be reoriented. Both curriculum content and methodology must be adapted to the needs of the different service levels through better integration of teaching and services, the development of in-service training and, in particular, the practice of research in a "learning-by-doing" context.

First Meeting on the Strengthening of Epidemiology in Ecuador

The first meeting on the strengthening of epidemiology was held from 27 to 30 August 1985 at Chorlavi, Ibarra City, Ecuador. It was attended by 25 epidemiologists, administrators, and planners from the Ecuadorian Social Security Institute, Guayaquil State University, Quito Central University, the National Epidemiological Administration, ININMS, CONACYT, the Undersecretariat for Health, and the Juan César García Institute of Health Research.

The agenda included items on epidemiological services, research, and training, and four general presentations were made: the use of and prospects for epide-

miology in the Americas, a diagnosis of epidemiological practice in Ecuador, a diagnosis of the health situation in Ecuador, and the epidemiology of occupational diseases.

The following conclusions were reached in the discussions of epidemiological services and research and education:

Services

Organization of epidemiological services. The central administrative bureau now chiefly engaged in defining norms, supervising, and directing the administration of programs for communicable, parasitic, and chronic diseases, needs to broaden its functions. It was proposed that this process begin with a change of its present name, Dirección de Control y Vigilancia Epidemiológica (Department of Epidemiological Control and Surveillance), to Dirección Nacional de Epidemiología (National Department of Epidemiology). A new administrative bureau was also suggested and it was agreed that the Undersecretariat for Health should propose to the National Health Council the appointment of a multidisciplinary committee to study the proposed bureau, the potential administrative effects at the central, regional and local levels, and its possible implementation.

Epidemiological surveillance. The following salient points were discussed:

- Simplification of the present disease-reporting system in regard to the choice of diseases under surveillance, statistical forms, and information flow.
- Strengthening of the analysis and response capability, particularly at the local level.
- Definition of the concept of a basic administrative unit and its relationship to surveillance.
- Implementation of new techniques for determining the magnitude of chronic and environmental diseases, including work-related health problems. The present use of case-reporting as an indicator for problems of hypertension, diabetes, and cardiovascular disease has not yielded the desired useful results. It was recommended that fresh approaches be studied so that the necessary adjustments might be made without delay.
- Incorporation of a more dynamic epidemiological content into the traditional reference and research functions of the Izquieta Pérez National Laboratories of Guayaquil and Quito. To accomplish this purpose, greater coordination was suggested between the epidemiological professionals at the central and regional levels and the researchers at the Institute, together with joint research on specific health problems.

Diagnosis of the health situation. There was consensus that diagnosis of the health situation is the core of epidemiological work at the central, provincial, and local levels. The activities in this connection currently in progress in the ININMS and the National Epidemiological Administration, with PAHO's cooperation, form a starting point.

Program Evaluation. The limited use made of epidemiology in program evaluation was emphasized. As an initial strategy it was recommended that epidemiological techniques be incorporated into evaluation procedures through methodical cooperation, programmed at the central level, with the technical units of the Social Security Institute and Ministry of Health.

Research and Training in Epidemiology

In the discussion of this subject, some of the limiting factors and possible ways of surmounting them were presented. It was agreed that the establishment of priorities for epidemiological research depended on the Ministry's defining its general policies on biomedical research. The problems created by a lack of properly trained researches, a lack of epidemiological research, and limited use of research findings were discussed in relation to in-service training, formal academic instruction in epidemiology, Ecuador's basic public health course, and the alternatives of continuing education. It was hoped that clearly spelling out a standard of medical practice consistent with the points made in the document "Diagnóstico de la práctica epidemiológica en Ecuador" (Diagnosis of the Practice of Epidemiology in Ecuador) would contribute to an adjustment of training and instruction in epidemiology, which was identified as the main problem to be solved for the strengthening of epidemiological practice in the country.

Three courses of action were considered for promoting the use of epidemiological knowledge acquired in surveillance and research:

- Reorientation of the Ministry's *Boletín Epidemiológico* and the *Revista del Instituto Izquieta Pérez* (Journal of the Izquieta Pérez Institute) as media for the dissemination of epidemiological information in tandem with the Ministry's current effort to set up a national documentation center.
- Financial and technical support to encourage and develop applied research, including the participation of health personnel in the entire research process.
- The development in Quito and Guayaquil of an ongoing process for selecting priority areas of epidemiological research based on an analysis of the health situation. This activity will be coordinated by the epidemiological units.

Finally, for the short term it was proposed that a

high-level epidemiological refresher course be conducted for the young epidemiologists in charge of the central level units of the Ministry and Social Security Institute and of the Guayaquil unit.

Activities to Strengthen Epidemiology in Argentina

The Ministry of Health and Social Welfare of Argentina is promoting, together with the provincial health ministries, a series of measures to strengthen and reorient the practice of epidemiology in the country, with special emphasis on systematic analysis of the health situation from existing data, epidemiological surveillance, and the study of emergency situations in individual provinces.

As the opening stage in this effort, a course in epidemiology has been sponsored by the Ministry of Health and Social Welfare and the Pan American Health Organization and conducted in the Dr. Juan H. Jara National Epidemiology Institute (INE), at Mar del Plata. This course of about 200 teaching hours was held from 5 November to 3 December 1985. It was attended by 28 regular students, four of them members of the INE staff, and 24 other students from the federal provinces and territories and other national institutes. Also present were professionals from the Undersecretariat for Programs in the Ministry, the School of Health of Buenos Aires National University, and all persons with teaching responsibilities in INE courses. The subject matter centered on three thematic units: principles and basic methods in epidemiology; epidemiological surveillance and the investigation of emergency situations; and uses of epidemiology in the planning, management and evaluation of health services. A unit on sampling was also included and lectures were given on some specific health problems.

As a follow-up to the course, the students participated in the Seminar on the Epidemiology of Argentina, held at Mar del Plata from 4 to 6 December 1985 for the following purposes:

- To establish the basis for the design of a project to strengthen epidemiology in order to diagnose the country's health and identify priority problems.
- To frame proposals for training consistent with health policies, which take into account the structure and organization of the services and the levels of functional responsibility.
- To establish general guidelines for epidemiological research that address the health-disease process as both a resultant and a determinant of the conditions of life in a society.

This seminar was attended by 78 professionals representing 21 of the country's jurisdictions, the Undersecretariat for Health Programs (National Health Promotion and Protection Directorate, National Directorate of Institutes, National Directorate of Primary Care), the National Institutes of Epidemiology, the Schools of Public Health of Buenos Aires and Córdoba, and the Pan American Sanitary Bureau.

The participants were divided into five groups to study the following topics: epidemiology services, personnel training, and general research guidelines. The conclusions and recommendations of the several groups were studied and consolidated into a final report. The leading recommendations are summarized as follows:

Epidemiology Services

- To guide efforts toward the inclusion of epidemiology as a basic component of every activity developed in the health sector.
- To emphasize the application of the epidemiological criterion in decision-making at all political and technical levels.
- To draw up jurisdictional health diagnoses based on existing information, which take account of the institutional and health aspects in order to detect problems and establish priorities, and which offer alternative courses of action to the political and technical levels.
- To use instruments that help refine the analysis of available information by improving the techniques for the selection and registration of data and the interpretation of indicators.
- To adapt epidemiological models to local programming, taking due account of community participation.
- To develop a system of epidemiological analysis that covers communicable, noncommunicable and occupational diseases in addition to such aspects as risk factors, technologies and drugs.
- To improve epidemiological surveillance in existing programs.
- To improve the dissemination of epidemiological information through the issuance of timely communications and bulletins that are attractive and of meaningful teaching content with a view to providing feedback to the system and useful information to users of the services and the community.
- To identify public and private laboratories and upgrade them for the formation of a nationwide network.

Personnel Training

- To plot a training profile for each level of com-

plexity of the health service system so as to improve the performance of activities in its area of competence.

- To formulate the type of training for each level.
- To use—as needed at each level—the resources available for training: in-service training, workshops, courses at a distance, INE courses, courses for public health graduates, and special basic and refresher training courses.
- To promote access for management levels to courses of practical content that will enable them to process and analyze data for application in the health field, and to promote access for personnel at operational levels to courses stressing the importance of proper data generation.
- To maintain a system of continuing education in occupational training and assure access to it at the levels of higher complexity.
- To strengthen the documentation centers (INE, public health schools, health secretariats, and PAHO) with updated bibliographies, and to circulate the most important material.

General Research Guidelines

- To carry further the analysis of mortality and its trends as an approach to the diagnosis of the health situation and to improve the quality of data.
- To evaluate the information on morbidity, particularly as to its quality.
- To explore other data sources and classification criteria.
- To study risk factors so as to take preventive action against modifiable conditions, and to devise predictive instruments for the purpose of identifying high-risk population groups for special care. Risk factors for some harmful conditions identified could be used in intervention strategies or to verify their local importance.
- To evaluate the impact of intervention measures and the use made and functioning of health services, activities, and technologies.

Malaria Vaccines: State of the Art

Background

Despite the remarkable results of the intensive efforts made against malaria between the 1950s and the 1970s, the disease has remained a major health problem in many tropical and subtropical countries.

The situation during the past 15 years clearly shows that the worldwide elimination of malaria cannot be achieved with currently available means, and the present antimalaria strategy is therefore based on realistic concepts of malaria control within the general strategy of primary health care.

However, even at modest target levels of malaria control, the same constraints that aborted global malaria eradication will continue to operate, namely financial and administrative difficulties as well as technical problems. The latter include widespread resistance of anopheline vectors to insecticides, the occurrence and spread of chloroquine resistance and the increasing development of multidrug resistance of *Plasmodium falciparum* in large tropical areas, the exophilic behaviour of certain anopheline vectors, and factors associated with human ecology such as migration and social attitudes. These obstacles have made the traditional antimalaria armamentarium less effective.

In reaction to this most unsatisfactory and dangerous situation, the UNDP/World Bank/WHO Special Program for Research and Training in Tropical Diseases in cooperation with the Malaria Action Program has planned and implemented research aiming at the improvement of malaria control. Part of this program pursues the development or improvement of tools and methods of the traditional type, while another part is devoted to the exploration of innovative approaches such as vector control through biological agents, and the control of the malaria parasite through vaccines.

Research on immunization against malaria has made outstanding progress over the past years so that there is a distinct possibility that malaria vaccines will play a role in malaria control in the not too distant future.

Current Approaches to Malaria Vaccine Development

Until approximately six years ago, before the advent of the cell fusion (hybridoma) technique for the production of specific monoclonal antibodies, most research towards malaria vaccines was based on the use of whole parasites as antigens. Although this approach proved to be successful with whole, inactivated sporozoites of *P. falciparum* and *P. vivax* in man, it has been realized that the quantities of antigen required were quite substantial. This has been ascribed to the simultaneous challenge by a multitude of antigens, the

majority of which is not inducing protective immunity, thus misleading the vertebrate host's immune response. This is also one of the reasons why man's immune response to malaria in nature takes a long time to build up. Moreover, the concept of vaccination with whole parasites became increasingly unacceptable as it would be practically impossible to obtain them in a very clean form, i.e. free of mosquito debris in the case of sporozoites, or free of blood substances in the case of asexual blood stages, and gametocytes. In all cases there would also be the risk of contamination, especially with viruses, the control of which poses major technical problems. Last but not least the production of adequate quantities of antigenic material from whole parasites is too expensive and time consuming to be a feasible source of vaccines.

It has conclusively been shown that the immune response to pure parasite antigens is much more effective and faster than that to the multitude of antigens contained in whole parasites.

Malaria vaccines will therefore be based on pure parasite antigens which specifically stimulate protective immune responses. Protective antigens are present in several of the developmental forms of the parasite and future vaccines may contain antigens from one or more of these. At present, most of the relevant research concerns *P. falciparum*.

The strategy for malaria vaccine development involves the identification and characterization of protective parasite antigens, cloning of the corresponding genes and their expression in bacteria, analysis of their nucleotide sequence and deduction of the amino acid sequence of the encoded molecule. The protective epitope, i.e. the immunogenic portion of the antigen molecule, may then be produced by genetic engineering methods or by chemical synthesis.

In attempting to identify protective plasmodial antigens, attention has been focussed on those antigens which are exposed to the immune system, either on the surface of the parasite or on the membrane of the infected erythrocyte. Vaccine targets currently envisaged are: (i) sporozoites, (ii) asexual erythrocytic stages, and (iii) gametes and other forms developing in the mosquito midgut.

The three main types of malaria vaccine now being developed will have different effects in the vaccinated subject and can be expected to be applied in different population groups and epidemiological situations. Immunity in malaria is stage-specific, so that a sporozoite vaccine would not be expected to protect against transfusion-induced malaria due to the presence of asexual erythrocytic forms in the transfused blood. Nor would a gamete-based vaccine be expected to protect against sporozoite-induced infection and the subsequent development of disease.

The gene encoding the protective sporozoite antigen of *P. falciparum* has been cloned and the antigen produced in *Escherichia coli*. The immunodominant epitope has been synthesized chemically and the possibility of producing the antigen in vaccinia and other genetically engineered microorganisms is being explored. Several putative protective antigens of the asexual erythrocytic stages of *P. falciparum* have been identified and the genes coding for some of these have been cloned. The target antigens of transmission-blocking immunity have been identified and gene cloning is in progress. It is therefore clear that several candidate antigens/vaccines will become available for evaluation before long.

Cautions and Reservations

The development of malaria vaccines is an entirely new area, and much of the current enthusiasm in this field is based on optimism and hope. There is good justification for this attitude on the basis of experimental studies, but this does not exclude the possibility of failure in producing vaccines which are cheap and well tolerated and do confer high protection of long duration. A variety of technical questions are also awaiting solutions, namely the selection of suitable carriers and, if so required, adjuvants.

Probably all these problems will be adequately solved given sufficient time, but even then caution is required with forecasts regarding the operational availability of malaria vaccines since there is a long way from the essential preclinical development to the completion of Phase III trials in humans, i.e., the moment that a vaccine can be registered.

Expected Contributions of Malaria Vaccines to Malaria Control

Current indications are that the three types of malaria vaccine will become available for field testing and that each will possess its own functional characteristics. A sporozoite vaccine, if fully effective, would prevent the successful establishment of plasmodial development in the host and thus induce sterile immunity. Parasitaemia, asexual or sexual, would therefore not occur; clinical illness would not supervene and the subject would remain incapable of infecting mosquitos. A vaccine of this type if applied to human populations sufficiently widely could effectively interrupt the natural transmission of malaria, irrespective of the prevalent endemic level. However, subjects effectively immunized against sporozoites would probably remain susceptible to challenge with asexual erythrocytic stages of the parasite and, following such challenge, i.e., transfusion of infected blood, would show para-

sitaemia and clinical illness and would develop gametocytaemia and become infectious to mosquitos. The operational indications of the sporozoite vaccine will largely depend on the duration of protection. In determining the operational indications, it will be important to assess the role of natural challenge as a potential booster of protective immunity.

An asexual erythrocytic stage vaccine is expected to induce an immunity which operates by restricting the replication of asexual blood stage parasites without necessarily inducing sterile immunity. Consequently its function will be to reduce the morbidity and mortality due to malaria. However, persons immunized by this type of vaccine will probably remain susceptible to sporozoite infection and the parasite's development in the liver will occur unimpeded; low grade asexual parasitaemia may occur and gametocytogenesis may evolve normally so that immunized persons would remain capable of infecting mosquitos. Asexual blood stage vaccines, therefore, seem unlikely, if used alone, to achieve the interruption of transmission of malaria in any endemic area.

Asexual blood stage vaccines would be used in highly susceptible groups in endemic areas to induce a level of immunity that would prevent serious illness following infection. The objective would be to confer a degree of protection equivalent to that which develops only after several infections in endemic areas. Infection might boost the vaccine-induced immune response.

The third type of vaccine will operate by inducing in the human host serum antibodies which effectively block the fertilization of females by male gametes within the mosquito gut or inactivate the fertilized zygote or the ookinete. Such transmission-blocking vaccines seem capable of interrupting malaria transmission at the mosquito level, but will neither protect the human host against sporozoites, hepatic forms, and asexual blood stages nor prevent the development of gametocytaemia. However, they are expected to reduce the overall rate of malaria transmission in endemic areas and thereby play an important role in malaria control. Such vaccines would be used in combination with a protective vaccine against sporozoites and/or asexual erythrocytic stages.

Of the three different types, only the asexual blood stage vaccine would seem likely to induce an immunity similar to that acquired by populations living in highly endemic regions. The most appropriate circumstances for the use of an asexual blood stage vaccine on its own may, therefore, be in areas of high endemicity where it may be used specifically for the young children of the community, particularly those under four years of age who bear the burden of malaria morbidity and mortality. The aim here would be to induce in the young child by limited vaccine administration an immunity which would eliminate serious morbidity and mortality, while still permitting reinfection and gametocytogenesis which would continue to boost the vaccine-induced immunity.

Sporozoite and transmission-blocking vaccines, which might be used with the aim of interrupting transmission, will both need to be administered to all ages in as complete a coverage as possible to be effective. Repeated vaccination at such intervals as are required to maintain effective immunity would also be necessary until interruption of transmission is achieved. Both sporozoite and transmission-blocking vaccines may have special application in limiting the epidemic spread of malaria, while the sporozoite vaccine seems especially suitable, as an adjunct or a replacement of personal drug prophylaxis, for the protection of non-immunes who enter endemic areas for occupational or recreational reasons, particularly in areas where drug-resistant parasites are prevalent. A sporozoite vaccine could also be used for the protection of young children in highly endemic areas, although booster doses may be required. Such usage could with time reduce natural infections and require extended vaccination of other, older groups.

Eventually, when all three vaccine types are available, their use in combination may be desirable. However, it must be realized that epidemiological, economic and logistic considerations may impose the use of single rather than multiple vaccines. Apart from the specific requirements of safety and efficacy assessment, such factors will also demand that all vaccine types be tested and evaluated independently in field circumstances before their use in combination is tested.

Ethical Aspects of Malaria Vaccine Trials

All trials should be conducted in accordance with the principles laid down by the World Medical Assembly of 1975 on Ethics and Human Experimentation and this aspect of the studies will be paramount. Informed consent of volunteers must be obtained in every case during Phase I-III trials. In tropical countries this means that the information should be given to the volunteer in writing or translated into a language and form that are well understood by each person concerned. In trials involving infants or children informed consent should be obtained from relatives in accordance with national legislation.

Each trial protocol should be agreed upon or prepared by the principal investigator involved, signed by him and approved by a local/national ethical committee. The safety of the volunteers in the trial is the primary consideration of the ethical committee in giving its approval of the study and of the principal investigator in carrying it out. However, the relevance of

the study and the chance of acquiring useful knowledge from it must also be considered before approving any new project.

Vaccine Development Phases

Preclinical development

The primary purpose of preclinical studies of advanced candidate experimental vaccines is to produce information on which to base a decision on whether to proceed with Phase I clinical trials (such preclinical studies are therefore often referred to as Phase 0). In addition, the data obtained are frequently used to improve or modify the experimental product and to gain insight into expected results in humans. Evidence is required which supports the proposition that the experimental vaccine is safe for use in man and that it will produce functional immunity. Requirements depend upon the type of vaccine and method of manufacture but in general are based on specific analyses and on *in vitro* and *in vivo* tests which characterize, as far as possible, the product in terms of content, purity, sterility, immunogenicity and toxicity. The experimental vaccine proposed for clinical trials should be produced in accordance with Good Manufacturing Practice and tested following the guidelines published by WHO and by national regulatory authorities.

Clinical and Field Trials of Malaria Vaccines

The overall objectives of malaria vaccine trials are the assessment of the safety, tolerability, and efficacy of the vaccines in individuals of different age, ethnic or geographical origin and malaria experience, as well as the determination of optimum conditions for the induction and maintenance of functional immunity. Furthermore, the epidemiological impact of immunization against malaria should be determined, including assessment of the acceptability of and compliance with immunization procedures in communities or population groups exposed to malaria risk.

The following phases of clinical and field trials have been defined:

Phase I. Trials, initially carried out in healthy adult male non-immune volunteers, will take place under close medical scrutiny and be sited in areas where malaria is not endemic. The objective of these trials will be to assess human local and systemic tolerability and immune responses to a malaria antigen(s) which has been shown to be safe and immunogenic during preclinical (Phase 0) studies. The test vaccine will be administered to determine the optimal dosage schedules for Phase II trials. The trials may also include comparison with a carrier, if included in the vaccine(s) and with a placebo, and will be double blinded whenever feasible. The conduct of such trials should comply with local/national regulations. Following acceptable safety and tolerance studies in healthy non-immune volunteers, Phase I trials may be extended to infected, semi-immune volunteers in the target populations in different ethnic groups, as well as to special groups.

Phase II. The aim of the Phase II trial is to demonstrate protective immunity of a malaria vaccine, as well as to continue to monitor its safety, tolerability and acceptability. Initially this may be assessed by experimental challenge (Phase IIa). These studies can only be undertaken in special centers where such challenge is undertaken and is ethically accepted. The prerequisite for initiating Phase II trials should be the demonstration (from the Phase I trials) of adequate safety, tolerability and acceptability; indications of the induction of functional immunity will have been obtained from preclinical (Phase 0) or Phase I studies. Phase IIb studies will be extended to population groups which are exposed to natural challenge and therefore may not necessarily be carried out in a residential facility (Phase IIb). There may be, therefore, some overlap between Phase IIb and Phase III since Phase IIb trials will have to take into consideration challenge by natural infections under a variety of epidemiological conditions.

Phase III. The major emphasis of these trials will be placed on vaccine efficacy; acceptability, safety and tolerability will be monitored in a way also appropriate to the detection of reactions occurring at moderate or low frequency. Phase III trials will be generally open trials carried out in a target population under natural challenge and may also provide an opportunity to study the impact of the vaccine(s) on the community. Initially they may be small-scale pilot studies before arriving at field trial proportions. Such trials should also be carried out in areas of differing malaria endemicity and transmission.

Phase IV. This phase, which follows registration of the vaccine(s) will be largely devoted to the monitoring of vaccine safety and efficacy and of the impact of the vaccine(s) on the epidemiological situation, with a view to optimizing the strategies of vaccine deployment.

Supplementary Benefits of Malaria Vaccine Research

Laboratory-based research related to malaria vaccine development is producing a number of tools that are expected to be of major importance to malaria epidemiology and diagnosis. Among these tools is a test system which reliably identifies sporozoite infections in mosquitos. In addition to being vastly superior and less time consuming than conventional mosquito dis-

section, the test provides also a *Plasmodium* species diagnosis of the sporozoites. For better applicability the original radioimmunoassay has been adapted to the use of enzyme markers.

Antigen detection tests and DNA probes hold considerable potential for improving and simplifying malaria diagnosis. While in an earlier phase of development, sensitive methods are already in field evaluation, preliminary results of which are encouraging.

(Source: Statement on the Development of Malaria Vaccines, Document WHO/MAP/TDR, 1985.)

Biotechnology: Its Potential for Health in Latin America and the Caribbean

The knowledge that has been explosively produced in recent years in microbiology, molecular biology, biochemistry, genetics and other disciplines has set off an unprecedented development of biotechnology and given it an increasingly important part to play in the socioeconomic advancement of countries. Judicious application of the latest discoveries in gene-splicing, the production of monoclonal antibodies, protein engineering, etc., to the solution of problems in the fields of health, food production, energy and the environment has given birth to technologies that have made themselves felt in the industrialized countries. The effort to control diseases and conquer health has already scored triumphs whose implications are publicized almost daily in the mass media.

Biotechnology is a general term that includes any technique that uses living organisms (parts of organisms or products obtained from such organisms) to produce or alter products, to improve animals or plants or to develop microorganisms for specific purposes.

One important feature of biotechnology is its interdisciplinarity, for it relies on the basic sciences, although popular lore and tradition have been decisive factors in many biotechnological advances. Since the dawn of civilization, human societies have deliberately selected organisms for the improvement of crops, livestock, the quality of foods, and the preparation of fermented products. As biology has elucidated the functioning of the cell, and particularly its molecular and regulatory mechanisms, it has become possible to develop more efficient production processes.

One of the outstanding features of biotechnology is that the entire process can go forward at different levels of scientific and technical knowledge. Between the popular lore of traditional biotechnologies and the basic knowledge of modern science there is a whole gamut of degrees of biotechnological sophistication.

Traditional biotechnological processes arose out of empirical practices such as the production of fermented liquids and bread. Today, the advances made in cell biology, molecular genetics and biochemistry have spurred the development of a modern, or new biotechnology (NBt). This is the name given to the use of organisms modified by the recombinant DNA (rDNA) technique. With this technique the genetic makeup of organisms can be changed at will. NBt also embraces procedures based on cell fusion, which include the fusion of plant protoplasts and the production of hybridomas that secrete monoclonal antibodies.

Whereas traditional biotechnology selects plants, animals and microorganisms created by crosses of varieties or gene transfers mediated by natural mechanisms, NBt switches the specific genes that code for a desired character through direct chemical manipulation of the chromosomes of the donor and recipient species. In this way interspecific barriers are surmounted and chimeras can be developed that express foreign genes on a high-yielding industrial scale. Thus, insects can be obtained that express mammalian genes, plants that express microbial genes, bacteria that express human genes, fungi that express components of viruses of higher mammals, and viruses that express proteins of other species of virus.

The cell (or viral) genome can also be dissected to obtain organisms without the genes that make them pathogenic. This opens up a new strategy for the production of vaccines and new methods for the control of animal and plant diseases based on the substitution of modified microorganisms in certain ecological niches.

Applications in Medicine

Many gains in the prevention of infectious disease have been made without any great understanding of the mechanism of immunity or of the nature of the pathogens. It is clear, however, that empirical knowledge is not enough to control the infectious and parasitic diseases that plague extensive segments of the world's population. The physician faces the necessity of fully understanding the molecular mechanism that regulates cell differentiation, genetic expression and the immune response in order to undertake with improved prospects of success alternative measures for the prevention and treatment of the acute infectious diarrheas, acute respiratory infections, malaria, trypanosomiasis, filariasis, schistosomiasis, leishmaniasis, leprosy and the enteroparasitic diseases, which attack tens of millions of persons in the tropics. Designing for new drugs for their treatment and obtaining antigens that are usable in diagnosis and prevention will require a better understanding of the molecular biology of the causative pathogens. This will not be achieved without research policies conducive to the answering of basic questions as a precondition for solving applied problems.

Diarrheal diseases are the leading cause of infant mortality in the Region. Oral rehydration therapy has reduced mortality, but leaves morbidity unaffected. It is estimated that many infants under one year of age suffer four to six episodes of diarrhea a year.

In probably one third of the cases of infant diarrhea the etiologic agent is a rotavirus. The rotavirus genome has recently been synthesized *in vitro,* reverse transcribed, and inserted into *Escherichia coli,* another etiologic agent of diarrhea. Bacteria clones containing copies of rotavirus genes have been identified. In some of them the amino acid sequence of the proteins codified by these genes has been or is being established. Even now DNA probes can be used for the diagnosis and identification of the virus in feces, and a vaccine is being tested. DNA probes are also being tested for identification and typing of *E. coli.*

More than 900,000 cases of ***malaria*** were reported in Latin America and the Caribbean in 1984, but the real number is estimated to be five times greater.[1] The control techniques used in recent decades—insecticide spraying and chemoprophylaxis—pose problems owing to the development of resistance to insecticides in the vector and to drugs in the parasite. Because of this, efforts are in progress to obtain specific antigen proteins of sporozoites and merozoites for the development of immunizing agents.[2] A simple molecule located in the sporozoite membrane has been identified and seems to be a good candidate for that purpose. While it appears to be essential for the development of the parasite and its entry into the liver cell, it also stimulates the production by the host of antibodies that can neutralize sporozoite infectivity. The gene that controls the production of this protein in *Plasmodium falciparum* has already been isolated and cloned and it has been established that the antigenic portion of the protein has only four amino acids. *P. falciparum* antigens can be synthesized chemically or produced in bacteria by rDNA techniques. Monoclonal antibodies have played a central role in the isolation of these protective antigens and are also expected to be of use in the detection of antigens circulating in infected humans and the detection of infection in vectors; in the latter case, also for determining the species of plasmodium infecting the mosquito. This is of importance for epidemiological surveys of affected areas and for the evaluation of prevention and control measures. DNA probes have recently begun to be tested for the diagnosis of infections. Vector control techniques using larvicidal biologicals are also being tested.

It is calculated that the number of persons infected in Latin America by *Trypanosoma cruzi,* the etiologic agent of ***Chagas' disease,*** exceeds 12 million. Study of the antigens of trypanosomes can yield a battery of alternative proteins for use as more sensitive and specific antigens in diagnostic tests. Another possibility is that monoclonal antibodies and probes may prove more effective than the methods currently in use for the detection of parasitemia. This will permit a more objective evaluation of the effects of antiparasitic drugs.

In regard to ***leishmaniasis,*** probes are needed for differential diagnosis of the etiologic agent in skin lesions. This would afford a faster method for certifying the diagnosis, inferring the response to current drugs, and evaluating new therapeutic agents.

Until a few years ago, the ***thalassemias and other hemoglobinopathies*** were the only diseases in which molecular biology could be said to have made some meaningful contribution to practical medicine. Methods based on the use of polymorphisms detected by the cleavage of DNA with restriction enzymes have already yielded important data on other genetic diseases: Duchenne's muscular dystrophy, mental retardation syndrome with a fragile X chromosome, Lesch-Nyhan syndrome, phenylketonuria, and retinoblastoma.

Molecular dissection of the ***poliovirus*** has made it possible to identify the immunogenic proteins that elicit neutralizing antibodies. These polypeptide fragments have been chemically synthesized, and their inoculation into animals has shown that they confer effective protection. Moreover, this protection is as efficient as that afforded by inoculation with the entire protein or

[1] See: Status of the Malaria Programs in the Americas. *Epidemiological Bulletin* Vol. 7, No. 1, 1986.

[2] See: Malaria Vaccines: State of the Art, in this issue, page 6.

the virus itself. These procedures can become the strategy of choice for obtaining vaccines against pathogenic viruses currently difficult to culture.

With rDNA techniques viral chimeras can be made consisting of the genome of an attenuated virus of proven immunogenicity to which is added the gene coding for the immunogenic protein of another virus. The first successful tests have been made of viral chimeras consisting of vaccinia viruses carrying genes of the surface antigen of the hepatitis B virus and vaccinia viruses carrying the gene coding for hemagglutinin from the influenza virus.

Genetic manipulation of the chromosomes of bacteria and viruses will also permit removal of the genes that make them pathogenic and the elimination of adverse reactions to vaccination while preserving the antigenicity of the microorganism.

Applied molecular biology will also have a considerable impact on other fields of medicine, particularly in the early diagnosis and treatment of neoplasms, congenital anomalies, and hereditary metabolic diseases.

Impact in Latin America and the Caribbean

NBt will have a considerable impact in Latin America and the Caribbean. In some cases this impact will be beneficial through the development of vaccines and faster methods of medical and veterinary diagnosis. Application of the new plant tissue and cell culture methods and rDNA technology to obtain plant species resistant to the high concentrations of aluminum present in tropical soils will make it possible to extend crop-growing to marginal areas. In other cases it may have harmful economic and social consequences already observed, when raw materials from exporting countries are supplanted by other products manufactured or improved by biotechnology in industrialized nations.

However attractive the development of NBt may prove for the countries in the Region, there are still many problems to be solved by traditional biotechnology, without either rDNA technology or monoclonal antibodies. There are still several countries that do not make their own vaccines even though the requisite technology was described years ago. Many fermentation industries in Latin America and the Caribbean are still primitive in their operation, in spite of which the profits earned from their captive markets are large enough to allow them to disregard so elementary a resource as the improvement of microbial strains by conventional methods in order to improve their production. In some cases there is very little use of reactors despite the importance and necessity of introducing reactor fermentation technology for the improvement of outmoded production methods. Actually, the design of biological reactors is a patent necessity for the Region. Drug production in rural areas requires a classical technology entirely independent of rDNA and monoclonal antibodies but of great economic and social importance to the rural communities of several countries in the Region. Although classical, this technology still poses many problems, the solutions to which are not to be found in the biotechnology textbooks of the industrialized countries because they have had no need to use it.

Conclusions

In all but a few countries of Latin America and the Caribbean, research and development and the status of industry are closely correlated with the economic and social level. The trend is for even the poorest countries to try to develop technologies of their own that will allow them a standard of living commensurate with their expectations. Many countries in the Region have some of the human resources needed for successful biotechnology programs, and in their policies technological development is seen as a priority for the attainment of autonomy and to extricate themselves from dependence on more advanced countries. However, it will not be easy to convert this theoretical potential into practical accomplishments. New scientific knowledge can be applied to the solution of problems in the Region only with the active participation of institutions and individuals of several countries.

The outlook will be favorable only if a serious effort is made to surmount the limitations imposed by the exiguity of the existing basic scientific structure, the lack of communication between academic institutions and the production system, the limited technological infrastructure, the scarcity of financing and the lack of promotion for biotechnology. All technological development and adaptation is based on policies and economic motives. Any attempt to impose technological innovation in a policy vacuum, without social acceptance and offering no obvious economic benefits must fail. Acceptable development in this area is possible only if all the production sectors of a country perceive biotechnology as necessary to national and regional development. It is then that personnel devoted to the discipline will find effective employment in the production system and appreciation for their accomplishments.

(*Source:* Based on the report Estado actual, tendencias y perspectivas de investigación en biotecnología en América Latina, PAHO Document PNSP/85-25.)

Diseases Subject to the International Health Regulations

Cholera, yellow fever, and plague cases and deaths reported in the Region of the Americas up to 30 September 1986.

Country and administrative subdivision	Cholera Cases	Yellow fever		Plague Cases
		Cases	Deaths	
BOLIVIA	–	*23*	*17*	*71*
La Paz	–	23	17	71
BRAZIL	–	*9*	*8*	*2*
Ceará	–	–	–	2
Goiás	–	5	5	–
Mato Grosso	–	3	2	–
Roraima	–	1	1	–
CANADA	*1*[a]	–	–	–
COLOMBIA	–	*2*	*2*	–
Arauca	–	1	1	–
Meta	–	1	1	–
PERU	–	*64*	*56*	–
Ayacucho	–	1	1	–
Cuzco	–	4	3	–
Junín	–	20	16	–
Madre de Dios	–	9	9	–
San Martín	–	30	27	–
UNITED STATES OF AMERICA	*2*	–	–	*4*
California	–	–	–	1
Louisiana	1	–	–	–
Maryland	1[a]	–	–	–
New Mexico	–	–	–	3

[a]Imported case.

Acquired Immunodeficiency Syndrome (AIDS)

Human Immunodeficiency Virus

The Executive Committee of the International Committee on Taxonomy of Viruses (ICTV) has endorsed the following name for the retrovirus implicated as the cause of acquired immunodeficiency syndrome (AIDS):

human immunodeficiency virus

and has recommended that it be used as the English vernacular name to replace previously used designations. This name will be used henceforth in all WHO publications and documents. The names "lymphadenopathy-associated virus" (LAV) and "human T-cell lymphotropic virus type III" (HTLV-III), and the combined abbreviation LAV/HTLV-III, should no longer be used. Although ICTV has not recommended any abbreviation, "HIV" may be used in order to avoid constant repetition of the name. However, the recommended name should preferably be written out in full upon its first occurrence in a given text, thus: "human

immunodeficiency virus (HIV)"; the abbreviation alone may be used thereafter. Care should be taken to avoid referring to the name as being "ICTV-approved"; it is, as noted above, the recommended English vernacular name (ICTV "approves" only international names).

ICTV has recommended only an English vernacular name of the virus. The French and Spanish equivalents recommended by WHO are *virus de l'immunodéficience humaine"* and *"virus de la inmunodeficiencia humana,"* respectively.

WHO Activities for the Prevention and Control of Acquired Immunodeficiency Syndrome

During its Seventy-seventh Meeting held in January, 1986, the Executive Board of the World Health Organization adopted the following Resolution:

Conscious that acquired immunodeficiency syndrome (AIDS) and other manifestations of human immunodeficiency virus (HIV) infection are becoming a major public health concern in many areas of the world and may thereby represent a hindrance to the attainment of health for all by the year 2000;

Recognizing that international alertness and preparedness are urgently required, as no country can consider itself immune to infection from HIV;

Noting that neither therapeutic agents nor vaccines are currently available for the treatment and prevention of AIDS;

Considering that public information and education as well as the assurance and use of safe blood and blood products are at this time the only measures available that can limit the further spread of AIDS:

1. ENDORSES the Director-General's report on WHO activities for the prevention and control of AIDS;[1]
2. NOTES with satisfaction:
   1) the steps taken by the Director-General to cooperate with Member States in this field;
   2) the assistance of the WHO collaborating centers on AIDS and other agencies in laboratory, epidemiological, clinical, and prevention and control activities regarding HIV;
3. URGES Member States:
   1) to maintain vigilance and carry out as necessary public health strategies for the prevention and control of AIDS;
   2) to share information, in all openness, with the Organization and other Member States on AIDS incidence, the seroprevalence of HIV, laboratory methods, clinical experience, and approaches to prevention and control of HIV infection;
   3) to call upon the Organization as necessary for support in the prevention and control of AIDS and other HIV infections;
4. REQUESTS the Director-General:
   1) to further develop activities within the WHO program on AIDS:
      a) to ensure the exchange of information on HIV, its epidemiology, laboratory and clinical aspects, and prevention and control activities;
      b) to prepare and distribute guidelines, manuals and educational materials;
      c) to assess commercially available HIV antibody test kits, develop a simple, inexpensive test for field application, and establish WHO reference reagents;
      d) to cooperate with Member States in the development of national programs for the containment of HIV infection;
      e) to advise Member States on the provision of safe blood and blood products;
      f) to promote research on the development of therapeutic agents and vaccines, simian retroviruses, and epidemiological and behavioral aspects of HIV infection;
      g) to coordinate collaborative clinical trials of antiviral and other drugs which have been demonstrated in human early phase trials to show efficacy in the treatment of AIDS and/or AIDS Related Complex.
   2) to seek additional funds from extrabudgetary sources for the support of national and collective programs of surveillance and epidemiology, laboratory services, clinical support, and prevention and control.

Meeting of AIDS Test Kit Manufacturers

Introduction

One of the main components of the World Health Organization's AIDS Control Program is assistance to member countries in carrying out local research on the epidemiology and diagnosis of infection by the human immunodeficiency virus (HIV) and AIDS. This requires action to enable countries that do not have test kits for determining the presence of antibodies to HIV to obtain them.

[1] Document EB77/42.

WHO intends to work closely with manufacturers to ensure the availability of these test kits. This was the main topic of a meeting held in Geneva on 31 January 1986 with the manufacturers of laboratory kits for the detection of antibodies to the virus associated with AIDS.

There is optimism that international technical cooperation, stimulated by the WHO program, will contribute significantly to the success of the AIDS control effort. The disease has become widespread and is an important public health problem. By December 1985 a total of 17,500 cases of AIDS had been reported in 71 countries (42 in the Americas and 19 in Europe).

Aspects of AIDS and associated diseases were examined—mortality rates, the different ways of transmitting HIV within a community and the infection's clinical manifestations, such as lymphadenopathy, immune deficiencies, a syndrome similar to acute mononucleosis, bacterial infections of the respiratory and gastrointestinal tracts, chronic diarrhea, and neurologic disorders.

Participants analyzed screening and confirmatory tests for the presence of antibody to HIV. Every screening test currently in use is a form of the ELISA test. Tests have to be simple and economical so that they may be performed and their results interpreted with a minimum of laboratory equipment. They must also be stable, and usable in widely varying field conditions. Two types of screening test using immunoblot (immunoprecipitation) and immunofluorescence techniques were examined; in both methods experience is required to interpret the results. Progress has been made in the commercial production of immunoblot nitrocellulose strips prepared with a viral antigen as a screening test.

It was noted that commercial tests of the ELISA type are basically large-scale screening tests to determine the presence of antibodies to HIV in blood donated for transfusion and the preparation of blood products. By themselves, they do not provide firm evidence of HIV infection; additional confirmatory tests are required.

The commercial kit manufacturers who participated in the meeting described the technical features of each of the tests.

Needs for Kits for the WHO AIDS Control Program

The manufacturers were asked to consider the possibility of supplying free kits for demonstration purposes in training workshops on laboratory techniques to be used under WHO's AIDS control program. Also, for each of the workshops to be held in different countries, kits from two or three manufacturers will be chosen so that the participants will learn to use them. Kits from different manufacturers will be rotated so that all available products can be used.

With a view to an uninterrupted supply of commercial kits for routine use under screening programs in member countries, and in view of the very limited means of many developing countries, WHO hopes that manufacturers will set moderate prices for their products. PAHO/WHO will be able to use its country offices to facilitate the needed business arrangements to the benefit of both member countries and kit suppliers.

Recommendations

It is recommended that commercial test kit manufacturers include in the specifications for their tests information on the origin and characteristics of the HIV strain used in the test and on the cell line used for its production. Another important point is the purity of the antigen.

WHO should establish an internationally accepted nomenclature for HIV strains that would include, for instance, the place of origin of the pure culture (United States, United Kingdom), the serial number of the strain and the year when the pure culture was obtained. Another important element in strain nomenclature could be the clinical status of the person from whom the pure culture was taken (AIDS, AIDS-related complex, asymptomatic).

Course on Serological Diagnosis of Acquired Immunodeficiency Syndrome (AIDS)

This course, inaugurated by the President of the National Institute of Health of Spain, took place at the Centro Nacional de Microbiología, Virología e Inmunología Sanitarias (National Health Center for Microbiology, Virology and Immunology) in Majadahonda, Madrid, Spain, from 10 to 15 February 1986. The course content included epidemiological aspects of AIDS in Europe and the Americas, immunology, pathology, electronic microscopy, and the latest contributions on the subject made by the study group of the National Cancer Institute (USA). Demonstrations and practical applications enabled the participants to gain a thorough knowledge of techniques such as ELISA, direct immunofluorescence and Western Blot. Discussions and seminars ensured the proper interpretation of test results. Ten students from nine countries attended the six workdays which lasted from 9 in the morning until 6-8 in the evening.

Publications

Infecciones respiratorias agudas en los niños. Scientific Publication 493. Washington, D.C., Pan American Health Organization, 1986. 130 pp. ISBN 92 75 31493 4. Price: $US 8.00.

This publication reiterates the importance of public health problems posed by acute respiratory infections (ARI) in children. It has been especially prepared for distribution in the Region of the Americas and deals, in various sections, with the following aspects: morbidity and mortality due to ARI; anatomical and physiological aspects; contributing factors related to the child; clinical ARI syndromes; general laboratory diagnosis of ARI; etiologic agents, diagnosis and vaccination; treatment of ARI; sequels of ARI; areas for future research, and training.

STD Interchange

This periodical bulletin aimed at disseminating pertinent information on research and control of sexually-transmitted diseases is published by the Division of Sexually-Transmitted Diseases of the Centers for Disease Control (USA). The bulletin is available only in English. Interested readers may obtain further information by writing to: Barbara McCollum, TIS, Center for Prevention Services, Centers for Disease Control, Atlanta, Georgia 30333, U.S.A.

Calendar of Courses and Meetings

International Health in an Era of Economic Constraint: The Challenge

That is the theme of the International Congress of the World Federation of Public Health Associations (WFPHA) to be held in Mexico City from 22 to 27 March, 1987. The Congress will bring together health professionals from over 45 countries to discuss and exchange ideas and experiences in international health. It is the fifth triennial international congress organized by the WFPHA, a worldwide consortium of 45 national public health associations joining efforts to improve personal and community health and to strengthen the public health professions. The Mexican Society for Public Health will host the event.

For more information write to: Susi Kessler, M.D., Executive Secretary, World Federation of Public Health Associations, c/o American Public Health Association, 1015 15th Street, N.W., Washington, D.C. 20005, USA, or Dr. José Luis Luna, General Secretary, Local Coordinating Committee, Mexican Society for Public Health, Insurgentes Sur 1397, 6° piso, 03920 Mexico City, Mexico.

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