MEETING OF THE TASK FORCE ON SURVEILLANCE FOR EMERGING AND REEMERGING INFECTIOUS DISEASES

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This is a report of the Second Meeting of the Task Force for Emerging and Reemerging Diseases Surveillance of the Pan American Health Organization (PAHO) held in Rio de Janeiro, Brazil, from 6 to 8 December 1997.

The document contains a summary of activities being carried out by the World Health Organization (WHO), PAHO, and their partners in the race to detect and respond to the threat posed by emerging and reemerging diseases in the Americas.

As a result of the discussions at the Rio de Janeiro meeting, the members of the Task Force endorsed the recommendations made during their first meeting (held in Toronto in November 1996), and added the following:

The Pan American Health Organization should:

- Maintain and reinforce the regional surveillance of malaria, dengue, tuberculosis and antimicrobial resistance.
- Promote a surveillance system with clearly define objectives, reporting pathways, outputs and feedback mechanisms to the beneficiaries.
- Promote the use of the syndrome approach to increase sensitivity and improve immediate response to change in disease trends, while maintaining disease based surveillance for specificity and accuracy.
- Promote a sentinel surveillance system:
  - Establish or strengthen sentinel programs for the surveillance of *Plasmodium falciparum* (with emphasis on monitoring of drug resistance), dengue hemorrhagic fever, blood borne pathogens, and antimicrobial resistance.
  - Support the initiative on surveillance for emerging infectious diseases in the Amazon basin and extend it to other subregions, such as the Southern Cone.
  - Include data provided by countries on antibiotic resistance and make them available through the PAHO WEB site.
  - Review and revise the existing pneumococcal sentinel surveillance system to transition this demonstration project to an efficient, economical part of the routine regional surveillance, and consider extending this to other pathogens.
  - Develop feasibility studies for the establishment of sentinel surveillance demonstration projects for other infectious diseases when knowledge of circulating strains is relevant to public health actions.
- Identify critical shortfalls in availability of diagnostic reagents and promote a regional production.
- Organize a regional data base for collecting reports of notifiable diseases from all countries on a periodic basis. Encourage common case definitions and standards for reporting, and provide consolidated information on selected diseases to participating countries. Explore the development of pilot surveillance initiatives in Member States, that take advantage of communication advances.
Welcoming Remarks and Objectives of the Meeting

Participants were given a warm welcome by Dr. Eloy Garcia, who expressed his satisfaction at having the FIOCRUZ campus host the “Meeting of the Task Force on Surveillance of Emerging and Reemerging Diseases.”

Dr. Garcia further indicated that he found the subject of the meeting very appealing, and one in which FIOCRUZ has been interested for the past few years. The Foundation, affiliated with the Ministry of Health of Brazil, is one of the oldest research centers in the country, working in several health fields. Among those, emerging and reemerging diseases are becoming an increasing public health concern which conceivably affects not only the population of Brazil, but that of other countries as well.

Dr. Garcia emphasized that the scientific contents of the meeting would be presented by many leaders in the field, making this gathering unique and very informative. The discussions surrounding each presentation and the final report would further the understanding of the complex nature of this subject. Therefore, he forecasted excellent results from the discussions, and underlined that only in rare opportunities are researchers, health officials and other professionals involved in health planning for emerging and reemerging diseases in developing countries brought together.

Dr. Garcia thanked the organizers of the workshop, Dr. Christina de Albuquerque Possas (FIOCRUZ) and Dr. Gabriel Schmunis (PAHO) as well as all the speakers, and expressed his strong appreciation of everybody’s participation and contribution to the debate.

Dr. Stephen Corber, Director, Division of Disease Prevention and Control of the Pan American Health Organization added his own welcome to the participants and provided an overview of the activities carried out so far by Member Countries, the Task Force on Surveillance for Emerging and Reemerging Infectious Diseases and PAHO. In 1995, PAHO, assisted by the Task Force, prepared a Regional Plan of Action on Emerging and Reemerging Diseases. The goals of the Plan were similar to those of the World Health Organization (WHO) and the U.S. Centers for Disease Control and Prevention (CDC), i.e., to improve regional surveillance; to strengthen national and regional infrastructures for early warning and rapid response to infectious diseases; to promote applied research in diagnosis, epidemiology and prevention, and to strengthen the regional capacity for effective implementation of prevention and control strategies.

Following approval of the Regional Plan, a meeting was held in Goiânia, Brazil, in March, 1996, to define priorities for the institutional strengthening of emerging infectious diseases surveillance. As a result of this meeting, it was recommended that a syndrome based system be adopted for disease detection with laboratory confirmation of cases; that each country define the syndromes of national interest and include those of regional and international consequences; that core data consist of hospital morbidity, mortality, and antimicrobial resistance. In addition, countries should ensure continuing interaction between epidemiologists and laboratories. Finally, it was recommended that PAHO promote the implementation of these surveillance systems in the countries of Latin America.

As part of his introduction, Dr. Corber presented the final report of the Meeting of the Task Force on Surveillance for Emerging and Reemerging Infectious Diseases held in Toronto, Canada, on 13-14 November 1996 (Document PAHO/HCP/HCT/97.01), and highlighted the conclusions and recommendations of the report, as well as the results of the Survey on National Capability for Surveillance of Emerging and Reemerging Infectious Diseases in Latin America and the Caribbean included as part of that document.

Dr. Corber further indicated that one objective of the current meeting was to review activities carried out by the countries and PAHO/WHO in regard to the surveillance of emerging and
reemerging diseases: syndromic approach to surveillance, detection of and response to outbreaks, strengthening of laboratory networks, detection of antibiotic resistance, and surveillance of blood borne diseases. Another objective was to analyze, discuss and make recommendations regarding a PAHO proposal for a Regional Surveillance System of Emerging and Reemerging Diseases (see p. 45).
In view of the serious threat to the health of populations posed by communicable diseases in general (figure 1), and by emerging diseases in particular, the World Health Organization has determined, through its Emerging and Other Infectious Diseases Program (EMC), that the following strategies must be in place for the world to be on the alert and able to contain communicable diseases:

- Development of strong national disease surveillance and control programs;
- Establishment of global networks of centers, organizations and individuals to monitor diseases;
- Rapid information exchange through electronic links to guide policies, international collaboration, trade and travel, and
- Effective national and international preparedness, and rapid response to contain epidemics of international importance.

The contribution of WHO to emerging and other communicable diseases control includes global monitoring and alert systems; global information systems; national and regional preparedness for communicable disease surveillance and control, and international preparedness for communicable disease surveillance and control. Some of the specific areas in which EMC is actively involved include antimicrobial resistance, cholera and epidemic dysentery, cerebrospinal meningitis, hemorrhagic fevers (including Ebola and dengue), hepatitis A, C, E and others, HIV/AIDS, influenza, legionellosis, plague, rickettsial infections, streptococcal infections, transmissible spongiform encephalopathies, viral encephalitis, yellow fever and zoonoses.

The objective of the activities carried out in this regard is to ensure international preparedness and response by achieving international consensus formulation on surveillance and control, providing a WHO surveillance and case definition manual, and preparing to respond to epidemics. In addition, operational and epidemiological research is needed to ensure that the most cost-effective surveillance and control approaches will be promoted (i.e. meningitis working group, hemorrhagic fever surveillance, simple diagnostic tests). An international coordinating group on vaccines for diseases of epidemic potential, and the facilitation of international outbreak response are part of these efforts.

The purpose of national and regional initiatives for strengthened surveillance control is to ensure that consensus norms and standards are integrated into national epidemic preparedness. These norms will apply to surveillance case definitions and methodologies, communicable disease control strategies, and reference reagents and laboratory norms.
Figure 1. Death due to selected infectious diseases, 1995
Estimates by the World Health Organization

Total deaths (51.9 million)

Other causes
67%
(34.5 million)

Infectious
diseases
33%
(17.3 million)

By main mode
of transmission

Person-to-person
65% (11.2 million)

Animal-borne
0.3% (0.06 million)

Insect-borne
13% (2.3 million)

Food, water and
soilborne
22% (3.7 million)
There are five major components of the global monitoring and alert systems:

- The *International Health Regulations* are currently under revision. The Regulations, which up to now require mandatory notification of cholera, plague and yellow fever, after the revision will require reporting of five acute syndromes, i.e. respiratory, diarrheal, neurological, hemorrhagic, and antimicrobial response. The new Regulations are now being field tested, and an operational manual is being developed. Once in place, the revised International Health Regulations will include descriptions of the best public health practices according to prevailing epidemiological conditions. A practical handbook will be provided and 24-hour availability of information will be ensured.

- The *WHO Collaborating Centers on Communicable Diseases*. The capacity of these institutions is being assessed in order to identify gaps in technology and geographic distribution (figure 2).

- The *Antimicrobial Resistance Monitoring Network* is being expanded to eight developing countries. This component includes laboratory training combined with workshops for policy formulation. In addition, an industry working group and a strain bank are being established to strengthen this area of surveillance.

- The *Rumor and Outbreak List* is an information system that receives outbreak notifications from around the world. The reports received are verified through regional offices and country representatives; once confirmed, relevant information is widely disseminated.

- *Specialized Disease Surveillance Networks* are actively maintained through regional offices and other Headquarters programs. Priority subjects for these networks include influenza (vaccine composition), Creutzfeld-Jacob disease (better understanding of disease's epidemiology) and HIV infection and AIDS (national and regional estimates of HIV infection).

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**Figure 2. Emerging and other communicable diseases worldwide distribution of WHO collaborating centres**
In order to further strengthen infectious disease surveillance, EMC has established military alliances which link 45 military laboratories with the WHO Collaborating Center Network; 21 military laboratories will be linked with the WHO Antimicrobial Resistance Monitoring Network, and training courses will be provided for the staff of five African countries in 1997.

The Emerging and Other Communicable Diseases Surveillance and Control Program of the WHO has implemented various initiatives to ensure epidemic preparedness. On one hand, subregional teams have been established to strengthen laboratory activities, surveillance, control, and epidemiological and operational research (Ethiopia, Kenya, Côte d’Ivoire, Vietnam and Zimbabwe).

In addition, EMC is involved in providing global information access, in collaboration with UNAIDS and the World Bank, in order to ensure most appropriate connectivity to Internet at surveillance sites (local telephone service, radio to telephone, radio to satellite). Information (data, problems, needs) is managed through moderated mail lists in this system.

Global information access provides electronic links among:

- 142 WHO country offices and 6 regional offices
- 190 ministries of health and agriculture
- over 200 WHO collaborating centers
- 110 national influenza centers
- over 50 Antibiotic Resistance Monitoring (ARM) national reference laboratories
- over 45 Gonorrhea Antibiotic Susceptibility Program (GASP) national laboratories or regional groups
- over 60 HIV sentinel surveillance sites
- 190 UNAIDS country sites
- World Bank resident missions, regional hubs and key collaborative sites
Regional Activities: Surveillance of Emerging and Reemerging Diseases in the Americas

Activities of the Pan American Health Organization Carried Out in the Region During 1997

Surveillance in public health is the systematic and constant collection, management, analysis and interpretation of data required for planning and evaluation. A regional surveillance system for infectious diseases is currently being developed, and antimicrobial surveillance for selected pathogens is already in place. The latter includes the participation of national public reference laboratories in several countries of the Region.

The following is a description of several collaborative activities carried out by PAHO since 1996, in order to develop or strengthen infectious diseases surveillance in the Americas. Planned activities for 1998 and beyond are also presented.

Strengthening the regional capability for emerging and reemerging diseases surveillance

This project aims to strengthen epidemiological intelligence capabilities in the public health sector by preparing effective plans for data collection, analysis, investigation and prompt intervention through:

• The strengthening of regional infectious disease surveillance networks as well as the capacity to implement effective prevention and control strategies; and

• The development of a national and regional infrastructure for the early warning of and rapid response to the threat of diseases. This would be achieved through multidisciplinary training programs.

National surveillance systems in the Americas reflect varying degrees of development. In general, epidemiological investigations of health problems are characterized by person, place and time whether the problem concerns the emergence of a new disease, changes in resistance patterns of known pathogens, or other. The principles of data gathering, management, and analysis are essentially the same in all aforementioned situations. The most stringent requirements apply to data collected from patients at the point of observation. A system with a relational data base designed to effectively handle patient data will almost certainly be able to handle the clinical, exposure and demographic data required for epidemiological analysis and public health action. PAHO is in the process of setting up such a system. It will make use of available Internet technology to build e-mail and Intranet systems (closed access) for communications in collaboration with the Latin American and Caribbean Center on Health Sciences Information (BIREME) in Brazil. The e-mail/Intranet system provides for the installation of a communications post in each country or point of observation. Access to the system will be granted to ministries of health and PAHO/WHO Country Representative Offices in each country; the Canadian Laboratory Centers for Disease Control (LCDC), and the U.S. Centers for Disease Control and Prevention (CDC) and Department of Defense. All participants will have equal access to the common database for analysis. The system will be enhanced by automatic feedback capabilities that will make the collected data available to
all participants. Ministries of health will be responsible for data management and analysis, as well as publication of the results obtained from information gathered and analyzed in each country. PAHO’s Regional Program will be responsible for system setup, coordination, monitoring and training, as well as data analysis from a regional standpoint (for additional details see section V).

Once the project is finalized, surveillance systems and corresponding infrastructures will be in place which are capable of monitoring emerging pathogens and diseases as follows:

1. Confirmation of current epidemics;
2. Assessment of health and socioeconomic impact and likely evolution of the problem; and
3. Determination of local response capacity, identification of most effective control measures, and assessment of additional immediate needs.

Introduction of the system at the national level will begin during the last quarter of 1997, one subregion at the time. The first subregional meeting will take place in conjunction with the conference Health Crisis and the Internet (an international meeting on harnessing the Internet for disasters and epidemics) to be held in Colombia in November. A second subregional meeting will be held in December in Nicaragua for participants from all Central American countries, followed in 1998 by meetings in Brazil, Mexico, the Andean Area and the Southern Cone.

**Surveillance of selected pathogens**

Infectious diseases transmitted by blood transfusion

Preventing infectious disease transmission through blood transfusion in developing countries is a difficult task. Even when policies and strategies are in place, necessary resources are not always available. Laboratory testing of blood donors is an effective preventive measure against transmission of blood-borne infectious diseases. Nevertheless, actual effectiveness depends on the coverage of blood donor screening. A study of the potential risk of acquiring an infectious disease through receipt of a tainted transmission was conducted in seven countries of South America (Bolivia, Chile, Colombia, Ecuador, Peru, Paraguay, and Venezuela) and five countries in Central America (Costa Rica, El Salvador, Honduras, Nicaragua, and Guatemala). Information was obtained from official reports on the prevalence of the disease and the proportion of donors screened for infectious diseases in each country.

Analysis of these data indicated that 9 out of the 12 countries screened 100% of donors for the HIV virus; only 3 reported complete screening for hepatitis B (HBV). Coverage of screening for hepatitis C (HCV) did not reach 100% in any country. Furthermore, in 6 countries there was no screening for syphilis at all, and only 2 screened for T. cruzi. Estimates of the risk of acquiring HIV through blood transfusion was much lower than the risk of acquiring HBV, HCV, or T. cruzi, due to a significantly higher coverage of screening for HIV, and lower prevalence rates of HIV infection. An index of infectious disease transmission through blood transfusion was calculated for each country. The highest value was obtained in Bolivia (222 infections per 10,000 transfusions); in other countries the index ranged from 60 to 100 infections per 10,000 transfusions. The risks were lower in Honduras (7 per 10,000), Ecuador (15 per 10,000) and Paraguay (19 per 10,000).

Results of the aforementioned study underline the need for development of an information system that allows an assessment of the status of blood screening for infectious diseases. Data from the study, which were only partially available in the past, will serve as baseline against which future achievements may be measured.

Since 1993, the screening of blood for infectious agents has improved in several countries. In Chile, Colombia and Costa Rica, for example, screening for HCV was made mandatory, and coverage of serology for that infection increased. Laws that regulate blood transfusion practices have been promulgated in Guatemala and Peru. Nevertheless, the situation needs improvement. Implementation or expansion of screening for HCV remains a priority in most countries. Increased donor screening for T. cruzi should be made a priority in Bolivia and, possibly, in Peru. Continuous collection of information on blood donor screening for infectious diseases is essential in order to maintain support for this endeavor and consequently, sustain or expand blood donor screening at country level. PAHO will continue to monitor the potential for transmission of diseases through blood transfusion.
Selected enteric pathogens (*Salmonella*, *Shigella*, *Escherichia coli* O157:H7, *Vibrio cholerae*)

The purpose of this project is to enhance laboratory and epidemiological infrastructure and to strengthen expertise in the Region for the surveillance of targeted enteric pathogens. An additional objective is to establish a network of national reference laboratories for the diagnosis of said pathogens in order to ensure a sustainable approach to their prevention and control in the Americas. As a result of the project, participating countries will enhance their surveillance capability for *Salmonella*, *Shigella*, *E. coli* and *V. cholerae* needed to define the magnitude of the problem, and allow for the formulation and implementation of appropriate national prevention and control programs through:

1. Identification of emerging serotypes and prevailing antibiotic resistance patterns;
2. Development of short and long term training programs to strengthen laboratory and epidemiological surveillance and control capabilities;
3. Development and implementation of protocols to enhance quality assurance and proficiency testing for antibiotic sensitivity of selected enteric pathogens.

Implementation of this project started with a workshop in FIOCRUZ, Brazil, in November 1996. Participants included experts from reference laboratories for enterobacteria from Argentina, Brazil, Chile, Costa Rica, Mexico, Peru and Venezuela, as well as their counterparts from LCDC (Canada). The discussion focused on standardization of techniques for antibiotic sensitivity evaluation, and protocols for quality assurance, proficiency testing and epidemiological surveillance. In order to standardize assay materials used in different countries, antibiotic disks, dispensers for retrospective and prospective antibiotic sensitivity evaluation, as well as other reagents were provided. LCDC prepared and distributed samples for proficiency testing, and analyzed the results.

Workshop participants were also trained in the Public Health Laboratory Information System (PHLIS) developed by the CDC (United States). This system provides electronic data entry screens (modules) to reporting sites. Data are introduced and reported within hours, without the need for computer programming. PHLIS has the capacity for a hierarchical reporting scheme, i.e. it allows reporting to multiple, successively higher levels. Furthermore, a database is created at every reporting level so that all data reported or entered at a site are included in the database at that site.1

Participants at the FIOCRUZ workshop recommended that the regional surveillance network be expanded so other countries could acquire the same capabilities regarding standardization of techniques for surveillance of antimicrobial resistance, and knowledge of PHLIS. As a result, the workshop held at FIOCRUZ was replicated at the Caribbean Epidemiology Center (CAREC) in November 1997. This second workshop was attended by professionals from Bahamas, Barbados, Jamaica, St. Lucia, Suriname and Trinidad and Tobago.

Because techniques to produce antiserum against different *Shigella* species are not available in some countries, and given the importance of this reagent for identification of isolates, it was also recommended that countries in these circumstances acquire such capability. In compliance with this recommendation, another workshop was held in Venezuela, in July 1997, to provide training in the production of antiserum for the identification of *Shigella* species. Participants from Chile, Ecuador, Mexico, Paraguay, Peru, and Venezuela had an overview of sera and antiserum production, titration of antisera, reagent conservation, and other subjects and practiced identification of different serotypes of the most common *Shigella* species. At the end of the workshop participants were able to set up their own production facility.

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1 PHLIS is used in all 50 state public health laboratories, as well as the District of Columbia, Guam, Canada, CAREC, and the seven countries that participated in the FIOCRUZ workshop. Disease modules included are animal rabies, *Campylobacter*, *Escherichia coli* O157:H7, *Lyme disease*, *mycobacteria*, respiratory and enteric viruses, human and nonhuman *Salmonella*, *Shigella*, and drug resistant *Streptococcus pneumoniae*. 
Drug susceptibility of *Mycobacterium tuberculosis*²

For some countries, drug-resistant tuberculosis is a significant threat to tuberculosis control, since only a few effective drugs against M. Tuberculosis are available. In particular, the spread of strains resistant to the two most important drugs, isoniazid and rifampicin, could have serious consequences for the epidemiology and control of the disease. Individuals infected with resistant strains are less likely to be cured, and their treatment is much more expensive.

The true worldwide magnitude of the problem is not known, but available information suggests that resistance could be increasing in some areas. Unfortunately, in several countries, antibacterial susceptibility testing cannot be performed, whether because of limited resources or lack of know how.

Because of these limitations, in 1994 the WHO Global Tuberculosis Program, together with the International Union Against Tuberculosis and Lung Disease (IUATLD) initiated an antituberculosis drug resistance surveillance project. The purpose of the project was to measure the prevalence of antituberculosis drug resistance in several countries of the world using a standardized methodology. Another objective was to study the correlation between the level of drug resistance and various national treatment policies. To that end, data were collected, especially from regions identified as having potential problems. Two major strategies were agreed upon: a) standardized surveys and/or surveillance would be implemented on representative samples of tuberculosis patients in various countries; and 2) proper bacteriological methodology in local laboratories would be ensured through proficiency and technical support by a network of reference laboratories. Laboratory testing was included for isoniazid, rifampicin, ethambutol dihydrochloride, dihydrostreptomycin sulphate and streptomycin sulphate.

Surveillance provided an overview of the degree of drug resistance in the world. Drug-resistant strains were found in all 35 countries surveyed. Median prevalence of drug resistance among new tuberculosis patients was 10%, ranging from 2% to 40%. The prevalence of multidrug resistant tuberculosis was generally low. Overall, the median prevalence of primary multidrug resistant tuberculosis was 1.4%, ranging from 0 to 14%. In areas with poor tuberculosis control the prevalence of drug resistance was higher. In the Americas, the Dominican Republic was identified as a ‘hot spot’, as overall prevalence of primary drug resistance in this country reached 41%; multidrug resistant tuberculosis showed a prevalence of 6.6%. This was probably the result of a deficient National Tuberculosis Program, self-medication practices, an irregular drug supply, and the unregulated treatment of tuberculosis patients by private practitioners. Worrisome levels of primary multidrug resistance (4.6%) were also recorded in Argentina in an infectious disease hospital with a growing AIDS patient population. The rest of the continent, including the United States, presents relatively little multidrug resistant tuberculosis. This was particularly reassuring in the case of Brazil, which has a high tuberculosis burden.³

Dengue and *Aedes aegypti*

At the 1947 Directing Council Meeting of the Pan American Health Organization held in Buenos Aires, a proposal for the eradication of *Aedes aegypti* was approved and hailed as the solution for the continental problem posed by dengue and the potential threat of urban yellow fever. *Aedes aegypti* eradication became an official policy of the Organization and an eradication campaign was sponsored by PAHO.

Fifteen years later, and after investing millions of dollars, the success of this campaign was reflected in the fact that, by 1962, more than 20 countries had achieved eradication (figure 3). Unfortunately, after 1962, only three additional countries succeeded in eliminating the vector. Furthermore, not all the countries of the Region were willing to go through with eradication efforts. By the end of the 1960s, countries that had achieved eradication started to become reinfested. Over time, in most countries, *A. aegypti* programs lost political priority, and reinfestation surveillance gradually declined. At present, with the exception of Bermuda, Canada, and Chile, all countries of the Americas have been reinfested. During 1997, the mosquito reappeared in Uruguay, 39 years after its eradication.

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³ Ibid.
Campaigns against *A. aegypti* undertaken in the Region also eradicated urban yellow fever. The last epidemic of the disease occurred in Brazil 55 years ago. However, the high-density of *A. aegypti* in urban centers of enzootic areas constitutes a potential risk of urbanization of yellow fever. An example of this risk is illustrated by the epidemic that occurred in Peru in 1995, where 492 human cases of jungle yellow fever and 192 deaths were reported.

Dengue and dengue hemorrhagic fever are an increasing problem for the countries of the Region, as has been shown by several recent extensive and explosive epidemics. In 1995 and 1996, over 200,000 cases of dengue were reported, 80% of them in Brazil. Through July 1997, almost as many cases as during the whole of 1996 had been reported (figure 4). Still more alarming is the emergence of dengue hemorrhagic fever. The latter began in Cuba in 1981, and it gradually disseminated to other countries of the Region. More than 42,000 cases of dengue hemorrhagic fever have been reported in 25 countries between 1981 and 1996 (figure 5).
Figure 4. Reported number of cases of dengue and dengue hemorrhagic fever in the Americas, by subregion, 1995, 1996 and 1997

Number of cases

South America  North America  Central America  Caribbean  English/French Caribbean

*Information as of June 1997

Figure 5. Reported number of cases of dengue hemorrhagic fever in the Americas, by country, 1981-1996

Number of cases  42,172  
Deaths  581  
Case fatality  14%
In addition, there has been an alarming increase in the number of cases of dengue hemorrhagic fever in the present decade (more than 28,000) when compared with the number reported in the 1980s (13,200 cases). This increase is not surprising due to the number of circulating viral serotypes.

In 1995, in light of the worsening situation, PAHO’s Directing Council recommended the establishment of a technical group to study the feasibility, opportunity, and desirability of preparing a continental plan for the eradication of *Aedes aegypti*. In 1997, the Directing Council established a task force with the purpose of elaborating a continental plan to combat the mosquito, based on national plans. The main objective of the continental plan is to increase actions against *Aedes aegypti* in order to reduce infestation levels as close to zero as possible, with a view to future eradication of the mosquito and the consequent elimination of circulating dengue viruses. The goal would be to interrupt transmission of dengue in the Americas through a progressive reduction in the number of areas infested by *Aedes aegypti*.

The proposed strategy consists of five gradual stages: from initial actions to intensify and expand the fight against the vector including an increase in surveillance in high-risk areas, to the implementation of the eradication phase and final surveillance to prevent reinfection.

The first stage consists of preventing dengue epidemics, dengue hemorrhagic fever and urban yellow fever through epidemiological surveillance and combat of *A. aegypti* in high-risk areas.

The objective of the second stage is to prevent dengue outbreaks by reducing the proportion of dwellings infested by *A. aegypti* to less than 1%. The successive stages would include the interruption of dengue transmission, eradication of *A. aegypti*, and surveillance of reinfection.

In any case, future eradication of the vector depends on creative problem solving that tackles the negative contributing factors present in most countries. In order for the plan to succeed, there must be political will and resources to support it. The plan must have the highest priority. The cornerstone of the effort stands on the elimination of man-made containers, such as bowls, tires, and barrels that can serve as breeding sites for the mosquito. The development of an effective strategy requires the participation of various disciplines, such as behavioral psychology, engineering, education, mass communication and sociology and anthropology, as well as the community at large.

The continental plan provides cost estimates of each operational component of the eradication program, to underline the importance of weighing required resources when selecting a strategy to fight *A. aegypti*. The calculations are based on actual information provided by 23 countries; population data were used to estimate program costs for 11 countries for which information was not provided. If all countries were to carry out the program simultaneously, the estimated cost of eradication activities would reach US$ 1,657 million per year, over a period of three to four years. Direct measures against the vector account for 84.5% of the total cost; epidemiological surveillance, 4.3%; community participation and communication, 10.1%; and sanitation, 1.1%. There was consensus among task force members that most funds for implementing the plan should come directly from the countries themselves.

During 1997, PAHO, through its in-country and Regional staff, provided technical cooperation to 15 countries for the development of plans, implementation of activities, and evaluation of control measures. In addition, technical cooperation by the Centers for Disease Control and Prevention (USA) and the Pedro Kouri Institute (Cuba) contributed to strengthen 29 national reference laboratories in order to maintain a network for quality control of dengue diagnosis and for diagnosis training.

Brazil provided assistance to Uruguay in the implementation of initial actions to combat *Aedes aegypti* following confirmation of reinestation. Finally, a rapid exchange of information was fostered among Central American countries to distribute updated information and assist in the timely alert of neighbors to risk situations.

**PROPOSED ACTIVITIES FOR 1998**

**Surveillance of antimicrobial resistance**

In January 1998, a meeting will be held in Mexico City, Mexico, to discuss the results of quality control activities and to evaluate sensitivity tests of *Salmonella*, *Shigella* and *Vibrio cholerae* isolates to antimicrobial drugs carried out by the network of laboratories during 1997.
Participants will represent the Latin American laboratories which were part of the project, and their Canadian counterparts. The possibility of expanding the project to include antibiotic sensitivity testing of Campylobacter jejuni, as well as the attempt to define the role of E. coli O157:H7 in the etiology of uremic hemolytic syndrome in specific countries of Latin America will be also discussed at the Mexico meeting.

Reduction in the frequency and impact of drug resistance requires a better understanding of all factors contributing to or hampering effective control. Physicians and laboratory personnel in both the private and public sectors are not yet integrated into an ongoing information system which could better indicate the status of antimicrobial susceptibility. This integration is an important component of a more efficient and effective surveillance system that provides an information basis for action. However, health sector reform and decentralization are changing the role of ministries of health in most countries of Latin America: from health care providers to regulators. Therefore, it is expected that public health laboratories will not expand their activities in the medium term. Expanding a surveillance system for antimicrobial resistance from enterobacteria to other species will imply looking for new partnerships, for instance, with professional associations in which public and private sector professionals may interact and cooperate to build a sentinel surveillance system which approaches “real-time.” Such a system would be able to monitor trends, and detect and investigate drug resistance. One such possibility is to cooperate with a Latin American professional society that, through its membership in different countries, contributes to monitor antimicrobial susceptibility. PAHO, through its technical cooperation program, will strengthen the association’s quality of the testing, and analyze the results of sentinel surveillance of antimicrobial sensitivity in terms of time, space and population. In addition PAHO will periodically distribute the results of antimicrobial susceptibility testing through the Organization’s web page.

The project will progressively add new partners, and will be implemented in several stages. The objective of the first phase is to achieve e-mail communication, followed by file transfer and reporting on a few agents of public health importance which are suitable for sentinel surveillance. The initial list of agents to be monitored includes Enterococcus faecium and E. faecalis, Streptococcus pneumoniae, Klebsiella pneumoniae, Acinetobacter spp, Pseudomonas aeruginosa and Staphylococcus aureus. The list will be updated from time to time, as necessary.

**Strengthening the regional capability for surveillance of emerging and reemerging diseases**

The surveillance system described in the first few paragraphs of section IV will be implemented in the countries of Central and South America (activity began on December, 1997). Workshops for training ministry of health and PAHO staff will be held in Uruguay for countries of the Southern Cone, and in Venezuela for the countries of the Andean Area. Additional workshops will be held in Brazil and Mexico. As part of the workshops, the traditional surveillance system based on case reporting of selected communicable diseases (which will be identified for each participant country) will be strengthened. In addition, the role of the laboratory in this endeavor will be reinforced, as well as the concept of syndrome based surveillance. Discussions will include the new International Health Regulations and their implementation in the Americas.

**STREPTOCOCCUS PNEUMONIAE: EPIDEMIOLOGICAL SURVEILLANCE OF ANTIBIOTIC RESISTANCE IN LATIN AMERICA**

This presentation revisited the results of a study on epidemiological surveillance of Streptococcus pneumoniae in Latin America, originally presented at a meeting of the Technical Advisory Committee and Coordinators of the study held in Cuernavaca, Mexico, in July of 1997. The study was based on a very strict research protocol, which defined inclusion criteria, case definitions and laboratory quality control. Six countries participated in the protocol: Argentina, Brazil, Chile, Colombia, Mexico and Uruguay.

Acute respiratory infections due to S. pneumoniae and Haemophilus influenzae are a major problem in the Region of the Americas. It is thus important to know the number of agents and serotypes, in order to formulate an adequate conjugated vaccine for use by the countries of the Region. The studies presented here also provide important...
information on resistance of pneumococci to antimicrobials. Figure 6 shows the Pan American Health Organization’s Surveillance network and the proportion of S. pneumoniae serotypes in each country.

Figure 6. Pan American Health Organization pneumococcal surveillance network and proportion (%) of *Streptococcus pneumoniae* serotypes, by country.
ARGENTINA

During the period 1994-1996, 554 isolates of Streptococcus pneumoniae had been collected from children under the age of 5 years in 14 hospitals throughout the country. The median age of the 402 children who participated in the study was 14 months. Predominant diseases were pneumonia, with and without pleural effusion (59.1%); meningitis (22%); and sepsis (10.8%). Sixteen children had multiple site infection. Clinical specimens were collected from blood (46.1%), pleural fluid (31.5%), cerebrospinal fluid (17.0%), and other fluids (5.4%). Of the 36 serotypes detected, the most frequent types and factors were: 14, 5, 1, 6B/6B, 7F, 9V, 19A, 19F, 16A and 23F. Serotype 14 accounted for 30% of all isolates, while 23F had the lowest frequency: 2.2%. The 7 most frequent serotypes (including 6A/6B as one) showed an accumulated frequency of 74.1%; furthermore, the sum of the 10 most common serotypes accounted for 80% of all isolates. Resistance (R) to penicillin (P) was observed in 24.4% of isolates, with 13.3% presenting intermediate resistance, and 11.1% high resistance (MIC between 2 and 4 mg/l). Of the 121 resistant Streptococcus pneumoniae, 59.7% were type 14 and 36.4% were type 23F. Serotypes 14, 6, 19, and 23 were associated with 87% of the resistance. Significantly fewer penicillin resistant Streptococcus pneumoniae were isolated from cases of meningitis (9.6%) than from pneumonia (27.7%) and sepsis (31.4%) (p<0.0015 and p<0.02, respectively). Resistance to cefotaxime was 11.7% (3.8% with MIC=2mg/l). Cefuroxime and imipenem resistance was 20% and 8%, respectively. Resistance to cotrimoxazole was high and associated with penicillin resistance (RR:2.11; p<.00001). Tetracycline resistance was 13%, and 12 and 7 isolates of two different serotypes were resistant to chloramphenicol and erythromycin, respectively. No resistance to rifampicin and vancomycin was found, and only 1% of serotypes presented intermediate resistance to ofloxacin. Serotype 14 showed high association with penicillin resistance (60.3%) when compared to other serotypes (p<.00001).

BRAZIL

Laboratory surveillance for S. pneumoniae began in Brazil in 1993, following a PAHO led regional initiative (SIREVA or Sistema Regional de Vacunas) supported by the Brazilian Ministry of Health. The principal goal of this surveillance system was to determine the prevalence of various S. pneumoniae serotypes and the degree of antimicrobial resistance. Initially, the study was implemented in Belem, Recife, Belo Horizonte and Sao Paulo. Most recently, however, and stimulated by the results of the SIREVA project, other regions of the country started to send isolates from invasive diseases to the Instituto Adolfo Lutz, the national reference center for bacterial meningitis. Between 1993 and May 1997, 725 isolates were studied. They corresponded to children under 6 years of age with pneumonia (34.2%), meningitis (64.2%), and other clinical diagnoses (1.6%). Isolates were obtained from cerebrospinal fluid (59%), blood (25%), pleural fluid (15%), and other clinical samples. Geographic distribution of isolates was as follows: 19 from the North; 145 from the Northeast; 47 from the Midwest; 439 from the Southeast; and 75 from the South. In all, 40 different serotypes were identified. Serotypes/groups with the highest frequencies were 14 (22.8%); 6 (16%); 1 (11.5%); 5 (7.5%); 18C (5.4%); 19F (5%); 23F (4.5%); 9V (4%); 19A (3.5%), and 9N (2.4%). The sum of these accounted for 82.6% of the total isolates studied. Some regional differences in frequencies were observed.

Twenty two percent of isolates presented resistance to penicillin, as determined by MIC. High resistance (HR) was observed in 1% of isolates, and intermediate resistance (IR) in 21%. A regional variation in resistance was also observed. Among penicillin resistant isolates, 4.1% were also resistant to erythromycin, 3.5% to cefotaxime, 97% to sulfametoxazole-trimethoprim. No resistance to vancomycin or chloramphenicol was observed. Multiresistance was detected in 6% of penicillin resistant isolates. Serotypes associated with resistance were 14 (42.9%); 6B (20%); 23F (14.4%); 19A (11.8%); 19F (6.2%), and 6A (4.1%). There was also a higher association of penicillin resistance in children under the age of 2 years (24.7%) when compared to those 2 years of age and older (14.1%). There was no association between resistance and clinical diagnosis.

CHILE

From March 1994 to March 1996, 202 isolates of S. pneumoniae were collected in Chile from children under the age of 5 years; of those, 71% came from children under 2 years of age. Clinical
diagnoses of these cases included meningitis (36%), pneumonia (30%), and sepsis (11%). Clinical specimens were obtained mainly from blood (51%) and cerebrospinal fluid (20%). The most common serotypes were 14 (17.3%), 1 (14.4%), 5 (13.9%), 6 (9.4%), and 19 (8.4%). Resistance to penicillin was high at 30% (11% presented HR, and 19%, IR). Antibiotic resistance was equally distributed among clinical diagnoses. The most resistant strains were types 14, 6, 19 and 23. Resistance to cefotaxime was 8%, of which 4% presented HR and 4%, IR. Despite the fact that serotype 1 was the second most common, it presented no penicillin resistant strains, and only 1 of 28 isolates of serotype 5 was penicillin resistant. S. pneumoniae was isolated in spite of the fact that 22% of the children had previously received antibiotic treatment. The case fatality rate among 146 cases with complete clinical data was 11.1%; 12 cases had sequelae.

**COLOMBIA**

This study was conducted in two periods. The first period encompasses July 1994 through March 1996; the second, April 1996 to May 1997. In the first phase, 324 S. pneumoniae isolates were collected, and in the second, 120. For the first 324 isolates, 42% of cases had a clinical diagnosis of pneumonia, and 40% were meningitis. The seven most frequent serotypes included 14 (22%); 5 (11%), 23F (9.5%), 6B (9%), 1 (9%), 19F (7%) and 6A (6%). The frequency of isolates with diminished susceptibility to penicillin (DSP) was 11.7%; 8.7% of isolates showed intermediate level resistance and 3.1%, high level resistance. Multiple resistance was detected in 8 isolates (8.7%). Sixty percent of the high resistance isolates were serotype 23F.

Of the 120 isolates from the second period, meningitis was the clinical diagnosis in 57.3% of cases, and pneumonia, in 35%. Seven of the most frequent serotypes included: 14 (27.5%); 23F (16.7%); 6B (12.5%); 19F (9.2%); 5 (7.5%); 1 (3.3%) and 4 (2.5%). The frequency of isolates presenting DSP was 27.5%; 18.3% of isolates showed IR, and 9.2% HR. The serotype distribution of S. pneumoniae in Colombia was similar during the years of study, although patterns of antimicrobial resistance increased from 12% to 27.5%.

**CUBA**

A total of 112 isolates available since 1993 were characterized. Serotype 14 accounted for 36 isolates (32.1%), followed by serotypes 19 (15.1%), 23 (10%), and 6 (7%). Other groups and types included: 5, 1, 11, 2, 9, 15, 8, 33, 7, 13, 24, 34, 29, and 3. In terms of resistance, 48% of isolates were resistant to penicillin; 45% to amikacin; 43.2% to gentamicin; 40% trimethoprym-sulfametoxazole; 18.2% to chloramphenicol; 18% to tetracycline, and 16% to streptomycin. Of all resistant strains, 34.7% were type 14, and 26% were type 23.

**MEXICO**

The relative prevalence of capsular types of Streptococcus pneumoniae and antimicrobial susceptibility in children under 5 years of age was studied. Of 220 isolates collected, 33 of the 90 known types were found. Type 23F (18.2%) was the most frequent, followed by types 6A+ 6B (15.0%), 14 (10.0%), 19F (7.7%), and 19A (6.8%). The sum of the seven most common serotypes (considering 6A and 6B as one) accounted for 65.9% of all isolates. High penicillin resistance was found in 49 strains (22.2%), 31 of which corresponded to type 23F. Ninety five (33.1%) were resistant to chloramphenicol, 29 (13.1%) to erythromycin, and 24 (10.9%) to cefotaxime. No strains were resistant to vancomycin.

**URUGUAY**

For three years, from June 1994 to May 1997, a surveillance study of 261 systemic infections by S. pneumoniae was conducted. Of the 261 cases studied, 67.8% were younger than 23 months of age, and 45 were less than 6 months, including 13 newborns. S. pneumoniae was the most frequent diagnosis (63%), with severe forms predominating between the ages 6 months and 24 months. The case fatality rate was low (1.9%). Meningitis was frequent among babies under 6 months of age; the fatality rate among these cases reached 25%. Out of 247 typed isolates, 24 different groups/types were recognized. In descending order, the seven most common types were:
4, 5, 1, 6A/6B, 3, 7/7F, and 19A. If these types were to be included in a conjugated vaccine, 79.7% of patients would be protected. Types 14 and 5 predominated during the three year study. Type 14 was common among children older than 6 months of age, and type 5 among younger ones.

Resistance to β-lactam antibiotics deserves special attention. In 1994, resistance was 25%, but by 1997, it had increased to 39%. This figure is somewhat low due to the lower resistance observed in isolates from cerebrospinal fluid; however, in isolates from blood and pleural fluids, resistance reached 52%. Patients treated in public institutions presented resistance in 28% of cases, while among patients from the private sector, resistance was 51%. A high proportion of type 14 isolates were resistant to penicillin and to trimethoprim/sulfamethoxazole. High resistance to penicillin and third generation cephalosporins was confirmed by MIC, and reached 22.5% and 9.0%, respectively. Resistance to cotrimoxazole (45%) persisted during the study period. Multiresistance was rare. However, resistance to antibiotics other than β-lactams was documented: 4.5% for erythromycin, 6.5% for tetracycline, and 2% for chloramphenicol. Reduced susceptibility to rifampicin and vancomycin was not observed. Studies carried out in adults with systemic infections during the same period also revealed resistance to penicillin and cephalosporins averaging about 11%.

**REGIONAL SUMMARY**

Between February 1993 and April 1996, 1649 sterile-site isolates of *Streptococcus pneumoniae* were collected from invasive pneumococcal infection in children 5 years of age and younger in Argentina, Brazil, Chile, Colombia, Mexico and Uruguay. Fifty percent of all isolates were obtained from children with lower respiratory tract infection, and 51.5% were isolated from blood (see figures 7 and 8). Capsular types 14, 6, 5, 1, 23F, 19F, 19A, 7F, 9V, 18C, 3, 4, 16F, 9N and 15B were the most prevalent throughout the Region, accounting for 87.7% of all isolates (see figure 9). Diminished susceptibility to penicillin was identified in almost 25% of isolates; 16.7% presented intermediate resistance, and 8.3%, high-level resistance (Figure 10 presents penicillin resistance of *S. pneumoniae* by country.) Three customized vaccine formulae containing 7, 12 and 15 different capsular types were found to have regional coverage of 72%, 85% and 88%, respectively. Except for Mexico, there were no significant differences in the proportion of coverage among countries with the 7 and 15 valent vaccine formulae, after controlling for patient age and clinical diagnosis.

As a result of these studies, the laboratory capacity in all countries was strengthened, avoiding the need to send samples for processing abroad.
Figure 9. Cumulative frequency of *S. pneumoniae* serotypes

![Cumulative frequency chart]

Top 20 shown; 6 includes 6A and 6B

Figure 10. Decreased susceptibility to penicillin among *S. pneumoniae* by country

![Susceptibility chart]

Country
- Argentina
- Brazil
- Chile
- Colombia
- Mexico
- Uruguay
**COLLABORATIVE STUDY ON STREPTOCOCCUS PNEUMONIAE RESISTANCE TO TRIMETHOPRIM/SULFAMETHOXAZOLE**

A study, funded by WHO and using pneumococcal isolates collected during the surveillance study was initiated to:

a) evaluate reliability of E test for the determination of trimethoprim/sulfamethoxazole (TM/S) MIC testing for *S. pneumoniae*,
b) evaluate the use of horse blood versus sheep blood, and
c) measure resistance to TM/S in Latin America.

After a pilot project that served as the quality control component, the collaborative study was initiated with the participation of Brazil, Chile, Colombia, Mexico and Uruguay. A single protocol was used and, except for blood, all materials were distributed from a single source. Preliminary conclusions were as follows:

i. E test is generally easy to read
ii. Minor errors occur more frequently on sheep blood than on horse blood
iii. Major errors are rare
iv. E test is likely to be higher than the broth microdilution MIC regardless of blood supplement
v. Dilution errors occur most frequently when testing strains with MIC ≥ 4/76 mg/l (resistant)

There are some concerns with respect to the availability of horse blood in some countries and the inconvenience and impracticality of having to use horse blood supplemented MH agar for only one drug/bug combination.

Similar conclusions were obtained by the six participating laboratories. Susceptibility results are summarized in table 1.

<table>
<thead>
<tr>
<th>Country</th>
<th>Susceptible</th>
<th>Intermediate</th>
<th>Resistant</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number</td>
<td>Percent</td>
<td>Number</td>
<td>Percent</td>
</tr>
<tr>
<td>Brazil</td>
<td>79</td>
<td>32.4</td>
<td>44</td>
<td>18.0</td>
</tr>
<tr>
<td>Chile</td>
<td>26</td>
<td>25.0</td>
<td>42</td>
<td>40.3</td>
</tr>
<tr>
<td>Colombia</td>
<td>85</td>
<td>56.6</td>
<td>26</td>
<td>17.4</td>
</tr>
<tr>
<td>Mexico</td>
<td>42</td>
<td>36.5</td>
<td>33</td>
<td>28.7</td>
</tr>
<tr>
<td>Uruguay</td>
<td>35</td>
<td>29.1</td>
<td>31</td>
<td>25.9</td>
</tr>
<tr>
<td>Total</td>
<td>267</td>
<td>36.4</td>
<td>176</td>
<td>24.0</td>
</tr>
</tbody>
</table>
**SURVEILLANCE IN THE AMAZON REGION**

In view of the tremendous biological diversity within the Amazon/Orinoco region, and the major ecological changes in progress as result of deforestation, mineral extraction, agricultural development and human settlements, conditions in the area pose a high risk for the emergence of new infectious diseases, including zoonosis.

In addition to the growing population of permanent residents and increasing flow of migratory populations from other areas seeking to colonize the land, there are unprecedented movements of a diversity of outsiders, such as mineral prospectors, soldiers, guerrillas, cocaine producers, biologists, ecological tourists, and others, through previously uninhabited forested areas. Many of these outsiders are highly mobile, and transit rapidly between isolated jungle areas and major urban centers, mainly within the region, but also in other parts of the Americas, Europe and Asia. Consequently, there is a threat for transmission and amplification of new and old pathogens. Venezuelan hemorrhagic fever is a good example of a new disease which probably resulted from agricultural practices implemented by colonists in an area where the zoonotic cycle of the arenavirus was being maintained. The recent reemergence of jungle yellow fever, plague, bartonellosis and malaria in Peru, and of Bolivian hemorrhagic fever and antimalarial resistance in several parts of the Amazon, are also examples of health problems of great magnitude. In view of the rapid dissemination of *Aedes aegypti* in the Region, there is a potential risk of recrudescence of dengue in areas already affected, and of spread of the mosquito to new areas. This could lead to explosive epidemics of dengue and the emergence of dengue hemorrhagic fever. Moreover, the presence of the mosquito in towns and cities located in the enzootic areas of jungle yellow fever may lead to the urbanization of this arboviral disease.

Furthermore, with airports scattered throughout the Amazon and Orinoco basins, it is possible for a person who is incubating yellow fever or in the acute phase of the disease to travel to any urban area infested with *Ae. aegypti* but free of disease, including major cities such as Rio de Janeiro, Buenos Aires or Miami. This situation could give rise to urban transmission.

Other serious health problems likely to increase or already on the rise in the Amazon region include antimicrobial resistance and HIV infection.

In response to these challenges, the establishment of a network of epidemiological surveillance for detection and monitoring of emerging infectious diseases in the Amazon/Orinoco region has been proposed. The objective of this proposal is to establish a network of laboratories in five countries of tropical South America, namely, Bolivia, Brazil, Colombia, Peru and Venezuela. The network will be able to perform active surveillance based on a syndrome approach. It is anticipated that this type of surveillance will allow detection of viral, parasitic and bacterial diseases. In addition, antimalarial and antimicrobial resistance will be monitored.

As an initial step, an organizational meeting is planned for representatives of key national institutions from Bolivia, Brazil, Colombia and Peru, and from the United States (Centers for Disease Control and Prevention, the University of Texas at Galveston, and two Department of Defense laboratories, one in Peru and one in Brazil). The Brazilian Ministry of Health, FIOCRUZ and the Brazilian Army Biological Institute will participate as well. The purpose of the meeting is to define strategies to implement surveillance in the region. Participants will address performance and implementation needs, including human resources, training, reagents, supplies and equipment. Other issues to be discussed include communication requirements to connect local health structures and institutions to national and international reference agencies. An advisory committee may be formed to help monitor and improve the project. Plans will also be prepared to conduct a workshop on clinical identification and case management, and epidemiological surveillance of selected emerging infectious diseases.

An implementation plan for the Amazon Basin Surveillance Network is an expected result of the meeting.
IV
National Activities

ARGENTINA
PUBLIC HEALTH LABORATORIES AND THE DIAGNOSIS OF EMERGING DISEASES

The occurrence of emerging diseases in recent years has forced a reevaluation of several technical and scientific concepts, applied to infectious agents for over a century. As a consequence, there is an immediate need to strengthen the capacity to react to infections in an accurate and timely fashion. In addition, there is a need to identify etiologic agents, both for rapid treatment and for the implementation of transmission control measures.

Experiences in Argentina have demonstrated that a good laboratory infrastructure is crucial when dealing with emerging diseases. In turn, laboratory strength is also dependent on established scientific research experience and well trained human resources. Laboratories should have staff capable of identifying and characterizing specific etiological agents. In addition, all laboratories in the network should have trained staff, so that the entire system (national laboratory network) is able to respond with the required speed. A strong infrastructure, inter-laboratory cooperation and quality control are all fundamental elements of a successful network.

The laboratory network must also feed the information it produces to the epidemiological surveillance system quickly and continuously. The effectiveness of collaboration between laboratory systems and epidemiological surveillance has been demonstrated in Argentina in the Tuberculosis Control Program and in the prevention of transmission of blood borne infections by transfusion (such as T. cruzi in Chagas disease). However, in Argentina, it was not until the cholera epidemic (that reemerged in the Region of the Americas in Peru in 1991) that the advantages of joint work between the national system for epidemiological surveillance and the national laboratory network became evident.

The cholera epidemic

The first case of cholera was reported in Argentina in the summer of 1992 and was caused by Vibrio Cholerae O1 biotype El Tor, serotype Ogawa, producer of cholera enterotoxin (CT). The epidemic started in the province of Salta, and spread to neighboring areas in the provinces of Formosa and Jujuy. Sporadic cases later occurred in other areas following population movements from infected areas. By June 1995, four epidemic outbreaks had occurred, mainly during the summer months. National health authorities decided that only bacteriologically confirmed cases of cholera would be reported in the country. In consequence, hospital laboratories performed an essential role in diagnosing cases. Once diagnosed, isolation, biochemical characterization and serogrouping of V. cholerae O1 were done by the reference laboratory. Coordination was achieved through implementation of a national laboratory network (Red Nacional de Laboratorios), intensive training of human resources, methodological development, and quality control for diagnosis, under the direction of the Department of Bacteriology, National Institute of Infectious Diseases (INEI, from the Spanish Instituto Nacional de Enfermedades Infecciosas).

Between 1992 and 1995, the Department of Bacteriology of the National Institute of Microbiology “Carlos G. Malbran” (national reference laboratory) completed the serotyping, toxin
detection and antibiotic resistance profile of 1,382 isolates of *V. cholerae* O1 received from all over the country. As in the rest of Latin America, *V. cholerae* O1 was systematically identified as El Tor. However, contrary to the rest of the Region, Ogawa was the most prevalent serotype (91.8%) in Argentina, and 99.2% of isolates produced CT with ELISA. During the second and third outbreaks, only 24 (1.7%) isolates presented resistance to antibiotics. Among them, 7 were resistant to tetracycline. In addition, 5 isolates presented unusual multiresistance accompanied by b-lactamase activity with third generation cephalosporins.

**Hemolytic uremic syndrome and its association with verocytotoxin-producing* E. coli**

Hemolytic uremic syndrome (HUS) is associated with a diarrheal prodrome accompanied by gastrointestinal loss of electrolytes, water, proteins and red cells, causing hypovolemia, hemoglobinemia, and hypoproteinemia, favoring acute renal failure. Renal symptoms include macro or micro hematuria, proteinuria, oliguria, or anuria. Oliguria may lead to fluid retention and hypertension which, together with uremia and anemia, can lead to heart failure.

Most HUS patients recover after 2 or 3 weeks, without sequelae. However, 10-year follow up studies of renal function in HUS patients indicate that recovery is complete in only 70% of cases. The pathogenicity of HUS results from renal capillary damage at the endothelial level caused by large amounts of cytotoxins liberated by verotoxin-producing *E. coli* (VTEC). These cytotoxins are biologically and genetically homologous to the toxin produced by *Shigella dysenteriae*.

It has been estimated that, in the Americas and Europe, around 90% of children with HUS have some evidence of infection by VTEC; serotype O157:H7 is responsible for 70% of cases. In Argentina, HUS in children is exclusively associated with strains of *E. coli* O157:H7. In 1996, the laboratory network for cholera and diarrhea diagnosis provided 250 samples from cases of diarrhea, hemorrhagic colitis and HUS to the INEI reference center. Of all HUS cases, 75% were associated with VTEC infection.

One study in progress in Argentina is investigating the incidence of VTEC among humans, cattle and beef, and dairy products. The study includes a network of laboratories from the five largest cattle producing provinces. The Clinical Bacteriology Laboratory, Department of Bacteriology, INEI, is the reference center.

**Bacterial antibiotic resistance**

Resistance of *Enterococcus* spp to glycopeptides has increased 14% to 20% in developed areas (Europe and the United States, respectively). This alarming situation has prompted the implementation of specific research and control measures, such as the search for reservoirs among farm animals, the identification of resistance mechanisms and their genetic localization, and the implementation of strict control measures in cases of hospital infection. In Latin America, even though some cases of vancomycin resistant *Enterococcus* spp have been documented, the high prevalence of multiresistant Gram-negative bacilli infections is more alarming.

In Argentina, penicillin resistance of respiratory system pathogens, such as that of *Streptococcus pneumoniae* (24%) or *Haemophilus influenzae* (15%), is on average similar to that observed in Europe and the Americas. However, some enteropathogens, like *Salmonella* spp or *Shigella* spp, show an alarming proportion of isolates with resistance to first line drugs.

For over 5 years, outbreaks of nosocomial infections of multiresistant salmonellas have been reported, particularly in hospitals located in areas along the rivers of the northeast: in Buenos Aires, Entre Rios, Corrientes, Santa Fe, and Misiones. The study of these microorganisms showed that all isolates have an extended spectrum b-lactamase and CTX-M2, as well as AAC(3)II and AAC(6)I inactivating enzymes of aminoglycosides. The corresponding genes are located in a conjugate plasmid of high molecular weight. These resistant genes were also detected in *Vibrio cholerae* isolates during the second and sixth epidemic cholera outbreaks.

The new cephalosporins and aminoglycosides are first line drugs for treatment of severe infections. The most efficient resistance mechanism involves the production of b-lactamas, inactivating enzymes of extended spectrum, and enzymes that modify aminoglycosides, respectively. In terms of the emergence of new resistance mechanisms, location of the genetic determinants involved has an important epidemiological meaning: while resistance arising from
mutations in the bacterial chromosome is transmitted only to progeny, genes located in mobile elements could be transferred horizontally between and within species, significantly increasing the potential for dissemination.

In order to control resistance levels, there is a need to establish regional strategies for the use of antimicrobials to prevent development of new mechanisms of resistance, and significantly decrease those already in existence. It is necessary, therefore, to provide training on standardized methods for sensitivity studies, design quality control programs for microbiological diagnosis, and develop national reference laboratories to verify, characterize and be alert to the development of new resistance mechanisms. Such national reference laboratories should also be in charge of coordinating the network. In Argentina, this role has been assumed by the Department of Bacteriology (at the INEI) which is part of the WHO international program of antimicrobial resistance surveillance, or WHONET. Since 1994, the INEI has participated in the coordination of a national network of 22 laboratories from different geographical areas of Argentina.

**Tuberculosis**

Rapid detection and identification of disease producing mycobacteria are important for public health. In order to implement effective preventive and treatment measures, tuberculosis must be detected early, and must be differentiated from other mycobacteriosis.

In advanced stages of the disease, it is possible to detect bacilli simply and quickly by microscopic examination of lesion samples. However, this method is not sensitive enough to detect bacilli in earlier phases of the disease; furthermore, it does not allow differentiation between tuberculosis and other mycobacteria. This requires culture. Most pathogens in the genus *Mycobacterium* replicate very slowly, therefore, detection and identification through culture is time consuming. This delay often diminishes the usefulness of microbiological studies.

The species identification is based principally on phenotypic characteristics, through conventional biochemical assays. These have to be done from well developed cultures, and may last hours (for *Mycobacterium tuberculosis*) or up to 40-60 days (for environment mycobacteria).

All laboratories of the tuberculosis diagnostic network in Argentina use bacilloscopy. Isolation through culture is performed by nearly 100 laboratories; 18 of them perform sensitivity tests and identification using biochemical tests. Two national laboratories carry out characterization by biochemical procedures and hybridization.

Since 1968, the National Tuberculosis Control Program has surveyed the magnitude and characteristics of *Mycobacterium tuberculosis* resistance to antibiotics; the last trial was conducted in 1994. Initial resistance trends of tuberculosis unrelated to AIDS have not changed since 1968, the date of the first national trial. However, acquired resistance trends have increased, especially in recent years due to multiresistance (simultaneous resistance to at least isoniazid and rifampicin). Despite this, resistance levels are not yet alarming.

The analysis of AIDS related tuberculosis resistance shows a different situation, both for initial and acquired resistance. Rates are significantly higher, specially for the former, which was found to be associated with nosocomial spread of multidrug resistant strains in urban areas. Although there is a constant increase in AIDS associated tuberculosis cases, especially in the city of Buenos Aires, and in the provinces of Buenos Aires, Santa Fe and Cordoba, most health services have adopted measures to prevent hospital transmission (National Tuberculosis Program, October 1997 report).

**Dengue**

Between 1905 and 1911, several cases of dengue were reported in the north of Argentina. In 1916, an outbreak of 15,000 clinically diagnosed cases was described in an area of the country bordering the Uruguay river.

In 1955, it was estimated that *Aedes aegypti* covered an area of 15 million km², bordered in the south by the city of Buenos Aires. By 1963, *Aedes aegypti* was considered eradicated. However, between April and October 1997, 12 cases of dengue were reported, the first occurrence since 1916.

At present, the Ministry of Health reports that *Aedes aegypti* is present in the same region as in 1955, encompassing a subtropical area in the north and a temperate area in the center, which
includes the city of Buenos Aires. In preparation for the future, the Ministry of Health is strengthening entomological actions through community-based participation programs. Laboratories are building a network for diagnosis by MAC ELISA at the Arboviruses Laboratory of the National Institute of Viral Diseases “Dr. Julio I. Maiztegui.”

Hantavirus pulmonary syndrome

Until 1993, hemorrhagic fever with renal distress (HFRS), geographically restricted to Asia and Europe, was the only disease known to be caused by hantaviruses. In 1993, however, a new clinical entity emerged in the Americas (United States). The disease, hantavirus pulmonary syndrome (HPS), is characterized by severe acute respiratory distress; its etiological agent was identified as a new hantavirus that was named Sin Nombre Virus. Hantavirus pulmonary syndrome is a viral zoonosis transmitted to humans by inhalation of excreta of infected rodents.

In Argentina, infection of wild and laboratory rodents as well as subclinical human infections were reported between 1983 and 1985. Clinical cases presenting both as HFRS and HPS were retrospectively diagnosed between 1987 and 1996.

In March 1995, the first case of a familial outbreak of hantavirus pulmonary syndrome (HPS) was notified in El Bolson in the south of Argentina. As of 15 December 1996, a total of 77 cases of HPS had been notified (48% fatality rate) from three geographical areas of the country: South, North and Central regions. During the spring of 1996, a new outbreak occurred around El Bolson. Of the 18 cases reported from El Bolson and San Carlos de Bariloche, 3 affected local physicians, one of whom—during the prodrome of her illness—traveled to Buenos Aires for care. While she was still in the hospital, two physicians who provided her care developed HPS, 27 and 28 days after the first contact. These data suggested, for the first time, the possibility of person-to-person transmission of hantavirus pulmonary syndrome.

Epidemiological data support person-to-person transmission in Andes HPS

A retrospective case control study was carried out to identify risk factors associated with HPS infection. The results of this study indicate that people who have had physical contact with an HPS patient or their body fluids, and shared a room with an HPS case were at increased risk of acquiring the disease.

Molecular features of hantavirus pulmonary syndrome outbreak in Argentina support a hypothesis of person-to-person transmission

Human exposure to hantavirus occurs mainly by inhalation of contaminated rodent excreta; person-to-person spread has never before been documented. An increase in HPS cases, from 6 in 1995 to 20 in the spring of 1996, was detected around a southwestern town in Argentina, and in physicians residing 900 miles away who had contact with those cases. Person-to-person transmission was evaluated by comparing the viral sequence homology, following PCR amplification, of 16 epidemiologically linked HPS human cases (nosocomial or household contacts). Nine cases were reported from the same geographic area, and 1 occurred in northern Argentina.

Phylogenetic analysis revealed that all Chilean and Argentinean case sequences constitute a distinct Andes lineage. Although variants circulating in the south of both countries were very similar (nucleotide differences <10%). The most outstanding result was that all 16 epidemiologically linked cases had the identical M segment sequences, and, partial G1, G2, and 3í non-coding S fragment sequence homologies. On the other hand, two contemporary cases from the same geographical area had differing sequences. No significant differences were found in molecular mechanisms of transmission, such as glycosilation signals, hydrophilic pattern or repeat sequences in the 3í untranslated region. While the panhandle structure was maintained, in accordance with the predicted secondary structure of Andes S segment RNA virus, differences in the folding related to other Hantaviruses were found. This is the first direct genetic evidence consistent with person-to-person transmission of an Andes hantavirus.

In addition to molecular studies, nosocomial and population seroprevalence studies were also carried out in order to estimate the prevalence of hantaviral antibodies in health care workers and residents of El Bolson. Only three individuals, none of whom worked in the health care field,
had antibodies which reacted to Hantavirus antigens. The overall seroprevalence in the population was 0.73%, which is comparable to previous results of seroprevalence studies conducted in central and northern Argentina and in the United States. These data suggest that residents of El Bolson are not at increased risk of hantavirus infection.

As of 31 October 1997, a total of 114 cases of HPS and 47 deaths (case fatality rate: 41%) had been reported in Argentina. All cases displayed the clinical characteristics of HPS, but renal involvement and hemorrhagic manifestations were also observed in some patients. All reported cases had etiologic laboratory confirmation, either by ELISA detection of IgM, serologic conversion or specific PCR.

**Brazil**

**Conceptual Framework for Surveillance of Emerging Diseases**

There is an increasing awareness of the global threat posed by the unexpected dissemination of new and emerging infectious diseases worldwide. Feasible strategies must be advanced that address the emergence of infectious disease. In Latin America, in most cases, harmful human interventions in the environment lead to a deterioration of the quality of life and threaten the ecological balance, leading to the emergence of pathogenic agents and disease dissemination. These consequences are further favored by development projects and deforestation, increased occupational and spatial population mobility, intensification of travel and migration, urban crowding, extreme poverty, inadequate land use and the improper use of drugs and pesticides leading to resistance. The following is a discussion of the challenge to existing epidemiological surveillance structures and practices in Latin America brought about by this increasingly complex global health scenario.

Shifting paradigms require transcending existing limits of public health and medical practice, and overcoming the restricted medical focus placed on the human species. It becomes necessary to move epidemiological surveillance schemes into what is now called “ecosystem health surveillance”, based on an “epidemiology of complexity,” which constitutes an interdisciplinary approach of environmental and social disciplines.

**Why should routine surveillance be revised?**

Routine surveillance looks for pathogenic agents or diseases that are already known or have been previously described. By nature, surveillance does not search for unusual or unexpected events or changes in populations and environments. Awareness of the unusual, through rumors and human perception, is the foundation of a broader concept of surveillance, and requires movement towards a social and ecosystem approach to health surveillance.

**Conceptual and political issues**

Both in Latin America and worldwide, traditional surveillance policy fails to deal with the unexpected. Among policy makers there is a conceptual misunderstanding of new, emerging and reemerging diseases resulting from incomplete comprehension of the dynamics of disease evolution. First, it is necessary to understand that diseases and pathogenic agents are not static entities, but suffer constant change and evolution. In fact, natural selection does not always occur in the long term, but can happen very fast. Some policy makers minimize the importance of new and emerging diseases and often view them as problems of developed nations. These officials tend to emphasize “traditional” diseases that “persist” (static concepts) as “the real and underevaluated problems of the poor.” However, most diseases formerly identified as traditional are now rapidly changing their pattern of occurrence and dissemination. These illnesses are not static, neither are their agents or vectors.

**The need for a “specific surveillance system”**

In Latin America, conditions favoring the emergence and reemergence of infectious diseases and drug resistance require «specific surveillance systems», with a strong scientific and technological
component. Systems must be able to anticipate a broad range of risk factors and to focus on syndromes and unexpected diseases, rather than just reportable diseases. In addition, the system must not only focus on routine events, but it must be able to deal with the unknown, respond to rumors, and detect changing reservoir and vector behaviors. Furthermore, it should be able to detect unusual disease patterns, identify drug and pesticide resistance, and follow-up on the consequences of human, animal and trade movement across borders.

The new approach requires the implementation of communication networks and the integration of scientific and technological inputs into routine surveillance procedures. Sharing strategic information on pathogenic agents, such as viruses, bacteria and fungi, requires the integration of plant and animal data. The addition of risk factors, pathogenic agent and disease information will facilitate the anticipation of risk and health consequences.

**Strengthening science and technology systems:**
*The Brazilian experience in reference research institutes and hospitals*

In 1995, the risk of dissemination of the Ebola virus, as well as other emerging diseases (such as HIV/AIDS, Sabia virus, Rocio, Oropouche, hantavirus and Brazilian purpuric fever) and reemerging diseases (dengue, cholera, malaria, tuberculosis, leishmaniasis) created critical situations in Brazil. The emergence in the Amazon forest of an unknown disease affecting Brazilian military personnel signaled limitations in the ability of Brazilian reference hospitals and public health laboratories to deal with emerging and reemerging infectious diseases. Analysis and recommendations were made at a seminar held by the Brazilian Project for the Strengthening of the Scientific Capacity of Reference Institutes and Hospitals. Main problems identified were a lack of adequate biosafety infrastructure for health facilities, laboratory and field work; gaps in information, and the need for specific task forces to coordinate immediate response at both the local and central levels.

At the seminar, there was consensus about the need to develop a highly sensitive surveillance system with a strong scientific and technological component capable of detecting suspect syndromes and unexpected diseases. A national list of priority syndromes and diseases was defined; it was agreed that disease selection criteria should be updated periodically. The system should be global in perspective, and should monitor changing behaviors of pathogenic agents, reservoirs and vectors, disease patterns, drug and pesticide resistance, and the possible risk factors resulting from development projects affecting the environment.

The new surveillance system should not be conceived as an independent structure. On the contrary, it should be part of the current National Epidemiological Surveillance System (SNVE). Participants in the Seminar also suggested that the Coordinating Board for Scientific and Technological Development of the Ministry of Health should be transformed into a new National Secretariat for Science and Technology in Health, with a broader scope. There was a consensus that emerging and reemerging infectious diseases in Brazil will demand extensive reform of the Brazilian state structure, in order to provide better coordination of national interventions, in collaboration with SNVE. In 1996, following the recommendations of the Seminar, the Brazilian project started to invest in capacity building in the main research institutes and hospitals, emphasizing immediate response and appropriate intervention. Additional funding was provided for human resources training in biosafety, and to improve the public health laboratory infrastructure. Recently, in collaboration with the Oswaldo Cruz Foundation, an evaluation of epidemiological information on emerging and reemerging diseases in Brazilian hospitals was initiated.

**What remains to be done**

a) Increase awareness: incorporate rumor information and move from data surveillance to effective local community action (figure 11a).

b) Strengthen the scientific and technological capacity and link surveillance to science and technology (figure 11b).

c) Build integrated databases, sharing health care data and modelling (figure 11c).

d) Define a new paradigm for specific emerging disease surveillance: reevaluate the exiting routine surveillance framework (figure 11d).
Figures 11a, b, c, and d summarize the concept proposed for a new surveillance system in Brazil.

**Figure 11a**

**INCREASING AWARENESS**

- Clinical
- Epidemiology expertise
- Laboratory network
- Medical education
- Rumors

**Figure 11b**

**THE CRUCIAL ROLE OF SCIENCE AND TECHNOLOGY**

**Research and Development Network**

- Biology
- Epidemiology
- Social Sciences
- Computer Sciences
- Mathematics
- Ecology
- Zoology
Figure 11c

BUILDING DATABASES AND SHARING HEALTH CARE DATA

- RUMOR ("POPULAR INFORMATION")
- EPIDEMIOLOGICAL INFORMATION NOTIFIABLE AND NON-NOTIFIABLE DISEASES
- MOSQUITO DATABASE
- TICKS DATABASE
- SMALL MAMMAL DATABASE
- RODENT DATABASE
- SPATIAL INFORMATION GIS APPLIED STATISTICS
- REMOTE SENSING VEGETATION FROM SATELLITES
- HEALTH STATE SECRETARIAT INFORMATION
- HEALTH CITY DEPARTMENT INFORMATION
- AGRICULTURE
- HOSPITAL IN-PATIENT INFORMATION
- VITAL RECORDS: BIRTH CERTIFICATES, DEATH DATA
- WEATHER RECORDS, CLIMATE DATA: PRECIPITATION AND HUMIDITY
- DEATH INVESTIGATIONS AND AUTOPSY INFORMATION

EMERGING INFECTIOUS DISEASES

Figure 11d

FRAMEWORK FOR SPECIFIC SURVEILLANCE SYSTEM FOR EMERGING DISEASE

- SURVEILLANCE SYSTEM
- SCIENCE AND TECHNOLOGY
- RUMORS
- COMMUNICATION NETWORKS
Development of National Infectious Diseases Surveillance

The approach Canada is taking in the future development of infectious disease surveillance is viewed within the context of a well established system of activities, some of which have been operating for many years; others are more recent.

A notifiable diseases system which reports aggregate data, and a complementary case by case reporting system form the core of these activities. Currently, 47 diseases are notified nationally, although the statutory obligation to report is only to provincial governments. The reporting structure, unfortunately, provides poor linkage between laboratory and epidemiological data, and has to cope with multiple software platforms for provincial databases.

One approach to dealing with this problem has been to develop specific surveillance programs related to specific databases or transmission routes. Examples include the Canadian Pediatric Surveillance Program, the Sentinel Hospital Reporting System, and surveillance programs for vaccine preventable diseases, AIDS/HIV, sexually transmitted diseases and tuberculosis.

The recognition of the multiplicity of needs, systems and programs has forced the Laboratory Center for Disease Control (LCDC) to begin to define a new strategy for public health surveillance which seeks to address priorities, data quality and standardization, as well as technological issues related to moving data and information around.

There is no doubt of the value, both in terms of preventing human illness or limiting the economic impact of disease, of early detection investigation and termination of outbreaks or epidemics of disease. In this regard, Canada has developed a process in the last few years to identify specific needs and enhance surveillance systems in several areas, including enteric, food and waterborne disease, and the surveillance of antimicrobial resistance.

In general, the process has gone through several stages:

- identification and prioritization of needs
- approach to agreement or buy in
- approach to development
- choice of technology and tools
- implementation and review

Identification and prioritization of needs

In general, the identification of needs is easy. There are no shortage of candidates in the area of infectious diseases. However, in keeping with the examples mentioned above, enteric diseases and antimicrobial resistance will be discussed. Recent national and international conferences on emerging infectious diseases have fully highlighted the importance of these areas. The ASM Task Force Report in 1995 stated:

“There is an urgent need for effective domestic and global surveillance of antibiotic resistance in animals and humans.”

This statement contains three key words:

- **Urgent**: Over the last 10 years, the United Kingdom has been observing the emergence of a multiple antibiotic resistant strain of *Salmonella typhimurium* (DT 104). This strain is aggressive and resistant to ampicillin, chloramphenicol, streptomycin, tetracycline, sulfonamides and trimethoprim. This strain is also found in North America.

- **Effective**: Nationally and internationally there is recognition of the need to provide a more effective, better coordinated collection of quality data; coordination of laboratory and epidemiological activities; standardization of approaches and methodology; and agreement in definitions.
• **Global**: People, food and animals move internationally, and the need for international sharing of data on related health issues is now recognized by the development of initiatives such as WHONET, SALMNET, PROMED, and others.

In Canada, and probably elsewhere, the difficulties arise when setting priorities. The reasons are several:

• **Regional interests**: In Canada, there are 12 jurisdictions, all with different priorities pertaining to the particular political and health interests of the province or territory concerned. Local priorities may differ from national ones, thus, the first priority of laboratories and health units is the community they serve.

• **Diversity of peoples**: In Canada work is done within a framework of multiple ethnic/cultural groups with equally diverse needs. First Nations Peoples have control of their own public health infrastructure, and are considered a partner in development of Federal health initiatives.

• **Resources**: There is considerable variation in availability of resources in terms of people, finances, laboratory facilities and computer related technology and skills.

**Approach to agreement**

Recognition of diversity at many levels in Canada has necessitated a process of consensus development mediated through conferences. The aim has been to have the project reviewed across jurisdictions and disciplines, and at multiple levels, in order to obtain the widest possible buy-in.

For infectious diseases, development of surveillance activities at the national government level includes:

• Identification and control of potentially serious and epidemic diseases
• Development and implementation of national prevention and control activities
• Monitoring and assessment of national prevention and control activities
• Publication of national statistics to aid national and local priority setting
• Contribution to the international surveillance of diseases (development of global policy)

This national perspective on data use must take into account at least six major issues which are influencing development of infectious disease surveillance:

• Reemergence of pathogens which have been of low public health significance for several generations in Canada, and the emergence of “new” pathogens.
• Development of multidrug resistant strains of bacterial pathogens within institutional settings and in the community.
• Risk of infection to persons with depressed immune systems.
• Social and demographic factors resulting in changes to population size and structure, individual and national wealth, and patterns of social abuses.
• Increased international contact via travel for commercial and leisure purposes, immigration (social, political and economic) and trade (particularly food and animals).
• Environmental change, including the effects of pollutants in health status, habitat invasion, and potential for increased contact with animals and insect borne infections.

Having agreed to develop a database, a series of key questions are asked about the storage and use of data to ensure that the surveillance activity is valid and serves the needs and purposes of public health at various levels. Such questions are:

• What data should be collected and by what process do we ensure the quality of data? e.g. completeness, timeliness, representativeness, consistency.
• Where should the database(s) be located and what options could be considered? e.g. multiple databases, centralized database.
• Who should have access to the database(s) and under what constraints? e.g. need to know, maintenance of patient confidentiality.
• What level or type of analysis of data is required to be consistent with local, provincial and federal responsibilities?
• What types of information outputs will need to be developed to meet needs of public health professionals, commerce, general public? What output options should be considered?

In addition, as an aid to decision making or priority setting, a series of criteria have been developed by which individual diseases can be scored. These are currently being applied against current and potential diseases on Canada’s national list of notifiable diseases. Criteria are: public perception of high risk; political perception of a need to respond to public concern; potential for spread in the population; increased incidence and/or severity of disease; unresolved control issues; potential for population-based control measures; international implications; and potential for impact on the health care system.

Approach to development of surveillance systems

The approach taken in the development of surveillance systems in Canada has been fundamental to partner buy-in. This is best illustrated by the current development of an integrated public health surveillance system in Canada called SPHINX (Spatial Public Health INformation EXchange). The system focuses on building a tool to assist and facilitate data collection, analysis and dissemination of information, and provide linkage to disease control, research and other health-related services.

Prior to SPHINX development, multiple, distributed islands of data existed in various formats and platforms, in multiple sections, with poor linkage and untimely analysis. In addition, this information was often poorly linked to the process of health policy development (see next page).

SPHINX is designed to gather health and health related data from multiple sources into a virtual data warehouse accessible by public health professionals at all levels of activity. The data warehouse will be linked to analytical applications such as Geographic Information Systems (GIS), and will have communications ability via electronic mail.

“SPHINX Demonstration Project Summary”

SPHINX is an integrated public health surveillance infrastructure designed to link and facilitate the activities of public health professionals from many disciplines and at multiple levels. The initial demonstration project is being developed in collaboration with Alberta Health, and will involve a number of regional health authorities and First Nations communities in that province.

SPHINX will interface with local data collection and processing packages, thus recognizing that an effective infrastructure must be able to «talk» to the existing database platforms at every level. As a public health surveillance tool, SPHINX is structured to answer specific needs relating to sharing and analyzing data at the local, provincial and national levels of aggregation, while ensuring personal confidentiality. Human case data will also be linked to a «warehouse» of complementary, risk factor data, including, for example, data relevant to agriculture and the environment. In addition, users will be able to access common analysis tools, particularly, geographic information systems which will provide geographic display of data. The structure of the system will facilitate both horizontal communication between stakeholders, and vertical cascading of information as alerts.

Central to the SPHINX demonstration project is a consensus process designed to ensure that essential needs are identified and addressed at every level, while fostering a sense of ownership by all stakeholders. SPHINX is also designed to have wide application to public health issues. The pilot phase will illustrate this by seeking to collect data on a limited number of non-communicable diseases and injury-related issues as well as the notifiable diseases.
Given the demands and complexity of such a system, buy-in at every level, from local public health authorities to provincial government, is essential. This partnership building is achieved by ensuring that the system not only meets the requirements of the local users, but will actually make their job easier and operate in a user friendly way. All of this is being built through a series of consensus meetings with very broad input from public health professionals.

Essentially, in recognizing that public health surveillance is impacted by many sectors and presently uses only some of the data available, SPHINX is providing a tool to make all this information more accessible to those who need it.

Choice of technology and tools

The technology options available for the development of surveillance infrastructure range from the highly sophisticated, integrated technology approach of SPHINX, to far less sophisticated but nevertheless effective paper based systems. In the development of some of the surveillance systems in Canada, the technology adopted has reflected the functional ability of the data contributors and the technology available to them.

For example, three years ago, the federal influenza surveillance program collected only laboratory confirmations of influenza and had no timely indicator of local influenza activity available at the national level. To improve this, about 250 sentinel physicians were recruited across Canada to report weekly consultation rates for influenza-like illness. However, problems emerged when participants were requested to report their data using only IVR technology. Basically, it was unsuccessful because physicians rapidly became frustrated with the (simple) reporting pathways. The system tremendously improved when physicians were asked to fax the data. Physicians now report using low-level fax technology, and the Federal government is free to develop more sophisticated fax technology to (1) generate computer controlled dial-up systems; (2) read characters and text directly into the FluWatch database (Teleform), and (3) fax reminders as well as summary reports of data.

The FluWatch program is based on commercial software adapted to the system's needs. An alternate approach would be to develop custom tools. The latter has been the LCDC approach in developing an integrated suite of computer applications known as CIPHS, which is designed to link and track laboratory and epidemiological data at the local level, and to link said data into systems such as SPHINX.

The first application of SPHINX is the Laboratory Data Management System (LDMS) for tracking and reporting specimens of human, animal, plant, food, environmental or synthetic sources. The data are held in a national database and can be linked to other «disease episodes» or data entities.

LDMS is the software component that manages data relating to specimens, results of tests and risk factors. Data management includes input and notification of data, query and retrieval, summarization, reporting and communication. The application is designed to be language independent; this is an important issue in Canada where there are two official languages. Screen text is stored in database tables and not programmed into the application code. An auxiliary application allows the text to be translated into another language, line by line. When translation is completed, the new language wording is automatically generated. Thus, it is a relatively easy task to translate the English screen into a Spanish or Portuguese version.

Implementation and review

A laboratory reporting mechanism for enteric disease is presently in the pilot stage of implementation. This project was the result of the recommendation of a national consensus conference three years ago, which recognized that there was no specific national collation of enteric disease data. For the one year pilot project, the decision was made to use a fax based weekly reporting system to collect aggregate data on the major enteric diseases for each province and territory.

Laboratories are being asked to give aggregate totals for each pathogen and additional information about outbreaks, serious sequelae and multiple drug resistance. In the first six months of the pilot, laboratories have been reasonably consistent in submitting weekly reports. In return, they receive a weekly aggregation and monthly summary of data, both of which are also sent to key public health officials in each province and territory. During the same period, almost
7,600 reports of infections were received for the major disease groups, over half of which were due to salmonellas.

The system has proved capable of picking up hot spots in reporting, such as the current problem with *Salmonella meleagridis*, indicating its potential as a warning system for outbreaks. The mechanism has also proved capable of collecting information on outbreaks and drug resistance, and finally, on travel related illness. Summarized data are faxed back to laboratories and provincial epidemiologists (within four days), and a summary is provided every four weeks. Laboratories and epidemiologists are encouraged to comment regularly on the system and its outputs, as part of a regular review process.

The potential of this system to identify trends and track outbreaks and occurrence of drug resistant strains for epidemiological purposes is becoming clear. A significant impact on the epidemiological study of disease trends, and identification of discrete incidents, can be made through the collation of laboratory data.

**Canadian Integrated Public Health System (CIPHS)**

The Canadian Integrated Public Health System (CIPHS) is a planned suite of computer applications and databases for acquisition, management, processing and communication of public health information.

In the future, CIPHS will incorporate a common logical data model and data dictionary, common standards for user interface, a filter for the replication of data, and a common pool of reusable tools and utilities. In addition, the CIPHS is intended to allow free exchange of data, and access to tools and utilities in the wider operating system environment, e.g., word processors, spreadsheets, statistical and graphics packages, electronic mail, and fax. The application development tools and database management system(s) employed are compatible with current industry and international standards.

CIPHS is language-independent. All text that appears on screens, such as labels on data fields and buttons, menu titles, menu items and help are not programmed into the application code but are stored in database tables. As described above, an auxiliary application allows line-by-line entry of this text in another language.

The first application to be developed in the CIPHS suite is the Laboratory Data Management System (LDMS). The focal point of this system is the specimen (human, animal, plant, food, environment or synthetic). Different database subcomponents and application screens are invoked according to specimen type. For human subjects, the system employs the standard patient and related data entities adopted from the LCDC Health Surveillance Data Model. These components provide a connection with epidemiological and surveillance data and their applications.

**INTERNATIONAL PERSPECTIVE OF THE SURVEILLANCE SYSTEM IN CANADA**

The international surveillance component of the Canadian System began with the episode of pneumonic plague in India in 1994. This event had major international repercussions due to the rapid transport of people by jet plane. With only 18 hours or less of travel time between New Delhi and Toronto’s Pearson Airport, there was little time for a thorough epidemiological assessment of the Indian outbreak. Similarly, not much time was available to develop and implement special procedures to monitor international arrivals from India before the first direct flight from that country was scheduled to arrive in Toronto. With the imminent arrival of this flight shortly after the detection of the plague outbreak, Pearson Airport came within 20 minutes of complete shutdown, due to threatened work stoppage. This and other outbreaks reinforce the need for global infectious disease surveillance and a coordinated international response.

Initial concern over outbreaks of infectious disease with international ramifications was heightened with the Ebola hemorrhagic fever outbreak in Zaire in 1995. Although this problem was quite distant to Canada, and active monitoring of the situation seemed to indicate that there was no real risk to Canadians; this situation changed dramatically when a refugee claimant from Zaire arrived at Pearson Airport and announced that he had just been in Kikwit, where he had
helped bury his mother. The country was totally unprepared for the eventuality of harboring someone potentially incubating this dreaded disease. There was no place to house this individual until the incubation period was over. The Quarantine Act of Canadian Law was hopelessly outdated as a tool to manage such a situation. Coping with this emergency stretched the system’s capacities to the breaking point. In the end, the entire outbreak in a distant land cost Health Canada approximately CAN$ 500,000.

Other incidents also have served to reinforce Health Canada’s commitment to strengthen its capacity in international surveillance. Following are some of the concepts that have shaped thoughts in this regard.

**National mandate**

Health Canada has a responsibility to protect the health of all Canadians, wherever they are. From an international perspective, there are three groups of concern: Canadians traveling to the site of an infectious disease outbreak, Canadians who work and live at the site, and Canadians (and other persons) who are returning from the site. Canada’s Travel Medicine Program works closely with the Department of Foreign Affairs to collect, analyze and disseminate information on any outbreak situation and advise on preventive measures to reduce the risk of exposure. Collecting accurate information is the major challenge.

**Humanitarian**

Again, there is concern with the concept of the global village, and the fact that infectious diseases can no longer be intercepted through quarantine action at national borders. We have to be concerned with any infectious disease outbreak anywhere in the world at any time, since the travel time from anywhere in the world is usually shorter than the incubation period of nearly all infectious diseases. The death of a nurse from Ebola in South Africa illustrated precisely how Ebola might occur in Canada, i.e., through the entrance of someone who is incubating the disease, becomes sick in Canada, seeks medical care in a local hospital where the attending physician forgets to inquire about the travel history, and infects one or more health care workers.

It must be recognized that any food can be grown anywhere, processed somewhere else and then widely distributed; the effects of food contamination can now occur on a much larger scale. In addition, it must be recognized that another pandemic like the 1918 flu pandemic would probably occur at great cost, with the possibility of significant irrational international response on a scale unforeseen to date.

In view of the above, Canada needs to participate more actively in addressing emerging disease outbreaks in other parts of the global village, in order to provide better support to national control efforts.

So far, the response has considered several paradigms:

We all recognize that national infectious disease statistics are “historic”. Earlier this year, Canada’s tuberculosis statistics for the calendar year 1995 were published, approximately 14 months after the end of the year in question. Prior to this time, the delay was two full years. The goal is to reduce this delay to less than 4 to 6 months. Nevertheless, such data produce historic trends; the systems are useful for defining the general infectious disease epidemiological profile for a given geographic area; these data are useful for defining general public health policies. However, these systems have limitations, especially in dealing with outbreak events. In fact of practice, these data are rarely used for outbreak detection. Direct telephone reporting by an astute health care worker is probably the most common way an outbreak comes to light. Internationally, however, outbreak information comes to light through the Internet and what may be called the “new paradigm”.

In this new paradigm, the information pyramid is flattened into a plane, and a public health event can spring to international attention from any place where someone is connected to Internet. With PROMED, there now is a global surveillance system composed of 15,000 self-selected persons who want to report infectious disease outbreaks. One major limitation of this new capability is that information is usually unverified and fraught with error and possible misinformation. In fact, one Achilles heel is its susceptibility to sabotage.
Finally, there are highly specialized systems, such as the Global Influenza Surveillance System, and targeted antimicrobial susceptibility surveillance laboratory networks such as the Tuberculosis Supernet.

Given these concepts and concerns, the Laboratory Centers for Disease Control is developing a Global Public Health Intelligence Network (GPHIN) as part of the National Health Surveillance System. Staffing for GPHIN has begun, as well as the establishment of the computer systems to permit global monitoring of multiple Internet-based information sources where public health events of potential international significance might be reported.

The primary purpose of the GPHIN will be to monitor international sources of information and detect health risks of importance. The system is broad in scope and initially will include communicable and non communicable diseases, as well as food and water safety. In the future, GPHIN will be expanded to commercial products, therapeutic products and devices, and environmental health risks.

A key component of the GPHIN will be the Internet. The Internet is central to global surveillance actions, communications with partners, and presentation of information on the World Wide Web.

The project is unique in its nature. The critical element in this type of surveillance activity is time. GPHIN will provide real-time, sensitive, verified information. It will share health risk information of international events for risk management responses and control and prevention measures. The system has four components, each feeding back to one another: global surveillance, verification and assessment, dissemination, and evaluation. It also introduces a human element at the very early stages of the risk assessment process, which will allow analytic decisions and proper actions to be promptly made.

GPHIN is not just another electronic surveillance tool for routine infectious disease incidence and prevalence or other ongoing environmental risk factors. Endemic infectious disease patterns do not abruptly change or significantly alter disease risk. Information on ongoing contamination of water, air or food in developing countries is also readily available. However, infectious disease outbreaks or changes in basic levels of environmental contamination may dramatically change risk. The uniqueness of GPHIN will lie in its ability to monitor abrupt changes (e.g. outbreaks of infectious disease or breakdowns in food supply and processing) in established patterns, so that increased risk to Canadians can be promptly identified and managed.

Ultimately, the system will be an early part of any response to international health crises, and will share information and communicate with partners through secure channels to facilitate the coordination of international response measures.

**UNITED STATES**

**GLOBAL EMERGING INFECTIOUS SURVEILLANCE AND RESPONSE**

In June of 1995, the President of the United States of America, recognizing that the infrastructure for infectious diseases surveillance was inadequate, issued directives that would help to strengthen a global emerging infections surveillance and response system. On this basis, a coordinated program to facilitate early recognition and control of new disease problems was established. Following is the text of Presidential Decision Directive NSTC-7:

“I have determined that the national and international system of infectious disease surveillance, prevention, and response is inadequate to protect the health of United States citizens from emerging infectious diseases. The mission of Department of Defense (DoD) will be expanded to include support of global surveillance, training, research, and response to emerging infectious disease threats. The Department of Defense will strengthen its global disease reduction efforts through: centralized coordination; improved preventive health programs and epidemiological capabilities; and enhanced involvement with military treatment facilities and United States and overseas laboratories. DoD will ensure availability of diagnostic capabilities at its three domestic and six overseas laboratories, using existing Department of Defense resources. DoD
will make available its overseas laboratory facilities, as appropriate, to serve as focal points for training of foreign technicians and epidemiologists.”

The objectives established by Presidential Decision Directive NSTC-7 are to:

i. Strengthen domestic infectious disease surveillance and response
ii. Collaborate to establish a global surveillance based on regional hubs linked by modern communications
iii. Strengthen research into diagnostics, treatment and prevention
iv. Ensure availability of drugs, vaccines, and assays
v. Expand missions and authority of US agencies
vi. Promote public awareness

Table 2 presents examples of emerging infectious diseases targeted for surveillance.

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<th>National level</th>
<th>International level</th>
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<tbody>
<tr>
<td>Escherichia coli O157:H7</td>
<td>Vivax malaria in Korea</td>
</tr>
<tr>
<td>Multidrug resistant pneumococcal disease</td>
<td>Ross River virus in Australia</td>
</tr>
<tr>
<td>Vancomycin-resistant enterococcal infections</td>
<td>Ciprofloxacin resistant <em>Campylobacter</em> in Thailand</td>
</tr>
<tr>
<td>Influenza A/Wuhan/96</td>
<td>Dengue in Central America</td>
</tr>
<tr>
<td>Hantavirus infections</td>
<td><em>Vibrio cholera</em> O139 in Asia</td>
</tr>
<tr>
<td>Cryptosporidiosis</td>
<td>Anthrax in Haiti</td>
</tr>
<tr>
<td>Multidrug resistant tuberculosis</td>
<td>Diphtheria in Eastern Europe</td>
</tr>
</tbody>
</table>

Approximate funding for 1998 fiscal year is as follows: Central Hub, US$ 800,000; research and development laboratories, $725,000; Army Hub, $400,000; Navy Hub, $400,000, and Air Force Hub $400,000.

Figure 12 shows the location of the Department of Defense hubs and laboratories for emerging infectious surveillance.
a) Center for Health Promotion and Preventive Medicine; b) Naval Health Research Center; c) Walter Reed Army Institute of Research; d) Naval Medical Research Institute; e) US Army Medical Research Institute.
ROLE OF THE DEPARTMENT OF DEFENSE GLOBAL EMERGING INFECTIONS CENTRAL HUB AT THE WALTER REED ARMY INSTITUTE OF RESEARCH

The Department of Defense’s Global Emerging Infections Central Hub at the Walter Reed Army Institute of Research is responsible for coordination and prioritization of surveillance efforts; establishing standardized methodologies; management of an integrated communications/data management system (LITS and PHLIS); receiving data for merger and analysis; coordination of Continental United States and Outside Continental United States laboratory support; monitoring quality of data collected and reported; dissemination of data as appropriate, and coordination and response activities.

Possible venues for obtaining emerging infections data on Department of Defense health care beneficiaries

Some possible venues for obtaining emerging infectious diseases data on Department of Defense health care beneficiaries include: sentinel clinical microbiology laboratories through the Comprehensive Health Care System; sentinel field and laboratory surveillance for emerging infectious diseases (e.g., invasive Streptococcus pyogenes, S. pneumoniae, adenovirus, influenza); unexplained deaths investigations; sentinel clinicians and emergency room syndromic surveillance; infectious disease specialist/travel clinic-based surveillance; hospitalization data; blood banks; and sexually transmitted diseases clinics. Figure 13 shows a map of proposed sites for Department of Defense beneficiary sentinel laboratory surveillance.

Figure 13. Proposed Sites for United States Department of Defense Beneficiary Sentinel Laboratory Surveillance
The role of overseas laboratories

Figure 14 presents the geographic distribution of Continental United States and overseas laboratories for emerging infections surveillance. The objectives of the Department of Defense overseas laboratory surveillance and response efforts are to establish regional sentinel surveillance for selected infections; to contribute to the development of regional medical surveillance infrastructure; to enhance diagnostic capabilities to evaluate the occurrence of emerging infections; to identify, facilitate, and evaluate control efforts for emerging infection problems; to perform routine monitoring of the incidence of selected infections; to identify and report on outbreaks; to coordinate Department of Defense training and response activities locally; and to provide staging platforms for intervention.

Initially, some surveillance modules have been selected for:

- Drug-resistant *Plasmodium falciparum* and *P. vivax* malaria
- Antibiotic-resistant diarrheal agents
- Influenza
- Hemorrhagic and other febrile infections

The objectives of training within the overseas laboratory surveillance program are to strengthen the internal infrastructure of the Department of Defense, as well as that of the host nation, and the Region’s Surveillance Infrastructure; to transfer epidemiology and microbiology skills for local sustainable surveillance; to facilitate replication of standard surveillance procedures at other sites and subsequently enhance data pooling, and to facilitate timely recognition and collaboration in outbreak control.

Figure 14. Continental United States and Overseas Laboratories for Emerging Infections Surveillance

a) Walter Reed Army Institute of Research; b) Naval Medical Research Institute; c) US Army Medical Research Institute.
There are several benefits to national security derived from the overseas laboratory surveillance program on infectious diseases, such as enhanced readiness through better medical threat estimates; early detection of importable emerging infections; improved evaluation of control measures; optimized treatments (e.g., appropriate antibiotics); enhanced regional stability from better disease control; assurance that research priorities reflect Commander in Chief needs; stronger international relationships; strengthened relationships with other federal agencies; strengthened international scientific relationships; strengthened host country surveillance; access to special capabilities (e.g., BSL-4 biocontainment and specialized diagnostics); expert help with outbreak investigation.

**UNITED STATES CENTERS FOR DISEASE CONTROL AND PREVENTION (CDC): SUPPORT OF CDC FOR BUILDING A LABORATORY NETWORK FOR SURVEILLANCE**

The Centers for Disease Control and Prevention (CDC) of the United States of America provide technical expertise to strengthen national laboratory capacity. CDC is currently involved in technical cooperation projects in several countries.

1. In Brazil, at the request of the Ministry of Health, CDC is collaborating on a project aimed at building a strong surveillance system, in the absence of a single national reference laboratory. The strategy includes building on existing expertise found among scientific staff working in several national scientific foundations. These facilities are primarily research oriented, and are generally well equipped and established.

Some advantages of using the existing system are:

- it is more economical since it uses available resources
- it utilizes established expertise of proven quality
- there is no need for significant new building or equipment

On the other hand, the use of existing systems presents some challenges. For instance, it sacrifices existing research infrastructure for applied and service work. In addition, due to the lack of a centralized facility, it is harder to test for multiple agents.

A needs assessment for strengthening the laboratory network will be conducted using a two team approach: one for laboratory support and laboratory biosafety, and a second for epidemiology and surveillance. The laboratory support team will examine specimen transport, receipt and tracking; quality control of tests; reagents production and distribution, including quality control; management of results; biosafety, and training requirements. The surveillance team will look at possible training opportunities linking laboratory and epidemiology; uses of surveillance data; reporting, including standardization and frequency of reports, and information management systems.

These are the first steps to revitalize the Brazilian health surveillance system. Continued collaboration is anticipated for several years to come.

2. Among other activities, an international course was conducted in Chile in April 1997, to provide training in the development of the influenza network. The course included training on the diagnosis of influenza and other respiratory viruses. The objectives of the training, which was attended by 23 participants from 17 countries, were to:

- strengthen laboratory diagnosis and surveillance of respiratory viruses;
- increase awareness of the significance of influenza surveillance; and
- emphasize the importance of influenza as a cause of morbidity and mortality.

The format of the course included keynote lectures on influenza surveillance and control: the global perspective; the role of WHO surveillance for vaccine strain selection; epidemiology and surveillance of influenza and other respiratory viruses; and the role of the laboratory in surveillance of respiratory viruses. The training also consisted of participant presentations of past experiences and future plans regarding respiratory virus surveillance.
A third aspect of the course was devoted to laboratory methodology for direct detection in clinical specimens; virus isolation and identification; serological diagnosis of influenza Respiratory Syncytial virus; molecular analysis of influenza, and identification of antiviral drug resistance in influenza.

The immediate goal of the workshop was to establish an active surveillance network for identification and characterization of currently circulating influenza strains. Long term goals were also identified: (a) timely collection of data appropriate for vaccine strain selection, and (b) establishment of a solid surveillance network capable of responding to newly emerging diseases, such as pandemic influenza.

3. In the area of dengue surveillance, a close collaboration has been established between CDC San Juan Dengue Laboratory and PAHO. This collaboration has contributed to extensive training in dengue laboratory techniques; provision of dengue diagnostic reagents, and the establishment of quality control and proficiency testing programs; and regional data collection and dissemination through PAHO. CDC has also provided assistance for outbreak response, as requested. Furthermore, an extensive laboratory network for dengue diagnosis has been established.

Challenges now facing the network include how to improve efficiency in the use of limited human and technical resources of the dengue laboratory, and most of all, how to control epidemic dengue.

4. In regard to hantavirus pulmonary syndrome surveillance, there has been close collaboration between CDC and PAHO, and between those institutions and Member States, namely, Brazil, Argentina, Paraguay and Chile, where outbreaks of the disease have occurred. Areas of collaboration include:

- training in laboratory diagnostics;
- training in pathology, including immunohistochemical staining;
- laboratory reagents to assist in local preliminary diagnosis;
- confirmation of suspect positive results;
- extended individual training for an Argentinian scientist;
- opportunity of similar training for other molecular biologists;
- assistance in outbreak investigations (Chile).

5. Potential areas for future collaboration:

- Food-borne disease surveillance: reestablishing food-borne disease surveillance, and the national molecular subtyping network; increasing sensitivity of laboratory based surveillance; molecular subtyping to discriminate between common species or serotypes (subtypes of common pathogens can be tracked like subtypes of the Salmonella surveillance system); better recognition of outbreaks, especially small disease clusters.
- Antimicrobial resistance: existing quality control and proficiency testing being provided by CDC to some laboratories collaborating with WHO in monitoring nosocomial pathogens. There is specific interest in vancomycin resistant strains of *Staphylococcus aureus* and resistant strains of *Streptococcus pneumoniae*.
- Collaborate with other surveillance networks being developed (several now exist).
- Monitor antiviral drug resistance in HIV, especially in countries like Brazil where drugs are provided free of charge to patients.
- Systematic monitoring of multidrug resistant tuberculosis.

6. Other opportunities

- Pertussis strain exchange and determination of vaccine efficacy.
- Response to current measles outbreak in Brazil.
• Emerging problems like urban leishmaniasis (co-infection with HIV), expanding distribution of schistosomiasis, and eradication of filariasis.
PAHO’S Proposal for a Regional Surveillance System

INTENSIFIED SURVEILLANCE OF EMERGING AND REEMERGING DISEASES

Traditionally, disease has been the focus of health systems and medical practices, a situation still largely persisting today. This paradigm has led to control efforts geared toward the enhancement of diagnostic and therapeutic measures, but has left little room for disease prevention, health maintenance and health promotion.

At the outset, new and reemerging diseases usually represent a small number of cases; only a sensitive surveillance system or high case-fatality rate will facilitate timely detection. Unfortunately, these diseases often go unreported until late in their course, preventing the immediate response and collaboration necessary to contain the risk of exposure and limit the number of cases.

With the acceptance that emerging and reemerging infectious diseases are an international problem requiring a world strategy, international actions are currently under way to develop and update detection systems in order to prepare and respond to these emergencies.

PAHO has prepared a Plan of Action designed to combat new, emerging, and reemerging infectious diseases in the Americas (Document PAHO/HCP/HCT/95.060) in which it identifies several objectives common to control plans prepared by both WHO and the CDC, namely:

- To strengthen international-level surveillance systems in order to reduce the occurrence of emerging diseases.
- To strengthen existing surveillance infrastructure (laboratories, research technology and communications).
- To strengthen and update international standards, guidelines, and recommendations.
- To increase the international capacity to respond to epidemics through effective use of scientific and technological resources.
- To strengthen research on emerging diseases, particularly with regard to the antimicrobial resistance of infectious agents.
- To give special attention to the training of all members of the health care team.
- To recommend to Member Governments the improvement of existing public health systems, the allocation of special resources to eliminate or control emerging and reemerging diseases and the coordination of public health activities with the international community.

The Region of the Americas is at high risk for infectious disease emergence. High risk conditions, exacerbated by the high population density of Latin American cities, are favored by the tremendous bio-diversity of the region, as well as by ecological changes induced by deforestation, mining, and agricultural development in previously unexploited areas. In the last decade, an observed increase in migration, in the transfer of people between rural and urban areas and in other large population movements in the Region have also contributed to the increasing risk of infectious diseases.
CURRENT EPIDEMIOLOGICAL SURVEILLANCE SYSTEMS

Existing surveillance systems for new or reemerging diseases need to be strengthened and adapted to the changing conditions of our Region. It is necessary to facilitate the ongoing analysis of information in order to predict epidemics caused by infectious diseases and identify factors in emergence as well as potential patterns of risk. Currently, surveillance system data are normally subject to delays and inaccuracies; the use of these data for early outbreak detection is problematic, since data are routinely processed, circulated and accumulated, without the opportunity to correct errors, make necessary adjustments, or perform the analyses needed to determine appropriate courses of action.

The most basic purpose of a communicable disease surveillance system is to identify outbreaks with sufficient foreknowledge to allow for timely interventions. Surveillance systems function through receipt of periodic (daily, weekly or monthly) reports from health care providers who summarize cases of specific diseases. This process can take several days, implying that a system reacting to reports of confirmed cases could not respond to an outbreak or epidemic in an adequate or timely manner. A good surveillance system does not guarantee sound decision-making, but it reduces the probability of error.

It is a mistake to consider that the designation of a disease or disorder for compulsory notification amounts to establishing a surveillance system for that disorder. In a surveillance system based on specific diseases, health workers diagnose according to case definitions; this has proven useful in determining disease incidence and assessing the impact of specific control measures. Unfortunately, in most areas of the Americas, the reporting systems are passive, offering little feedback to informants and demonstrating a lack of data monitoring, analysis, and corrective actions.

PROPOSAL OF A NEW APPROACH FOR EPIDEMIOLOGICAL SURVEILLANCE OF EMERGING AND REEMERGING DISEASES

Although no existing surveillance system can detect every event of public health interest, a syndromic approach to the surveillance of infectious diseases offers greater sensitivity and specificity. Compared with systems dependent on laboratory diagnosis for the identification of specific diseases, a syndrome-based surveillance system will provide for swifter, more timely reporting.

The low sensitivity of current surveillance systems, coupled with little available knowledge of emerging diseases, hinders the detection of cases and increases the risk of further disease exposure. With this in mind, epidemiological surveillance should be adopted in a broader sense and not used simply as a case count mechanism (morbidity and mortality). Instead, surveillance should provide the background knowledge upon which timely actions are based, furnishing data on morbidity and mortality, as well as information on risk factors and environmental analyses of circulating pathogens, vectors, and reservoirs, among others.

No data set exists that meets all the needs of epidemiological analysis, however it is possible to define a nucleus, or minimum data set, required for effective action. Despite the fact that epidemiological information is indispensable to planning and decision-making, the acquisition of a huge quantity of data is not justified. The availability of data is a necessary but insufficient condition; not only must data be available, its quality and accessibility must be ensured, and a thorough, pertinent analysis performed. Unfortunately, such criteria are rarely applied.

The usefulness of the data depends, then, upon the timely and accurate delivery of relevant information to appropriate personnel. Accordingly, there exists the need for an intensified Regional surveillance system for emerging diseases that complements the work done by the epidemiological sector in each country of the Region. Such a system should strengthen existing national systems, provide the technical support necessary to implement control measures in risk situations while respecting the national responsibility to follow up and analyze information, send out alerts, and carry out control measures.

This type of system should be sufficiently sensitive to detect not only common pathological processes in a given area or space, but uncommon or abnormal occurrences as well (either an increase in the number of cases, the presentation of new cases, or an increase in mortality of
unknown cause). In addition, the system should permit the monitoring and analysis of existing disease trends and the detection of health hazards and new processes of disease. System sensitivity should permit early detection (of the syndrome according to its clinical definition) allowing for immediate response, followed by laboratory testing to determine the infectious agent of disease, and if necessary, a readjustment of control measures. The laboratory is therefore a fundamental tool counted upon by epidemiologists to characterize disease occurrence, enabling the establishment of adequate control measures.

Given the characteristics mentioned, the syndromic approach makes it possible to detect a large number of cases of well-known diseases, but above all, it makes it possible to detect disease occurrences of unknown etiology. However, to be of value, reports of syndromic cases must be subsequently researched and the causative agent determined. In addition, it is imperative to take immediate control action, since to delay intervention inevitably results in a larger number of cases.

Surveillance systems should endeavor to increase detection sensitivity, strengthen epidemiological research, and improve the determination of etiologic agents. Data should be analyzed for the purposes of monitoring disease and evaluating the effectiveness of control measures. Currently, it is commonplace for surveillance systems to detect disease incidence, carry out epidemiological research and isolate causative agents; however, they do not clearly establish the underlying conditions of a given health problem. As a result, it is necessary to strengthen the concept of surveillance in order to integrate not only epidemiological and laboratory data, but other sources of information as well.

Information will be fed to the Regional Surveillance System by its member countries. It will be necessary to establish timely mechanisms of data collection and analysis at the Regional level in order to maintain up-to-date knowledge of the epidemiological situation, as well as identify potential risk conditions associated with specific cases or outbreaks of communicable diseases.

In order to achieve this, it will be necessary to establish a database capable of data exchange between various organizations. The system should:

- Collect data on vectors, reservoirs, and the environment;
- Collect mortality and morbidity data for specific diseases (or syndromes); this could be accomplished through exploratory research designed to determine the magnitude of mortality from unknown syndromes;
- Incorporate information from geographic information systems.

The changes occurring in various ecosystems, whether through human activities or environmental variation, have upset the complex balance of infectious agent to host (vector, mammal) and made possible the emergence of formerly recognized or hitherto unknown diseases. One example of this is the notable increase in the number of new infectious agents identified since 1973 (Table 3). The appearance of these new agents makes it necessary to seek human behavior modification in an effort to minimize the risk of these diseases.

### Table 3. Etiologic agents of infectious diseases identified beginning in 1973 *

<table>
<thead>
<tr>
<th>Year</th>
<th>Agent</th>
<th>Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>1973</td>
<td>Rotavirus</td>
<td>Diarrhea</td>
</tr>
<tr>
<td>1975</td>
<td>Parvovirus</td>
<td>Erythema infectiosum (fifth disease)</td>
</tr>
<tr>
<td>1976</td>
<td>Cryptosporidium parvum</td>
<td>Acute enterocolitis</td>
</tr>
<tr>
<td>1977</td>
<td>Ebola virus</td>
<td>Hemorrhagic fever</td>
</tr>
<tr>
<td>1977</td>
<td>Legionellae pneumophila</td>
<td>Legionnaires’ disease</td>
</tr>
<tr>
<td>1977</td>
<td>Hantaan virus</td>
<td>Hemorrhagic fever with renal syndrome</td>
</tr>
<tr>
<td>1977</td>
<td>Campylobacter spp</td>
<td>Diarrhea</td>
</tr>
<tr>
<td>1980</td>
<td>T-cell human lymphotropic virus (HTLV-1)</td>
<td>Leukemia</td>
</tr>
<tr>
<td>1981</td>
<td>Staphylococcus aureus</td>
<td>Toxic shock syndrome</td>
</tr>
<tr>
<td>1982</td>
<td>Escherichia coli</td>
<td>Hemorrhagic diarrhea, hemolytic syndrome</td>
</tr>
</tbody>
</table>
1982  HTLV-2  Leukemia  
1982  *Borrelia burgdorferi*  Lyme disease  
1983  Human immunodeficiency virus (VIH)  Human immunodeficiency virus  
1983  *Helicobacter pylori*  Gastric ulcer  
1988  Human herpesvirus - 6 (HHV-6)  Roseola subita  
1989  *Ehrlichia chaffeensis*  Human ehrlichiosis  
1989  Hepatitis C  Hepatitis  
1991  Guanarito virus  Hemorrhagic fever (Venezuelan)  
1992  *Vibrio cholerae O139*  Diarrhea  
1992  *Bartonella* spp  Bartonellosis  
1993  Hantavirus isolation  Pulmonary syndrome  
1994  Sabia virus  Hemorrhagic fever (Brazilian)  


If the area covered by epidemiological surveillance is expanded, not only can the occurrence of normal and abnormal phenomena be detected, but various activities can be carried out that prevent case occurrences or, at least, diminish the number of potential cases. This is especially valid with respect to those syndromes or diseases for which clear guidelines of prevention or specific treatment are not available.

The syndromic approach permits a) utilization of broader case definitions; b) work with clinical data; c) a faster response; d) discovery of new or not previously defined diseases, and e) the promotion of participation in reporting and response.

Syndrome reporting does not replace the surveillance of specific diseases, but rather tries to provide the system with the sensitivity required to detect new or abnormal processes, and ensure specificity of the later. In summary, syndrome detection facilitates reporting.

All diseases should be reported, but a report should be considered urgent when:

- The number of expected cases for a given space and period of time are surpassed;
- The disease in question has the potential to spread outside the community;
- The case-fatality is high;
- The situation is new or unexpected;
- A previously unrecognized syndrome occurs.

In addition, the report should include the following information:

- Origin and disease type, agent or syndrome.
- Number of cases and deaths; information indicating a primary case; indication of whether the syndrome is 'indigenous', imported or derived from another reporting or service area; epidemiological tests identifying a causative or vector agent; whether confirmation was made by laboratory diagnosis or through epidemiological research.
- Geographical assessment of the area affected and the population at risk, including a description of changes occurring in nature.
- Conditions that favor or reduce the probability of disease spread.
- Measures taken.

In view of the foregoing, the proposed epidemiological system will integrate national level reports of the diseases and syndromes agreed to. These data will be reported by country and political or administrative division within each country.
VI

Task Force on Surveillance of Emerging and Reemerging Diseases
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