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### EMERGING AND REEMERGING INFECTIOUS DISEASES AND ANTIMICROBIAL RESISTANCE

Despite significant progress, infectious diseases still pose a major threat to the peoples of the Americas. The appearance of several new pathogens which cause severe disease, such as the human immunodeficiency virus (HIV), the agent of Lyme disease, hantavirus and others, and the resurgence of old pathogens, including those which cause cholera, plague, dengue hemorrhagic fever, and yellow fever, are having a considerable impact in the Region. Microorganism mutation is leading to drug and multi-drug resistance among strains of *Mycobacterium tuberculosis*, staphylococci, pneumococci, gonococci, malaria parasites and other agents, which in turn are becoming major obstacles to the control of these infections.

A Regional Plan of Action was prepared in 1995 to provide guidance to Member States in addressing specific problems, and in implementing regional and subregional measures for prevention and control of emerging and reemerging infectious diseases. A Task Force on Surveillance of Emerging and Reemerging Infectious Diseases was convened to assess the capacity to carry out surveillance of infectious diseases at the country level, and to define priorities for regional surveillance.

The Pan American Health Organization is promoting a three-pronged approach to deal with the health threats described above: emerging disease/syndrome surveillance; outbreak detection and response; and antimicrobial resistance surveillance and prevention. Strengthening of public health laboratory networks will provide support to this approach.

The capacity of all Member States to recognize, prevent, and respond to the threat of emerging and reemerging infectious diseases will provide the foundation for an effective national and regional response. PAHO will continue to help countries to address the threat of infectious diseases in a cost-effective and sustainable manner.

The Executive Committee is requested to review this document and make recommendations on surveillance, detection and control programs in the countries and regionally, and on the development and implementation of regional guidelines for surveillance, prevention and control of emerging and reemerging infectious diseases and antimicrobial resistance.

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## 1. Introduction

According to the definition of the Institute of Medicine of the United States of America (1992), emerging diseases are those whose incidence in humans increased in the last 20 years. Reemerging diseases are those conditions that have reappeared after a significant decrease in incidence.

Two viral diseases, AIDS and dengue, are excellent examples of e in this Region. AIDS was unknown until early in the 1980s. Since then, the human immunodeficiency virus has been disseminated throughout the world.

Dengue, on the other hand, was a common disease whose incidence was greatly reduced during the 1960s and 1970s. The decline was due to interventions that almost wiped out the dengue vector, *Aedes aegypti*, from Mexico and continental Central and South America. In the 1980s, the mosquito returned with a vengeance and was responsible for an epidemic in Cuba that caused thousands of cases of dengue and hundreds of deaths. Since then, over 1.5 million cases have been reported in the Region.

Some of these epidemics are widely known to the public, while others remain ignored. Since 1993, mass media channels have provided the public all over the world with information on new and old threats of disease: Ebola virus in Africa and plague in India dominated the news. In the Americas, an adult pulmonary distress syndrome and its etiological agent, the *Sin nombre* virus, later recognized as a hantavirus, were found in the State of New Mexico, United States, and attracted great media attention. By comparison, a cholera epidemic in the Region during that same year—some three years after cholera was introduced to the Americas following an absence of a century—received little attention. Likewise, the press reported little on outbreaks of bubonic plague that have affected Peru since 1992. In fact, the latter epidemic remained unrecognized by the media as late as 1995, by which time there were already 2,000 cases with 90 deaths.

Other significant emerging and reemerging conditions include Lyme disease, diarrhea caused by cryptosporidiosis, and illness caused by *Escherichia coli* O157:H7 in the United States; dengue and yellow fever in Brazil; drug-resistant *Plasmodium falciparum* malaria in areas of the Amazon; hantavirus infections in the Southern Cone; cholera in many countries of Central and South America; and wide-spread antibiotic resistance in several species of bacteria.

In several instances, industrialized countries have responded to the challenge with remarkably rapid development of accurate laboratory methods to identify the disease-causing microbes. However, the diagnostic infrastructure, particularly in developing countries, must be expanded with a long-term commitment to capacity building.

The Organization has prepared a Regional Plan of Action<sup>1</sup> to provide guidance to Member States in addressing specific problems and in implementing regional and subregional measures for prevention and control of emerging and reemerging infectious diseases. The goals of the Plan are:

- (a) to strengthen regional surveillance networks for infectious diseases in the Americas;
- (b) to establish national and regional infrastructures for early warning of and rapid response to infectious disease threats through laboratory enhancement and multidisciplinary training programs;
- (c) to promote further development of applied research in the areas of rapid diagnosis, epidemiology, and prevention;
- (d) to strengthen the regional capacity for effective implementation of prevention and control strategies.

In 1996,<sup>2</sup> 1997,<sup>3</sup> and 1998 a Task Force on Surveillance of Emerging and Reemerging Infectious Diseases was convened to assess the Region's current capacity to carry out surveillance of infectious diseases at the country level and to define priorities for regional surveillance. The Task Force includes experts from several countries of the Region and from WHO. Guidelines for the implementation of a PAHO Regional Plan of Action for Combating Emerging and Reemerging Infectious Diseases were developed.

In response to recommendations of the Task Force, PAHO organized subregional meetings to develop and promote a surveillance system for emerging diseases, including antimicrobial resistance, which can report the occurrence of epidemiological events in real time, as well as provide rapid feedback and support. An electronic platform for the system is in development. Each country defines the diseases and syndromes of national interest, and includes in its reporting system those of regional and international interest. Further details regarding fulfillment of the Task Force's recommendations are provided in section 2 below.

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<sup>1</sup> Regional Plan of Action for Combating Emerging and Reemerging Infectious Diseases in the Americas. Doc. PAHO/HCP/HCT/95.060

<sup>2</sup> I Meeting of the Task Force on Surveillance for Emerging and Reemerging Infectious Diseases (PAHO/HCP/HCT/97.01)

<sup>3</sup> II Meeting of the Task Force on Surveillance for Emerging and Reemerging Infectious Diseases (PAHO/HCP/110/98).

The strategies adopted foster horizontal cooperation, especially among countries in the same subregion.

## **2. PAHO's Strategy and Technical Cooperation**

The Organization's technical cooperation activities have followed the recommendations of Directing Council Resolution CD38.R12 (1995). These activities have been aimed at achieving the goals of the Regional Plan of Action for Combating Emerging and Reemerging Infectious Diseases in the Americas. Activities have also been guided by recommendations of the Task Force on Surveillance of Emerging and Reemerging Infectious Diseases, which meets yearly to analyze progress and make suggestions for future technical cooperation.

The Organization's three-pronged approach to deal with the health threats described above is:

- emerging and reemerging infectious disease/syndrome surveillance, including the development and implementation of an electronic platform for instant communication of disease occurrence;
- outbreak detection and response;
- antimicrobial resistance surveillance and prevention.

PAHO activities for strengthening public health laboratories will provide crucial support to this approach. These areas of technical cooperation are carried out jointly by the Division of Disease Prevention and Control, Communicable Diseases Program (HCP/HCT) and the Division of Health Systems and Services Development, Essential Drugs and Technology Program (HSP/HSE).

### **2.1 *Emerging and Reemerging Infectious Disease/Syndrome Surveillance***

Communicable diseases continue to be the major source of illness and death in developing countries, but industrialized countries are becoming increasingly aware that they too are at risk from many emerging and reemerging infectious diseases. The socioeconomic development of many nations is being crippled by the burden of these diseases, which cause huge losses in foreign currency income and income from food trade and tourism as a result of epidemics of diseases such as cholera, plague, and dengue. Dengue has reemerged with dramatic force and is now endemic in most of the Americas. During 1998 alone, 770,000 cases were reported, with consequent losses in productivity and impact on health services.

The problem of emerging and reemerging infectious diseases must be approached from a regional perspective since these conditions no longer affect countries in isolation. For example, with the enormous increase in the frequency and speed of international travel, individuals infected during travel or residence abroad may introduce a disease into a previously unaffected area in a matter of hours.

Because of the above, with very few exceptions, all of the Organization's activities have a subregional focus and rely on intercountry technical cooperation. An example of this approach is the establishment of two subregional networks of laboratories for surveillance of emerging and reemerging infectious diseases, one in the Amazon region and another in the Southern Cone.<sup>4</sup> These are subregional initiatives which have been sponsored by the Organization in collaboration with the United States Centers for Disease Control and Prevention (CDC). A proposal for developing a Central American network is under consideration.

During 1998, PAHO also sponsored a technical cooperation project on hantavirus between Argentina and Chile in which the two nations collaborated in the areas of diagnosis, surveillance, the study of rodents, and research. In this context, support was also provided to cooperation activities between countries. For example, Argentina provided reagents for the diagnosis of hantavirus on a regular basis to other countries in Latin America. PAHO is also working very closely with several partners (national research institutes, ministries of health, national reference laboratories and others) to develop a regional surveillance system for infectious diseases, as well as to strengthen existing antimicrobial resistance surveillance programs for selected pathogens.

In order to strengthen the regional capability for emerging and reemerging infectious disease surveillance, plans for effective data collection, analysis, investigation, and prompt intervention are being prepared with the following objectives: (a) strengthening regional infectious disease surveillance networks as well as the capacity to implement effective prevention and control strategies; and (b) developing the national and regional infrastructure for early warning of and rapid response to the threat of these diseases.

Once in place, the new surveillance system will make use of available Internet technology to build e-mail and Intranet systems (closed access) for communications. Access to the system will be granted to ministries of health, all PAHO/WHO Country Representatives' Offices, selected national research institutions, and other partners. Validated data will then be made available through PAHO's web page. All participants will have equal access to the common database for analysis. Once surveillance systems and

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<sup>4</sup> Meeting to Establish a Network of Laboratories for the Surveillance of Emerging and Reemerging Infectious Diseases in the Amazon Region (PAHO/HCP/HCT/106/98) and the Southern Cone (PAHO/HCP/HCT/122/98)

corresponding infrastructures are in place, they will be capable of monitoring emerging pathogens and diseases for the confirmation of current epidemics; assessing the health and socioeconomic impact and likely evolution of the problem; determining the local response capacity; identifying the most effective control measures; and assessing the additional immediate needs. Standardization and harmonization of case definitions of diseases under surveillance is paramount for validation and comparability. This area of technical cooperation is coherent with WHO's global program, and is coordinated with WHO/CDS (Communicable Diseases Cluster) in the framework of the Task Force on Surveillance of Emerging and Reemerging Infectious Diseases.

## **2.2 *Outbreak Detection and Response***

Because of the need to expand the concept of surveillance to include not only information-collecting but also intervention, and to try to integrate all the actors from the public and private sectors into an ongoing reporting and response system, PAHO has proposed a team approach to confront infectious disease outbreaks. In programmatic terms, this is the newest strategy being implemented.

To complement the surveillance system, and in order for countries to be prepared to respond efficiently and effectively to the threat of infectious disease outbreaks, especially in post-disaster situations, the Organization is working with countries, initially in Central America, toward strengthening the subregional and national reaction capacity by means of multidisciplinary outbreak response teams. Active surveillance will also be strengthened to allow for the future identification of and response to infectious disease clusters.

The Communicable Diseases Program of PAHO has been preparing training materials, including some for social communicators, so that the general public will be better informed of outbreak situations through improved and more accurate press reports.

Once this strategy is operational, it is expected that countries will have national teams to deal with disease outbreaks, and will have replicated outbreak response training so that there will be as many outbreak response teams as deemed necessary in each country. The current approach proposes a long-term and sustainable strategy with the aim of having, in each country of the Region, a cadre of professionals trained and provided with the necessary tools (equipment) to lead the national response to outbreaks or public health threatening situations.

Training materials (Outbreak Response Manual) were tested by the first group of participants attending a course held in San Salvador, El Salvador, in January 1999. These trainees pilot-tested the format and materials of the course and were provided with the skills to become facilitators for future courses to replicate the training.

### **2.3 *Antimicrobial Resistance***

Drug-resistant strains of microbes are having a deadly impact in the fight against tuberculosis, malaria, cholera, diarrhea, and pneumonia—major diseases that together kill more than 10 million people worldwide each year. This is happening at a time when too few new drugs are being developed to replace those that have lost their effectiveness.

Some of the most common bacteria that are the major causes of death in children through acute respiratory infections, particularly *Streptococcus pneumoniae*, are becoming more and more resistant to antibiotics. Antibiotic resistance in hospitals throughout the Region threatens to leave medical and public health workers virtually helpless in the prevention or treatment of many infections. As an example, antibiotic-resistant bacteria are responsible for up to 60% of hospital-acquired infections in the United States. Resistance means that people with infections are ill for longer periods, and are at greater risk of dying. Disease epidemics are prolonged, as well.

A major factor that contributes to antibiotic resistance is the uncontrolled and inappropriate use of antibiotics. There is a need to prevent the improper prescription of these drugs by the medical community and the non-prescription use by the population at large, as well as to monitor the use of antibiotics in animal husbandry. In addition, implementation of legal and policy guidelines that mandate the rational use of antibiotics must be promoted.

An additional constraint in this area is the lack of reliable data to determine the real magnitude of antibiotic resistance in the Region and to provide baseline information for planning interventions. In order to address this situation and the misuse of antibiotics, PAHO feels that it is necessary to collaborate with the best and most influential individuals working in the countries on the issue, especially if changes in policy and health care practices are to be promoted in the near future. Some work is already in progress with organizations in several countries of the Region.

CDC has provided training in the use of the Public Health Laboratory Information System (PHLIS) to professionals from Bahamas, Barbados, Jamaica, Saint Lucia, Suriname, and Trinidad and Tobago. All activities in this area were coordinated and implemented jointly by HCP/HCT, the PAHO-directed Caribbean Epidemiology Center (CAREC), and HSP/HSE.

PAHO, together with WHO, the Ministry of Health of Venezuela, and the Pan American Society of Infectious Diseases, cosponsored the Pan American Conference on Antibiotic Resistance. The event was used to gather information on the current situation of antibiotic use and resistance in the Region. Several recommendations were issued which



will be incorporated into a 3-year plan for the prevention and control of antimicrobial resistance: strengthening surveillance, promoting policy formulation, encouraging participation of the pharmaceutical industry, monitoring the use of antibiotics in animal husbandry, and promoting proper prescription and use of these drugs.

Since 1996, PAHO, together with Canada's Laboratory Center for Disease Control (LCDC), has been collaborating with countries to strengthen their laboratory and epidemiological infrastructure and expertise for the surveillance of targeted enteric pathogens. Over US\$ 500,000 has been invested.

An expert committee met in Asunción, Paraguay, to develop a strategic plan for surveillance and prevention of antimicrobial resistance. The strategic approach relies heavily on technical cooperation among countries, especially in the areas of quality assurance and external quality control of laboratories in bacteria identification and antimicrobial susceptibility.

At the suggestion of the Task Force on Surveillance of Emerging and Reemerging Infectious Diseases, a page has been included in the PAHO Web site with data provided by countries on antibiotic resistance. In addition, hospital data on vancomycin-resistant enterococci are being collected.

### **3. Recent Technical Cooperation Activities**

Table 1 provides a summary of PAHO's recent technical cooperation activities in the area of emerging and reemerging infectious diseases, following recommendations of the Task Force.

Several technical documents and publications were published during 1998 to disseminate information in the area of emerging and reemerging infectious diseases:

- Métodos para trampeo y muestreo de pequeños mamíferos para estudios virológicos (PAHO/HCP/HCT/104/98);
- Meeting to Establish a Network of Laboratories for the Surveillance of Emerging and Reemerging Infectious Diseases in the Amazon Region (PAHO/HCP/HCT/106/98) and (PAHO/HCP/HCT/122/98);
- II Meeting of the Task Force on Surveillance for Emerging and Reemerging Infectious Diseases (PAHO/HCP/HCT/110/98);
- *Hantavirus in the Americas: Guidelines for Diagnosis, Treatment, Prevention and Control* (Technical Paper 47, 1999).

**Table 1: Technical Cooperation Activities in Response to Recommendations of the Task Force: Emerging and Reemerging Infectious Disease/Syndrome Surveillance**

Recommendation	Technical Cooperation Activity
<p>Maintain and reinforce regional surveillance of malaria, dengue, tuberculosis, and antimicrobial resistance.</p>	<p>In addition to annual case reporting of malaria by all countries, eight countries implemented a protocol for the evaluation of antimalarial drug susceptibility, of which Brazil, Colombia, Guyana, Peru and Suriname have already reported data. Six malaria outbreaks were reported during 1998 (Colombia, Ecuador, Guatemala, Honduras, Nicaragua, and Peru). Ten countries are currently reporting data on antimicrobial resistance. Nine countries monitor tuberculosis drug resistance; five more countries are starting the process.</p>
<p>Promote a surveillance system with clearly defined objectives, reporting pathways, outputs and feedback mechanisms.</p>	<p>Five subregional meetings were held to discuss a proposal for a surveillance system based on a combined approach of syndrome notification and specific disease reporting. As a result of each meeting, subregional groups of countries defined the syndrome/disease combination to be reported; the need to strengthen the link between the laboratory and epidemiological work was underlined; participants emphasized the need to maintain current disease-specific based surveillance systems, complemented by a syndrome approach. A set of criteria* was established to make reporting urgent: number of cases surpass the expected number for given space/time; disease may spread outside the community; high mortality rate/case fatality rate; and unknown or unexpected condition.</p>
<p>Identify critical shortfalls in availability of diagnostic reagents and promote a regional production.</p>	<p>ANLIS "Carlos Malbrán," Argentina, has provided reagents for hantavirus, and the Centro de Higiene, Venezuela, has produced reagents for the identification of various leptospira serovars, which are being tested.</p>
<p>Organize a regional database for collecting reports of notifiable diseases from all countries on a periodic basis.</p>	<p>A regional database was designed for this purpose and an electronic platform for data reporting and feedback is in development.</p>
<p>Encourage common case definitions and standards for reporting and provide consolidated information on selected diseases to participating countries.</p>	<p>The WHO/CDS Communicable Diseases Surveillance Kit was translated into Spanish and distributed to all Member States, and its use was promoted at subregional surveillance meetings.</p>
<p>Explore the development of pilot surveillance initiatives in Member States, that take advantage of communication advances.</p>	<p>A project to identify national web sites which report epidemiological data and to explore their validity and timeliness, in order to incorporate these data into a regional surveillance system, is being set in motion.</p>

\* It was agreed that definitions for above criteria would be further refined on a subregional basis.

## **4. Future Activities**

### **4.1 *Emerging and Reemerging Infectious Disease/Syndrome Surveillance***

Ongoing information dissemination activities will continue with the publication of hard copy and electronic versions of technical reports. Once the electronic platform for the disease reporting systems is fully operational, reported data will be posted for all partners to review.

The successful establishment of the Amazon and Southern Cone subregional networks of laboratories for surveillance of infectious diseases has provided the motivation to explore the feasibility of initiating a similar intercountry cooperation approach in Central America. This task will involve working with the countries to identify priorities, laboratory needs, and funding alternatives. Surveillance of blood-borne infections will continue with laboratory quality control and data dissemination.

The Communicable Diseases Program will continue to maintain an early epidemiological warning system among countries and to share information on emerging and reemerging infectious diseases, including outbreak reports. It will also continue to work with WHO in pilot testing the International Health Regulations, and in providing assistance to countries to obtain diagnostic reagents for rapid diagnosis and to strengthen laboratories.

### **4.2 *Outbreak Detection and Response***

Other activities in progress include the adaptation of outbreak investigations and response training materials and related training activities, and strengthening of laboratories for emerging and reemerging infectious disease agent identification. A rapid assessment of the national capacity of surveillance systems will be carried out in selected countries, especially in regard to their ability to detect and respond to outbreaks in a timely manner.

As mentioned above, training activities have been planned for six-person multidisciplinary teams from each selected country. These teams will include an epidemiologist, laboratory scientist, nurse, disaster/emergency specialist, armed forces health representative, and social communicator. Each national team will be trained in a subregional course. Equipment consisting of a field laboratory, reagents and other supplies will be distributed at the end of the course so that team members are fully prepared for the next outbreak situation.

A training-of-trainers approach will be promoted within each country to give the project sustainability. Thus support will be provided for national teams to replicate the training at the state, provincial, and local levels.

### **4.3 Antimicrobial Resistance**

Collaboration with LCDC will continue to support the ongoing surveillance of antimicrobial resistance of enteropathogens (*Shigella*, *Salmonella* and *V. cholerae*). These surveillance activities will supplement WHO's, which are directed to a broader number of pathogens and are mainly hospital-based.

In addition, implementation of the Regional Plan of Action for the Control and Prevention of Antimicrobial Resistance will begin. The Plan has two major components: capacity building (laboratory strengthening) for surveillance to determine the magnitude and impact of antimicrobial resistance; and capacity building to implement approaches to address the problem. The latter component includes gathering of information on current national policies, regulations and guidelines; development of approaches to promote rational use of antimicrobial drugs; and creation of awareness among health professionals, policy makers and the general public of the risk of antimicrobial resistance and the need to implement preventive practices.

Implementation of this program of activities will bring together HSP/HSE's expertise in laboratory strengthening and drug management and HPC/HCT's experience in disease surveillance and control. Many activities, especially in regard to laboratory strengthening, will rely on technical cooperation among countries.

As stated in other sections of the document, public health laboratory strengthening is a major component of the three strategies (emerging and reemerging infectious disease surveillance, outbreak detection and response, and antimicrobial resistance surveillance and prevention). The emphasis of technical cooperation activities in this area includes training for infectious disease agent identification; antibiotic susceptibility testing; reporting mechanisms and data management, analysis and interpretation; quality control and quality assurance; and provision of logistic and laboratory inputs, when necessary and feasible.

## **5. Issues for the Consideration of the Executive Committee**

The Executive Committee is requested to review this document and make recommendations on the progress of surveillance, detection and control programs at the country and regional level, and on the development and implementation of regional guidelines for surveillance, prevention and control of emerging and reemerging infectious diseases and antimicrobial resistance.