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Regional Office of the World Health Organization

NATIONAL FORUM OF LEPTOSPIROSIS OF NICARAGUA AND INTERNATIONAL MEETING OF COUNTRIES THAT ARE FACING OUTBREAKS OF LEPTOSPIROSIS IN THE AMERICAS

Report of the Meetings

Ministry of Health of Nicaragua
Ministry of Agriculture of Nicaragua
University of León, Nicaragua
Pan American Health Organization

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1. Introduction

Leptospirosis is a zoonotic disease with epidemic potential that has a significant impact on health in various parts of the world, including the Americas. Human infection results from exposure to infected urine of mammal hosts, either directly or through contact with contaminated soil or water.

The change of weather patterns such as heavy rains and floods, increase the risk of occurrence of severe epidemics of leptospirosis. About ten million people are affected by natural disasters in the Region of the Americas annually with an average of one hundred events each year, with the majority of them being storms/tropical cyclones and floods; the subregions most affected are the Latin Caribbean and Central America. Several outbreaks of leptospirosis have been documented in the Region, some of them in Nicaragua, which acquired significant experience in the subject.

Within the framework of the alert and response to diseases of epidemic potential and the International Health Regulations, the Pan American Health Organization (PAHO) in conjunction with the Ministry of Health of Nicaragua, Ministry of Agriculture of Nicaragua and the University of Leon of Nicaragua, organized the “National Forum of Leptospirosis of Nicaragua” and the “International Meeting of countries that are facing outbreaks of Leptospirosis in the Americas” with the objective of sharing experiences.

In this framework, the Area of Health Surveillance and Disease Prevention and Control from PAHO, together with the PAHO/WHO Country Office in Nicaragua and the Nicaragua Ministry of Health conducted a study titled “Leptospirosis Outbreaks in Nicaragua: Identifying Critical Areas and Exploring Drivers for Evidence-Based Planning”, which allowed to demonstrate the methodological utilization of the country's epidemiological information to support decision-making based on evidence. These studies, in addition to the experiences of Nicaragua, were part of the National Forum, in which the participants of the International Meeting also attended.

PAHO objective is to support countries to predict, detect, prevent and respond to outbreaks of leptospirosis, thus reducing mortality and severe cases during outbreaks, as well as reducing the number of cases in risk areas, primarily related to the environment. Through a better understanding of the epidemiologic situation in the Americas and possible driving factors, exchanging experiences between countries that have been facing outbreaks, publishing the recommendations developed by the working groups coordinate by WHO, discussing with countries and possible partners actions for risk areas and risk groups in the Region and identifying potential intersectoral partners.

Leptospirosis is a disease that requires a multidisciplinary approach, both in understanding its driving factors as in the intersectoral actions in prevention and response. Therefore, professionals from the health and agriculture sectors, academia, research institutes and international organizations were invited to these meetings, allowing an exchange of experiences between different levels of practice and knowledge.

2. National Forum of Leptospirosis of Nicaragua

2.1 Objectives

Present the results of the study conducted jointly with the Ministry of Health of Nicaragua (MINSA) and PAHO, which sought to document the analysis of the known driving factors of Nicaragua to identify risk areas for leptospirosis outbreaks; as well as present the experiences of the country on this issue, some of which were presented in technical meetings held in 2010.

2.2 Background in Nicaragua

Leptospirosis is an endemic zoonosis in Nicaragua, as seen by the statistics of the disease in the country. In 1995 there were 2,252 cases with clinical features of pulmonary hemorrhagic fever without jaundice that caused 48 deaths. With the support of the Centers for Disease Control and Prevention (CDC), the leptospira strain causing the outbreak was isolated and a new serovar was found: *Australis Nicaragua*.

In 1998, after Hurricane Mitch, outbreaks were reported in the Local Integrated Health Care Systems (in Spanish, Sistemas Locales de Atención Integral en Salud – SILAIS), of Estelí and Chinandega. In 1999, outbreaks were reported in the SILAIS of Río San Juan and Matagalpa; and in the municipalities Morrito, San Carlos, El Almendro and Waslala. Clear evidence of high rodent infestation was reported in crop fields of rice and other staples. Until approximately 2000 and 2002, the diagnosis of leptospirosis was based on clinical management and the laboratory confirmation was made using the microscopic agglutination test (MAT), conducted by the National Diagnostic and Reference Center (in Spanish, Centro Nacional de Diagnóstico y Referencia – CNDR).

Starting in 2003 and 2004, 78 positive cases and no deaths were reported; an active surveillance of febrile cases was initiated using the enzyme-linked immunosorbent assay (ELISA) IgM, developed and standardized by Nicaragua and approved by the Royal Tropical Institute of the Netherlands, which is used until today.

For the years 2005 and 2006, resources were strengthened and the quality of laboratory diagnosis was improved using a comprehensive clinical form to manage case of dengue and leptospirosis. In 2005, 91 positive cases were reported and in 2006, 104 positive cases and no deaths were reported.

In 2006, the School of Veterinary Medicine carried out a study for the isolation of leptospira in domestic animals, in the municipalities of El Sauce and Achuapa, in the department of León, finding 76% of horses, 56% of cattle and 41% of dogs infected.

During 2007 three outbreaks were reported in different territories. The most significant one with the highest number of cases and deaths reported was in November, after Hurricane Felix, in the SILAIS of León and Chinandega, which began during epidemiological weeks 43 and 44.

During the years 2008 and 2009, cases were reported by active surveillance in the country, which continued to use the same type of reagents for screening and confirmatory diagnostic tests. Sampling from the School of Veterinary Medicine in 2009 reported infection in domestic animals.

In 2009, 136 cases of leptospirosis were reported; in addition, the Technical Cooperation among Countries (TCC) was implemented with an ecosystem approach. The following activities were performed:

- Urine sampling from different species of domestic animals (cattle, swine, equine, canine) for the isolation and identification of serovars, as well as the expansion of activities for animal medication in municipalities reporting positive cases. The study was expanded to 7 SILAIS, within 15 municipalities, and isolation of leptospira in domestic animals reported: canine (30.7%), equine (29.7%), swine (27.5%) and cattle (26.9%). In coordination with the SILAIS Chinandega and the School of Veterinary Medicine, treatment of domestic animals was conducted in communities that reported human cases of leptospirosis.

- Strengthening of training activities for municipal multidisciplinary teams in different aspects, among which stands out the "early community warning" on febrile syndromes

In 2010, cases were reported in all 17 SILAIS of Nicaragua and beginning on epidemiological week # 43, outbreaks were reported in 73% of municipalities, with a total of 587 positive cases. The SILAIS with the highest number of cases were: Leon with 32%, Carazo with 16.1%, Managua with 12.7% and Chinandega with 9.8%, cases were mostly from rural areas.

Besides having the ELISA IgM laboratory diagnosis test, Nicaragua utilizes, in municipal laboratories, the rapid latex agglutination test for presumptive diagnosis based on clinical and epidemiological data, allowing for early detection and adequate

management of outbreaks at primary care level. For both methods of diagnosis, the confirmatory laboratory test is the microscopic agglutination test, MAT, performed at the central level in the National Diagnostic and Reference Center.

2.3 Participants

About 50 participants attended the Forum, including members of the Intersectoral Committee of Leptospirosis of Nicaragua, which included representatives of the Ministry of Health, Ministry of Agriculture, University of León and the Pan American Health Organization. Professionals from Nicaragua's local and department level were present from areas with very high incidence of leptospirosis, as well as national authorities from different sectors, universities and civil organizations representatives.

Participants from the International Meeting that was held in the two consecutives days following the Forum also attended the meeting. Among them were representatives from the Ministries of Health and Agriculture of the five selected countries that have been facing outbreaks of leptospirosis in the Americas: Brazil, El Salvador, Honduras, Nicaragua and the Dominican Republic.

In addition, were present representatives from the World Health Organization (WHO), the Pan American Health Organization, the WHO Collaborating Center on Leptospirosis of the Oswaldo Cruz Foundation (Fiocruz/Brazil) and the University of Minnesota that is part of the Global Leptospirosis Environmental Action Network (GLEAN).

2.4 Program and Summary of Presentations

The program was planned so that it allowed experiences to be shared and discussions about the progress related to leptospirosis to take place among Nicaragua's experts who work in surveillance, prevention and response to outbreaks of leptospirosis at various national institutions, as well as promote interaction with international experts on this subject. The agenda included presentations of the country experiences and the results obtained from the study conducted to identify the driving factors for leptospirosis outbreaks in Nicaragua, carried out jointly by the Ministry of Health of Nicaragua and PAHO (Nicaragua and Washington DC). Followed by plenary discussions that examined selected issues and developed recommendations. The participation of representatives from different sectors of Nicaragua as well as representatives from other countries, international organizations and research institutions allowed very productive work to be

done on a subject that have not had this level of interaction in the Region of the Americas.

- **Welcoming remarks and opening of the National Forum of Leptospirosis**
  Dr. Carlos Sáenz Torres, Ministry of Health/Nicaragua

Dr. Saenz welcomed the participants of the National Forum and began by giving a brief history of the outbreaks that occurred in Nicaragua since 1995, indicating the importance of civic participation in the control of the last two outbreaks, especially in respect to the timely identification of cases. He considered the National Forum a great opportunity in improving the control strategies of the disease and reducing human and economic costs for the country. He welcomed everyone wishing that they accomplish the objectives of the National Forum.

- **Epidemiological situation of leptospirosis in Nicaragua and the Intersectoral Plan**
  Dr. Edmundo Sánchez, Ministry of Health /Nicaragua
  Presented by Mr. Eduardo Jiménez, Zoonosis National Expert, MINSA/Nicaragua

Mr. Jiménez made an extensive presentation of the epidemiological situation of leptospirosis in Nicaragua, mentioning important and determining aspects for the appearance of leptospirosis outbreaks: environmental and climatic factors, as well as the socioeconomic status of the population. He outlined the epidemiological history of the disease in Nicaragua, mentioning the years with the most significant outbreaks in the country: 1995, 2007 and 2010. It was during these years that the characterization and identification of serovars in the country were made, the laboratory technique was improved, the isolation of leptospires in domestic animals was performed and, multidisciplinary and intersectoral teams started to be formed to control outbreaks. His presentation also showed the geographical boundaries of the area with the highest number of cases, known as "The Corridor of Leptospira", which is formed by Managua, León, Chinandega and Estelí, and their corresponding municipalities.

Finally, he described the response actions for outbreaks in the country, organized into three stages that include rodent control, chemoprophylaxis, community involvement, training of health personnel and health communication.

- **Identification of the driving factors for leptospirosis outbreaks in Nicaragua**
  Dr. Cristina Schneider, Advisor, Human and Animal Health Interface, IHR/ Alert and Response and Epidemic Diseases, HSD/PAHO-Washington

In her presentation Dr. Schneider talked about the methodology of the studies conducted in Nicaragua last year, through which it was possible to identify the different driving factors for the emergence of leptospirosis outbreaks. She explained how the risk stratification for leptospirosis was performed, starting from the criterion of productive zones that presented cases and of zones that did not, which enabled a final classification into three zones: critical, endemic and silent. She showed the results obtained with the involvement of other regions of the country in addition to those selected for the study.

Also, she highlighted that the most important finding was the relationship of soil type with critical areas as one of the driving factors for outbreaks; it was found that a combination of Cambisol soil type, of volcanic lava origin, and Andosol soil type, of volcanic ash origin, are the ideal environment for the longer survival of the bacteria.

She finished by presenting the importance of environmental and climatic factors in the emergence of outbreaks and the lack of studies with other methodological designs that can complement the ecological study analysis further.

- **Identification of possible environmental driving factors for leptospirosis outbreaks in Nicaragua**
  Ms. Patricia Nájera, GIS Expert/PAHO-Washington
  Presented by Dr. Cristina Schneider

During this presentation Dr. Schneider explained the methodology used by Patricia Nájera and the challenges to standardize climate data in order to conduct the study. Mrs. Nájera constructed indicators by municipality, and in addition worked with slopes and floodplains. A more in-depth analysis is still needed in order to include other pertinent variables, for example, the altitude of the terrain, a variable that is still being studied. Databases of storms and floods were used, but it was difficult to carry out a good detailed analysis by municipality. The most relevant finding about soil types was regarding soil pH, since alkalinity allows the bacteria to live longer. She stressed the importance of using agricultural soil as a driving factor for the presence of leptospirosis, because they exhibit higher water absorption and it establishes the difference between the Pacific and the Atlantic in the country.

- **Socioeconomic factors and vulnerability to leptospirosis outbreaks in Nicaragua**
  Dr. Jorge Bacallao, Biostatistician from the University of Habana/Cuba
  Presented by Dr. Cristina Schneider

Dr. Schneider explained that for this part of the study only three regions were included: León, Chinandega and Managua, because they contributed 50% of the cases. These regions are located in the Pacific region of Nicaragua, sharing epidemiologic and geographic risk factors, and Managua, as the capital, has the highest population density. She presented the methodology employed to build a Vulnerability Index; rates were managed logarithmically to avoid asymmetries in the distribution and three groups of rates were defined: low, medium and high. She emphasized the importance of unmet basic needs, physical condition of households, extreme poverty and basic sanitation in homes. She mentioned that basic services were a protective factor. The results showed that municipalities with the highest rates of leptospirosis are those with the lower socioeconomic status, therefore reinforcing the distinction between environmental risk factors and vulnerability to risk given by socioeconomic factors. Lastly, she suggested using the Vulnerability Index in order to target available resources to specific areas, as well as utilizing this tool for other diseases.

- **Preliminary analysis of the Inter-institutional Plan of comprehensive approach to leptospirosis**
  Dr. Aida Soto, National Officer/PAHO-Nicaragua

During her presentation Dr. Soto showed the results of the inter-institutional committee for leptospirosis and explained that they are organized based on the biological cycle of the disease, emphasizing on critical areas such as Leon and Chinandega for being endemic areas and in strengthening the leadership of the Ministry of Health. A study was conducted to characterize the source of infection and the most important findings were: 1) 71% of the cases occurred in endemic localities, 2) an accurate characterization of serovars and positive isolation in reactor animals and non-reactors in order to proceed with medication, 3) the availability and quality of the water in the communities of Chinandega; where 53% of these localities uses wells as a source of water supply and 2% uses the river, unfortunately data for León were not available. Dr. Soto also explained the importance of trapping in order to characterize housing infestation by rodents. Using this method it was found that 51% of the zones were infested by rodents. Lastly, she described the disease behavior during the period of 2009-2011, with

reduction in the past year, and made recommendations to carry out the same characterizations in other regions of the country.

- **Family and Community health model of Nicaragua, Citizen Participation**
  Dr. Luisa Amanda Campos, National Dengue Expert of MINSA/Nicaragua

In her presentation Dr. Campos explained how the Family and Community Health Model emerged with the support of national health policies and the need for strong community participation in more effective strategies for health prevention and promotion. She described the components of the model and the importance of citizen participation as a determining factor for changes in the health of the population, in strengthening the community network, within communication strategies and provision of information, as well as in the analysis of the health status. Finally, she presented how the model works through the service network; thereby bring able to characterize the population by demographic and socioeconomic indicators, focus resources to identify unmet basic needs, improve sanitary conditions and identify risk factors, among others.

- **Epidemiological surveillance of febrile syndromes in Nicaragua**
  Dr. Matilde Román, Responsible for the National Epidemiological Surveillance, MINSA/Nicaragua

Dr. Román presented the clinical and epidemiological criteria used by the national surveillance unit to monitor febrile and icterohaemorragic syndromes. She explained in what criteria is based the classification of suspected cases and that the confirmation of cases is carried out by the national reference laboratory. She stated that cases are reported immediate through the epidemiological file designed for febrile syndromes and showed how the information flows from the community to the central level, with subsequent feedback to the health units that reported the cases, whether they were confirmed or not. Lastly, she concluded her presentation by stating that case monitoring is carried out by the national epidemiological surveillance unit, by elaborating daily, weekly and monthly analysis of the area and by creating a monthly newsletter through which information is shared with all health units and relevant authorities.

- **Advances in the diagnosis of leptospirosis in Nicaragua**
  Dr. Alberto Montoya, Director of Medical Parasitology and Zoonoses at the National Diagnostic and Reference Center (CNDR, in Spanish), MINSA/Nicaragua
  Presented by Dr. Aida Soto

During her presentation Dr. Soto explained the different serological diagnostic techniques in the country, such as the gold standard technique of microscopic agglutination test MAT, which was used by the laboratory for the diagnosis of leptospirosis with more documentation since the outbreak of Achuapa in 1995 in Nicaragua. She explained the advantages and disadvantages of the diagnostic test MAT. She then explained that for the year 2001 the enzyme immunoassay technique type ELISA was standardized for early diagnosis of leptospirosis in humans and showed the advantages and disadvantages of the technique, with qualities such as: low cost, quality diagnostic (high sensitivity and specificity), early diagnosis, fast results and simple technique, among others. And with the introduction of the Latex-Lepto Kit in 2002 it was possible to carry out timely diagnosis during the acute stage of the disease. She then referred to the standardization of the Latex-Lepto Kit, showed the results of the effectiveness of the test as well as the advantages among which stood out its usefulness in the screening of suspected patients in remote areas, its easy reading and assistance in the control of outbreaks, the disadvantages of the technique is that it presents reactions with IgG anti leptospire with very high titers. To conclude she showed the impact of technology in the diagnosis and monitoring of the disease through earlier detection of outbreaks and explained the flowchart for the serological diagnosis.

- **Animal Leptospirosis in Nicaragua**
  Dr. William Jirón, Director of the School of Veterinary Medicine, UNAN-León/Nicaragua

His presentation began with images of sources of infection and with reference to the results of a study conducted by the CDC in Atlanta on the life habits of the population and the coexistence with domestic and non-domestic animals as an important risk factor for contracting the disease. He then presented the techniques used by veterinary medicine such as: MAT, PCR and initiating the implementation of the Latex-Lepto technique in animals. After that he made a brief chronological outline of the experience of veterinary medicine in leptospirosis, showing the most significant seroprevalences for the year 2006 in animal species as the: equine, bovine, canine and porcine, the objective was to set the cut-off point for MAT technique in animals. In 2007 with the leptospirosis outbreak in the area of La Leona in León, it was determined the animal species involved

in the transmission, detecting bovine and porcine. In 2009 the first isolations were carried out, finding the same groups of serovars that were found in the laboratory tests. He showed the strains found and their classification of virulence and in the same year the MAT technique was installed in veterinary laboratories. During the period 2010-2011 the trapping method was conducted, with a high prevalence of leptospirosis in rodents, 54% of rodents captured in the urban area of León were infected. He ended with the importance of creating a monovalent vaccine for serovars suitable for each country.

⌑ Experience in controlling outbreaks of Leptospirosis in Leon

Dr. Gilberto Moreno Avellán, Medical Epidemiologist, SILAS-Leon/Nicaragua

Dr. Moreno started his presentation with a characterization of SILAIS-León by describing the geography of the region, the distribution of health care network in the department, the chronology of outbreaks that occurred in Leon (according to epidemiological variables), the symptoms of clinical cases, and the co-occurrence with dengue. He continued explaining that with the help other countries it was possible to carry out the diagnosis of the disease, because clinical symptoms were similar to dengue and the disease did not present the characteristic clinical manifestations of leptospirosis, for subsequent antibiotic therapy. He explained that leptospirosis has the same behavior every year, the majority of outbreaks start in week 41 and cases are reported until week 45, he also identified climate as one of the driving factors. He continued by referring to the methodology used in the study of seroprevalence in the municipalities of El Sauce and Achuapa in 2007 and described the results of the study, which showed a considerable increase in the seroprevalence since the outbreak of 1995, in addition it was observed that the seroprevalence was similar for both municipalities. Based on the results obtained a risk stratification for the SILAIS is done, also during his presentation he showed risk factors for acquiring the disease and reservoirs of leptospire in the affected communities. To conclude, he presented the actions taken to deal with outbreaks, including: organization of services, pest control, training of health personnel, intersectoral meetings, and support of community agents, among others. As well as the difficulties for intervention actions, due to, for example, the dispersion of the cases.

⌑ Experience in controlling outbreaks of Leptospirosis in Chinandega

Dr. Octavio Chávez, Medical Epidemiologist, SILAIS-Chinandega/Nicaragua

Dr. Chavez also started his presentation with a description of the geography and health care network of the region, he briefly explained the history of outbreaks in the

department, and reported that the pathological behavior of the disease is similar to the department of León, reporting cases in the same epidemiological weeks, between week 36 and 44. He made a brief chronological outline of the outbreaks in the SILAIS, stating that the first outbreak occurred in the community of El Ojoche in 2007 and explaining that this area presented all environmental conditions and all driving factors for the disease to occur. He continued to explain outbreaks according to epidemiological variables and described one the determining factors for the occurrence of outbreaks: climate events. He briefly explained the sampling study in animals in order to identify serovars circulating in the area, which were presented previously. He continued his presentation by describing risk factors to the onset of the disease, such as disorganized urbanization, socio-cultural factors, among others, which does not present a characteristic clinical manifestation. In conclusion he presented what are the intervention activities, which consists of: community organization, institutional and intersectoral organization, communication of preventive measures, training of community agents, community epidemiological surveillance, bacteriological sampling of drinking water, among others.

2.5 Recommendations and Conclusions

Recommendations

- Conduct household surveys in order to take into account other involved variables, such as access to piped water, amount of water received, household water management and education on water management.
- Characterization of the sources of infection in critical areas and endemic zones to determine the state of the carriers of the bacteria and shedding of organisms in their urine
- Strengthening and involvement of all veterinary schools.
- Include the veterinary doctor among the health team, so that he/she works within Nicaragua's health model
- Development of studies to determine the proportion of asymptomatic cases and cases outside outbreaks with the support of sentinel surveillance
- Studies to establish the relationship of reservoirs and infection sites.
- Studies to assess the impact of chemoprophylaxis in animals and humans

Conclusions

- Strengthen the laboratories of schools of veterinary medicine in order to carry out molecular differentiation of strains
- Standardize the rapid test for veterinary medicine
- Review of the Technical Standards for Leptospirosis related to the definition of early warning and the criteria for chemoprophylaxis in both humans and animals.
- Strengthen intersectoral collaboration to control aspects such as the mobilization of cattle herds

3. International Meeting of countries that are facing outbreaks of Leptospirosis in the Americas

3.1 Objectives

- Share with other countries that are also facing outbreaks of leptospirosis the methodology developed for the study of risk stratification and analysis of driving factors conducted in Nicaragua. It is expected that it will serve as basis for the identification of risk areas of leptospirosis in other countries in Latin America.
- Exchange practices between countries with experience in facing outbreaks of leptospirosis
- Discuss among participants and obtain recommendations on actions to predict, detect, prevent and respond to outbreaks of leptospirosis in risk areas and risk groups, similarly to what was developed for outbreaks during disaster situations by the Global Leptospirosis Environmental Action Network (GLEAN)
- Collect and share brief information about the epidemiological situation and plans of action of the participating countries, as well as materials and websites of common interest, using a standard format for all countries
- Share the information obtained from the Forum and the International Meeting with other countries through the creation of a leptospirosis webpage in the PAHO-Washington, D.C website (Spanish and English).

3.2 Background in the Americas

Leptospirosis is an endemic disease with epidemic potential throughout the Region of the Americas. Many outbreaks have been recorded in the region of the Americas in recent years; among those outbreaks is the outbreak in Nicaragua in 2007. During the 2007 outbreak, there was an average of more than 1 case per week, although after a flood there were up to 100 cases reported in a period of two weeks. Another outbreak is that of Guyana in 2005, which caused six deaths and more than 40 probable cases in the first three days of flooding; and Brazil in 2008, with 3,493 confirmed cases after heavy rains and floods in the state of Santa Catarina.

The Region of the Americas has presented the vast majority of alerts for leptospirosis in recent years. Reviewing the HealthMap database that utilizes different online sources for real-time surveillance of emerging public health threats, 568 alerts for leptospirosis were found between 2007 and 2011 worldwide. More than half of them were located in

the Americas, particularly in Brazil (140 alerts), Nicaragua (53), the Dominican Republic (28) and Honduras (19).

The burden of disease is still not precisely estimated due to, on one hand, the lack of surveillance and on the other, the frequently disease misdiagnosis, especially in vulnerable populations. Leptospirosis, in its initial stages, have symptoms and signs similar to a variety of diseases, most frequently dengue, malaria, hepatitis, among others, in addition, laboratory diagnosis is not readily available in several countries of the Region.

The magnitude of the problem in tropical and subtropical regions can be largely attributed to climatic and environmental conditions, as well as result of the probability of humans and animals coming into contact with *Leptospira* polluted environments due to, for example, local farming practices or poor housing with inadequate disposal of household waste, resulting in different sources of infection. Studies in the Region show that men acquire the disease more frequently than women, probably because of their higher occupational exposure as rice farmers, slaughterhouse workers, or other occupations.

Leptospirosis is a disease that still has a long way to go, most of the countries of the Americas report cases, but few of them have a reliable surveillance system for this disease. It is important to prepare countries to identify and respond to outbreaks, thus avoiding high mortality.

Similarly, better understanding the epidemiological situation of the countries where it is known that outbreaks are occurring and identifying the areas of greater risk and the driving factors, allow countries to be better prepared in the prevention and training of health services in case leptospirosis outbreaks occur.

Leptospirosis is a great example of the human-animal-ecosystem interface, as part of the "One Health" framework, where cooperation between sectors is essential.

3.3 Participants

About 30 participants attended the International Meeting, including representatives from the Ministries of Health and Agriculture of the five selected countries that have been facing outbreaks of leptospirosis in the Americas: Brazil, El Salvador, Honduras, Nicaragua and the Dominican Republic. In addition representatives were present from the World Health Organization, the Pan American Health Organization, the WHO Collaborating Center on Leptospirosis of the Oswaldo Cruz Foundation (Fiocruz/Brazil)

and the University of Minnesota that is part of the Global Leptospirosis Environmental Action Network (GLEAN).

Members of the Intersectoral Committee of Leptospirosis of Nicaragua, which included representatives of the Ministry of Health, Ministry of Agriculture, University of León and the Pan American Health Organization, also participated in the meeting. Additionally, were present professionals from Nicaragua's local and department level from areas with very high incidence of leptospirosis.

3.4 Program and Summary of the presentations

The program of the international meeting allowed representatives from the health and agricultural sector of the selected countries to present information about their epidemiological situation and action plans, as well as share their experiences. There was also an opportunity to discuss the methodologies presented during the National Forum about the study carried out jointly between the Ministry of Health of Nicaragua and PAHO and its possible applications in the regional programs.

The agenda also included presentations by the World Health Organization, the Pan American Foot-and-Mouth Disease Center (PANAFTOSA/PAHO), the Oswaldo Cruz Foundation (Fiocruz/Brazil) and the University of Minnesota, followed by plenary discussions.

The discussions among participants made it possible to exchange operational views about the same subject, for example, which would be the definition of an outbreak of leptospirosis for the country; in addition to elaborate recommendations for new studies to be conducted and potential partners on the subject to predict, detect, prevent, and respond to outbreaks of leptospirosis in risk areas and groups.

- **Welcoming remarks and opening of the International Meeting**
  Dr. Jorge Prosperi, PAHO/WHO Representative in Nicaragua

Dr. Prosperi began the meeting by thanking and congratulating the participants, principally the representatives of each country that attended the event; for their support and contribution of their experiences regarding leptospirosis. He noted that leptospirosis is not only a problem that is of interest for the Ministry of Health, it is rather an inter-institutional and multi-sectoral job, with evidence-based intervention that will allow for a better control of the disease.

⌑ Welcoming remarks and the opening of the International Meeting

Dr. Carlos Sáenz, MINSA/Nicaragua

Dr. Saenz welcomed everyone on behalf of the government of Nicaragua and the country's health minister, the representatives of PAHO/WHO Washington, WHO Geneva and PAHO/WHO Nicaragua, as well as the participants from Central America and the Caribbean. He gave a brief speech about the importance of the international meeting, its contribution in improving contingency plans and epidemiologic surveillance of each country. He also stated the importance of sharing experiences about outbreak prevention, detection and control actions and discussions about the methodology used in studies conducted in Nicaragua and its implementation for other member countries. He ended by wishing success in fulfilling the objectives proposed for the international meeting.

⌑ History of Animal Leptospirosis in the Dominican Republic

Dr. Deyanira Bidó Estrella, Technical Division of Epidemiological Surveillance, Ministry of Agriculture/Dominican Republic

Dr. Bidó began her presentation with a chronological history of animal leptospirosis in the Dominican Republic, she then discussed the achievements of indentifying serovars, (Pemona being the most frequent the sevorar) the installation of the Unit for Leptospira with support of CEPANZO and the discovery of Icterohaemorragic in rats and mice.

She showed the statistical data of regions that present animal Leptospira, pointing out: Sto. Domingo, San Pedro de Macorís, the Seybo, Hato Mayor and Monte Plata, subsequently she presented the percentage of cases per year and by province, and explained the stratification of risk areas. She emphasized that monitoring is being conducted in silent areas to investigate what is happening in those provinces. She stated that after the implementation of the International Health Regulations it was decided to strengthen areas such as surveillance and laboratory diagnosis. She states that because a plan for zoonotic disease surveillance does not exist, neither an established national control program nor surveillance, but the responsible authorities are working on this and have a list of priority zoonotic diseases and surveillance protocols for these diseases. To conclude, she presented what the actions at the local level that includes sampling and treatment.

- **Experiences in Human Leptospirosis in the Dominican Republic**
  Dr. Emilia Peña, General Directorate of Epidemiological Surveillance, Ministry of Health/Dominican Republic

During her presentation Dr. Peña referred to the history of leptospirosis in the country, explaining chronologically the experiences that included: the mandatory reporting of diseases, establishment of standards for monitoring and control, surveillance of febrile syndromes, the regulation of the SINAVE and the establishment of a rapid response team. She described the experience of the first outbreak of leptospirosis that occurred in 2007. The outbreak was due to climatic events with high fatality rates and the main transmission mechanism was contact with soil, water or vegetation (through wounds or lacerations in the skin) that were contaminated with urine of infected animals. She also explained that the strategy for controlling the outbreak included antibiotic therapy in high-risk areas. She showed the rates of leptospirosis cases per week, years and provinces. The map had risk stratification by provinces and her and her team conducted an analysis according to the epidemiological variables and presented contingency plans for outbreaks, because they do not have a plan or a national program to make a more effective control of the pathogenesis and serovars identified until now.

She explained the importance of ecosystem changes, variations and climate change, as well as demographic and economic factors as drivers that favor the transmission of leptospirosis. To conclude she described the experience of the last outbreak that occurred in the region called “El Salado" in 2009. She stated that the lack of piped water is a determinant factor for the spread of the disease and the serovars found in animals and humans.

- **Experience of Human Leptospirosis in the Republic of Honduras**
  Dr. Reina Teresa Velásquez, Head of the Zoonoses Control Program of the Ministry of Health/Honduras

Dr. Velasquez started her presentation by describing the epidemiological history of the disease with its first report in 1964 and its first outbreak in 1995, which presented cases with clinical manifestations similar to cases from Nicaragua for the same year. In 1998 Honduras conducted a prevalence study, which reported 29% prevalence in the northern and center of the country with Hepatorenal clinical characteristics. Because of these events, in 1999 weekly disease alert report was established. She showed the behavior of the disease for years, weeks, age and by departments. She then presented risk stratification for each department. There are 18 serogroups found in humans and she showed the distribution of the serogroups by department. To conclude her

presentation she described how the program for zoonoses works. She said that other actors intervene in the contingency plans. She also explained that the activities of the national plan, the procedures followed for the confirmation of cases, the actions taken in an outbreak situation and the needs in order to prevent, detect and respond to outbreaks of leptospirosis.

- **Experience of Animal Leptospirosis in the Republic of Honduras**
  Dr. Carlos Espinoza Rodezno, Head of the Department of Epidemiology, Ministry of Agriculture/Honduras

During his presentation, Dr. Espinoza explained the limitations in performing an adequate epidemiological surveillance, the linkages and determinants of risk for acquiring the disease, the epidemiological history of leptospirosis in veterinary medicine, as well as the prevalence and main serovars detected in blood of cattle and swine. He described the results of studies conducted in two areas of the country, explained how passive leptospirosis surveillance is performed in animals, and that active surveillance is resuming in slaughterhouses. He showed the geographical distribution of serovars and the risky consequence of smuggling in borders' "blind sports" in the north, west and south. He explained the preventive and control measures for leptospirosis in livestock and the surveillance of domestic animals, described the activities in outbreaks situations and some relevant cases. To conclude he presented the major needs to detect outbreaks and the importance of implementing the International Health Regulations to strengthen intersectoral and interagency actions.

- **Experience of Leptospirosis in the Republic of El Salvador**
  Dr. Eduardo Suárez, Directorate of Infectious Diseases, Ministry of Health/El Salvador

In his presentation Dr. Suarez shared the country's experiences, the epidemiological history of this disease of mandatory reporting. He also discussed how cases occur in accordance with the rainy season and likewise with factors such as disorganized urbanization. Due to deaths the need to develop clinical guidelines for diagnosis was recognized. He showed the serovars detected from 2004 to 2011 in the country, shared data from confirmed cases and serovars isolated by department, municipality, sex, age and year with a strong relationship with flooded areas and places with difficulties for water drainage. He noted that the effects not only affect health but also the country's economy. He explained the tables with percentages of cases by department and the risk stratification. He said that the country has a national plan and a program for

surveillance, control and prevention of the disease, in which other institutions are involved. He mentioned the main activities of the plan and the program and the authorities' procedures against an outbreak. Specifically, the plan includes a good characterization of the outbreak, study of potential risk factors, among others; he also described the protocol that is followed for the confirmation of cases and gave a brief description of the organization of multisectoral teams involved in the control of outbreaks. To conclude, he referred to the needs for the control of outbreaks, pointing as an important point the training of recently graduated health professionals, included since undergraduate.

- **Experience of Leptospirosis in the Republic of Brazil**
  Dr. Eduardo Pacheco de Caldas, Zoonoses Surveillance Department, Secretariat of Health Surveillance/Brazil

In his presentation Dr. Pacheco described: how the health system is structured in Brazil in order to show where the zoonosis program is located; the timeline of the epidemiological background; the information system and the design of the reporting form of mandatory notifiable diseases. He highlighted the importance of the year in which the mandatory reporting of communicable diseases (including leptospirosis) was established. He also mentioned the importance of the year when the certification of information systems was conducted. All reportable diseases are collected from the primary care unit to a national database. He then explained the prioritization of departments based on classification by frequency of cases, with the objective of reducing mortality and strengthening surveillance, identifying areas of risk, establishing control methodologies for leptospirosis reservoirs and training medical personnel. He presented the registered cases in a period of 5 years in the country, fatality rates, total number of cases by department; and stressed the effect of population density on rates in some cities. In the epidemiology of the urban and rural areas, the climate and environment are determinant factors. On the other hand, the culture, occupation and sanitary conditions are risk factors, with an animal reservoir as the source of infection. To conclude, he presented the risk stratification of the country and explained that there is no national plan but a surveillance system and a program with control, prevention and detection activities.

Experience in Animal Leptospirosis in the Republic of Nicaragua

Dr. William Jirón, Director of the School of Veterinary Medicine, UNAN-León/Nicaragua

During his presentation Dr. Jiron discussed the factors for the transmission of the disease: behavioral and climatic factors, exposure to rodents during the rainy season and how socio-demographic factors are related to occupation. He presented data about: animal reservoirs by department and by species in the last year; the coordination to perform the same procedures of human medicine in veterinary medicine, such as the latex technique; the isolates of animal reservoirs from the areas where cases occur. Dr. Jiron described the actions carried out for prevention and gave as an example education and early diagnosis of animals to trigger interinstitutional working teams in the control of focus. To conclude he emphasized strengthening the implementation of health standards for transporting animals to other regions and abroad.

Global Leptospirosis Environmental Action Network

Dr. Eric Bertherat, Pandemic and Epidemic Diseases, WHO/Geneva

In his presentation Dr. Bertherat referred to the health perspective on leptospirosis, mentioning important and unique aspects of the disease. He explained that to estimate the magnitude of the problem of leptospirosis, WHO, in 2006, appointed a committee to evaluate the global severity of the disease, which resulted in alarming numbers and found that outbreaks occur after climatic disasters. He presented, as an example, what happened in the Philippines in 2009, after weather events the incidence of leptospirosis cases had a considerable increase. Given this situation, guidelines for controlling outbreaks were evaluated and many questions and concerns were found about the actions against outbreaks. He highlighted as an important point the revision of antibioprophylaxis measures, taking into account risk groups, such as pregnant women, at the time of treatment protocols. He explained what GLEAN is, with whom it is composed, its function, its objectives and its priorities. Furthermore, he stated that since GLEAN's priorities are outbreaks that have occurred after climatic disasters, the outcome of all this work is a plan of action for five years with 4 levels of intervention. He highlighted the importance of definition and differentiation of the seasonal behavior of the disease compared to outbreaks, for this reason he recommended that defining an epidemiological threshold would greatly help optimize heath resources. Finally, he closed by giving his recommendations for the control of outbreaks and his conclusions about the extent of the disease and the work that is still to be done.

- **Leptospirosis in the LAC Region-Systematic Review**
  Dr. Martha María Pereira, WHO Collaborating Center on Leptospirosis, Fiocruz/Rio de Janeiro-Brazil

During her presentation Dr. Pereira presented the results of the systematic review and explained the importance of improving knowledge about leptospirosis, for this reason an agenda and protocol have already been developed, in order to establish the knowledge gaps regarding the clinical and epidemiological management of leptospirosis. During epidemic outbreaks and emergency situations, the main challenges faced are: misdiagnosis in the first clinical presentation; shortage of simple rapid tests for laboratorial confirmation and concomitant outbreaks of other acute febrile illnesses that are confused with Leptospirosis. Priority should be given to the most important knowledge gaps such as: diagnostics, therapeutic alternatives and vaccines. In addition, information about the serious forms of the disease are also needed in epidemiological aspects, to make more accurate clinical differentiation, case definition and differentiation of the pulmonary form. To finalize she presented a summary of the major knowledge gaps about leptospirosis in the region.

- **Eco-epidemiology of Leptospirosis**
  Dr. Claudia Muñoz Zanzi, Assistant Professor of Epidemiology at University of Minnesota/GLEAN-WHO

During her presentation Dr. Munoz gave an extensive explanation about what eco-epidemiology consists of and the several factors that influence it (taking into account during the analysis that they are dynamic): the variety of pathogens, the factors that affect the prevalence in reservoirs, as well as risk behaviors, risk perception and cultural factors. She continued explaining the methodology used in the study conducted in Chile, with the objective of understanding the dynamic of transmission between species and the probable routes of transmission. She concluded with a brief explanation of the preliminary results of the study.

- **Laboratory Network for Zoonotic Diseases - Articulating Diagnostic Laboratories in Public and Animal Health**
  Dr. Alfonso Clavijo, Diagnostic Advisor, PANAFTOSA/PAHO

In his presentation, Dr. Clavijo discussed the disadvantages of the isolated work of animal and human health laboratories, such as low quality in diagnosis and duplication of efforts, which is a justification for including the human-animal interface. He

continued discussing the basic principles of a network of laboratories that includes: quality standards, competency of laboratory personnel, standardized protocols and teams, adequate bio-security, timely reporting (surveillance), and capacity evaluation through diagnostic scenarios. He talked about the importance of defining the purposes of the network to strengthen laboratory systems and surveillance, as well as to assure and maintain quality. Subsequently, he discussed the steps to create a network of public and animal health laboratories and explained that they would have to define the participants, as well as the short-term and long-term objectives of the laboratories in the network. Quality control should be one of the basic factors that contribute to the future of the network, which includes multiple actions such as: standardization of the reagents, education and training of personnel. He finalized by mentioning the challenges in the establishment of these laboratory networks, stating that one determinant factor is the economic financing of these actions.

- **Application of the methodology of Risk Stratification and Identification of Driving Factors of Leptospirosis Outbreaks**
  Dr. Cristina Schneider, Advisor, Human and Animal Health Interface, IHR/ Alert and Response and Epidemic Diseases, HSD/PAHO-Washington

Dr. Schneider briefly explained the public health importance of leptospirosis as the cause of infections, the implications it has for health systems in Latin America and the relationship to natural events, climate, and geography in the Central American region with the presence of disease outbreaks. She also explained the importance of taking into account other variables such as socio economic factors. In addition, she described how the methodology can be implemented in participating countries and made suggestions for the revision of contingency plans for leptospirosis outbreaks and surveillance plans. She stressed the need to identify the capabilities that we have and to determine what we need in order to strengthen, improve, acquire or establish surveillance for leptospirosis. She mentioned the importance of epidemiological data collection for the disease, as well as the evaluation of the impact of the implemented strategies for the control of outbreaks by participating countries. Lastly, she stated that summaries of the WHO guides for important public health events have been made, in order to facilitate the task of the Rapid Response Teams and explained how the vulnerability index can be a tool used to focus and optimize resources in risk areas previously defined by health surveillance teams.

⌑ **Using Environmental Information to Identify Risk Areas**
Ms. Patricia Nájera, GIS Expert/PAHO-Washington
Presented by Dr. Cristina Schneider

Dr. Schneider showed the different resources and internet tools for mapping areas of environmental risk, through the different environmental and climatic variables such as: types of soil, rainfall, topography, slope, hurricane path, earthquakes, among others. Finally, she provided the links to explore these web pages and stated that in the near future, these tools will be used for the analysis of public health events.

3.5 Recommendations and Conclusions

Recommendations

- Develop studies in order to better understand the kinetics of the disease both in the period of low incidence (preparatory phase) and the period of high incidence or seasonal increase (response phase).
- Analytical studies on the pathogenesis and immunity of the disease for the development of alternative therapies and creation of vaccines.
- Establish the algorithm for the rapid test for the diagnosis of leptospirosis.
- Identify and support technically a reference laboratory for Central America for the diagnosis of leptospirosis.
- Create a reliable indicator for epidemiological surveillance in order to evaluate silent and endemic areas (suggestion: proportion of ELISA tests for leptospirosis in febrile patients).
- Conduct further ecological analysis with more environmental variables in the country

Conclusions

- Proposal of multicenter studies in pilot sites for risk factors and to evaluate surveillance systems, understanding the natural history of the disease
- Establish a working group to design a preliminary proposal for eco-epidemiological studies and operational research through pilot or sentinel sites.
- In order to evaluate strategies on population dynamics of rodents, the Brazilian Ministry of Health offers technical assistance in methodological aspects for the implementation of eco-epidemiological studies.

- With the support and technical assistance of the WHO Collaborating Center (FIOCRUZ) the identification of a Subregional laboratory in coordination with PAHO was carried out.

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Annex 2. Agenda

First Day – National Forum:

Presentation of the results of the study conducted to identify driving factors for outbreaks of leptospirosis in Nicaragua and country experiences

Tuesday, August 14, 2012, from 9:00am to 5:00pm	
Opening Session 9:00- 9:15 am Dr. Carlos Sáenz Torres	
9:15-9:40am	Epidemiological situation of leptospirosis in Nicaragua and the Intersectoral Plan *Dr. Edmundo Sánchez, DPE, MINSA/ Nicaragua*
9:40-10:05am	Identification of the driving factors for leptospirosis outbreaks in Nicaragua *Dr. Cristina Schneider, PAHO/Washington*
10:05-10:30am	Identification of possible environmental driving factors for leptospirosis outbreaks in Nicaragua *Ms. Patricia Nájera, PAHO/Washington*
10:30-11:00am	*Coffee Break*
11:00-11:15am	*Questions and answers to the first block of presentations* *Moderator Mr. Eduardo Jiménez MINSA*
11:15-11:40am	Socioeconomic factors and vulnerability to leptospirosis outbreaks in Nicaragua *Dr. Jorge Bacallao, University of Habana/Cuba*
11:40-12:05pm	Preliminary analysis of the Inter-institutional Plan of comprehensive approach to leptospirosis *Dr. Aida Soto, PAHO/Nicaragua*
12:05-12:30pm	Family and community health model of Nicaragua, Citizen Participation *Dr. Luisa Amanda Campos, MINSA/Nicaragua*
12:30-1:30pm	*Lunch*
1:30-1:45pm	*Questions and answers to the second block of presentations* *Moderator Mr. Eduardo Jiménez MINSA*
1:45-2:10pm	Epidemiological surveillance of febrile syndromes in Nicaragua *Dr. Matilde Román MINSA/ Nicaragua*
2:10-2:35pm	Progress of the diagnosis of leptospirosis in Nicaragua *Dr. Alberto Montoya, MINSA/ Nicaragua*
2:35-3:00pm	Animal Leptospirosis in Nicaragua *Dr. William Jirón, School of Veterinary Medicine, UNAN-León*
3:00-3:25pm	Experience in controlling outbreaks of Leptospirosis in León *Dr. Gilberto Moreno Avellán, SILAIS- León/Nicaragua*
3:25-3:50pm	Experience in controlling outbreaks of Leptospirosis in Chinandega *Dr. Octavio Chávez, SILAIS-Chinandega/Nicaragua*
3:50-5:00pm	Discussion, conclusions and recommendations *Moderator Mr. Eduardo Jiménez MINSA*

Second and Third Day – International Meeting:

Presentation of the epidemiological situation and plans of action of the countries, as well as methodologies and group work

Wednesday, August 15, 2010, from 9:00 am to 5:00 pm	
9:00 - 9:15am	Event Inauguration *Dr. Jorge Prosperi and Dr. Carlos Saenz*
9:15 - 9:30am	Presentation of the representatives of the participating countries
9:30 - 10:00am	Dominican Republic *Dr. Deyanira Estrella, Ministry of Agriculture* Dominican Republic *Dra. Emilia Peña, Ministry of Health*
10:00–10:30am	Honduras *Dr. Reina Teresa Velásquez, Ministry of Health* Honduras *Dr. Carlos Espinoza Rodezno, Ministry of Agriculture*
10:30 -10:45am	*Coffee Break*
10:45 -11:00am	Questions and answers to the first block of presentations *Moderator - Dr. Aída Soto, PAHO/Nicaragua*
11:00 -11:30am	El Salvador *Dr. Eduardo Suárez, Ministry of Health*
11:30 -12:00pm	Brazil *Dr. Eduardo Pacheco de Caldas, Ministry of Health*
12:00 -1:00pm	*Lunch*
1:00–1:30pm	Nicaragua *Dr. William Jirón, Ministry of Agriculture*
1:30 - 2:00pm	Discussion about leptospirosis outbreaks in selected countries *Moderator - Dr. Aída Soto, PAHO/Nicaragua*
2:00 - 2:30pm	Burden of disease and Global Leptospirosis Environmental Action Network (GLEAN) *Dr. Eric Bertherat, WHO/Geneva*
2:30 - 3:00pm	Leptospirosis in the LAC Region - Systematic Review *Dr. Martha Pereira, Fiocruz, MoH/Brazil*
3:00 – 3:30pm	Eco-epidemiology of Leptospirosis *Dr. Claudia Munõz-Zanzi, GLEAN/University of Minnesota*
3:30 – 4:00pm	Laboratory Network for Zoonotic Diseases *Dr. Alfonso Clavijo, PANAFTOSA/PAHO/Brazil*
4:00 – 5:00pm	Questions and answers to the third block of presentations *Moderator - Dr. Aída Soto, PAHO/Nicaragua*

Thursday, August 16, 2012, from 8:30 am to 3:00 pm	
8:30 – 9:00am	Application of the methodology of stratification of risk areas *Dr. Cristina Schneider, PAHO/Washington D.C. and* *Dr. Jorge Bacallao, University of Habana/Cuba*
9:00 – 9:30am	Using Environmental Information to Identify Risk Areas *Ms. Patricia Najera, PAHO/Washington, D.C.*
9:30am – 3:00pm	Plenary discussion Recommendations of the meeting

Questions for the discussion:

1. What would it be an operational definition for an outbreak of leptospirosis? Taking into consideration the seasonal increase of the disease
2. What kind of studies are recommended for the region on this topic?
3. How could we continue the cooperation to improve capacities in the prevention and response to outbreaks of leptospirosis? (Participating countries, WHO/PAHO and collaborators).

Annex 3. Abbreviations

CDC	Centers for Disease Control and Prevention, United States
CNDR	National Diagnostic and Reference Center (in Spanish, Centro Nacional de Diagnóstico y Referencia
ELISA	Enzyme-linked Immunosorbent Assay
Fiocruz	Oswaldo Cruz Foundation, Brazil
GIS	Geographic Information Systems
GLEAN	Global Leptospirosis Environmental Action Network
IgG	Immunoglobulin G
IgM	Immunoglobulin M
MAT	Microscopic Agglutination Test
MINSA	Ministry of Health of Nicaragua
PAHO	Pan American Health Organization
PANAFTOSA	Pan American Foot and Mouth Disease Center
SILAIS	Local System of Integrated Health Care, Nicaragua
UNAN	The National Autonomous University of Nicaragua (in Spanish, Universidad Nacional Autónoma de Nicaragua
WHO	World Health Organization

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