

122nd Session
Washington, D.C.
June 1998

Provisional Agenda Item 4.8

CE122/14 (Eng.)
13 April 1998
ORIGINAL: ENGLISH

HANTAVIRUS

Since 1993, when an outbreak of hantavirus pulmonary syndrome was detected for the first time in the southwestern United States of America, several outbreaks or sporadic cases have been notified in Argentina, Brazil, Canada, Chile, Paraguay, and Uruguay. Outbreaks of this disease produce high case-fatality rates and have aroused widespread fear in the affected communities and great concern among the national health authorities.

In light of this situation, the 40th Directing Council of the Pan American Health Organization (September 1997) adopted a resolution (CD40.R14) calling on the Member States to strengthen the mechanisms for collaboration among the countries and promote information, education, and communication geared toward the community to ensure the adoption of good environmental sanitation practices. That same resolution requests the Secretariat to create a task force to issue recommendations on surveillance, diagnosis, treatment, and prevention of the infection. The task force met in March 1998 to review and approve the guidelines on hantavirus.

This document summarizes the historical background and current epidemiological situation of hantavirus infection. It also reports on PAHO activities to date in this area and presents a proposal for ongoing activities.

The Executive Committee is requested to review this document and to make recommendations on the progress of the surveillance and detection activities of the Bureau in support of the Member States.

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EXECUTIVE SUMMARY

In 1995 the Directing Council adopted Resolution CD38.R12 encouraging the implementation of the Regional Plan of Action for Combating New, Emerging, and Re-emerging Infectious Diseases in the Americas. According to the available studies, hantavirus is a viral infection that has been present for some time in the Region, but its clinical symptoms have only recently been described.

Since 1993, when an outbreak of hantavirus pulmonary syndrome was detected for the first time in the southwestern United States of America, several outbreaks or sporadic cases have been notified in Argentina, Brazil, Canada, Chile, Paraguay, and Uruguay. Outbreaks of this disease produce high case-fatality rates and have created widespread fear in the communities affected and great concern among the national health authorities.

In light of this situation, the 40th Directing Council of the Pan American Health Organization (September 1997) analyzed the problem and adopted a resolution (CD40.R14) calling on Member States to strengthen the mechanisms for collaboration among the countries and promote information, education, and communication geared toward the community to ensure the adoption of good environmental sanitation practices. The same resolution requests the Director to create a task force to issue recommendations on surveillance, diagnosis, treatment, and prevention of the infection. The task force was established and its members met in March 1998 to discuss and approve a draft of a technical guide to hantavirus in the Americas. It issued recommendations on epidemiological surveillance, diagnosis, treatment and prevention of hantavirus infection. In addition, PAHO supported technical cooperation among Member States and produced the following technical documents: (a) *Métodos para trampeo y muestreo de pequeños mamíferos para estudios virológicos*, and (b) *Technical Guide to Hantavirus in the Americas*. The Guide will be formally published and distributed prior to the 25th Pan American Sanitary Conference.

The present document provides an update of the epidemiological situation of hantavirus infection in the Americas, and reports on PAHO activities to date in this area. It also proposes to the Committee activities to be carried out by the Bureau. Some of those activities will represent a continuation of ongoing ones.

It has been determined from historical serological studies that hantavirus was circulating in the Region before clinical cases were detected, which means that cases are likely to appear in other areas where the virus exists. In view of this, it is necessary to improve surveillance, laboratory diagnosis, and mechanisms for the prevention and control of emerging diseases, especially hantavirus, as stipulated in the Regional Plan approved by the 38th Directing Council (September 1995).

1. Background

In 1995 the 38th Directing Council reviewed the strategies for prevention and control of new, emerging, and re-emerging diseases, elaborating the Regional Plan of Action, which has four goals: (1) strengthening regional surveillance networks for infectious diseases in the Americas; (2) establishing national and regional infrastructures for early warning of and rapid response to infectious disease threats through laboratory enhancement and multidisciplinary training programs; (3) promoting the further development of applied research in the areas of rapid diagnosis, epidemiology, and prevention; and (4) strengthening the regional capacity for effective implementation of prevention and control strategies. Hantavirus pulmonary syndrome, just identified in 1993, is considered to be a new emerging disease.

The 40th Directing Council (September 1997) adopted a resolution (CD40.R14) on hantavirus, requesting the Member States to intensify surveillance measures for the detection of hantavirus pulmonary syndrome; strengthen the capacity to establish collaboration agreements and mechanisms among the countries for developing a diagnostic laboratory network for this pathology; promote multidisciplinary intersectoral research on the ecology of the infection, with a view to defining prevention measures appropriate to the epidemiological situation; and promote, through information, education, and communication geared to all levels of the community, the adoption of good environmental sanitation practices. That same resolution requested the Director of PAHO to create, in the short term, a task force to issue recommendations on hantavirus infection/disease with respect to epidemiological surveillance, diagnosis, treatment, and prevention; to promote and support horizontal cooperation between Member States; and to prepare a report on this topic for the 25th Pan American Sanitary Conference.

In 1993 an epidemic outbreak of a disease heretofore unknown in the Region occurred in the Four Corners area of the southwestern United States. Due to its pulmonary manifestations and the fact that it was caused by a hantavirus, the disease was called hantavirus pulmonary syndrome (HPS). It was determined that the epidemic had been caused by a new hantavirus, which was called the Sin Nombre virus after the valley in which the disease first occurred. Since then, as of July 1997, a total of 173 cases have been notified in 28 states, including 20 cases diagnosed prior to 1991. In Latin America, cases of hantavirus infection have surfaced in Argentina, Brazil, Chile, Paraguay, and Uruguay. These epidemics are described under Section 2 of this document.

Hantavirus pulmonary syndrome (HPS) is an acute, serious, zoonotic viral disease characterized by fever, myalgia, and gastrointestinal symptoms. Some patients also present with acute respiratory failure, hypotension, and cardiogenic shock. The case-fatality rate ranges from 35% to 60% in the countries of the Hemisphere.

Several wild rodents appear to be the reservoir for hantavirus. In the United States, the predominant species are the *Peromyscus* mouse and the *Sigmodon hispidus* rat. In Argentina the presence of hantavirus infection has been determined both serologically and virologically in *Oligoryzomys flavescens*, *Oligoryzomys longicaudatus*, *Akodon azarae*, and *Bolomys obscurus*. In Paraguay *Calomys laucha* has been implicated as the reservoir.

It is presumed that most people are infected by inhaling aerosols of the dry or fresh remains of feces, urine, or saliva from infected rodents or by direct contact with the excretions. It also is possible to contract the infection from bites. During an epidemic outbreak in Argentina in 1996, there were indications of person-to-person transmission; however, to date it has not been possible to establish the precise mode of transmission in that outbreak.

The available information seems to indicate that there is a complex of hantaviruses that cause HPS. For example, in the United States, several species of hantavirus have been associated with the pulmonary syndrome: Sin Nombre, Bayon, Black Creek Canal, New York; however, the vast majority of infections are attributed to the Sin Nombre virus. Moreover, differences have been identified in the genetic structure of the hantaviruses isolated from HPS cases in Argentina (Andes, Lechiguana, Pergamino), Brazil (Juquitiba), and Paraguay (Laguna Negra).

There is no specific treatment for HPS. Patients should be treated in intensive care units, with special attention to lung function; treatment should involve maintenance of internal equilibrium with avoidance of overhydration, which can lead to pulmonary edema. The differential diagnosis should consider plague in areas endemic for that disease. A careful clinical examination together with laboratory tests should also be conducted in order to confirm the etiologic agent.

Control measures consist of reducing contact with rodents through domestic hygiene, impeding access by rodents to living areas, clearing of areas around dwellings, and rodent control with the careful use of rodenticides and/or other methods. Given the possibility of person-to-person transmission, it is recommended that universal biosafety measures be adopted during the treatment of suspected or confirmed cases.

2. Epidemiological Situation

Because specific diagnostic methods did not become available until 1993, only Argentina, Canada, and the United States have made retrospective diagnoses of clinical cases of unknown etiology or of clinical cases attributable to another etiology with serum samples available to make the retrospective diagnosis. In Paraguay, in contrast, symptomatic and serological clinical cases were reported during an outbreak in 1995. In Argentina, Bolivia, and several other countries positive serology for hantavirus infections

were detected as early as 1985 in specimens collected during serological surveys to detect *T. cruzi* infection. A 3.1% prevalence was found (20/542) (see figure). Some retrospective studies showed that between 1983 and 1991, 60 clinical cases of respiratory distress consistent with HPS but lacking laboratory confirmation had occurred. Of 32 suspected cases of HPS, 9 cases of leptospirosis were confirmed.

Individuals Studied and Those with Positive Hantavirus Antibodies, 1985



Source: Weissenbacher MC, Cura E, Segura EL, Hortal M, Luc u Baek, Ypmg Kyu Chu, Ho Wang Lee. Serological Evidence of Human Hantavirus Infection in Argentina, Bolivia and Uruguay. *Medicina* (Buenos Aires) 1996;56:17-22

Retrospective studies have pointed to similar situations in Canada and the United States. Likewise, in Brazil a 7% prevalence (35/500) of hantavirus antibodies was observed in sera taken from several populations in the Amazon region in the 1970s (Pinheiro F, unpublished data); subsequent studies detected hantavirus antibodies in various human and mouse populations. More recently (1997), studies conducted by the Adolfo Lutz Institute found a 4.1% (2/48) prevalence of the Sin Nombre virus in the State of São Paulo. In addition, among patients in São Paulo with suspected leptospirosis but negative for that disease, a prevalence of 1.6% (6/358) was observed in 1995; in Paraná, the figure was 5.1% (7/136) in 1997.

To date, 432 cases of hantavirus pulmonary syndrome (Table 1) have been notified in the Region. All of this indicates that hantavirus was circulating in the Americas prior to its recognition by professionals in the United States in 1993.

Table 1. Cumulative Reported and Confirmed Cases of Hantavirus Pulmonary Syndrome in the Region of the Americas, 31 March 1998

Country	Number of Cases
Argentina	142
Brazil	6
Canada	25
Chile	44
Paraguay	34
United States	179
Uruguay	2

Source: Departments or ministries of health of the above countries

In Argentina the first two cases were retrospectively diagnosed clinically and serologically in Salta Province in 1991. From 1991 to 1997, a cumulative total of 48 cases were reported in Salta; 24 in Río Negro Province; 17 in Buenos Aires; 12 in Chubut; 5 in Santa Fe; 2 in the Federal Capital, and 1 in Neuquén.

In Brazil the first 3 cases were reported in 1993 in the State of São Paulo; 1 case was reported in Matto Grosso in 1995 and 2 new cases in São Paulo in 1996.

In Canada the first case occurred in 1989, followed by 1 in 1990, 1 in 1992, 8 in 1994, and 3 in 1995 and 1997, respectively.

To date, 44 cases in three regions have been reported in Chile, where the first case was diagnosed in 1995.

In Paraguay the first 24 cases were diagnosed in 1995 in the El Chaco region (Department of Boquerón, cities of Filadelfia and Loma Plata). In that same region 7 cases were reported in 1996 and 3 in 1997. Judging from the characteristics of the research conducted, the 1995 cases represent the cumulative prevalence for that year and not the annual incidence.

In the United States, the first case was identified retrospectively in Utah. From 1975 to 1990, a total of 19 cases occurred in California, Colorado, Idaho, Kansas, North Dakota, South Dakota, New Mexico, Washington, and West Virginia. Table 2 summarizes all cases of hantavirus infection in the United States since 1991.

In Uruguay, the first two cases were diagnosed in 1997 in the departments (provinces) of Canelones and Rocha.

Table 2. Notified Cases of Hantavirus Infection in the United States of America, by State, 1991-1997*

State	Number of Cases	State	Number of Cases
Arizona	22	New York	1
California	13	North Carolina	1
Colorado	10	North Dakota	2
Florida	1	Oklahoma	1
Idaho	7	Oregon	5
Illinois	1	Rhode Island	1
Indiana	1	South Dakota	4
Iowa	1	Texas	10
Kansas	6	Utah	5
Louisiana	1	Virginia	1
Minnesota	2	Washington	13
Montana	5	Wisconsin	1
Nevada	7	Wyoming	1
New Mexico	28		

*Excludes 20 cases diagnosed before 1991

Source: U.S. Centers for Disease Control and Prevention

Table 3 presents the number of cases of hantavirus infection in the Americas and the number of political divisions affected.

The disease affects people of all ages and ethnic groups, as well as both sexes (although men predominate) and, usually, people over the age of 14. Most infections have occurred in rural settlements and houses or garages infested with infected rodents.

Table 4 presents the cumulative cases of hantavirus infection, by sex and age, by country in the Americas.

3. Previous Technical Cooperation

In 1991 the Organization began to provide technical cooperation to several countries to combat hantavirus based on how they were affected by the disease. Below is a list of the activities carried out:

- Technical assistance to Argentina (1995 and 1996), Brazil (1994), and Paraguay (1995). PAHO sponsored the visit of a virologist from Argentina to the United States to perform the genetic characterization of the hantavirus isolated in Argentina.

Table 3. Reported Cases of Hantavirus Infection in the Americas and Political Divisions Affected,^a by Country and Year, 1991-1997

Country		1991	1992	1993	1994	1995	1996	1997	Total	Case-Fatality
Argentina	Cases	2	5	10	13	10	42	29	111	44%
	Deaths	1		4	4	8	21	10	48	
	No. provinces	1	2	3	4	4	5	7	7	
Brazil	Cases			3		1	2		6	N/A
	Deaths			2		1	2		5	
	No. states			1		1			2	
Canada	Cases ^b		1		8	3	3	3	20	35%
	Deaths				3	1	2		7	
	No. provinces		1		3	3	3	3	3	
Chile	Cases					2	3	15	20	60%
	Deaths								12	
	No. regions					1	1	3	3	
Paraguay	Cases					24	7	3	34	38%
	Deaths					11	1	1	13	
	No. departments					1	1	1	1	
United States	Cases ^c	3	9	48	32	24	22	15	173	45.3%
	Deaths								78	
	No. states							28	28	
Uruguay	Cases							2	2	N/A
	Deaths							1	1	
	No. departments							2	2	

^a Number of political divisions affected; includes only cases for which breakdown is available.

^b Includes two cases that occurred prior to 1991, one of which resulted in death.

^c One case by place of residence; 1 case in 1959; period 1960-1990 = 19 cases.

N/A = not applicable

Source: Ministries of health, : U.S. Centers for Disease Control and Prevention, Canadian Laboratory Center for Disease Control

- Financial support for studies in Argentina to identify the reservoir of the virus and implement control measures.
- Organization of a subregional meeting in Argentina (April 1996), with the participation of professionals from that country and representatives of Bolivia, Brazil, Chile, Paraguay, United States, Uruguay, and Venezuela. The objectives of the meeting were to present an update on the epidemiological situation in the countries and determine the need for diagnostic laboratories, the production of reagents, virological and ecological research, and epidemiological surveillance.

Table 4. Cumulative Cases of Hantavirus Infection by Sex and Average Age, Region of the Americas, December 1997

Country	Cases					Age (years)	
	Total	Men		Women		Average	Range
		Number	%	Number	%		
Argentina	111	81	73.0	30	27.0	31	5 - 71
Brazil	6	6	6.0	-	-
Canada	20	15	75.0	5	25.0	42	16 - 62
Chile	20	15	75.0	5	25.0	26	1 - 41
Paraguay	34
United States	173	107	61.9	66	38.1	37	11 - 69
Uruguay	2	2	100.0	-	-	...	29 - 48

Source: Ministries of health, U.S. Centers for Disease Control and Prevention, S/CDC, Canadian Laboratory Center for Disease Control

- Sponsorship of a project for technical cooperation among countries for Argentina and Chile (1997-1998) in which the two nations would collaborate in areas such as diagnosis, surveillance, the study of rodents, and specific research.
- Publication of a guide on handling hantavirus reservoir species: *Métodos para trampeo y muestreo de pequeños mamíferos para estudios virológicos*. This was a joint publication by the United States (Centers for Disease Control and Prevention), Argentina, and Chile. The publication was distributed to all Spanish-speaking Member States through the PAHO/WHO Country Offices.
- A report on hantavirus in the Americas was prepared for use by the task force as a background paper in the elaboration of the *Technical Guide to Hantavirus in the Americas* (see below). This background document provided an update on hantavirus in the Americas, especially HPS, detailing its incidence, case descriptions, affected countries, regions, case-fatality rates, and diagnostic, prevention, and treatment methods.
- A technical guide to hantavirus in the Americas was prepared with the collaboration of experts from the countries affected by the epidemic. The guide includes virological aspects, reservoirs, human infection, treatment, diagnosis, prevention, control of transmission, and research needs.
- A task force of experts was established in response to Resolution CD40.R14 on hantavirus. The members of the task force met in March 1998 to discuss and approve the draft of the *Technical Guide to Hantavirus in the Americas*. The finalized Guide will be distributed to the Member States of the Executive

Committee of PAHO on 20 May 1998, and will be formally published and distributed prior to the Pan American Sanitary Conference.

4. Programmed Activities

In order to meet the countries' demands and assist them in fulfilling the mandate of the Directing Council regarding hantavirus infection, the PAHO Program on Communicable Diseases has programmed the following activities:

- (a) Promotion of regional production of the antigens necessary for the diagnosis of hantavirus infection (ongoing).
- (b) Support for technology transfer and training for the diagnosis and treatment of HPS (ongoing): funds allocated in 1998-1999, \$10,000 (plus regular staff time).
- (c) Promotion of specific research in the areas determined by the task force (ongoing): funds allocated in 1998-1999, \$15,000 (plus regular staff time).
- (d) Response to the demands of Member States for technical assistance: funds allocated in 1998-1999, \$15,000 (plus regular staff time).

With the above activities and resources, the Bureau expects to satisfy the needs and demands of Member States for technical cooperation, and to continue to support technical cooperation in order to strengthen the regional capacity for research, and for the diagnosis and treatment of hantavirus pulmonary syndrome.

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