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Epidemiological Assessment of Tuberculosis. Trends in Some Countries of the Americas

Introduction

The continuity of the tuberculosis transmission chain that keeps the disease endemic in the population depends on multiple factors. Prominent among them are the prevalence of sources of infection, mainly, cases of bacillary pulmonary tuberculosis; the number of persons infected by each case; and the probability of infected individuals contracting the disease as a result of infection.

The number of infected persons per case depends on the site and type of tuberculosis and the behavior of the patient. The number of exposed persons and the degree of exposure, which in turn depend on population density and type of housing, also influence the number of infected persons. The probability of contracting the disease depends mainly on the infecting dose and on the immune status of the host, and therefore, on age, sex, nutrition and concomitant diseases. In relation to the latter it is well known, for example, that diabetes and the use of corticosteroids increase the risk of acquiring the disease. Similarly, infection with human immunodeficiency virus (HIV) significantly increases the risk of contracting tuberculosis (usually about 10%), among infected persons. Infection with HIV interferes with the cellular immune mechanism responsible for destroying mycobacteria. In developed countries such as the United States of America, the age group infected

with tuberculosis and infected with HIV do not overlap much; in developing countries, however, both infections have greater prevalence in young adults, which could bring about an increase in tuberculosis if HIV infection spreads. In Brazil, 17% of the AIDS cases are discovered through tuberculosis.

In developed countries, improvement of socioeconomic conditions contributed to a gradual reduction of approximately 5% annually of endemic disease; and when control measures such as diagnosis, treatment, vaccination and chemoprophylaxis were added, this reduction reached 14% annually in countries with better health programs(1). The decrease in mortality from tuberculosis in the countries of nothern Europe and the United States of America began at the end of last century, long before chemotherapy. In less developed countries, however the effect of socioeconomic development is much smaller and a decrease in endemic disease does not occur without an effective control program. This control program must have enough coverage and quality to be able to break the transmission chain. Although the latter goal is more difficult to attain, the impact of such a program may be greater in a developing country. In developed countries the disease occurs among the aged population, as a consequence of old infections, and cannot be prevented by the principal control activities.

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Epidemiological Indicators

In general, evaluation of the status of tuberculosis is based on a combination of estimates of three indicators, i.e., risk of infection, incidence, and mortality, along with knowledge of socioeconomic and sanitary conditions in the country and the quality and coverage of program activities. The most frequently used indicators are discussed below.

Risk of infection, or the probability of an individual being infected in a year. Obtaining this indicator requires prevalence studies of infection, with tuberculin tests in representative samples of the child population, repeated at several years intervals. This is the most useful indicator; however, vaccination with BCG, infections with nontuberculous mycobacteria and the mobility of the population make its obtention difficult.

Case incidence, especially of smear positive pulmonary tuberculosis in young adults. This indicator is useful only when the case detection program achieves good coverage, its intensity is maintained relatively constant, and there is good reporting and quality of registration.

Mortality. This indicator is greatly affected by the program for case finding and treatment, and usually decreases more rapidly than transmission. In the absence of control measures its trend is similar to that of the risk of infection and incidence. It is useful as an indicator in countries with high mortality where mortality reduction is a priority objective.

Current Situation and Trends in Incidence and Mortality

In 1983 an analysis of the information available on annual reported incidence of new cases and mortality from tuberculosis in countries of the Americas with more than 100,000 population was performed at the PAHO/WHO Regional Office. The work was done with the cooperation of the WHO Collaborating Center for Tuberculosis Epidemiology in Santa Fe, Argentina. The resulting document was distributed to countries with the request that they provide the Collaborating Center, on a regular basis, with annually updated information on reported cases by age, site and bacteriology; and on mortality by age. With those data a second document(2) was prepared, on which this paper is based.

In general, for the population of the developed countries in the Region—Canada and the United States of America—annual reductions of nearly 6% in the risk of becoming ill from tuberculosis are estimated. These countries lack an "active" control program with national coverage, but have ample

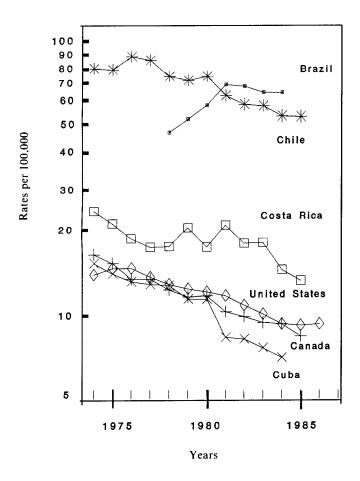
resources for highly effective diagnosis and treatment in addition to the historical trend resulting from their socioeconomic development. In recent years reported incidence in the United States has stabilized at 10% above expected figures. The two most important factors affecting this trend are the immigration of persons with a greater prevalence of infection and risk of becoming ill—from countries of Southeast Asia and Latin America—and the rapid spread of infection with HIV.

In countries of Latin America the trend varies according to the level of development, quality of the health care system, and coverage and quality of control measures. The average reduction is estimated at 6% annually. There is a latent period of several years between improvement or deterioration of program activities and its reflection in the indicators. Hence a program with improved organization will initially produce an increase in reported casesespecially smear positive—followed by a reduction in mortality and a stabilization of reporting, then a reduction in incidence, greater among young people. It should be reiterated that the epidemiological indicators cannot be interpreted independently of operational factors of the programs, especially with respect to data obtained from the notification registries.

Trend differences in Latin America can be illustrated by the tuberculosis situation in some countries (Figure 1). Cuba, for example, has a good health care delivery system and a well-organized tuberculosis control program; coverage of practically 100% of children with BCG; case finding among patients with respiratory symptoms who consult the general health services, through sputum smear and culture; and treatment with high compliance. The result has been an annual reduction of incidence of 9.6% since 1978, and juvenile tuberculous meningitis has not been observed for 10 years. The incidence level reached is similar to that in Canada and the United States, although the average age of cases is lower.

On the other hand, Costa Rica, with a much slower reduction—approximately 6% annually in incidence before 1975 and around 9% annually in mortality—has also reached very low levels. This is partly explained by an effective, ongoing program, although of limited coverage in some areas due to lack of integration of symptomatic case finding into the social security health services system. From 1977 to 1983 sharp increases in reporting and a continued decline in mortality were observed; this can be interpreted as an increase in diagnoses—in large measure through immigration due to political instability in Central America—followed by good treatment of the cases detected. A reactivation of the

Figure 1. Reported incidence of tuberculosis (per 100,000 population) in Brazil, Canada, Chile, Costa Rica, Cuba and the United States of America, 1974-1986.



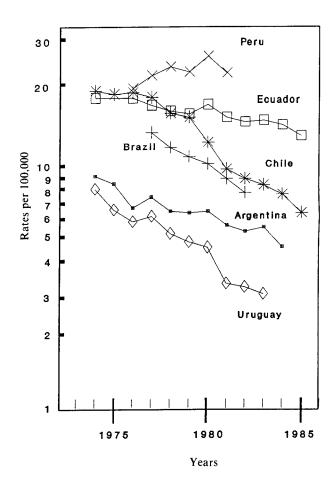
program, currently in progress, should give rise to a new peak in the detection of cases.

In Brazil the existent program, which had less than 600 health services units and approximately 23,000 specialized beds, was gradually merged into the general health services of the States in the 1970s. Currently approximately 4,000 health services units are incorporated into an integrated program, with less than 3,000 specialized beds, almost all in general or chest hospitals. At the same time, notification increased from 47,000 cases in 1974 to 88,000 in 1984 and stabilized at an estimated 80% of the real incidence that can be detected with the technology available in the country. Information at the national level represents an average of the trends and levels of the problem, as well as of the coverage and quality of information, in the individual States. An average minimum reduction in real incidence of 6% annually can be assumed; mortality in state capitals, on the other hand, is declining by 11% annually, which is

probably a good reflection of the national trend (Figure 2). The annual risk of infection is estimated at approximately 0.9%, ranging from 0.2% in the south to 2% in the north of the country.

In Chile the intensity of case finding efforts has increased yearly. This may be observed through the annual number of sputum smears performed in the country for diagnosis of tuberculosis. Treatment has also improved, currently utilizing an abbreviated scheme of seven months including just one month of daily treatment with completely supervised administration. As a result of the real reduction in incidence and greater case-finding efforts, the reported incidence decreased gradually by 5.6% annually from 1976 to 1985, while the yield, as measured by the proportion of positive sputum smears, decreased rapidly. Mortality decreased by 9.9% annually between 1981 and 1985.

Figure 2. Tuberculosis mortality (per 100,000 population) in Argentina, Brazil, Chile, Ecuador, Peru and Uruguay, 1974-1985.



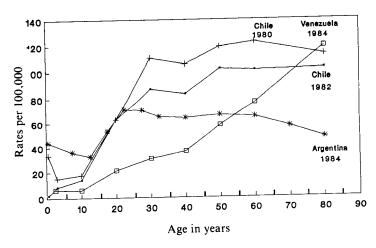
It is more difficult to interpret data from countries where the program and the information systems are inefficient. In Mexico, for example, it is estimated that less than half the cases are reported; l0 years ago the number of reported cases was almost the same as the number of deaths registered by the vital statistics system. The increase in reported cases is not due to extension of the program but to the incorporation of the cases treated by the Social Security health care system into the reports of the services of the Ministry of Health. The 7% annual reduction in reported cases from 1974 to 1978, when there were no changes in the program, may be real; however, this would not be true for real incidence rates which are probably much higher.

In countries with high incidence such as Haiti, Bolivia, Paraguay and Peru, the problems of coverage of the health infrastructure coincide with the scarcity of resources for tuberculosis control activities. This is the case especially with respect to the provision of drugs, and supervision of services with integrated actions necessary to maintain case finding and assure compliance with treatment. As a result the reported incidence, although high, is much lower than the real incidence. In addition, interruption of treatment for lack of drugs or abandonment by patients produces a large number of drugresistant cases which survive a long time and contribute to maintenance of the transmission chain. Changes in incidence in these countries are basically due to variations in case finding intensity and completeness of registration. This is observed especially in Haiti.

In spite of the limitations described, mortality seems to be decreasing continuously in most countries, reflecting gradual improvements in treatment and, in general, in the quality of the tuberculosis program and the health care systems in the Region (Figure 2).

The age distribution of tuberculosis incidence rates illustrates another aspect of the problem (Figure 3). Although the magnitude of the rate depends greatly on diagnostic coverage, it shows the risk accumulated in countries by age cohorts. In developed countries incidence increases in proportion to age, as a result of risk accumulated over a lifetime, and exposure to greater risks in prior decades. In developing countries the risk of infection is high and the "pool" of uninfected is rapidly exhausted, which explains the peak incidence of disease among young adults. In Venezuela the curve by age is similar to that of a developed country, whereas in Argentina there is still a peak among the young. In Venezuela the older age groups were exposed to greater risks than in Argentina, but that situation has been re-

Figure 3. Reported incidence of tuberculosis (per 100,000 population) by age-groups in Argentina (1984), Chile (1980 and 1982) and Venezuela (1984).



versed in the last 40 years. In Chile the curve by age is changing; the risk is high but has rapidly diminished in recent years.

Conclusions

Appropriate analysis of the data on incidence and mortality, accompanied whenever possible by information on the risk of tuberculosis infection or the prevalence of infection among children, allows measurement of the long-term result of tuberculosis control measures as well as the effect of nonspecific factors, including socioeconomic development and development of the health care system. For most of Latin America, levels of annual reductions close to those of developed countries of the Region have been achieved through organized control programs. The average reduction is estimated at 6% annually at the very least, which would reduce real rates by half in 11 years and the absolute number of cases in 18 years. These estimates refer to real incidence, since observed incidence depends on operational factors and will probably increase as coverage of the program improves and new diagnostic methods become available. A real increase in many countries is also possible, if HIV infection spreads rapidly.

Given that data interpretation should lead to program improvement and should be made in relation to programs, PAHO/WHO has assigned priority for next year to developing a system of evaluation of

program operations through periodic information from countries, similar to that already existing for epidemiological information. The basis for this system will be discussed, in November 1987, by a working group which will propose basic indicators on coverage and quality of interventions—BCG vaccines, case finding and treatment—and criteria to assess strategies, resources and intermediate activities for national and international use.

References

- (1) Styblo, K. Epidemiology of Tuberculosis. VEB Gustav Fischer Verlag Jena, 1984.
- (2) Pan American Health Organization. *Tuberculosis: Incidencia y Mortalidad*. PNSP/87-11, Washington, D.C., 1987.

(Source: Tuberculosis, Maternal and Child Health Program, PAHO.)

Epidemiological Activities in the Countries

Workshop on Improvement of National Information Systems and Development of Epidemiology

The Latin American and Caribbean Association for Education in Public Health (ALAESP) and the Association of Schools of Public Health (ASPH) of the United States of America, under the sponsorship of the Pan American Health Organization (PAHO), are holding a series of meetings, during 1987, at different Latin American schools of public health to explore new forms of cooperation among the schools of both associations aimed at institutional development, strengthening of educational capabilities, and development of research capabilities.

The meetings are based on the following key topics: Analysis of public policies in the health and development context; health information and epidemiology; health economics and financing; human resources for health; technological process in health; and health services systems.

The workshop on Improvement of National Information Systems and Development of Epidemiology was held in Caracas, Venezuela, from 25 to 29 May 1987. The following institutions participated: ALAESP; ASPH; the Schools of Public Health of the University of North Carolina, Columbia University, the University of Southern Florida, and the Central University of Venezuela; the Ministry of Health and Social Welfare of Venezuela, and PAHO. The Schools of Rio de Janeiro and of Medellín were invited to the meeting but were unable to attend.

Current problems in epidemiology practice and training in the Region of the Americas were dis-

cussed, and each of the participating schools presented a status report on their courses and problems.

It was noted that efforts to achieve the strengthening of epidemiology in countries of the Region have already begun. Special mention was made of the comprehensive development project for epidemiology in Venezuela and the projects in the schools of public health of Medellín, México, and Rio de Janeiro; PAHO's activities for information dissemination by means of the *Epidemiological Bulletin* and the project for dissemination of selected bibliography (underway) were underlined, as well as its support and encouragement for meetings on the subject in the Region.

The group was of the opinion that basic epidemiology activities should include the analysis of health situation; epidemiological surveillance; evaluation of the impact of programs, services and techniques; and epidemiological research. The need to strengthen the schools of public health in epidemiology, was recognized as an important way to support development of human resources in this area.

To achieve a strengthening of epidemiology in schools of public health, the group recommended consideration of projects for institutional strengthening; development of academic and research capabilities; and establishment of an interschool network.

With regard to institutional strengthening the following proposals were made: Development of information systems including a system that would permit identification of the various types of resources available in the area of epidemiology; development of mechanisms and strategies for exchange of scientific and technological information on epidemiology; development of educational material on epidemiology; and creation and encouragement of mechanisms to improve relations between educational institutions and epidemiology services.

As for strengthening of academic capabilities, there were recommendations to study and develop different educational levels in epidemiology, in accordance with needs; to review curriculum contents of courses in the area; to develop new educational technologies applicable to the teaching of epidemiology; to implement programs for continuing education in epidemiology; to explore the use of nontraditional educational strategies, including "at distance" education and implementation of exchange programs for epidemiology teaching staff and students among educational institutions, for which the possible use of sabbaticals and internships should be explored.

For the strengthening of research, proposals were made to improve educational capabilities in methodology, with special emphasis on the interdisciplinary aspects of epidemiological research; to increase research administration and management capabilities; to carry out interinstitutional epidemiological research; to develop mechanisms that would permit broad dissemination of epidemiological research findings and favor the application of results in modifying health status; and to promote faculty exchange.

Finally, in regard to the establishment of an interschool network the group was of the opinion that the existence of shared problems, the possibility of cooperation among institutions, and the need to preserve the autonomy of participating institutions in administrative, technical, and financial aspects, suggest the creation of an interinstitutional network, with an epidemiology chapter, as a possible mechanism for achievement of the objectives. The structure of this network should be adapted to its function, and financing should be sought from agencies and institutions that have economic resources available. All exchange activities, including resource mobilization, would be the responsibility of each chapter, with collaboration from ALAESP, ASPH, and PAHO.

The epidemiology chapter should be open to all institutions which partitipate in the network (ALAESP-ASPH) and that are interested in epidemiology and health information systems. It was decided that the epidemiology chapter would be responsible for defining the desirable level of international cooperation, taking into account the needs, weaknesses, and strengths of participating schools.

Recent Activities in Argentina

Based on recommendations of the Epidemiology Seminar of Argentina held in Mar del Plata in December 1985, the National Commission on Epidemiology of Argentina (CONEP) defined activities for the reorientation and strengthening of the practice of epidemiology at different jurisdictional levels of the country. These activities center around the strengthening of analytical capability for health situation diagnosis, starting with utilization of available data; and strengthening of the capability to investigate and respond to unusual situations, including documentation through written reports for publication.

Since December 1985, CONEP has had monthly meetings to program, discuss and adjust proposed activities. In support of the latter, information dissemination and follow-up activities were foreseen, as well as advice for projects under implementation and periodic meetings for presentation of projects already performed.

Contact was maintained with 20 of the 22 participating jurisdictions. As of May 1987, 13 jurisdictions had begun data analysis as proposed and 9 were analyzing mortality based on available data. Eight health emergencies were investigated, and two of the eight resulting reports have been presented for publication. Furthermore, the epidemiology course of the Dr. J.H. Jara National Epidemiology Institute was reformulated.

In April 1987 a workshop took place at the Dr. E. Coni National Epidemiology Institute in Santa Fe, with the participation of epidemiologists and statisticians from the national level; from the national institutes of epidemiology and the schools of public health; from the jurisdictions Capital Federal, Chaco, Neuquen and Santa Fe; from Paraguay and Uruguay as special guests; and PAHO consultants. At the workshop the analyses presented by three jurisdictions were discussed and the importance of interaction between statisticians as producers and epidemiologists as users of information was stressed; this interaction was considered necessary for improvement of the relevance and quality of analyses as well as of the data on which they are based.

The working proposal of CONEP was adjusted, based on the experience gained, as follows:

To continue monthly meetings and to conduct, every six months, an analysis of progress achieved, evaluation and adjustment of activities, including preparation of a written report. To expand every other meeting to

include study sessions on epidemiology as a way of keeping up to date and providing ongoing training.

- To continue to support the analytical approaches initially proposed and to promote them in jurisdictions where they have not yet been implemented. To that end it is proposed that regional workshops be held in order to enrich health situation analysis in provinces which have similar geographic-political areas, populations and health problems. Epidemiologists and statisticians should participate in these work sessions, as they did in the Santa Fe workshop, as a means of achieving the benefits of integration and interrelation at a working level.
- To intensify efforts to increase selective dissemination of information within feasible limits, including preparation and distribution of a newsletter on CONEP activities.
- To hold a workshop with participation of epidemiologists, planners and statisticians in order to promote closer relations and define the cooperation among them which is needed to enhance the contribution of epidemiology to improved planning, management and evaluation of the health services system at the national and jurisdictional levels.
- To define the strategies for adapting the mission and functions of epidemiology at the different jurisdictional levels.

National Workshop on Epidemiology, Asunción, Paraguay

The First National Workshop on Epidemiology was held in Asunción, Paraguay, on 2-4 October 1986, sponsored by the Ministry of Public Health and Social Welfare and the Pan American Health Organization (PAHO). It was attended by 56 participants from the Ministry of Public Health and Social Welfare, the National University of Asuncion, the Institute of Social Welfare, the Health Department of the Armed Forces, the Police Health Department, and the Paraguayan Association of Nurses.

The objectives of the workshop were to review the current situation of epidemiology in Paraguay and to analyze lines of action to broaden the use of epidemiology in the planning, administration, and evaluation of health services and actions. The agenda, carried out through theoretical presentations of general topics, group discussions, and plenary meetings, covered the following four subjects:

epidemiological information in Paraguay; epidemiology services in Paraguay; human resources development in epidemiology; and epidemiological research.

Epidemiological Information in Paraguay

Population data are, in general, reliable; they come from the decennial censuses and are disseminated through demographic publications. Births and deaths are registered both by health services and by the Civil Register. Attempts are being made to improve the problem of significant underregistration. Around 23% of certified deaths are due to ill-defined causes.

In regard to morbidity, there exist records in outpatient clinics, family and individual records, reports of clinics, medical records, daily censuses, data on discharges, weekly lists of cases of notifiable diseases, and others. Nevertheless, morbidity information is still limited due to incomplete coverage, since the public subsector is practically the only one notifying; diagnoses are performed without laboratory testing; health administrators do not recognize the importance of statistical recording and reporting; there is a lack of forms for timely reporting of data; training and supervision of statistical personnel are inadequate; and health personnel must perform too many functions.

Analysis of information is not very common. A minimal analysis of the health situation is performed at the different levels, and there is practically no analysis of information on degenerative diseases, cancer, physical growth, mental health, or operation of services.

Epidemiological information in the country is disseminated mainly through an epidemiological bulletin and a yearbook of the department of biostatistics, but it is little utilized. All groups recognize the need for using this information when setting standards and for technical and administrative decisions.

Documentation on epidemiology is available at the libraries of the School of Medicine, the Rectory, the Institute of Tropical Medicine and, to a lesser extent, the Ministry of Public Health and Social Welfare.

Epidemiology Services in Paraguay

The Department of Biostatistics of the Ministry of Public Health and Social Welfare and the National Service for Epidemiology and Zoonoses are the sources for health information in Paraguay. They collect data from the health services through forms filled out for outpatient consultation and hospital discharges. They have vital statistics data (birth and death certificates) and data from the 1982 national census, and the 1985 census taken for the poliomy-elitis control program. Data from primary sources (volunteer health workers and lay midwives) are not very reliable and there is no effective communication with other sectors, such as agriculture and cattle husbandry. Programs for control of certain pathologies take advantage of some of the statistical data for early detection and control of epidemics. An early detection system has been set up for malaria and vector control, and a similar system has also been developed for diseases preventable by vaccination, tuberculosis, and leprosy.

Laboratory diagnoses are carried out at various levels. Routine tests and those of low complexity are performed at the local level; laboratory tests of medium complexity at the regional level; and tests of greater complexity, beyond the means of the population with scarce resources, at the central level.

It was proposed that the Central Laboratory of the Ministry of Public Health and Social Welfare carry out its functions, which are: a) to formulate procedural standards for various laboratory techniques; b) to act as an educational and research center; c) to meet the demands of the sector; d) to become a reference center for confirming diagnoses, establishing etiologies or types of germs and strains circulating in a community, facilitating selection of the most suitable antimicrobic agents, and ensuring better epidemiological surveillance; and e) to supervise directly or indirectly the laboratories under the Ministry of Public Health and Social Welfare.

Health services and programs are often unable to obtain from the central level the human and financial resources needed for evaluation which discourages directors from undertaking activities of this nature.

Human Resources Development

The health system should have epidemiologists at central and regional levels with functional responsibilities for their development. The establishment of an inservice training program for the entire health system is considered essential; this program should be adapted to the needs of each level and to the various regional demands. Furthermore, it should have continuity, beginning with basic courses in epidemiology using the workshops methodology, of an interdisciplinary and intersectoral nature; these should be followed by a national course in epidemiology for appropriate staff, with more in-depth training supported by foreign educators. Only when

there is a need for greater development or specialization should staff be sent abroad for training.

Epidemiological Research

Health situation analyses for the whole country, conducted at the central level, consist of descriptive, not very systematic studies, limited by the quality of available data. It is essential to enhance these studies by using multidisciplinary working groups. This is already being done for the study of mortality in Paraguay.

Data are being collected for the studies of risk factors; studies so far conducted are incomplete and insufficient for the formulation of health policies. Evaluative studies have not normally been incorporated into health programs, despite their acknowledged importance. The most prominent are those done by the Immunizations Program, by the National Malaria Eradication Service, by the Maternal and Child Health Program—on the use of oral rehydration therapy—and the study on public health dentistry—on the impact of the use of sodium fluoride on reducing dental caries. The lack of human and financial resources makes it difficult to carry out the studies that the country needs, and the few existing ones are insufficiently disseminated. As epidemiology develops in Paraguay, priorities will be established for epidemiological research.

Recommendation

A working group coordinated by the Director of the National Service for Epidemiology and Zoonoses should be established to prepare a project for the strengthening of epidemiology in Paraguay based on the conclusions of this workshop.

First National Seminar on Epidemiology, Lima, Peru

The First National Seminar on Epidemiology was held in Lima, Peru, on 25-28 September 1986. It was organized by the Peruvian Society of Epidemiology under the auspices of the Ministry of Health, the Pan American Health Organization (PAHO), the Peruvian College of Physicians, and the Peruvian Association of Medical Schools (ASPEFAM). The main objective of the seminar was to analyze the health situation in Peru and the status of epidemiology in its theoretical, educational, service, and

research-related aspects in order to formulate recommendations and adopt resolutions on how to strengthen this discipline in the country.

This event was attended by 110 participants from various specialties assembled in five working groups to discuss the following official presentations: Epidemiological analysis of the health situation in Peru; currents of epidemiological thought in Peru; current state of epidemiology services in Peru; teaching of epidemiology and training of epidemiologists;

and relationship of epidemiology with other specialties. In addition, a round table dealt with the topic "Perspectives for epidemiology."

In order to allow for the full development of epidemiology at different levels, the participants requested that the Minister of Health establish a Bureau of Epidemiology within the central administration of the Ministry, and re-establish the corresponding structures at the departmental level, support hospitals, and peripheral services.

Acquired Immunodeficiency Syndrome (AIDS)

Consensus Statement on Laboratory Testing

The third meeting of the WHO Collaborating Centers on AIDS was held in Washington, D.C., on 6 June 1987 in conjunction with the Third International Conference on AIDS. The meeting was called to inform the Collaborating Centers of the current status of the WHO Special Program of AIDS and to discuss their role in the Program. A consensus was reached regarding the following: the transmission of

human immunodeficiency virus (HIV); HIV infection and health workers; and the present status and future developments in laboratory testing of HIV. The consensus statements on the first two of these issues were published in the *Epidemiological Bulletin*, Vol. 8, No. 1-2, 1987; the third one is transcribed below.

Present Status and Future Developments in Laboratory Testing for HIV

Introduction

The following types of tests are available or under development:

- measurement of antibodies against viral antigens;
- measurement of neutralizing antibodies;
- detection of viral antigens;
- detection of viral RNA or cDNA;
- virus isolation and characterization of virus isolates from various geographical regions.

Measurement of Antibodies Against Viral Antigens (anti-HIV)

Determination of anti-HIV should consist of a primary screening test to be followed by confirmation with a second supplemental assay based on a different test principle. Current antigen-antibody binding assays have a high degree of specificity and sensitivity. Second generation tests using recombinant antigens or future use of synthetic peptides promise to improve sensitivity and particularly specificity. Generally these test systems measure anti-

bodies of the IgG class, but test systems measuring specific IgA and IgM antibodies are needed also and should be developed further.

Although more specific ELISA or other antigenbinding assays may in the future make supplemental (confirmatory) tests unnecessary, reactivities indicating presence of anti-HIV obtained with any of the currently available screening tests should be confirmed by another test method. Western-blots (immunoblots) are the most widely used and reliable tests, but radioimmunoprecipitation (RIPA) or immunofluorescence may be used. The latter should, however, only be used by laboratories with extensive experience with this test system.

Test systems should be developed which detect antibodies to HIV1 and HIV2 either together in one test or individually. The antigenic specificities of HIV isolates from different parts of the world should be continuously characterized to assure that the diagnostic method covers the antigens of the viruses prevalent in a given region. Simplified, less expensive tests should be developed further. These test systems should have at least the same sensitivity as currently used test systems, but a slight decrease in specificity might be acceptable.

Measurement of Neutralizing Antibodies

Neutralization tests are used for research purposes and for evaluation of antibody responses following vaccination. The biological relevance of the antibodies measured by the various test systems needs further study and all test systems must be standardized, so that results obtained in different laboratories can be compared.

Detection of Viral Antigens

The tests available today need further clinical and technical evaluation. They are not recommended for routine diagnosis or screening of blood donors. Increase of HIV p24 antigen in serum has been associated with progression of disease but this does not occur in all cases. Decrease of HIV p24 in serum has been taken as an indication of a decrease of HIV replication and is used for evaluation of the effectiveness of antiviral therapy. These preliminary observations require additional studies. Absence of detectable antigen does not guarantee lack of infec-

tiousness of a given serum, semen, body fluid or organ.

Detection of Viral RNA or cDNA

Methods for detection of viral RNA or cDNA in routine diagnostic laboratories are under development and may offer the most sensitive test systems for direct demonstration of HIV in fluids or tissues.

Virus Isolation and Characterization of Virus Isolates from Various Geographical Regions

Techniques are still cumbersome and time-consuming but have been considerably improved, so that an almost 100% isolation rate can be achieved if multiple blood samples are examined. An optimized standard protocol should be worked out and made available to laboratories using this technique for basic or clinical studies. Virus isolates should be characterized to monitor the emergence of variant or new antigenic types.

Standardization and Reference Reagents

All of the above-mentioned test systems need further standardization. International antibody units should be established and appropriate reference reagents (both antigens and antibodies) should be prepared. The WHO Collaborating Centers on AIDS should play an active role in the preparation and evaluation of these reference reagents and WHO standards should eventually be established. WHO should also establish a repository of HIV1 and HIV2 as well as simian immunodeficiency virus (SIV) isolates. In addition it would be desirable to prepare a list of available clones of human and simian retroviruses.

Human T-Cell Lymphotropic Virus Type I and Type II (HTLV-I and HTLV-II)

The prevalence of HTLV-I and HTLV-II in various population groups should be monitored, but there seems to be no current need for general screening of blood or organ donors for HTLV-I and HTLV-II.

(Source: Wkly Epidem Rec, 62 (30) 1987.)

AIDS Surveillance in the Americas

Cumulative number of cases and deaths.

Subregion	Cases	Deaths	First report	Last report	
Country REGIONAL TOTAL	47,923	26,490			
	4.161	1.367			
LATIN AMERICA ^{a)}	256	121			
ANDEAN GROUP	2 2	1	31 Dec 85	18 Sep 8	
Bolivia	57	34	31 Dec 86	31 Mar 8	
Colombia	52	6	31 Dec 85	15 Sep 8	
Ecuador	44	6	30 Jun 82	15 Sep 8	
Peru Venezuela	101	74	31 Dec 84	18 Sep 8	
	174	90			
SOUTHERN CONE	164	51	31 Dec 83	30 Jun 8	
Argentina	95	22	31 Dec 83	30 Jun 8	
Chile	42	9	31 Dec 84	30 Jun 8	
Paraguay	14	8	31 Dec 83	30 Jun 8	
Uruguay	13	0	31 Dec 83	50 5 an c	
BRAZIL	2,013	734	31 Dec 82	15 Sep 8	
CENTRAL AMERICAN ISTHMUS	139	83	21.14 07	20 1	
Belize	2	2	31 Mar 87	30 Jun 8	
Costa Rica	31	18	31 Dec 83	30 Jun 8	
El Salvador	12	6	31 Dec 85	30 Jun 8	
Guatemala	27	27	30 Sep 86	30 Jun 8	
Honduras	29	13	30 Jun 85	30 Jun 8	
	19	0	18 Sep 87	18 Sep 8	
Nicaragua Panama	19	17	31 Dec 84	31 Mar 8	
MEXICO	534	177	30 Jun 81	30 Jun 8	
LATIN CARIBBEAN ^{b)}	1,055	162			
	4	3	31 Dec 86	30 Jun	
Cuba	200	35	31 Dec 85	31 Mar	
Dominican Republic Haiti	851	124	31 Dec 83	31 Mar	
	(24	353			
CARIBBEAN	624		31 Mar 87	30 Jun	
Anguilla	2	0		30 Jun	
Antigua	3	3	31 Dec 85	30 Jun	
Bahamas	126	56	31 Dec 85	30 Jun	
Barbados	44	27	31 Dec 84	30 Jun	
Cayman Islands	2	2	31 Dec 85	30 Jun	
Dominica	5	3	31 Mar 87	30 Jun	
French Guiana	84	60	31 Dec 86	30 Jun	
Grenada	6	5	31 Dec 84	30 Jun	
Guadeloupe	51	28	31 Dec 86	30 Jun	
Guyana	4	2	30 Sep 86	30 Jun	
Jamaica	26	23	30 Jun 86		
Martinique	27	17	31 Dec 86	30 Jun 31 Jul	
Montserrat	0	0	31 Jul 87		
Netherlands Antilles	18	10	31 Mar 87	30 Jun	
Saint Lucia	6	2	31 Dec 84	11 Sep	
St. Christopher-Nevis	1	0	31 Dec 85	31 Dec	
St. Vincent and the Grenadines	3	2	30 Jun 85	31 Dec	
Suriname	6	5	30 Jun 84	30 Jun	
Trinidad and Tobago	199	106	30 Jun 83	15 Sep	
Turks and Caicos Islands	4	2	31 Dec 86	30 Jun	
Virgin Islands (UK)	0	0	31 Mar 87	31 Mar	
Virgin Islands (US)	7	0	31 Mar 87	14 Sep	
NORTH AMERICA	43,138	24,770			
Bermuda	62	43	31 Dec 84	30 Jun	
Canada	1,258	657	31 Dec 79	14 Sep	
United States of Americab)	41,818	24,070	30 Jun 81	14 Sep	

a) French Guiana, Guyana, and Suriname included in Caribbean.

b) Puerto Rico included in USA.

Progress in Epidemiology

In Volume 3 (No.2) of Chronic Diseases in Canada, there appeared the following quotation: "Epidemiology in the 1980s - Need for a Change?" "It thus seems mandatory for epidemiologists to learn from clinicians and to focus their attention not only on risk factors but also on the individual on whom these risk factors are acting. In this way we may maximize the benefits to be learnt from the community study of disease patterns and safeguard against potential hazards of manipulating risk factors in individuals who are not at risk. For although clinicians should always be aware that the individual he sees with disease is merely part of a spectrum of disease in the community, the epidemiologist should not forget that the disease pattern he describes in the community reflects only the aggregate of many diverse and often unique individual results. I therefore call for epidemiology to free itself of inappropriate dependence on statistical analysis and 'disease-oriented' approaches and to focus more on the essential constituent of both epidemiological and clinical practice - the individual." (1)

These are provocative comments, but not unfamiliar. Epidemiologists have been told many times that they lose sight of the individual in their preoccupation with aggregate data. When curiosity led me to read the whole article, I found that the author was saying something far more interesting. His main point was that epidemiology tends to ignore two groups of people: those with known risk factors who remain disease-free and those without known risk factors who fall prey to disease. The first group holds the secret of protective factors and the second holds the secret of causes still unknown. Thus, instead of regarding these two groups of people as untidy departures from a neat causal model, we should be pursuing them with the fervour of a bloodhound. The point of the article is not so much that epidemiologists ignore the individual but that they ignore certain important categories of individuals.

It is much easier to make this mistake in the study of noninfectious diseases. Infectious disease epidemiologists have always been highly attuned to exceptional cases. For example it was the rarity of smallpox in milkmaids that gave Jenner the clue to cowpox vaccine. But in the study of heart disease and cancer, the complexity of the multiple cause model distracts the investigator's attention from the

exceptional cases. These tend to be regarded more as nuisance than as opportunity.

It is not difficult to estimate the size of the exceptional categories. The results of multivariate risk computations are used to define high risk and low-risk groups. Then, from cohort studies one determines the proportion of high-risk subjects who actually develop the disease and the proportion of cases belonging to the low-risk group. An example cited by Tunstall-Pedoe comes from the U.K. Heart Disease Prevention Project (2). Only 7% of the high-risk group had a heart attack during the 5-year period of observation, whereas 66% of heart attacks occurred outside the high-risk group. Which is more important to an epidemiologist, the 7% or the 66%?

The 66% may be less important because it may not reflect anything exceptional at all. If high levels of risk factors are not widespread, most cases of diseases will occur among the lower-risk majority. These cases can be regarded as the "natural" level of the disease arising from the inevitable deterioration of human substance rather than from exogenous causes. But before we dismiss the importance of disease among the low-risk, there is one question that we should ask. Does the incidence of the disease among the low-risk vary substantially over space or time? If it does, we may suspect the existence of other potentially important but as yet unidentified causes. These causes could be genetic, but they could also be exogenous. For example, the absence of certain trace elements in an environment could accelerate the "inevitable" deterioration of the cardiovascular system.

Let us turn now to the other category of exceptional people, the high-risk who escape the disease. The escape may be more apparent than real, of course, if the duration of follow-up is brief or if competing diseases are powerful. Nevertheless, experience suggests that for many diseases there may be a numerically significant group that is high on risk factors but low on incidence. Intensive study of such individuals could lead to the identification of protective factors. Our knowledge of protective factors seems less complete than our knowledge of risk factors. In fact, the long and ever increasing list of risk factors, particularly for cardiovascular disease, tends to make epidemiology a rival to economics as the dismal science. Any protective factor that we

could identify would be good news, especially if it were other than genetic and thus more immediately amenable to intervention.

It might also be rewarding to adopt a more integrated approach to the study of risk factors and protective factors. Instead of regarding them as separate, we should ask how a risk factor and a protective factor could interact. A recent epidemiological study of cervical cancer found that serum beta-carotene appeared protective (3). Even more interesting, however, was their evidence that smoking might be related to cervical cancer by virtue of its depressing effect upon beta-carotene. Observations such as these herald the coming of a more sophisticated era in epidemiology when we will begin to knit up the ravelled sleeve of causation.

References

- (1) Orchard, T.J. Epidemiology in 1980s—need for change? Lancet 2:845-6, 1980.
- (2) Tunstall-Pedoe, H. Paunches and the prediction of coronary heart disease. Br Med J 288:1629-30, 1984.
- (3) Harris, R.W.C., Forman, D., Doll, R., Vessey, M.P. and Wald, N.J. Cancer of the cervix uteri and vitamin A. *Brit J Cancer* 53:653-9,1986.

Editorial Comment

This is yet another thought-provoking article that stresses the fact that very often the highest frequencies of undesired events happen among people who have been described as being at low risk according to the state-of-the-art.

There could be much discussion about whether or not knowledge about health-disease processes in a community can be achieved satisfactorily by the simple aggregate of individual results. Although undisputably necessary, this approach may not be sufficient. Regardless of this "individual/social" question, Professor Buck's message cannot be stressed enough: fuller use should be made of the "discordant" cells — unexposed but diseased, and exposed but non-diseased individuals— to gain better insight into the causal process when asking "how else could the observed results be explained?"

(Source: Carol Buck. First published in Chronic Diseases in Canada, Vol. 7, No.3, 1986.)

Regional Course on Gerontology, Geriatrics, and Administration of Services for the Elderly

Introduction

Progress in activities in gerontology, geriatrics, and the administration of services for the elderly, in developing countries with high aging levels of their population, is hindered by the lack of theoretical and practical courses on these subjects in medical training and related programs. Furthermore, the possibility of Latin American countries basing their programs on geographic and demographic circumstances very different from their own is high, since available information and guidelines come, for the most part, from developed countries.

Based on the above, PAHO's Program of Health of the Elderly in February 1986 organized a working group of Latin American experts in care of the elderly to discuss the content, methods, and general characteristics of the First Regional Course on Gerontology, Geriatrics, and Administration of Services for the Elderly.

Course Profile

This training activity was designed in modules, with a one-week module for each of the three aspects mentioned in the course title. In addition, during the course a field project was to be carried out which would be useful in designing a care program for elderly persons.

The course was intended for participants from several disciplines, medical as well as others related to the subject, including: nurses, social workers, sociologists, and anthropologists. Special attention was given to promoting the selection of participants involved in care of the elderly in Spanish and Portuguese-speaking countries; preferably from those which had already established a policy of support to programs for the elderly, or where important research on the subject of the elderly had been conducted recently, or was being conducted. Partic-

ipants should have direct responsibility—at present or in the near future—for care programs for the elderly, educational functions, or research activities.

Course Development

The course was held in Buenos Aires, Argentina, from 3 to 21 November 1986, under the coordination of the National Institute of Social Services for Retirees and Pensioners (INSSJP). As the educational unit for the second module, the "Ingeniero A. Rocca" Institute of Geriatrics of the Italian Hospital also participated. General coordination of the course was the responsibility of PAHO's Program of Health of the Elderly.

The course was attended by 15 participants from eight countries: Argentina (6), Brazil (1), Chile (1), Dominican Republic (1), Mexico (1), Paraguay (1), Peru (3), and Uruguay (1). Twelve of the 15 participants were physicians; there was also a sociologist, a psychologist, and a social worker. There were five coordinators; in addition, the first module involved 13 instructors; the second, 18; and the third, 10. All of the instructors were nationals, from various public and private institutions.

The general objective of the course was to familiarize the participants with the principal characteristics affecting elderly persons, in order to facilitate the development of a plan of action that would lead this social group to active and productive participation in communities from which it has been unjustly excluded.

The specific objectives were:

Gerontology module: to interpret the social situation of the elderly; to identify conditioning factors, and to identify factors which could be modified by short-term programs.

Geriatrics module: to evaluate the health status of the elderly, and to identify medical and community techniques and resources to help improve the quality of services. Administration module: to apply the principles of administration to the design of programs and services for the elderly, and to identify the principal components of the institutions and the productive interaction among them.

Field project: to use newly acquired knowledge in the preparation and development of a health program for the elderly in a community, within the framework of the strategy of primary health care.

The field project consisted of preparing a health care program for the elderly in a town located in the interior of the province of La Pampa. The design followed the conceptual framework of the strategy of primary health care. Demographic and health material and statistics were made available for its preparation, as well as background information on the population aged 60 and over. The field work was led by a coordinator and two assistants, one for each group of participants. The work was carried out during the entire course and involved six hours a week of work group meetings. At the end of the course a lecture was given on "The Elderly in Latin America and the Caribbean: Current Situation and Perspectives."

Comments

By following up some of the participants, PAHO's Program on Care of the Elderly has observed that in the seven months since conclusion of the course over one third of them have been involved in establishment of programs for the elderly (Dominican Republic, Paraguay, Uruguay), services and organization of similar courses at the national level (Mexico), research (Brazil, Chile), or management of establishments for elderly persons (Uruguay). Currently, a second course is being organized (9-27 November 1987) which will incorporate several suggestions made by participants—in an anonymous evaluation—and by organizers of the first one.

To our Readers

We regret the delays experienced in publication of recent issues of the *Epidemiological Bulletin* which have been largely due to logistic problems. In order to bring the publication up to date, Volume 8 will consist of a total of only three issues; we trust this will facilitate our bringing the *Bulletin* to you in a more timely manner.

Diseases Subject to the International Health Regulations

Total cholera, yellow fever, and plague cases and deaths reported in the Region of the Americas in 1986.

Country and	Cholera	Yellow fever Cases Deaths		Plague
administrative subdivision	cases	Cases	Deaths	cases
BOLIVIA	-	26	19	94
Cochabamba	_	1	1	-
La Paz		25	18	94
BRAZIL	-	9	8	58
Bahía			****	21
Ceará		_		3
Goiás		5	5 2	
Mato Grosso	_	3	2	34
Paraiba	_			34
Roraima		1	1	_
CANADA	1	-	-	-
Ontario	1ª	_		_
COLOMBIA	-	6	6	-
Arauca		1	1	_
Guaviare		2	2	_
Meta		1	1	_
Putumayo		1	1	_
Santander	_	1	1	
PERU	-	118	98	-
Ayacucho	_	3	3 4	_
Cuzco		5 7	7	
Huánuco			18	
Junin		26	16	
La Libertad		1	-	
Madre de Dios	-	18	13	_
Pasco		2	1	
San Martín	_	55	50	
Ucayali		1	1	
UNITED STATES OF AMERICA	22	-	-	10
Arizona	-	_	_	1
California	-	_	_	3
Florida	1	_	_	_
Georgia	1		_	
Louisiana	18 1 ^a	_	_	
Maryland	1-			1
Nevada	_ 1a		_	
New Jersey	1	-		5
New Mexico	_	_		,

a_{Imported} case.

Calendar of Meetings

International Workshop on Research Towards Global Control and Prevention of Tuberculosis: With an Emphasis on Vaccine Development

This Workshop will be held from 3 to 5 November 1987 in the Hyatt Regency Hotel in Bethesda, Maryland, United States of America. The topics will include: past and present approaches to tuberculosis control and prevention; the pathogenesis of tuberculosis and its implications for vaccine development; molecular biology of the Mycobacteria; immunology; vaccine development; new drug development; and future directions and priorities.

Registration is required. Further information may be obtained from: Marcia J. Aaronson, Conference Coordinator, International Studies Branch, Fogarty International Center, National Institutes of Health, Bethesda, Maryland 20892, USA.

Conference on International Travel Medicine

This Conference will be held from 5 to 8 April 1988 in Zurich, Switzerland, under the auspices of the World Health Organization, the U.S. Centers for Disease Control, the Swiss Federal Office of

Public Health, the London School of Hygiene and Tropical Medicine, and the British Public Health Laboratory Service.

This event will bring together health professionals involved in the development and implementation of preventive measures, and those who provide health advice to travelers or temporary residents abroad. The ultimate goal of the Conference is to improve the protection of the travelers' health by more effective and more uniform recommendations.

Among the topics to be discussed are the following: health risks for short term travelers and for temporary residents in developing countries; malaria; vaccine preventable diseases, vaccines; traveler's diarrhea; sexually transmittable diseases; AIDS and other infections not preventable by immunization; non-transmittable illnesses, e.g. due to air/sea travel, high altitude, psychic impairment, accidents; health aspects of selected risk groups, e.g. pregnant or nursing women, children; International Health Regulations, health advice to travelers; and medical care and health insurance abroad.

Further information may be obtained from: Conference on International Travel Medicine, Interconvention AG, c/o Swissair, CH-8058 Zurich Airport, Switzerland.





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