

New, Emerging, and Re-emerging Infectious Diseases

In recent years considerable attention has been given to the serious threat posed by new, emerging, and re-emerging infectious diseases.¹ The magnitude of the problem is illustrated by the appearance of several new pathogens causing disease of marked severity, such as the human immunodeficiency virus (HIV) and other retroviruses, arenaviruses, hantaviruses, and Ebola virus. Simultaneously, old pathogens — including those which cause cholera, plague, dengue hemorrhagic fever, and yellow fever — have re-emerged and are having a considerable impact on the Americas.

Mutations leading to drug-resistant and multi-drug-resistant strains of *Mycobacterium tuberculosis*, enterobacteria, pneumococci, malaria parasites, and other agents occur continuously. Drug resistance is becoming a major obstacle to the control of these infections in many parts of the world, including the Americas.

In response to these alarming trends, PAHO convened a meeting of international experts to discuss strategies for the prevention and control of new, emerging, and re-emerging diseases. As a result of this meeting, held 14–15 June 1995 in Washington, D.C., a Regional Plan of Action was pre-

pared in order to develop regional and sub-regional approaches and to guide Member States in addressing specific problems. The Regional Plan of Action was subsequently presented to the XXXVIII Meeting of the PAHO Directing Council in September 1995, which adopted a resolution (CD38.R12) supporting the goals of the Plan. PAHO thus joined the World Health Organization and an impressive array of other health organizations and institutions that had developed or were developing strategic plans to address emerging infectious disease threats.

The Regional Plan of Action for Combatting New, Emerging, and Re-emerging Infectious Diseases in the Americas will serve as PAHO's blueprint for implementing programs and initiatives on emerging infections in the Western Hemisphere. The following report gives an overview of some of the most significant emerging and re-emerging disease problems in the Americas and summarizes the goals and objectives of the Regional Plan of Action.

EMERGING INFECTIONS IN THE AMERICAS

A complex combination of factors has contributed to the recognition of an increasing number of new, emerging, and re-emerging infectious diseases in both developed and developing countries of the Americas. Cholera, for example, returned to the Western Hemisphere in epidemic proportions in 1991. Since then, over 1 million cases and 9 000 deaths have occurred in Latin America. PAHO has estimated that more than a decade and over US\$ 200 billion will be required to control the regional epidemic. International commerce may have played a role in the reintroduction of

¹ Emerging diseases are defined as those whose incidence in humans has increased in the past two decades, and re-emergence is the reappearance of a known disease after a significant decline in incidence.

Sources: (1) Pan American Health Organization. New, emerging, and re-emerging infectious Washington, DC: PAHO; 2 August 1995. (Document CD38/17). (2) Regional plan of action for combatting new, emerging, and re-emerging infectious diseases in the Americas, based on the report of the workshop on combatting emerging infectious diseases: challenges for the Americas, Washington, DC, 14–15 June 1995. (Document PAHO/HCP/HCT/95.060).

Vibrio cholerae to this Region. Factors contributing to the resurgence of cholera included poor public sanitation, inadequate water treatment, and high levels of poverty and unsatisfactory living conditions.

Tuberculosis (TB) may also be on the rebound. Between 200000 and 250000 cases have been reported annually in the Americas since 1980, with substantial variability in reporting completeness and accuracy (1). Case notifications are estimated to represent roughly 40% to 70% of true incidence (2). Although data from case notifications may not be adequate to confirm resurgence of TB, the experience of some countries with stable and relatively reliable reporting systems does suggest that it is a growing problem. There are four factors that seem to be contributing to a resurgence of TB: the HIV/AIDS epidemic, drug resistance, increases in marginalized populations, and neglect of public health infrastructure in general and of TB control specifically. An estimated 330 000 individuals in the Region were co-infected with TB and HIV in 1992 (3).

HIV/AIDS may be the most devastating example of the potential impact of a newly emerging infectious disease on global health. The HIV/AIDS pandemic has been pivotal in drawing the attention of public health experts to the problem of infectious diseases and to the need for increased surveillance and research. HIV infection and other sexually transmitted diseases illustrate the impact of changes in demographic conditions and social standards, modification of the global environment, and the mutability of microorganisms. The discovery of HIV has also led to the identification of other etiologic agents with similar modes of transmission (through sexual contact, blood contamination, and perinatal acquisition), such as HTLV-I and HTLV-II, which are associated with myelopathy/tropical spastic paraparesis in the Caribbean and Brazil (4).

The dramatic impact of HIV/AIDS on public health is due in large part to the

multiple opportunistic infections that develop in association with this condition (5). Besides the interaction with TB, noted above, HIV/AIDS is also interacting with common tropical diseases such as Chagas' disease — producing unusual clinical manifestations (6) — and with new and emerging infections. Experience with some HIV-related infections, such as diarrheal disease caused by *Cryptosporidium*, has led to their increased recognition in broader populations. Even "new" diseases are being recognized with increasing frequency as a result of an expanding population of persons with HIV/AIDS; for example, three new species of microsporidia were first described in HIV-infected individuals in North America and the Caribbean. HIV-induced immunosuppression has also been found to affect susceptibility to cervical cancer caused by human papillomavirus.

Although worldwide in scope, the emergence of dengue and dengue hemorrhagic fever (DHF) as a major public health problem has been most dramatic in the Americas, where the mean annual number of reported DHF cases increased almost 80-fold between 1989 and 1994 compared with the preceding six-year period (1983–1988). In 1995 explosive outbreaks of dengue struck Brazil, Venezuela, and Central America. Dengue (types 1, 2, and 4) has now become hyperendemic in many countries of the American tropics; in addition, dengue type 3 virus activity reappeared in the Region in 1994 after an absence of 16 years. The resurgence of dengue/DHF in this Region is largely due to the reduction in most countries of programs to eradicate *Aedes aegypti*, the mosquito vector of dengue. As a result, the current geographic distribution of *Ae. aegypti* is similar to what it was prior to the successful eradication campaigns of the 1950s and 1960s. Other contributing factors include uncontrolled urbanization, population growth, and increasing poverty (7–9).

Yellow fever, which usually occurs sporadically among persons exposed to the

infection in forests, re-emerged forcefully in Peru in 1995, causing the largest outbreak in the country's history. A total of 499 cases were notified in 1995, with a fatality rate approaching 40% (Ministry of Health, Peru, 1995).

Oropouche fever is another arthropod-borne viral disease of importance in the Americas. Major outbreaks have occurred in urban centers of the Amazon region of Brazil, mostly in Pará State, during which over 300 000 persons were infected. In the 1990s Oropouche fever spread to cities of the western Amazon area, causing severe outbreaks, as well as to urban centers in Panama and Peru (10).

In the latter country, a resurgence of human plague began in October 1992, after 40 to 50 years during which only sporadic cases had been reported. The upsurge in this flea-transmitted disease was associated with expanding rodent populations brought on by increased availability of cereal grain food sources.

Influenza, like yellow fever and plague, has caused considerable illness and death among humans for hundreds of years. Several pandemics have occurred during the 20th century, the most important being the 1918 influenza A pandemic, which claimed more than 20 million lives; less severe pandemics occurred in 1946, 1957, 1968, and 1976. It is likely that an influenza pandemic will strike again, but it is not possible to predict when (11).

The South American arenaviruses provide an important example of how exploitation of new areas for human settlement and agriculture increases the likelihood that new infectious diseases will emerge. While some recently discovered members of this group of rodent-borne viruses are not pathogenic to humans, three of them cause important health problems: Junín virus (Argentine hemorrhagic fever), Machupo virus (Bolivian hemorrhagic fever), and Guanarito virus (Venezuelan hemorrhagic fever). Humans come into contact with

these emerging infections when they move into new areas where the viruses are circulating in wild rodents; the rodents may enter ecologically disturbed areas, allowing the viruses to spread widely (12).

Vulnerability to emerging infections is not limited to the developing countries of the tropics. In 1993, the United States of America experienced the largest waterborne disease outbreak ever recognized there, owing to contamination of an urban water system with *Cryptosporidium*. Also in 1993, the emerging bacterial pathogen *Escherichia coli* 0157:H7 caused a multi-state foodborne disease outbreak of hemorrhagic colitis and hemolytic uremic syndrome (13).

Likewise, a previously unknown hantavirus was identified in the four-corners area of the United States (Arizona, Colorado, New Mexico, and Utah) as the etiologic agent of hantavirus pulmonary syndrome. This infection, which was linked to exposure to infected rodents, has primarily affected otherwise healthy adults, with a cumulative mortality approaching 50% (14). Illness associated with hantavirus is increasingly being recognized elsewhere in the Americas, including Argentina, Brazil, Chile, and Paraguay.

Finally, antimicrobial resistance is perhaps one of the gravest threats among the problems presented by emerging infections (15). The problem is well documented in the United States, where increasing levels of drug resistance have been noted in infections acquired both in the community and in health care institutions. This situation is viewed by infectious disease experts as a crisis that could lead to a "post-antibiotic" era (16). Although less well documented, significant levels of antimicrobial drug resistance are increasingly being detected in Latin America. The threat from antimicrobial resistance in the developing countries of the Western Hemisphere may outweigh that which is present in the United States and Canada, since conditions that encourage the development of anti-

crobial resistance are widespread throughout Latin America. They include over-the-counter sale of antibiotics and frequent self-medication; overcrowding and suboptimal infection control practices in many hospitals; minimal regulation of antibiotic usage within or outside of hospitals; scarce documentation of clinical trial results of newer antibiotics; and almost nonexistent surveillance and reporting of antimicrobial resistance patterns (17).

GOALS AND OBJECTIVES OF THE REGIONAL PLAN OF ACTION

The Plan lists four goals, each with several associated objectives:

Goal 1: Strengthening regional surveillance networks for infectious diseases in the Americas

Well-run surveillance networks are invaluable tools for disease monitoring and assessment. Surveillance should detect, promptly investigate, and monitor emerging pathogens, the diseases they cause, and the factors influencing their emergence.

Several surveillance networks are presently functioning in the Americas, including ones for cholera, influenza, dengue, and antimicrobial resistance (WHONET), and those established as part of the polio eradication and measles elimination programs. In addition, the Caribbean Epidemiology Center, the Pan American Foot-and-Mouth Disease Center, and the Pan American Institute for Food Protection and Zoonoses have important functions in the surveillance of human and animal diseases.

Regional leadership and coordination must be provided to enhance these existing capacities by strengthening and linking established laboratories and surveillance facilities (objective 1-A). Consideration should be given to establishing a regional steering committee for emerging infectious

disease surveillance that will develop priorities for regional surveillance, in close coordination with the countries (objective 1-B). The committee could include representatives of leading institutions in the countries.

Surveillance systems that are closely linked with reference diagnostic services function as early warning systems for emerging infections. Therefore, it is necessary to develop uniform guidelines for Member States that provide for programmatic links between surveillance and reference diagnostic services, emphasizing that such services are inherently governmental functions and responsibilities (objective 1-C).

Goal 2: Establishing national and regional infrastructures for early warning of and rapid response to infectious disease threats through laboratory enhancement and multidisciplinary training programs

A program for early warning and rapid response to emerging infections has a number of components, including human resources, laboratory facilities, communications networks, and supplies. An organizational structure must be developed that integrates the different infrastructural elements, provides for basic logistical support (e.g., procurement, specimen handling and storage, and shipping of specimens to reference facilities), and has sufficient political/governmental support to integrate the program into overall national health priorities (objective 2-A). Development of a long-term plan for fiscal support and budgetary management (objective 2-B) is essential.

Appropriately trained personnel will be a critical component. Therefore, mechanisms must be established to assign, redeploy, and maintain the necessary human resources through training and career development programs (objective 2-C). Training should target medical as well as

laboratory personnel, and a career path providing advancement opportunity should be established to ensure retention of skilled personnel.

The necessary facilities must be secured for laboratory-based diagnosis and research, clinical evaluation and care, and training (objective 2-D). A comprehensive survey of suitable laboratory and epidemiologic facilities should be conducted and their capabilities assessed. It is necessary to define the complement of minimal laboratory and epidemiologic capabilities that should be available at each level (local, national, subregional, and regional), develop guidelines and standard procedures, and assist governments in implementing these guidelines.

Different communication mechanisms are appropriate at different levels. There is a need to develop communications links among program participants that are "level-appropriate" and to emphasize feedback to and participation of communities (objective 2-E).

Goal 3: Promoting the further development of applied research in the areas of rapid diagnosis, epidemiology, and prevention

Objects of applied research include diagnostics, treatment, prevention, surveillance, development of products, and socioeconomic factors affecting disease transmission.

Each country must determine its own research priorities regarding emerging diseases. However, three broad categories of applied research deserve particular priority: diagnostics, epidemiology/prevention effectiveness, and clinical studies.

Development of rapid, simple, and cost-effective diagnostic techniques for emerging pathogens of importance in the Americas is a high priority (objective 3-A). It would be useful to develop reagents that could be produced by a regional reference center or by local laboratories, depending on their capabilities. Studies of the cost-

effectiveness of various diagnostic tests should be carried out.

Efforts in epidemiologic and prevention effectiveness research must be expanded (objective 3-B). Research in the latter area should include the development and testing of innovative interventions, including vaccines, to control or prevent emerging diseases.

It is essential to standardize the clinical diagnosis and treatment of newly emerging diseases. Clinical research protocols must be designed to answer critical questions on the pathogenesis and spectrum of emerging infections (objective 3-C).

Goal 4: Strengthening the regional capacity for effective implementation of prevention and control strategies

Prevention and control strategies will complement goals 1-3 and can be viewed as the "action" and "feedback" components of the Regional Plan of Action. Three broad areas related to prevention and control strategies deserve particular attention: information dissemination, antimicrobial resistance, and outbreak evaluation and control.

Emphasis will be placed on developing systems and programs for information dissemination (objective 4-A). These plans should make effective use of the press, including radio, television, newspapers, and other media, to disseminate information such as disease-specific prevention and control guidelines for communities and individuals.

Education programs for the health consumer and health provider on the inappropriate use of antibiotics and the development of antimicrobial resistance must be developed and rapidly implemented (objective 4-B). Ways should be sought to reduce easy availability of over-the-counter antimicrobial agents, and assistance to the countries in developing rational drug policies should be intensified.

Finally, regional outbreak control measures must be enhanced (objective 4-C). Guidelines for contingency situations should be updated, and a system for rapid procurement of vaccines, reagents, insecticides, and antimicrobials for prompt response to outbreaks should be available.

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