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HANTAVIRUS

Since 1993, when an outbreak of Hantavirus pulmonary syndrome (HPS) was detected for the first time in the southwestern United States of America, several outbreaks or sporadic cases of HPS 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, which met in September 1997, adopted a resolution calling on the Member States to strengthen the mechanisms for collaboration among the countries and promote research, education, and communication geared toward the community to ensure the adoption of good environmental sanitation practices. That same resolution (CD40.R14) requests the Secretariat to create a task force to issue recommendations on surveillance, diagnosis, treatment, and prevention of the infection.

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 activities to carry out in the present year and 1998.

The Subcommittee on Planning and Programming is requested to make observations and issue its recommendations on the progress of the surveillance and detection program and on the proposal for developing a regional guide for the surveillance, prevention, and control of Hantavirus infection.

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EXECUTIVE SUMMARY

In 1995 the Pan American Health Organization adopted 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 circulating in the Region—an infection whose clinical symptoms have only recently been described.

Since 1993, when an outbreak of Hantavirus pulmonary syndrome (HPS) was detected for the first time in the southwestern United States of America, several outbreaks or sporadic cases of HPS 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, which met in September 1997, analyzed the problem and adopted a resolution calling on Member States to strengthen the mechanisms for collaboration among the countries and promote research, education, and communication geared toward the community to ensure the adoption of good environmental sanitation practices. That same resolution (CD40.R14) requests the Secretariat to create a task force to issue recommendations on surveillance, diagnosis, treatment, and prevention of the infection.

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 submits a proposal for activities to carry out in the present year and 1998.

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 positive for the infection. 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.

1. Background

In June 1995 the Pan American Health Organization presented strategies for the prevention and control of new, emerging, and re-emerging diseases, implementing 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, by definition, falls within this context.

The 40th Directing Council, which met in September 1997, adopted a resolution 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 (CD40.R14) requests the Director of PAHO to create, in the short term, a task force to issue recommendations on Hantavirus infectiondisease 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 (unnamed) virus. 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 further on (Epidemiological Situation).

Hantavirus pulmonary syndrome (HPS) is an acute, serious, zoonotic viral disease characterized by fever, myalgia, and gastrointestinal symptoms. Some patients also present 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 is 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 logicaudatus*, *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, since it 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 andor 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 have only been available since 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. Argentina, Bolivia, and several other countries have had a history of Hantavirus infections since 1985, confirmed through specimens collected during serological surveys to detect *T. cruzi* infection. A 3.1% prevalence was found (20542) (Figure 1). Some retrospective studies showed that between 1983 and 1991, 60 clinical cases of respiratory distress consistent with Hantavirus pulmonary syndrome (HPS) but lacking laboratory confirmation had occurred. Of 32 suspected cases of HPS, 9 cases of leptospirosis were confirmed.

Figure 1. Individuals Studied and Those with Positive Hantavirus Antibodies, 1985

Fuente: 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 (35500) 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, studies conducted by the Adolfo Lutz Institute found a 4.1% (248) prevalence of the Sin Nombre virus in the State of São Paulo in 1997. In addition, among patients in São Paulo with suspected leptospirosis but negative for that disease, a prevalence of 1.6% (6358) was observed in 1995; in Paraná, the figure was 5.1% (7136) in 1997.

To date, 366 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 U.S. professionals in 1993.

Table 1. Cumulative Reported and Confirmed Cases of Hantavirus Pulmonary Syndrome in the Region of the Americas, 3 October 1997

Country	Number of Cases
Argentina	111
Brazil	6
Chile	20
Canada	20
Paraguay	34
United States	173
Uruguay	2

Source: Ministers of Health

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 also reported in Matto Grosso in 1995 and 2 new cases in São Paulo in 1996.

In Canada the first case was reported in 1989, followed by 1 in 1990, 1 in 1992, 8 in 1994, and 3 in 1995 and 1997, respectively. To date, 20 cases in three regions have been reported in Chile, where the first case was diagnosed in 1995.

In the United States, the first case was identified retrospectively in Utah. From 1975 and 1990, a total of 19 cases were reported 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 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.

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: CDC

In Uruguay the first 2 cases were diagnosed in 1997 in the Departments of Canelones and Rocha.

Table 3 presents the number of cases of Hantavirus infection in Latin America and the number of political divisions affected (see also Figure 2).

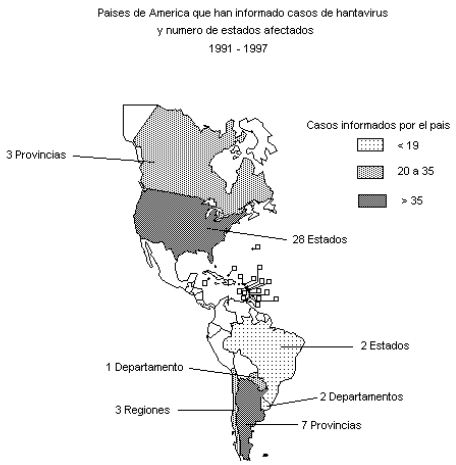
The disease affects people of all ages and ethnic groups, as well as both sexes (although men predominate) and, usually, people over the age of 14. Most infections have occurred in rural settlements and houses or garages infested with infected rodents. Table 4 presents the cumulative cases of Hantavirus infection, by sex and age, by country in the Americas.

Table 3. Reported Cases of Hantavirus Infection in Latin America and Political Divisions Affected,[a] by Country and Year, 1991-1997

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

[a] Number of political divisions affected, cumulative cases from the beginning.
[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.
NA = not applicable
Source: Ministries of Health, CDC, LCDC

Figure 2



Source: Ministries of Health, CDC, LCDC

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

	Cases					Age (years)	
		Men		Women			
Country	Total	Number	%	Number	%	Average	Range
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, CDC, LCDC

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.

- Financial support for studies in Argentina to identify the reservoir of 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, the United States, Uruguay, and Venezuela. The meeting's objectives 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.

- 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.

4. Programmed Activities

In order to meet the countries' demands and fulfill the mandate from the Directing Council, the Program on Communicable Diseases has programmed the following activities:

(a) Report on Hantavirus in the Americas: An update on Hantavirus in the Americas, especially Hantavirus pulmonary syndrome, detailing its incidence, case descriptions, affected countries, regions, case-fatality rates, and diagnostic, prevention, and treatment methods. Two consultants will be hired. End date: 15 November 1997.

Funds $ 4,000

(b) Preparation of a Guide to Hantavirus Reservoirs: This will be a joint publication by Argentina and Chile whose objective will be to identify and describe the reservoirs of the virus, determine their geographical distribution, and know their habits in order to adopt general control measures.

Funds $ 10,000

(c) Preparation of a Technical Guide to Hantavirus in the Americas: This technical guide will be prepared with the collaboration of six or seven experts from the countries affected by the epidemic. The content will include virological aspects, reservoirs, human infection, treatment, diagnosis, prevention, control of transmission, and research needs. A task force of experts has been created in response to Resolution CD40.R14 "Hantavirus." In early 1998 the members of the task force will be receiving the documents above for study and analysis, together with the existing information on the care and treatment of patients with respiratory distress andor hemorrhagic syndrome, in addition to the studies on possible person-to-person transmission. With this information distributed sufficiently in advance, the experts will meet in March 1998 to discuss and approve the content of the Guide to Hantavirus and to decide on future actions to combat and prevent Hantavirus infection. Date for distribution of the guide to the Member States of the Executive Committee of PAHO: 20 May 1998:

Funds (Guide) $ 10,000

Funds (meeting) $ 20,000

5. Conclusion

Regional Program activities to combat Hantavirus are:

(a) Preparation of a Guide to Hantavirus Reservoirs (November 1997)

(b) Preparation of a report on Hantavirus in the Americas (November 1997)

(c) Preparation of a Regional Guide to Hantavirus Prevention and Control. Meeting of the Task Force in March 1998 and availability of the Guide in May 1998.

(d) Promotion of regional production of the antigens necessary for the diagnosis of Hantavirus infection. (December 1997 to March 1998).

(e) Support for technology transfer and training for the diagnosis and treatment of HPS.

(f) Promotion of specific research in the areas determined by the Task Force.

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