Epidemiological Alerts and Updates

Annual Report 2015

Pan American Health Organization

World Health Organization
REGIONAL OFFICE FOR THE Americas

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Acronyms

CDC   United States Centers for Disease Control and Prevention

CHIKV   Chikungunya virus

IMS   Integrated Management Strategy

EW   Epidemiological week

ILI   Influenza-like illness

IHR   International Health Regulations

IVM   Integrated vector management

NFP   National Focal Point

PPE   Personal protection equipment

SARI   Severe acute respiratory illness

ZIKV   Zika virus

Cholera

Situation Summary

From the beginning of 2015 up to epidemiological week (EW) 48 of 2015, a total of 30,654 cholera cases had been recorded in three countries in the Americas: Cuba, 65; the Dominican Republic, 509, and Haiti, 30,080. Haiti reported 98% of the total number of cases in the Region. In addition, the Canada International Health Regulations (IHR) National Focal Point (NFP) reported one case case of cholera in a person with history of travel to Cuba. Mexico, which in recent years had reported cases, reported zero cases for 2015.

Meanwhile, for EW 33, Brazil reported the isolation of toxigenic *Vibrio cholerae* serogroup O1, serotype Ogawa in samples from a wastewater treatment plant in the Federal District.[1] The finding was confirmed by the National Reference Laboratory for the Diagnosis of Enteric Bacterial Infections of the Oswaldo Cruz Foundation (FIOCRUZ) in Rio de Janeiro.

Cuba

The cholera case reported by the Canada IHR NFP was the only one registered in Cuba between January and August 2015. That case generated an epidemiological investigation by Cuban public health authorities to determine the source of infection, and implement appropriate public health measures. No additional cases were reported in the country during those months.

On 29 August 2015, national health authorities reported that isolated cases of cholera had been confirmed in Holguin province in recent weeks and that major efforts were under way to control infection. Later, by 9 October 2015, it was reported that by EW 39, a total of 23 cases of cholera, *Vibrio cholerae* O1, serotype Ogawa, had been confirmed. Those cases were related to the drought affecting Holguin province, which caused the consumption of unsafe water. Cuban authorities intensified prevention and control activities in response to the situation. By 19 December 2015, a total of 65 cases of cholera had been confirmed. Prevention and control activities were ongoing.

Dominican Republic

In the Dominican Republic, between EWs 1 and 53 of 2014, 597 suspected cases of cholera were reported, including 10 deaths. When compared to 2013, these numbers represent a 69.5% decrease in reported cases, and 76% decrease in the number of deaths. However, between EWs 1 and 10 of 2015, 185 suspected cases of cholera were reported, including 9 deaths. These numbers represent an almost two-fold increase in the number of cases reported for the same period of 2014. This situation was considered to be closely related to the cholera dynamics in Haiti during the same period. The largest proportion of cases in 2015 was reported in the National District and the provinces of Monseñor Nouel, Santiago, and Santo Domingo.

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[1] http://portalsaude.saude.gov.br/index.php/o-ministerio/principal/secretarias/svs/noticias-svs/19567-monitoramento-ambiental-do-vibrio-cholerae.

Between EWs 31 and 32, a cholera outbreak was reported in the municipality of Bonao, Monseñor Nouel province. An irrigation canal was identified as the main source related to that outbreak, as notified in the Dominican Republic Epidemiological Bulletin for EW 32 of 2015. Furthermore, starting on EW46, there was an increase in the number of cases that lasted through EW 48 (Figure 1).

Figure 1. Suspected cholera cases from 2014 to EW 48 of 2015, Dominican Republic
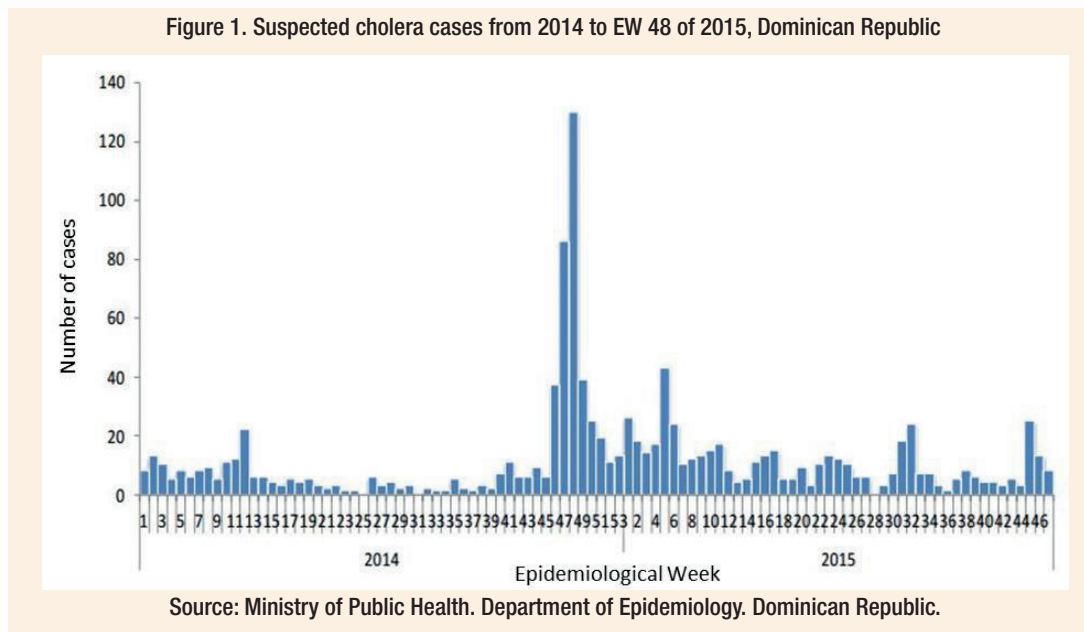
Source: Ministry of Public Health. Department of Epidemiology. Dominican Republic.

Haiti

2014

Between EWs 1 and 53 of 2014, 27,753 cases of cholera were reported in Haiti, with 296 deaths; these number represent a reduction of 53% and 50%, respectively, when compared to 2013.

While the overall number of cases registered in 2014 was well below the numbers recorded in previous years, between EWs 37 and 47 of 2014, there was an increase in the number of cases. In fact, between EW 1 and EW 36 of 2014, the weekly average of new cholera cases reported had been 251; that weekly average jumped to 918 new cases nationwide for EWs 37 to 47 of 2014. Four departments, Artibonite, Centre, Ouest and Nord, accounted for 90% of the cases reported in 2014; Ouest had the highest number of reported cases, i.e., 36% of the total. Between EWs 37 and 47, these four departments reported an average hospitalization rate of 70%. As of December of that year, the incidence rate and number of deaths from cholera decreased.

2015

Since the beginning of the cholera epidemic (October 2010) up to 12 November 2015, a total of 754,735 cases of cholera had been reported, including 9,068 deaths. The number of cases reported in 2015 exceeded the total number of cases registered in 2014. Actually, the number of weekly cases in 2015 was even higher than the number reported in 2012 (Figure 1). For example, from EW 1 to EW 7 of 2015, 7,225 new cholera cases were reported, 80% of which were hospitalized, and 86 deaths. Furthermore, as of EW 11, outbreak alerts were reported by the Haiti Ministry of Public Health and Population in 8 out of 10 departments in the country, indicating intense and widespread circulation of *Vibrio cholerae* at the community level.

As of EW 37 of 2015, a weekly average of around 600 new cholera cases and 5 deaths were reported. During EW 34 to 37 of 2015, the number of new cases remained stable, due to a decrease in the number reported in the department of Nord-Ouest, and a resurgence of cases in some communities, mainly in the department of Sud-Est.

The rapid and timely response to this situation led to a decrease in the number of cases in October and November of 2015 (Figure 2). The response was based on the reactivation of the Rapid Intervention Mobile Teams (EMIRA, per its acronym in French), and an awareness campaign addressed to the population throughout the country. Nonetheless, cholera transmission in Haiti remains endemic.

Figure 2. Number of cholera cases and case fatality rate in Haiti. January 2012 to 12 November 2015

Source: Ministry of Public Health and Population (MSPP). Epidemiology, Laboratory and Research Directorate (DELR). Report of the National Surveillance Network, Haiti.
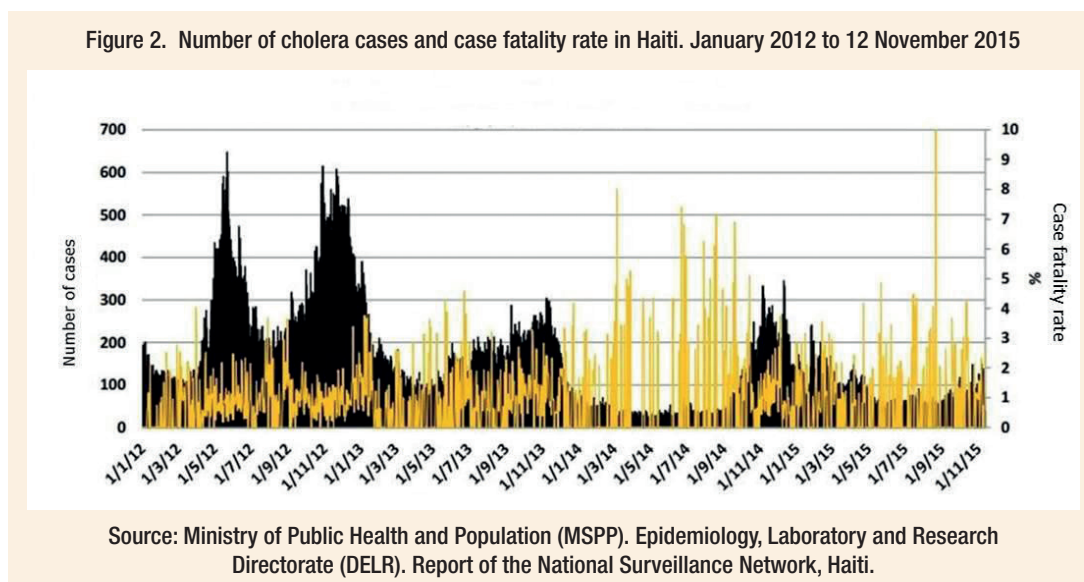
Mexico

In Mexico, in 2014, 14 cases of cholera were reported in two states: Hidalgo (13) and Querétaro (1). Since the beginning of 2015, no new cholera cases have been reported.

Recommendations

The 2014 Annual Report on Cholera, published by the World Health Organization,[2] emphasizes the fact that cholera is a public health event that can be predicted, prevented, and treated. Higher risk is associated with areas of limited access to health-care facilities, poor sanitation and lack of access to safe water. Prevention and preparedness, as well as early detection through surveillance, should enable health authorities to allocate resources and implement appropriate prevention and control measures.

Key factors for effective surveillance include the existence of a standard case definition; clear and simple mechanisms for data collection; reporting and data analysis procedures; rapid diagnosis of suspected cases, and laboratory confirmation; routine feedback of surveillance data, and appropriate coordination at all levels (i.e., community, health services, district, national, and international levels). Cholera surveillance should be part of an integrated disease surveillance system that includes local feedback, as well as information-sharing at the global level.

[2] Weekly Epidemiological Record. No 40, 2015, 90, 517-544. Available at: http://www.who.int/entity/wer/2015/wer9040/en/index.html

Given the persistence of cholera circulation in countries within and outside the Region of the Americas, the Pan American Health Organization / World Health Organization (PAHO / WHO recommends that Member States continue their efforts to ensure and maintain adequate sanitation and access to safe drinking water. Travelers headed to areas with cholera circulation should be informed of its modes of transmission, and the need for good personal hygiene, as well as consumption of safe water and foods, in order to minimize the risk of importing cases. The potential spread of cholera through imported cases will depend on existing water and sanitation conditions.

The Organization urged Member States to maintain cholera surveillance, as well as to continue implementing the recommendations of the Cholera Epidemiological Alert of 2 November 2012[3], transcribed below.

Surveillance

Under the IHR, the risk of public health events that involves cholera should be evaluated on the basis of Annex 2 of the IHR, and—in accordance with it—the WHO Contact Point for IHR should be notified.

The use of WHO's standardized case definition is recommended to obtain a more precise estimation of the cholera burden of disease at the global level, and to define more sustainable support strategies.

In countries where no cholera cases have been reported, recommendations are as follows:

- Monitoring the trend of acute diarrhea diseases, especially among adults.
- Immediate reporting of all suspected cases from the local to the central and peripheral levels.
- Investigation of all suspected cases and clusters of cases.
- Laboratory confirmation of all suspected cases.

In outbreak situations, the following measures are recommended:

- Intensified surveillance, including active case finding.
- Laboratory confirmation to monitor geographic spread and patterns of resistance to antibiotics.
- Weekly analysis of the number of cases and deaths by age, sex, geographical location and hospital admission.

Laboratory Diagnosis

Cholera is confirmed in the laboratory by the isolation of *V. cholerae* strains or by serological evidence of recent infection. It is important that public health laboratories in the Region be prepared to identify both Ogawa and Inaba serotypes.

Treatment

Cholera is a disease that responds satisfactorily to medical treatment. The first goal of treatment is the replenishment of fluids lost by patients' diarrhea and vomiting. Up to 80% of cases can

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[3] Cholera Epidemiological Update, 2 November 2012. Washington, D.C.: PAHO/WHO; 2012. Available at: http://www.paho.org/hq/index.php?option=com_docman&task=doc_view&gid=19243&Itemid

be treated by early administration of oral rehydration salts (WHO/UNICEF oral rehydration salts standard sachet).

Intravenous fluid administration is recommended for patients who have lost more than 10-20 ml/kg/h or patients with severe dehydration. Following replacement of the initial fluid loss, the best guide for fluid therapy is the recording of fluid losses and gains, and the adjustment of fluid therapy as necessary.

The administration of appropriate antibiotics, especially in severe cases, shortens the duration of diarrhea, reduces the volume of hydration fluids necessary, and shortens the time of excretion of *V. cholerae*.

Massive administration of antibiotics is not recommended, because it has no effect on the spread of cholera and contributes to bacterial resistance. With appropriate treatment, the case fatality rate of cholera is less than 1%.

In order to provide timely access to treatment, cholera treatment centers should be established for affected populations. These centers should be strategically located to maximize the number of affected individuals that may be treated in outpatient settings, based on case management protocols defined and agreed to by all parties.

Response plans must provide for coordination between treatment centers and healthcare centers, and various levels of community care in the corresponding communities they serve, and should include information dissemination on proper hygiene practices and public health measures.

Prevention Measures

The following recommendations are aimed at reducing transmission of fecal-oral infection of cholera in healthcare settings:

- Wash hands with soap and water or glycerine alcohol before and after patient contact.
- Use of gloves and gowns for close contact with patients, and contact with excretions or secretions.
- Isolation of patients in a single room or in cohorts.
- Separation of beds by more than one meter.
- Cleaning of debris and organic material with sodium hypochlorite (bleach) dilution (1:10).
- Environment cleaning with sodium hypochlorite (bleach) dilution (1:100).
- Persons who care for children that use diapers or incontinent adults must strictly follow the same precautionary measures cited above, especially those related to hand hygiene (after changing diapers and contact with excretions). It is also recommended that soiled diapers be changed frequently.

Preparedness and Response

The implementation of prevention activities in the medium and long term is crucial in the fight against cholera. Generally, the response to cholera outbreaks tends to be reactive and take the shape of an emergency response; this approach prevents many deaths, but not cholera cases themselves.

A coordinated multidisciplinary approach, supported by a timely and effective surveillance system is recommended for prevention, preparedness, and response. Key sectors that should

be involved are health care, water supply and sanitation, agriculture and fisheries, education, professional societies, non-governmental organizations, and international partners in the country.

Water Supply and Sanitation

Improving the water supply and sanitation remains the most sustainable measure to protect people from cholera and other waterborne epidemic diarrheal diseases. However, this approach may be unrealistic for those poorest populations in our Region.

Cholera is usually transmitted by food or water contaminated with feces. Sporadic outbreaks can occur anywhere in the world where water supply, sanitation, food safety, and hygiene are inadequate.

Travel and International Trade

Experience has shown that measures such as quarantine—to limit the movement of people-- and the seizure of goods are unnecessary and ineffective in controlling the spread of cholera. Therefore, restricting travel or imposing restrictions on food imports produced by good manufacturing practices, based solely on the fact that there is a cholera epidemic or endemic in a country, is not justified.

The persistence of cholera in and outside of the Americas increases the likelihood of imported cases. Information should be provided to travelers about the potential risks of cholera, the symptoms of the disease, and precautions to avoid it, and where to seek health care when symptoms are present.

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4. Dominican Republic. Boletín Epidemiologico, 2015. Available at:

   http://www.digepisalud.gob.do/?page_id=93&drawer=Boletines epidemiológicos*Boletín semanal

5. Mexico, Secretaría de Salud de México. Boletín Epidemiológico de la Dirección General de Epidemiologia. Available at:

   http://www.epidemiologia.salud.gob.mx/dgae/boletin/intd_boletin.html

Related links:

1. WHO cholera fact sheet: http://www.who.int/mediacentre/factsheets/fs107/en/index.html.

2. PAHO/WHO cholera health topic: www.paho.org/cholera.

3. Information on WHO's statement relating to international travel and trade to and from countries experiencing outbreaks of cholera:
   http://www.who.int/cholera/technical/prevention/choleratravelandtradeadvice231110.pdf.

4. Atlas of Cholera outbreak in La Hispaniola. PAHO/WHO. Available at: http://new.paho.org/hq/images/Atlas_IHR/CholeraHispaniola/atlas.html.

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Avian influenza

On 27 January 2015, the Canada IHR NFP notified WHO of one laboratory-confirmed case of human infection with avian influenza A(H7N9) virus. On 30 January, a second case was confirmed. Both individuals flew from Hong Kong, Special Administrative Region (SAR) of the People's Republic of China, to British Columbia, Canada, after traveling together through China. During their travels, they had been exposed to live poultry, but had had no direct contact with fowl.

The index case developed symptoms on 14 January and was seen by a physician the next day. Following laboratory-confirmation of influenza A, the case received antiviral therapy for five days. On 26 January, the case tested positive for influenza A(H7N9). The second case, who had underlying comorbidities, developed symptoms on 13 January, and was seen by a physician on that same day. On 19 January, the second case received antiviral therapy for five days. On 29 January, laboratory results were positive for avian flu virus A(H7N9). Neither individual was hospitalized; both recovered from their acute respiratory symptoms, and agreed to self-isolation at home.

Canada reported its case of H7N9 to PAHO/WHO, as mandated by the IHR for events that may constitute a public health emergency of international concern PAHO/WHO considered the risk of infection with influenza virus A(H7N9) to Canadians and other countries of the Americas to be low.

Avian influenza A(H7N9) is a subtype of influenza A virus previously detected in birds. The virus was first detected in humans in China in March 2013. Since then, nearly 500 human cases have been reported, nearly all of them from China. Most patients have become severely ill, and by January 2015, 185 had died.

Most human cases of influenza A(H7N9) have been linked to exposure to infected live poultry or contaminated environments, such as live poultry markets. Evidence suggests that the virus is not easily transmitted from person to person, and sustained human-to-human transmission has not been reported.

Public Health Measures

In Canada, tracing and monitoring of household and healthcare contacts were carried out for the two individuals infected. Follow-up of air flight passengers was not undertaken, as the cases were not symptomatic during the flight, and the incubation period had elapsed since the date of the flight. WHO continued to closely monitor the evolution of the global situation regarding H7N9, as well as conducting risk assessment and the overall risk associated with the H7N9 virus had not changed.

Recommendations

PAHO/WHO advises that travelers to countries with known outbreaks of avian influenza should avoid poultry farms, contact with animals in live bird markets, and any areas where poultry may be slaughtered. They should also avoid contact with any surfaces that appear to be contaminated with poultry or other animal feces. Travelers should also wash their hands often with soap and water and should follow good food safety and food hygiene practices.

PAHO/WHO does not advise screening at points of entry with regard to this event, nor did it recommend any travel or trade restrictions. As always, diagnosis of infection with an avian influenza virus should be considered in individuals who develop severe acute respiratory symptoms while traveling or soon after returning from an area where avian influenza is a concern.

PAHO/WHO urged countries to continue strengthening influenza surveillance, including surveillance of severe acute respiratory infections (SARI), and to carefully review any unusual patterns, in order to ensure reporting of human infections under the IHR, and to continue national health preparedness.

Detection of Avian Influenza due to Reassortant Viruses:
Public Health Implications for the Americas

Situation Summary

Canada

Starting in December 2014, the World Organization for Animal Health (OIE) began receiving reports of outbreaks of highly pathogenic avian influenza (HPAI) in North America due to new reassortant H5 viruses.[4] In early December, an outbreak of HPAI A(H5N2) was detected in Fraser Valley, south of the province of British Columbia, Canada. Other outbreaks, in commercial and non-commercial sites were detected in the same area following that report. These were the first reported outbreaks due to Eurasian H5 reassortant viruses in North America. A few months later, an outbreak of HPAI A(H5N2) was detected in birds in the province of Ontario. The latter was unrelated to the outbreak in British Columbia.

Under the supervision of the Canadian Food Inspection Agency (CFIA), depopulation, as well as appropriate cleaning and disinfection of all infected premises were conducted.

United States of America

From December 2014 to January 2015, the United States Department of Agriculture (USDA) received 14 reports of birds infected with HPAI viruses of Eurasian origin. Of those, 7 notifications were infection with HPAI A(H5N2), 6 were A(H5N8) and one was A(H5N1). These were the first reports of infection with H5 reassortant viruses in domestic and wild birds in the United States, and the first detection of HPAI subtypes A(H5N8), and (H5N1) in birds in the Americas. By April 2015, all 10 affected states[5] located along migratory bird routes had reported HPAI outbreaks of A(H5N2) to the OIE. Six states[6] along the migratory Pacific Route reported outbreaks of HPAI A(H5N8); and one state[7] reported birds infected with HPAI A(H5N1) (Figure 3).

The recent detection of these H5 reassortant viruses in birds in North America follows the introduction of genetically similar influenza A(H5N8) viruses in Europe. The H5N8 viruses detected in the United States and Europe are genetically similar to those found in Japan and South Korea in 2014. In North America, genomic sequences from the Eurasian A (H5N8) virus have combined with other circulating viruses resulting in the emergence of the new H5 reassortant viruses A(H5N1) and A(H5N2).

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4 Influenza aviar viruses are divided into two groups based on their ability to cause disease in poultry: high pathogenicity or low pathogenicity.http://whqlibdoc.who.int/hq/2005/WHO_CDS_2005.29.pdf.

5 Arkansas, South Dakota, Idaho, Kansas, Minnesota, Missouri, Montana, Oregon, Washington and Wyoming. These states are within the migratory routes of the Central, Mississippi and Pacific flyways.

6 California, Idaho, Nevada, Oregon, Utah, and Washington

7 Washington

National and local authorities in Canada and the United States have maintained enhanced surveillance of both domestic and wild birds. Furthermore, measures implemented to control the outbreaks in domestic birds remain in place, including quarantine, stamping out, controlling the movement of fowl within the country, and disinfection of infected premises/establishments. In response to the detection of HPAI viruses A(H5N8), A(H5N2), AND A(H5N1) in domestic and wild birds (including those collected by hunters), both countries conducted full epidemiological investigations and intensified surveillance.

Belize

On 23 January 2015, Belize's Agricultural Health Authority (BAHA) reported to the OIE an outbreak of low pathogenic avian influenza virus (LPAI) A(H5N2) in broiler breeder farms in the Cayo District. The Central Veterinary Laboratory provided the diagnosis, which was confirmed by the National Veterinary Services Laboratory, USDA (OIE's Reference Laboratory). Appropriate prevention and control measures were implemented by national authorities.

Recommendations

Both HPAI and LPAI viruses can spread rapidly among poultry through direct contact with waterfowl, other infected fowl, or through contact with fomites or surfaces contaminated with the virus. The infection of poultry with HPAI virus can cause severe disease, with high death rates. LPAI viruses infect poultry, but are more often associated with subclinical infection. Both types of viruses have the potential to cause human infection.

H5 avian influenza viruses, similar to those detected in Canada and the United States, have infected people in other parts of the world, therefore, the possibility of human cases associated with these avian influenza outbreaks cannot be excluded. Most human infections in other countries associated with these HPAI viruses have occurred after close contact with infected birds.

Even though there is a possibility of human infections with these viruses, in general, they are rare; when they have occurred, the viruses have not spread easily from person to person. So far, there have been no reported human cases of infection with avian influenza A(H5N8) or A(H5N1) reassortant viruses in the Americas. Also, there is no evidence to suggest that avian influenza viruses can be transmitted to humans through properly prepared poultry or eggs. A few A(H5N1) human cases have been linked to consumption of dishes made of raw, contaminated poultry blood.

Intersectoral Coordination

Control of the disease in animals is the first step in decreasing risks to humans. Therefore, it is important, both in the animal and human health sectors, to undertake prevention and control activities in a coordinated and collaborative manner. Efficient information sharing mechanisms should be established and/or strengthened to facilitate coordinated decision making.

Surveillance of Human Infections

People directly or indirectly exposed to infected birds, such as individuals involved in the culling and cleaning operations on affected farms, are at risk of infection. Therefore, appropriate personal protection equipment (PPE), and other protective measures to prevent zoonotic transmission among these operators are strongly recommended.

For early detection of animal-human transmission, surveillance of exposed persons is recommended: the occurrence of influenza-like-illness (ILI) or severe acute respiratory infection in persons who have been exposed to domestic, wild, or captive birds infected with avian influenza viruses.

Especially in areas of avian flu transmission, clinicians and health care workers should be alerted to the possibility of transmission (LPAI or HPAI) to humans among exposed individuals. Testing of patients with ILI or severe acute respiratory syndrome (SARI) who have had recent contact with birds infected with HPAI or LPAI should be considered in such areas.

Laboratory Diagnosis

The specific diagnosis of human infection with avian influenza is based on the detection of the viral genome by molecular techniques (polymerase chain reaction - PCR) in swab specimens (oropharyngeal or nasopharyngeal), nasopharyngeal aspirate or bronchoalveolar lavage (only in hospitalized patients), taken within the first 7 days (maximum 10) from the onset of symptoms.

The diagnostic algorithm includes an initial screening for influenza A or B followed by the identification of the specific hemagglutinin protein gene that will define the subtype (H1, H3, H5, H7 or other). All influenza A viruses that cannot be subtyped or those that are defined as an avian subtype (H5, H7, etc.) should be immediately sent, under appropriate conditions, to a reference laboratory or to a WHO Collaborating Centre for a more complete antigenic and molecular characterization.

In the Region of the Americas, as part of the Global Influenza Surveillance and Response (GISRS), 22 of the 24 National Influenza Centers and 3 national laboratories, have the capacity for molecular detection of H5 (and also to detect some H7 and H9). In addition, established mechanisms are in place for quality control and shipment of samples for complete characterization to the U.S. Centers for Disease Control and Prevention (CDC) in Atlanta, which is the WHO Collaborating Centre for the Region.

Antiviral treatment

Evidence suggests that some antiviral drugs, notably oseltamivir, can reduce the duration of viral replication and improve the prognosis. In suspected cases, irrespective of severity, oseltamivir should be prescribed as soon as possible (ideally, within 48 of the onset of symptoms) to maximize therapeutic benefits. The administration of corticosteroids is not recommended.

Figure 3. Avian A(H5N2), (H5N8), and (H5N1), among birds in the Americas, December 2014 – January 2015
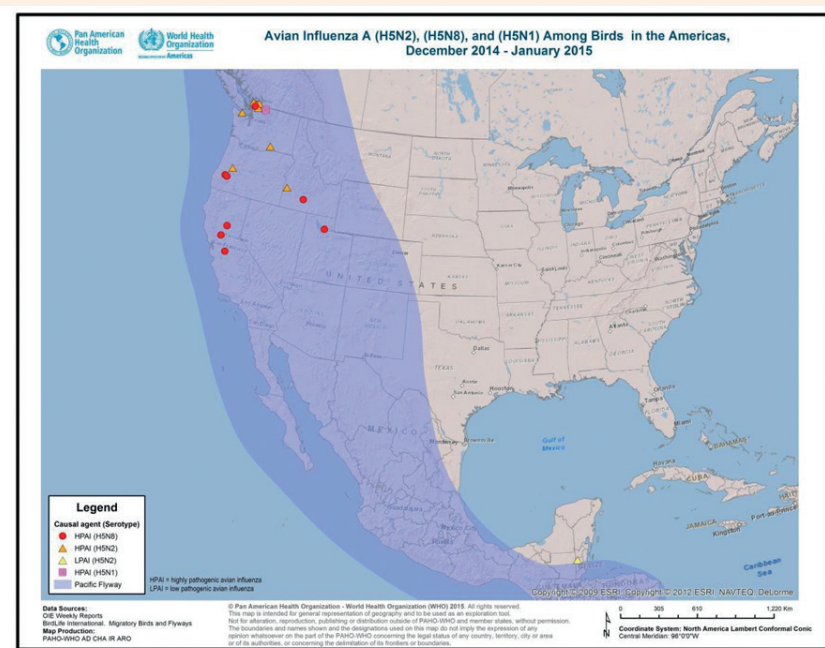
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7. United States. Centers for Disease Control and Prevention: Interim Guidance on the use of antiviral medications for treatment of human infections with novel influenza A virus associated with severe human disease. Available at: http://www.cdc.gov/flu/avianflu/novel-av-treatment-guidance.htm.

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Related Links

1. WHO Avian influenza factsheet: http://www.who.int/mediacentre/factsheets/avian_influenza/en/

2. WHO Avian influenza in humans: http://www.who.int/influenza/human_animal_interface/avian_influenza/en/

3. WHO Influenza – Information resources: http://www.who.int/influenza/resources/en/

4. WHO – Influenza at the Human-Animal Interface (HAI):
   http://www.who.int/influenza/human_animal_interface/en/

5. WHO – Avian influenza: food safety issues:
   http://www.who.int/foodsafety/areas_work/zoonose/avian/en/index1.html

6. FAO Avian Influenza – Food and Agriculture Organization of the United Nations: http://www.fao.org/avianflu/en/index.html.

7. WHO Avian influenza A(H7N9): http://www.who.int/influenza/human_animal_interface/influenza_h7n9/en/

8. WHO Disease Outbreak News: http://www.who.int/csr/don

9. PAHO/WHO Epidemiological alerts and updates: HYPERLINK "http://www.paho.org/epialerts" www.paho.org/epialerts

Measles: Implications for the Americas

Situation Summary

The Region of the Americas' interruption of endemic measles transmission in 2002 faces major challenges, due to the continued importation of the disease in several countries. From 2003 to 2014, the total number of imported cases reached 5,077, most of which occurred in 2011 (n=1,369), and 2014 (n=1,848). In 2015, a total of 147 cases had been reported as of EW 5; most of the latter cases were related to a large multi-state outbreak in the United States of America (Figure 4).

Brazil

In Brazil, between 2013 and 2015, a total of 971 confirmed measles cases were reported in the Federal District and nine states: Ceara, Espiritu Santo, Rio de Janeiro, Minas Gerais, Paraiba, Pernambuco, Sao Paulo, Santa Catarina, and Roraima. The highest proportion of cases was reported in the states of Ceara and Pernambuco.

Circulation of the measles virus was detected in Pernambuco on 19 March 2013. From then to 14 March 2014, a total of 224 confirmed cases, including one death, were reported in 24 municipalities. Children under 1 year of age were the most affected (49%, 110/224). The genotype identified was D8. The outbreak spread to the neighboring state of Ceara, which reported the first case on 25 December 2013.[8] As of 5 February 2015, a total of 718 cases had been confirmed in 31 municipalities. The onset of rash for the last case was 19 January 2015. No deaths had been reported. During this outbreak, children under 5 years of age were the most affected (37.1 %), followed by adolescents and adults aged 15-29 years (33.2%). A total of 51 cases remained under investigation in 12 municipalities. The onset of rash of the last suspected case was 2 February 2015. The genotype was identified as D8. Additionally, one case with travel history to Fortaleza, Ceara, was reported in a 40-year-old male, resident of the state of Roraima.

Canada

Two unrelated measles outbreaks were investigated in February 2015 in Canada. The first, on 3 February 2015, was reported by the Lanaudiere Public Health Department of the Agency for Health and Social Services[9] in Quebec province. This outbreak began in early 2015, with eight suspected measles cases that were linked to an outbreak in California, United States. These cases were all members of the same family, who had not been vaccinated for religious reasons. The second outbreak was reported on 2 February 2015 by Toronto Public Health,

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[8] Measles Epidemiological Bulletin – Ceara Health Secretary. Available at: http://www.saude.ce.gov.br/index.php/boletins.

[9] Lanaudiere Public Health Department of the Agency for Health and Social Services. Available at: http://www.agencelanaudiere.qc.ca/asss/Pages/default.aspx.

[10] Toronto Public Health. Available at: http://wx.toronto.ca/inter/it/newsrel.nsf/9a3dd5e2596d27af85256de400452b9b/880 1512dfd189fa685257de0005b0b86?OpenDocument.

Ontario province.[10] It consisted of four laboratory confirmed cases of measles: two children under the age of 2 years, and two adults from different families. As of the date of the report, no source had been identified, and there were no known links or contact between the cases. Contact tracing of exposed contacts was conducted.
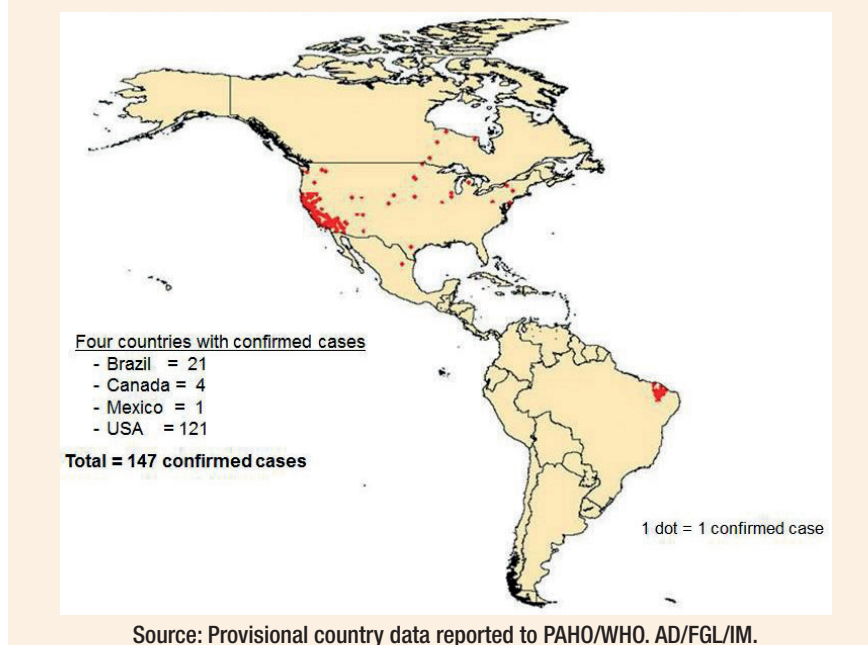
United States of America

A total of 121 measles cases had been reported in the Unites States of America from 1 January to 6 February 2015 in the District of Columbia and 17 states, as follows: Arizona, 7 cases; California, 88; Colorado, 1; District of Columbia, 1; Delaware, 1; Illinois, 3; Michigan; 1; Minnesota, 1; Nebraska; 2; New Jersey; 1; New York; 2; Nevada, 2; Oregon, 1; Pennsylvania, 1; South Dakota, 2; Texas, 1; Utah, 2; and Washington, 4. Most of these cases (103 or 85%), were part of a large, ongoing multi-state outbreak linked to an amusement park in California.[11] The outbreak likely started from a traveler who became infected with measles overseas, then visited the amusement park while infectious. However, as of the date of this report, no source had been identified. The ages for the cases reported ranged from less than 12-months to 59-years-old (media = 19-years-old). The measles genotype for the outbreak linked to an amusement park in California was B3, this genotype also caused a large outbreak in the Philippines in 2014.

Mexico

The Mexico IHR NFP reported two imported cases of measles with history of travel to the United States. The first case corresponded to a 22 month-old girl, resident of the state of Baja California Sur, Mexico, with history of travel to California from 16 to 18 December 2014. The girl developed exanthema on 30 January 2015. The second case was a 37-year-old female, unvaccinated, resident of the state of Nueva León, Mexico, who traveled to San Francisco, California, from 26 to 31 December 2014. Local and national authorities implemented appropriate prevention and control measures, and no secondary cases were reported related to the two imported cases.

Figure 4. Confirmed cases of measles, Region of the Americas, 1 January to 8 February 2015

Four countries with confirmed cases
- Brazil = 21
- Canada = 4
- Mexico = 1
- USA   = 121

Total = 147 confirmed cases

1 dot = 1 confirmed case

Source: Provisional country data reported to PAHO/WHO. AD/FGL/IM.

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[11] U.S. CDC Health Advisory. U.S. Multi-state Measles Outbreak, December 2014- January 2015.
http://emergency.cdc.gov/han/han00376.asp

Recommendations

Travelers

Prior to departure

1. PAHO/WHO recommends that all travelers over the age of 6 months going to areas with documented measles virus circulation be fully vaccinated against measles and rubella, preferably with the MMR (measles, mumps, and rubella) vaccine. Ideally, the vaccine should be administered at least two weeks before departure.

2. Infants who receive the MMR vaccine before their first birthday must be revaccinated according to their country's vaccination schedule.

3. Travelers who are not up to date on their vaccinations are at higher risk of contracting either disease when in close contact with travelers from countries where the viruses still circulate.

4. Exceptions to this recommendation include persons with medical contraindications for the measles and rubella vaccine, and infants under the age of 6 months.

5. Individuals who may be considered immune to measles and rubella include:

   ◖ Those with written documentation of measles and rubella vaccination; or

   ◖ Laboratory confirmation of rubella and measles immunity (a positive serological test for measles and rubella-specific IgG antibodies).

During the trip

1. Ensure that travelers are aware of the following symptoms:

   ◖ Fever

   ◖ Rash

   ◖ Cough, cold (runny nose), or conjunctivitis (red eyes)

   ◖ Joint pain

   ◖ Lymphadenopathy (swollen glands)

2. If travelers suspect they have measles or rubella, they should:

   ◖ Seek professional health care;

   ◖ Remain at the site of their current residence (e.g. hotel or home, etc.), or as advised by a health professional, except to seek professional health care;

   ◖ Avoid close contact with other people for seven days following the onset of rash;

   ◖ Avoid travel and visit to public places.

Upon returning

1. Travelers who suspect they may have measles or rubella should seek professional health.

2. If travelers develop any of the above mentioned symptoms, they should inform their physician of their travel history.

Clinicians and Health Care Providers

1. PAHO/WHO recommends the practice of requiring proof of immunity to measles and rubella in the health care sector (medical, administrative, and security personnel).

2. Sensitize private sector health personnel about the need to report immediately to the appropriate public health authorities any suspected cases of measles or rubella, since international travelers may seek medical assistance at private health care facilities. Prompt reporting of these diseases will allow a timely response from the national surveillance and response system.

3. Continue to remind health care workers to always ask patients for their travel history.

Persons and Institutions in Contact with Travelers, Before and/or After Their Trip

1. Advise personnel in the tourism and transportation sectors (i.e., hotels, airport, taxis, and other) to get fully immunized against measles and rubella, and make the necessary regulatory and operational arrangements to enable vaccination.

2. Conduct public awareness campaigns on the symptoms of measles and rubella, so travelers are able to recognize said symptoms, and know to seek immediate medical care. Information should be distributed at airports, ports, bus stations, travel agencies, airlines, and other such places.

Contact tracing of confirmed measles cases

1. Conduct contact tracing according to national guidelines for contacts identified and present in the national territory;

2. Consider the international implications that contact tracing may present, taking into account the following scenarios and operational aspects while conducting these activities:

   ◖ When a case is identified by national authorities of a Member State who requests another Member State to locate contacts whose residence is most likely within their country, national authorities are encouraged to use all coordination mechanisms in place to locate those individuals. Information available for action might be limited, and efforts should be warranted as resources allow. Health services should be alerted of the possible or actual presence of contacts in order to detect suspected cases.

   ◖ When a case is identified locally, and, depending on the timing of the natural history of the disease at detection:

   a. Current case: national authorities should obtain information about the possible location of contacts abroad and inform third party national authorities accordingly.

   b. Retrospectively identified case: according to the travel history of the case, national authorities should inform relevant third party national authorities as this occurrence might constitute the first signal of measles virus circulation, or of an outbreak, in the other country or countries concerned.

Operational Remarks

1. If no international conveyances are involved (e.g., aircrafts, cruise ships, trains) as a possible setting for exposure to a case(s), national authorities should contact their counterpart(s) through the IHR NFP network or other bilateral or multilateral programmatic mechanisms, with copy to the WHO IHR Contact Point for the Americas. The assistance of the WHO IHR Contact Point for the Americas can be requested to facilitate international contact tracing related communications.

2. If international conveyances are involved (e.g., aircrafts, cruise ships, trains) as a possible setting for exposure to a case(s), national authorities should activate existing mechanisms to obtain relevant information from carriers (e.g. airlines) to locate travelers, or establish such mechanisms, if absent. For subsequent communication between national authorities see the preceding paragraph.

Dissemination of Recommendations

PAHO/WHO urges national authorities to consider disseminating the recommendations outlined herein through:

◖ Public awareness campaigns to promote and enhance travelers' health before and after their trip, in order for them to adopt healthy behaviors in regard to measles vaccination, and recognize the signs and symptoms of the disease. It is also advised that travel medicine services or clinics, airports, ports, bus and train stations, airlines operating in the country, be involved.

◖ Travel agencies and other tourism related agencies, and diplomatic channels, so travelers know to take necessary actions prior to travel.

◖ The dissemination of existing national guidelines to clinicians and other health care providers, and timely dissemination of any newly developed protocol related to travelers.

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4. Portal de Saude. Secretaria de Estado de Saude de Roraima: http://www.saude.rr.gov.br/index.php/servicos-e-informacoes/noticias/noticias-outubro-2013/1102-caso-de-sarampo-e-confirmado-em-roraima-e-sesau-adota-medidas-controle (in Portuguese, accessed on 5 February 2015).

5. U.S. Centers for Disease Control and Prevention (CDC) Health Advisory. Health Alert Network: http://emergency.cdc.gov/han/han00376.asp (accessed on 5 February 2015).

6. The Public Health Department of the Agency for Health and Social Services of Lanaudiere, Quebec: http://www.agencelanaudiere.qc.ca/asss/Pages/default.aspx (accessed on 3 February 2015).

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Related links

◖ PAHO/WHO Immunizations website: http://www.paho.org/hq/index.php?option=com_content&view=category&layout=blog&id=956&Itemid=358&lang=en.

Middle East Respiratory Syndrome - Coronavirus (MERS-CoV)

Background

Middle East respiratory syndrome (MERS) is a viral respiratory illness caused by a coronavirus (CoV) that was first detected in Saudi Arabia in 2012. From that time through 5 June 2015, a total of 1,185 cases had been laboratory confirmed, including 443 deaths. Seven out of 10 cases were male (n= 1,165), and the average age was 49 years (ranging from 9 months to 99 years).

Most human cases of MERS-CoV infection have been attributed to person to person transmission. However, the virus does not spread easily from one person to another, unless there is close contact, such as when providing care to a patient without proper protection. Some scientific studies suggest that camels are an important reservoir for MERS-CoV, and the animal source of infection in humans. However, the specific role of camels in the transmission of the virus, and the exact route or routes of transmission is unknown.

On 3 June 2015, the WHO updated the risk assessment of this infection following an outbreak in the Republic of Korea, which began with an index case with a travel history to the Middle East (Bahrain, Qatar, Saudi Arabia, and the United Arab Emirates). This was the largest outbreak of MERS-CoV outside the Middle East. Thus far, there had been 36 confirmed cases of MERS-CoV infection, and three deaths related to the latter outbreak (case fatality rate, 8%). More than 1,500 contacts were monitored. Included among confirmed cases were health care workers who assisted patients with confirmed infection, and other patients who were being treated at the same health care facilities as the index case, as well as family members and close contacts of the cases. Some cases of tertiary transmission were reported.

By 5 June 2015, 25 countries from 5 continents[12] had reported cases. Most of them (> 85%) occurred in Saudi Arabia. From 1 January to 5 June 2015, a total of 239 new cases and 86 deaths were reported in 10 countries: China, Germany, Iran, Jordan, Oman, the Philippines, Qatar, the Republic of Korea, Saudi Arabia, and the United Arab Emirates.

Recommendations

In light of this situation, PAHO/WHO reiterated the recommendations published in its Epidemiological Alert of May 2013[13] urging Member States to strengthen health surveillance activities to detect any unusual event, including those that might be associated with MERS-CoV. Health professionals should be informed of the possibility of infection caused by this virus, and what measures to take if a suspected case is detected. Clinicians should have access to

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[12] Africa: Algiers, Egypt and Tunes; Americas: the United States of America; Asia: China, Iran, Jordan, the Republic of Korea, Kuwait, Lebanon, Malaysia, Oman, the Philippines, Qatar, Saudi Arabia, Turkey, the United Arab Emirates, and Yemen; Europe: Austria, France, Germany, Greece, Italy, the Netherlands, and the United Kingdom.

[13] Human infection caused by novel coronavirus, Epidemiological Alert, 10 May 2013. PAHO/WHO; 2013. Available at: http://www.paho.org/hq/index.php?option=com_docman&task=doc_view&Itemid=270&gid=21469&lang=en

information for the appropriate clinical management of patients with acute respiratory failure, and septic shock, as a result of severe infection caused by MERS-CoV, with special emphasis on measures to prevent the spread in health care facilities. PAHO/WHO also recommends that health care workers have access to up to date information on the illness, be familiar with the principles and procedures for handling MERS-CoV infections, and be trained to inquire about a patient's travel history, in order to relate this information to clinical data.

PAHO/WHO does not recommend any type of screening at entry points regarding this event, nor any restrictions on travel or trade.

PAHO/WHO urged Member states to implement and continue to follow infection control procedures to reduce or minimize the occurrence of infections in health care setting, including those associated with MERS-CoV. Further details on additional measures are provided below.

Epidemiological Surveillance

Because the clinical presentation of MERS-CoV infection is similar to other viral respiratory infections, cases are not always suspected and identified early. Therefore, strict compliance with prevention and infection control measures is essential.

PAHO/WHO recommends that Member States strengthen surveillance for severe acute respiratory illness and to carefully review any unusual patterns. Additionally, health care workers must be trained to ask patients about their travel history, and to relate said information to the patient's symptoms. Recently reported cases stress the need for health care workers to suspect MERS-CoV infection in travelers who present a clinical picture consistent with MERS-CoV, and who have recently returned from areas where the virus has been circulating.

An epidemiological investigation and laboratory testing for MERS-CoV is advised for individuals who meet the following criteria:

a) Any person with acute respiratory disease of any severity, within 14 days before the onset of the disease, who had close contact[14] with a probable or confirmed MERS-CoV infection case while the case had the disease.

b) Any person with a clinical picture consistent with SARI, for which infection by known respiratory viruses has been ruled out, and who in the last 14 days prior to the onset of symptoms has been in areas where the virus has been circulating.

International Reporting

National authorities are requested to report all probable and confirmed MERS-CoV infection cases to the WHO IHR Regional Contact Point within 24 hours of classification.

For the purposes of classification and reporting, the current definitions for probable and confirmed cases are available at: http://www.who.int/csr/disease/coronavirus_infections/case_definition/en/index.html

Laboratory Testing

PAHO/WHO encourages Member States to follow the WHO interim recommendations for laboratory testing for MERS-CoV. The general recommendations for laboratory diagnosis are available at: Ihttp://www.paho.org/hq/index.php?option=com_docman&task=doc_download&gid=30509&Itemid=270&lang=en.

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[14] Close contact includes:
- Any person who provided care to a probable or confirmed case, including health care workers or family, or who had other similar close physical contact.
- Any person who was in the same site (e.g. residing or visiting) to a probable or confirmed case in the period in which the case presented symptoms.

Any laboratory testing to detect this virus should be performed according to the capacity of the national laboratory system, in appropriately equipped laboratories, by staff trained in the relevant technical and biosafety procedures (under BSL2 conditions, only for molecular assays). When the diagnostic capability is not available at the national level, PAHO/WHO recommends that samples of any unusual or unexpected SARI case or SARI cluster of unexplained etiology, including suspected cases of MERS-CoV, be forwarded immediately to the WHO Collaborating Center for influenza and other respiratory viruses, at the U.S. CDC for additional testing.

Clinical Management

To date, knowledge of the clinical features of MERS-CoV infection is limited, and there is no prevention or specific treatment for the virus (e.g., vaccine or antiviral). However, WHO has developed a series of interim recommendations for the management of patients with the infection, in line with the management of severe acute respiratory infections.[15] In December 2013, WHO convened an international network of clinical experts to discuss treatment options, such as the use of convalescent plasma or highly neutralizing antibodies against MERS-CoV. Currently, there are no evidence based clinical studies to recommend these options. WHO and the International Consortium of Emerging Infections and Severe Acute Respiratory Infection have developed and made available research protocols and forms for clinical research on emerging diseases that cause serious respiratory syndromes, such as MERS-CoV, and avian influenza A(H5N1) and A(H7N9). The detailed objectives and methodology are available at: http://www.prognosis.org/isaric/.

Infection Prevention and Control in Health Care

PAHO/WHO stresses the importance of the rigorous application of health care infection prevention and control measures, and advises Member States to follow the provisional WHO guidelines for infection prevention and control in health care settings when dealing with probable or confirmed MERS-CoV cases. These guidelines are available at: http://www.who.int/csr/disease/coronavirus_infections/IPCnCoVguidance_06May13.pdf?ua=1.

The use of personal protective equipment for specific procedures must be based on risk assessment. Further details and recommendations for infection prevention and control of epidemic and pandemic-prone infections are available on the WHO website: http://apps.who.int/iris/bitstream/10665/112656/1/9789241507134_eng.pdf

International Travel and Trade

The Organization does not advise the implementation of health screening at points of entry in relation to this event, nor that any international travel or trade restriction be applied.

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3. WHO – Update on MERS-CoV transmission from animals to humans, and interim recommendations for at-risk groups. Available at: http://www.who.int/csr/disease/coronavirus_infections/MERS_CoV_RA_20140613.pdf?ua=1.

Related links

◀ WHO - Coronavirus Infections: http://www.who.int/csr/disease/coronavirus_infections/en/.

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[15] http://www.who.int/csr/disease/coronavirus_infections/InterimGuidance_ClinicalManagement_NovelCoronavirus_11Feb13u.pdf?ua=1.

Rabies

Background

Rabies is caused by the rabies virus, of the *Rhabdoviridae* family, and *Lyssavirus* genus, which infects domesticated and wild animals, and is transmitted to humans through rabies infected saliva (through skin and mucous membranes, by bites and scratches).

The incubation period is variable, but usually ranges from 2 to 8 weeks. In very rare occasions it can be as short as 10 days or as long as several years. The first symptoms of rabies include a sense of apprehension, headache, low-grade fever, malaise, and vague sensory changes (paresthesia), often in the site of an animal bite. Once symptoms appear, the disease is almost always fatal. Hence the importance of post-exposure prophylaxis with both the vaccine and immunoglobulin, according to the severity of the case.

For the case definition and clinical approach, it is essential to relate a person's exposure to a suspected rabid animal in an area where the disease has been occurring in humans and animals. The best strategy to prevent human cases is through the vaccination of pets, mainly dogs, and through timely and appropriate use of prophylaxis for persons exposed to rabies.

Situation Summary

While human rabies transmitted by dogs is in the process of elimination in the Americas, some countries of the Region continue to report human rabies cases transmitted by dogs. From the beginning of 2014, the following countries reported human cases of canine-borne rabies: Bolivia, 6 cases; Brazil, 1 case; the Dominican Republic, 1 case; Guatemala, 2 cases; and Haiti, 3 cases.

In addition, canine rabies cases had been reported in areas where no cases had been previously reported, such as northern Argentina (Jujuy and Salta), Brazil (Mato Grosso do Sul), Paraguay (Loma Plata), and areas declared free of canine rabies over 10 years ago, such as the region of Arequipa in Peru. The latter is the first time canine rabies has been reintroduced in an area that had been officially declared free of canine rabies.

Rabies is entirely preventable, and the occurrence of human cases is related to failures in canine vaccinationcampaigns, health promotion activities, and surveillance and control by health care systems, in addition to limited access to health care services. The cases described in this report were concentrated in urban areas, and around international borders; they are related to poverty and/or unfavorable environments. Because the situation reflects limitations in access to universal health care, it requires the prompt attention of health authorities.

> Anyone exposed to the rabies virus should receive post-exposure prophylaxis
>
> The prevention of human rabies must be a joint effort involving veterinary and public health services. Safe and effective vaccines for preventing animal rabies are available, as are vaccines for administration to humans pre and post suspected exposure.

Recommendations

PAHO/WHO reiterates its recommendation to the countries of the Americas about the need to improve canine vaccination, and to have post-exposure prophylaxis available (WHO pre-qualified rabies vaccines and immunoglobulin) to respond to potential suspected cases. PAHO/WHO also emphasizes that health care workers should be trained in the detection of suspected cases, and the prompt administration of prophylaxis. In addition, PAHO/WHO recommends countries:

◖ Plan and implement mass canine vaccination campaigns until appropriate and sustainable immunity levels are achieved (above 80% of the estimated canine population). This is the most efficient and cost-effective method for the control and elimination of human rabies transmitted by dogs. Vaccination of domestic animals (mainly dogs) has been shown to decrease the occurrence of human disease up to its elimination. Canine vaccination coverage should be a basic management indicator for national rabies control programs.

◖ Raise public awareness to ensure persons seek immediate medical attention for suspected exposure to the rabies virus.

◖ Use effective and safe WHO pre-qualified vaccines for humans for pre and post-exposure prophylaxis, following WHO's Guide for Rabies Pre and Post Exposure Prophylaxis in Humans available at: http://www.who.int/rabies/PEP_Prophylaxis_guideline_15_12_2014.pdf?ua=1.

◖ There are no contraindications for post-exposure prophylaxis for pregnant women, infants, the elderly or immunocompromised individuals, including children with HIV/AIDS. The number of people attacked by dogs who fall within the WHO categories of exposure I, II, and III,[16] for whom prophylaxis was not recommended, is an indicator of universal health care access in areas where anti-rabies prophylaxis is indicated because of a persistent risk.

◖ Inform the public and health care workers that cleaning wounds and getting post-exposure vaccinations as soon as possible after contact with an animal suspected of having rabies can prevent the onset of rabies in 100% of exposures.

◖ Remind health care workers to begin immediate post-exposure treatment for exposed persons; treatment should only be halted if the attacking animal shows no signs of rabies while under observation.[17] Dead animals, whether by slaughter or otherwise, must be tested for rabies; the results should be forwarded to the veterinary and public health services responsible for planning and implementing control activities in the area where the exposure occurred.

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[16] Categories of exposure and post-exposure prophylaxis are defined in the WHO Expert Consultation on Rabies. Second report. WHO Technical Report Series No. 982. Available at:
http://who.int/iris/bitstream/10665/85346/1/9789240690943_eng.pdf.
[17] The recommended observation period for dogs is 10 days.

- Raise awareness among health care workers to consider rabies as a possible diagnosis in patients showing acute or progressive encephalitis; provide training on the timely and appropriate prophylaxis to those exposed.

- Acquire human immunobiologicals (WHO pre-qualified vaccines and immunoglobulin) and canine rabies vaccine in order to respond to a potential human rabies case.[18]

PAHO/WHO reiterates its recommendations published in Epidemiological Alerts on rabies in 2010, 2011 and 2014, regarding the need to develop strategies to ensure access to pre-exposure prophylaxis for persons, based on the risk characterization of areas considered most at risk of exposure to rabies, for example, individuals at risk of bat and other wild animal bites, especially those who live in or visit rainforests.

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[18] In support to national program activities, PAHO/WHO provides Member States the use of the vaccine procurement system through the Revolving Fund.

Yellow Fever

Situation Summary

Over the past decade, in the Region of the Americas, cases of yellow fever were reported in Argentina, Bolivia, Brazil, Colombia, Ecuador, Paraguay, Peru, and Venezuela. In 2015, only Bolivia, Brazil, and Peru reported yellow fever virus circulation.

In December 2015, the Bolivia IHR NFP reported the detection of an epizootic (deaths of non-human primates) in the municipality of Monteagudo, Department of Chuquisaca. The analysis performed by the National Center for Tropical Diseases (CENETROP) indicated positive results for yellow fever. No human cases were detected in relation to the epizootic.

In July 2014, Brazil declared the reemergence of yellow fever virus in the country, due to epizootics in non-human primates in which the presence of the virus was confirmed. Between July 2014 and June 2015, seven human cases of yellow fever, including four deaths, were confirmed. The distribution of cases by location of exposure was: Goias (5 cases); Mato Grosso do Sul (1 case); and Pará (1 case). All cases were male with ages ranging between 7 and 59 years. None of the cases had been vaccinated against yellow fever. Additionally, the Health Secretariat of Rio Grande do Norte reported the investigation of the death of a patient in Natal in July 2015, for whom initial tests for yellow fever were positive. The patient had no history of travel to endemic areas, and no other cases had occurred in the municipality;[19] the last evidence of yellow fever transmission in that municipality dated back to 1930.[20]
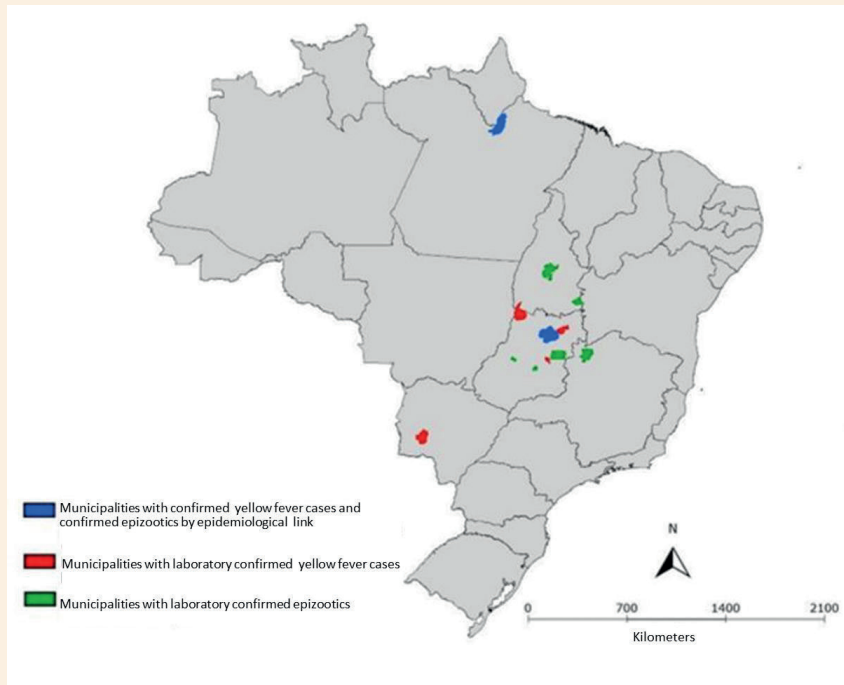
Yellow fever epizootics were also confirmed in the states of Tocantins (1 municipality in 2014 and 4 in 2015), Goiás (3 municipalities in 2015), Minas Gerais (1 municipality in 2015), Para (1 municipality in 2015), and in the Federal District (1 municipality in 2015).

The occurrence of human cases and epizootics of yellow fever is an indication of viral circulation of the virus, which in Brazil was confined to the center-east region of the country (Figure 5).

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[19] State Secretariat of Rio Grande do Norte:
http://www.saude.rn.gov.br/Conteudo.asp?TRAN=ITEM&TARG=101194&ACT=&PAGE=&PARM=&LBL=NOT%CDCIA.

[20] Brazil, Ministry of Health Web-Portal: http://portalsaude.saude.gov.br/index.php/cidadao/principal/agencia- saude/21464-esclarecimento-sobre-caso-suspeito-no-rn.

Figure 5. Geographical distribution of confirmed human cases and epizootics of yellow fever, Brazil, July 2014 - December 2015

Municipalities with confirmed yellow fever cases and confirmed epizootics by epidemiological link

Municipalities with laboratory confirmed yellow fever cases

Municipalities with laboratory confirmed epizootics

Source: Brazil. Ministry of Health. Publication: "Situação Epidemiológica / Dados" accessed 28 December 2015 at: http://portalsaude.saude.gov.br/index.php/situacao-epidemiologica-dados-febreamarela.

In Peru, up to EW 49 of 2015, 56 suspected cases of yellow fever had been reported, including three deaths. Of the reported cases, 11 had been confirmed, 12 had been classified as probable, and the rest were ruled out. The number of probable and confirmed cases combined in 2015 (23) was higher than the number observed in 2014 (15).

In descending order, the confirmed and probable cases were geographically distributed, by department, as follows: Loreto, 8 cases; Junin, 5 cases; San Martin, 5 cases; Pasco, 2 cases; and Cusco, Huanuco, and Madre de Dios, 1 case each.

Recommendations

The occurrence of epizootic and human cases in certain areas of the Americas is indicative of a remaining risk for urban yellow fever, primarily due to the high density and broad presence of *Aedes aegypti*, combined with the movement of persons to and from areas of sylvatic circulation of the virus. Currently, climate changes resulting from the El Niño phenomenon are expected to continue into 2016. These changes could impact the incidence, geographical distribution, and seasonal transmission of various vector-borne diseases, among them, yellow fever.

Considering that the yellow fever virus is circulating in various areas of the Region, in addition to the situation generated by El Niño, PAHO/WHO advises Member States to establish and maintain the capacity to detect and confirm cases, update health care professionals on how to detect and treat cases appropriately, and to maintain adequate vaccination coverages among at risk populations. Below are key recommendations related to yellow fever surveillance, clinical management, and prevention and control measures.

Surveillance

Yellow fever epidemiological surveillance must be aimed at achieving early detection of viral circulation to allow for the timely adoption of appropriate control measures to prevent new cases; interrupting outbreaks; and preventing the reintroduction of the disease into urban areas. To achieve its purpose, surveillance should monitor:

- clinical cases consistent with the classic form of the disease, based on WHO's case definition;
- febrile jaundice syndrome, usually conducted through sentinel sites; this method applies a more sensitive case definition, and rules out cases based on laboratory testing;
- epizootics;
- post-vaccination events allegedly attributable to yellow fever vaccination.

Laboratory Diagnosis

Yellow fever laboratory diagnosis is done by detecting viral genetic material in blood or tissue by polymerase chain reaction, and through serological testing for IgM antibodies.

Viral Testing

In the acute phase (viremic period) viral RNA can be detected in serum by molecular techniques, such as conventional or RT-PCR. A positive result obtained with appropriate controls confirms the diagnosis.

Viral isolation can be performed by intracerebral inoculation in mice or in cell culture. Nevertheless, due to its complexity, it is rarely used as a diagnostic method; its use is recommended for research studies only as a complement to public health surveillance.

Serologic Testing

Serology (detection of specific antibodies) is useful for yellow fever diagnosis during the acute and convalescent phases of the disease, i.e., after day 6 of the onset of symptoms. A positive IgM reaction by ELISA (MAC-ELISA or other immunoassay) in a sample taken following day 6 of the onset of symptoms is presumptive of recent yellow fever infection. Moreover, the diagnosis may only be confirmed by demonstrating a four-fold increase in antibody titer in paired serum samples by using quantitative techniques.

The fact that serological tests may produce cross-reactions must be taken into consideration, especially in areas with circulation of various flaviviruses. Therefore, in such places, once infections by other causal agents have been ruled out as part of the differential diagnosis, serological confirmation should include other more specific techniques, such as plaque neutralization test (PRNT). In any case, the results of serological tests should be carefully interpreted, and should take into account the patient's vaccination history.

Post-mortem Test

Liver histopathology is the "gold standard" for post-mortem diagnosis of suspected yellow fever cases. The analysis includes the typical microscopic description of yellow fever lesions (midzonal necrosis, fatty change, among others), detection of Councilman bodies (pathognomonic), and immunohistochemistry, which reveals viral proteins within the hepatocytes. In addition, molecular methods for fresh or paraffin preserved tissue may also be used for confirmation of suspected cases.

Serum samples from the acute phase are considered potentially infectious. All laboratory personnel who handle yellow fever samples in a laboratory setting must be vaccinated against yellow fever. The use of Class II certified biosafety cabinets for the handling of samples is also recommended, as well as extreme caution to prevent puncture accidents.

Because the differential diagnosis of yellow fever includes hemorrhagic fevers caused by arenaviruses, samples should be handled under BSL3 containment conditions, and a risk assessment and analysis of the medical history should be conducted before handling samples in the laboratory setting.

Clinical Management

There is no specific antiviral treatment for yellow fever, therefore, supportive therapy is critical. Severe cases should be treated in intensive care units. General supportive therapy includes the administration of oxygen, intravenous fluids, and vasopressor medication to treat hypotension and metabolic acidosis. Gastric protection should be included to reduce the risk of gastrointestinal bleeding.

Treatment of severe cases includes mechanical ventilation, treatment of disseminated intravascular coagulation, use of frozen fresh plasma to treat hemorrhage, antibiotic treatment of secondary infections, and management of liver and kidney failure. Other supportive measures include the use of nasogastric tube for nutritional support or prevention of gastric distention, and dialysis for renal failure or refractory acidosis. The treatment of mild cases is symptomatic. Salicylates should not be used as they can produce hemorrhage.

Differential Diagnosis

The different clinical forms of yellow fever must be differentiated from other febrile diseases that progress with jaundice, hemorrhagic manifestations, or both. In the Americas, the following diseases should be considered in the differential diagnosis of yellow fever: leptospirosis; severe malaria; viral hepatitis, especially the fulminating form of hepatitis B and D; viral hemorrhagic fevers; dengue; typhoid and typhus fever; and hepatotoxicity or fulminating secondary hepatitis due to drugs or toxic products.

Patient Isolation

A patient infected with yellow fever virus should avoid contact with the *Aedes* mosquito for at least the first 5 days of illness (viremic phase). The use of bed nets is advised (with or without insecticide treatment), or remaining in places protected by intact window/door screens. Health personnel caring for patients with yellow fever should be protected from mosquito bites by using repellents and wearing long sleeves and pants.

Prevention and Control Measures

Vaccination

Vaccination is the single most important measure for preventing yellow fever. Preventive vaccination can be administrated as part of a child's routine vaccination schedule or in one-time mass campaigns to increase the vaccination coverage in at risk areas, as well as for travelers to yellow fever risk areas. Yellow fever vaccination is safe and affordable, providing effective immunity against yellow fever within 10 days for 80-100% of vaccinated individuals, and 99% immunity within 30 days. A single dose of yellow fever vaccine is sufficient to confer

sustained immunity and life-long protection, and it does not require a booster dose. Serious adverse events are rare.

Given the limited availability of the vaccines, national authorities are advised to carry out assessments of vaccination coverage against yellow fever in at risk areas, in order to target vaccine distribution. Additionally, a national reserve of the vaccines should be maintained to respond to potential outbreaks.

Yellow fever vaccine is contraindicated in the following cases:

- People with acute febrile disease, whose general health status is compromised

- People with a history of hypersensitivity to chicken eggs and/or their derivatives

- Pregnant women, except in an epidemiological emergency, and at the express advice of health authorities

- People with disease related (e.g., cancer, leukemia, AIDS, etc.) or drug-related immunosuppression

- Children under 6 months old (check the vaccine's laboratory insert)

- People of any age with a thymus-related disease

Vector Control

The risk of urban yellow fever transmission can be reduced through effective vector control strategies. Combined with emergency vaccination campaigns, spraying with insecticide to kill adult mosquitoes during urban epidemics can reduce or halt yellow fever transmission, while populations are vaccinated to acquire immunity. Mosquito control programs in sylvatic areas are not feasible.

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Zika Virus Infection and Associated Neurological and Autoimmune Conditions

Description

The disease is caused by the Zika virus (ZIKV), an arbovirus of the flavivirus genus (family Flaviviridae), phylogenetically very similar to other viruses, such as dengue, yellow fever, Japanese encephalitis, and West Nile virus.

The Zika virus is transmitted by the bite of mosquitos of the genus *Aedes* in urban areas as well as in the wild. After an infected mosquito bite, the onset of symptoms follows an incubation period of 3 to 12 days. The infection may present itself as asymptomatic or with moderate clinical manifestations.

In symptomatic cases, symptoms appear abruptly and include: fever, non-purulent conjunctivitis, headache, myalgia and arthralgia, asthenia, maculopapular rash, edema of the lower limbs, and less frequently, retro-orbital pain, anorexia, vomiting, diarrhea, or abdominal pain. The symptoms last from 4 to 7 days, and are self-limiting. Complications, whether neurological or autoimmune, are rare, and originally were only detected in the epidemic in French Polynesia.

Background

The Zika virus was first isolated in 1947 in the Zika forest (Uganda), in a Rhesus monkey during a study of wild yellow fever transmission. It was first isolated in humans in 1952, in Uganda and Tanzania. It was not until 1968 that the virus was isolated from human samples in Nigeria.

Between April and July 2007, the first major outbreak of Zika virus fever occurred on the island of Yap (Micronesia). That outbreak lasted 13 weeks; 185 suspected cases were reported, 49 of which were confirmed, and 59 were classified as probable cases. *Aedes hensilii* was identified as the likely vector, but the presence of the virus in the mosquito could not be determined.

Subsequently an outbreak occurred in French Polynesia, in late October 2013. Around 10,000 cases were reported; of those, approximately 70 cases presented severe complications, including neurological disorders (Guillain-Barre syndrome, meningoencephalitis), and autoimmune conditions (thrombocytopenic purpura, leukopenia). An investigation was carried out to determine the association between said complications and primary or secondary co-infection with other flaviviruses, especially dengue virus. The vectors were *Aedes aegypti* and *Aedes polynesiensis.* In 2014, cases were also reported in New Caledonia and in the Cook Islands.

No deaths attributed to Zika virus infection were reported in the aforementioned outbreaks.

In the past seven years, sporadic cases have been reported among travelers to Thailand, Cambodia, Indonesia, and New Caledonia. Recent outbreaks of Zika fever in various regions of the world signal the potential spread of this arbovirus across territories where the vector (*Aedes*) is present.

Situation in the Americas: Chronological Summary

Zika Virus Infection

February 2014. Chilean public health authorities reported a confirmed case of autochthonous Zika virus infection in Easter Island,[21] which coincided with the presence of other transmission foci in the Pacific Islands: French Polynesia, New Caledonia, and the Cook Islands. The presence of the virus in Easter Island was reported until June 2014, and has not been detected since then.

May through October 2015. In May 2015, Brazilian public health authorities confirmed autochthonous transmission of Zika virus in the northeastern part of the country. As of October of 2015, 14 states had confirmed autochthonous virus transmission: Alagoas, Bahia, Ceará, Maranhão, Mato Grosso, Pará, Paraíba, Paraná, Pernambuco, Piauí, Rio de Janeiro, Rio Grande do Norte, Roraima, and São Paulo.

In October, the Ministry of Health of Brazil reported an unusual increase in the number of cases of microcephaly in the state of Pernambuco, in northeastern Brazil. The state of Pernambuco reported, on average, 10 cases of microcephaly per year. However, since the beginning of 2015 through 11 November of that same year, there had been 141 cases of microcephaly detected in 44 of the 185 municipalities of that state.

Colombian health authorities reported the detection of the first autochthonous case of Zika virus infection in the state of Bolívar.[22] As of 1 December 2015, 26 out of 36 territorial entities in Colombia had reported autochthonous circulation of the virus.

Given the increased spread of Zika virus in the Region of the Americas, PAHO/WHO urged Member States to set up and maintain the capacity to detect and confirm cases of Zika virus infection in order to prepare the health services for a potential increase in demand at all levels of the system; and to implement an effective public communications strategy to reduce mosquito populations, particularly in areas where the vector *A. aegypti* is present.

November 2015. The Ministry of Health of Brazil reported a situation similar to that of Pernambuco in the states of Paraiba[23] and Rio Grande do Norte. In Rio Grande do Norte, 35 cases of microcephaly had been reported between August and mid-November 2015.[24] Later, the state of Piauí[25] reported an unusual increase in the number of microcephaly cases.

In response, the Ministry of Health of Brazil declared a national public health emergency,[26] and health authorities investigated the cause of the event. Clinical, laboratory, and ultrasound analysis of mothers and newborns were ongoing.

By then, El Salvador, Guatemala, Mexico, Paraguay, Suriname, and Venezuela had each confirmed autochthonous Zika virus circulation.

1 December 2015. Nine Member States in the Region of the Americas had confirmed autochthonous transmission of Zika virus: Brazil, Chile (Easter Island), Colombia, El Salvador, Guatemala, Mexico, Paraguay, Suriname, and Venezuela.[27] Around the same time, 18 states in Brazil had confirmed autochthonous circulation of the virus: Amazonas, Pará, Rondônia, Roraima, and Tocantins in the North region; Alagoas, Bahía, Ceará, Maranhão, Paraíba, Pernambuco, Piauí, and Rio Grande do Norte in the Northeast region; Espírito Santo, Rio de Janeiro, and São Paulo in the Southeast region; Mato Grosso in the Central-West region; and Parana in the South region.

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[21] Information available at: http://web.minsal.cl/node/794

[22] https://www.minsalud.gov.co/Paginas/Confirmados-primeros-casos-de-virus-del-zika-en- Colombia.aspx

[23] http://paraiba.pb.gov.br/saude-discute-notificacao-de-casos-de- microcefalia-na-paraiba-nesta-sexta-feira/.

[24] http://www.saude.rn.gov.br/Conteudo.asp?TRAN=ITEM&TARG=96603&ACT=&PAGE=&PARM=&LBL=Materia.

[25] http://www.saude.pi.gov.br/noticias/2015-11-13/6805/nota-casos-de- microcefalia.html.

[26] http://portalsaude.saude.gov.br/index.php/cidadao/principal/agencia-saude/20629-ministerio-da-saude-investiga-aumento-de-casos-de-microcefalia-em-pernambuco.

[27] Notification from the IHR NFPs of Brazil, Chile, Colombia, El Salvador, Guatemala, Mexico, Suriname, and Venezuela.

Congenital Anomalies

October 2015. The Brazil IHR NFP reported an unusual increase in microcephaly cases in public and private healthcare facilities in the state of Pernambuco, in northeastern Brazil.[28]

17 November 2015. Given the unusual increase in cases of microcephaly in some northeastern states of Brazil, PAHO/WHO called upon Member States to remain alert to the occurrence of similar events, and to notify their occurrence through the channels established by the IHR.

At that same time, the Flavivirus Laboratory at the Osvaldo Cruz Institute confirmed that Zika virus genome had been detected through RT-PCR in amniotic fluid samples of two pregnant women from Paraíba whose fetuses had been diagnosed with microcephaly by ultrasound.

Syndrome description: Microcephaly is a neurological disorder in which the occipitofrontal circumference is smaller than that of other children of the same age, race, and sex. It is defined as a head circumference of 2 standard deviations (SD) below the mean for age and sex or below the second percentile.

Microcephaly can be caused by a variety of genetic and environmental factors, and children with the condition may present developmental problems. In general, there is no treatment for microcephaly, but early intervention can help improve the child's development and quality of life. According to preliminary analyses of the investigation conducted by Brazil's health authorities, the greatest risk of microcephaly or congenital anomalies in newborns is associated with Zika virus infection in the first trimester of pregnancy. (See also *Neurological syndromes* below).

24 November 2015. Health authorities of French Polynesia reported an unusual increase of central nervous system malformations in fetuses and newborns during 2014-2015, coinciding with the Zika virus outbreaks on the islands. Out of 17 recorded malformations, 12 were fetal cerebral malformations or polymalformative syndromes, including brain lesions; five infants were reported to have brainstem dysfunction and absence of swallowing reflex. None of the pregnant women described clinical signs of Zika virus infection, but four women were found positive by IgG serology assays for flavivirus, suggesting a possible asymptomatic Zika virus infection. Further serological tests were under way. Based on the temporal correlation of these cases with the Zika epidemic, French Polynesian health authorities hypothesized when mothers were infected with the virus during the first or second trimester of pregnancy, Zika virus infection may be associated with these abnormalities.

28 November 2015. The Ministry of Health of Brazil established the connection between the increase in the number of cases of microcephaly and Zika virus infection, by detecting Zika virus genome in the blood and tissue samples of a baby from the state of Pará. The newborn presented microcephaly and other congenital anomalies, and died within five minutes of being born. The confirmation of the presence of the viral genome was provided by the Evandro Chagas Institute, in Belém, Pará, a national reference laboratory for arboviruses.

30 November 2015. By this date, 1,248 cases (99.7/100,000 live births) of microcephaly, including 7 deaths, had been reported in 14 Brazilian states. These events were under investigation. In 2000, the prevalence of microcephaly in newborns in Brazil was 5.5 cases per 100,000 live births, and in 2010, 5.7 cases per 100,000 live births. This data shows a twentyfold increase vis-a-vis the rate observed in previous years. Data was obtained from the Live Births Information System, which collects epidemiological data on pregnancy, births and congenital anomalies, in addition to the socio-demographic characteristics of the mothers.[29]

Figure 6 illustrates the distribution of microcephaly cases in the Region, and microcephaly rates in Brazil.

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[28] http://www.paho.org/hq/index.php?option=com_docman&task=doc_view&Itemid=270&gid=32286&lang=es
[29] http://www2.datasus.gov.br/DATASUS/index.php?area=0205

Figure 6. Countries and territories with confirmed cases of Zika virus (autochthonous transmission), 2014- 2015, and rates of microcephaly by state, Brazil, 2010-2014 and 2015
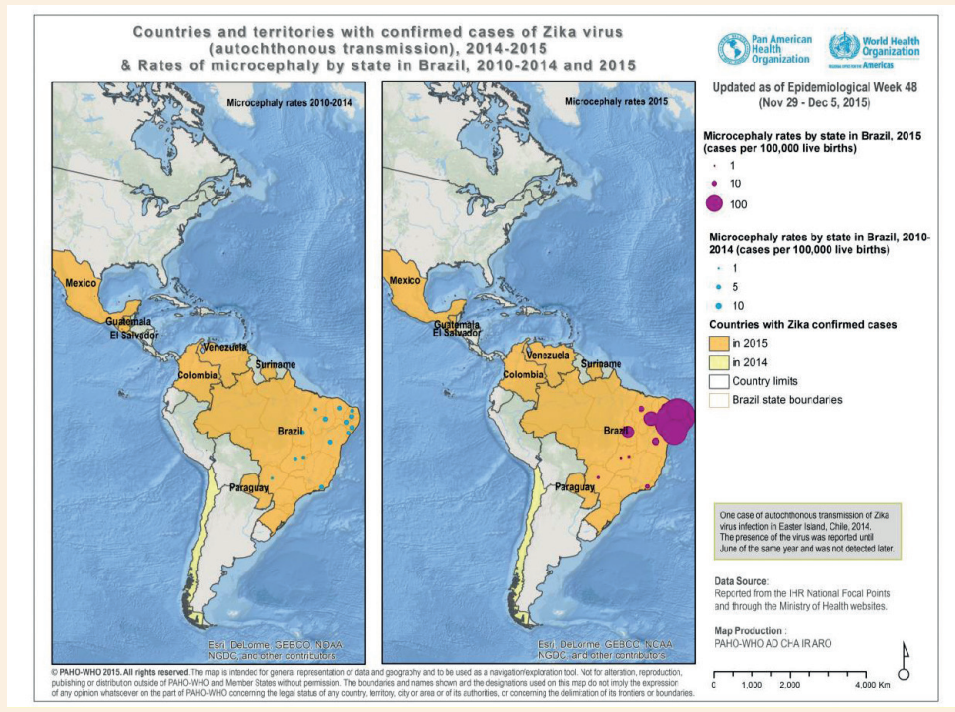
Neurological Syndromes

In July 2015, the Brazil IHR NFP reported the detection of neurological syndromes in patients with recent history of Zika virus infection, especially in the state of Bahía. Up to 13 July, a total of 76 patients with neurological syndromes had been detected. Of those, 55% (42/76) were confirmed cases of Guillain-Barré syndrome (GBS); 5 cases had other confirmed neurological disorders; 4 were ruled out, and 25 were still under investigation. Among those cases with GBS, 62% (26/42) had symptoms consistent with Zika virus infection.

Additionally, on 25 November 2015, the Aggeu Magalhães Research Center of the Oswaldo Cruz Foundation Institute reported that, of 224 suspected dengue patients whose samples had been analyzed for Zika virus infection, 10 had been confirmed positive. Of those 10 patients, 7 had developed neurological syndromes.

During the Zika virus outbreak in French Polynesia, 8,750 suspected cases were detected;[30] of those, 74 patients presented neurological or autoimmune syndromes following an illness consistent with Zika virus infection. Of those, 42 were confirmed GBS, 37 of which had presented previous viral syndrome.

Neither event established a causal relation with Zika virus; nonetheless, the hypothesis cannot be ruled out.

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[30] It is estimated that about 32.000 persons were infected.

Deaths Related to Zika Virus

As of 28 November 2015, the Ministry of Health of Brazil had reported three deaths associated with Zika virus infection. The first fatal case was an adult male with no neurological disorders, but with history of lupus erythematosus, chronic use of corticosteroids, rheumatoid arthritis, and alcoholism. Although he was hospitalized as a suspected dengue case, the final laboratory diagnosis by RTp-PCR was Zika virus infection. Zika virus genome was detected in blood, brain, liver and spleen samples, as well as in a pooled sample (brain, liver, and kidney). Zika virus was also identified through partial sequencing of the virus.

The second fatal case was a 16-year-old female from the Benevides municipality in the state of Pará. This case presented no neurological disorder, and was hospitalized as a suspected case of dengue. The onset of symptoms (headache, nausea, and petechiae) happened on 29 September 2015; the patient died in late October. Zika virus infection was confirmed by RTp-PCR. The third fatal case was the newborn previously described (28 November 2015).

Recommendations

Considering the spread of Zika virus transmission in the Region of the Americas, and the fact that the disease's vector is present in most countries of the Region, PAHO/WHO updated the recommendations on surveillance, and emphasized previous recommendations regarding other diseases borne by the same vector. The Organization also urged Member States where the *Aedes* mosquito is present to continue their efforts to implement an effective communications strategy aimed at reducing its density.

Given the increase in the number of cases of congenital anomalies, GBS and other neurological and autoimmune syndromes in areas where Zika virus is circulating, and their potential relation to the virus, the Organization recommended that Member States establish and maintain the capacity to detect and confirm Zika virus cases; prepare healthcare facilities for the possible increase in demand at all healthcare levels, as well as specialized care for neurological syndromes; and to strengthen antenatal care.

Below are the key recommendations related to surveillance, case management, and prevention and control measures.

Surveillance

Zika surveillance should be based on existing surveillance systems for dengue and chikungunya, and take into account differences in the clinical presentation of each infection. As appropriate to the country's epidemiological situation, surveillance should be aimed at (i) determining if the Zika virus has been introduced to an area; (ii) monitoring the Zika virus once introduced, or (iii) monitoring the emergence of neurologic and autoimmune complications of the disease.

In countries without autochthonous Zika virus transmission, the recommendation is to:

◖ Test for Zika virus in a percentage of patients with fever and arthralgia, or fever and arthritis of unknown etiology (e.g., those with negative test for malaria, dengue, chikungunya, and febrile rash illnesses). Cross reactivity with dengue serology tests should be taken into account, especially if the patient has had a prior dengue infection. Early detection will allow the identification of circulating strains, the proper characterization of the outbreak, and implementation of a proportionate response, and

- Strengthen event-based surveillance to detect the first cases. Based on the experiences of Brazil and Colombia, health authorities must be on alert for the emergence of clusters of cases of rash febrile syndrome of unknown etiology (in which dengue, chikungunya, measles, rubella, and parvovirus B19 have been ruled out), and laboratory tests for Zika virus detection.

In countries with Zika virus autochthonous transmission, the recommendations are to:

- Monitor temporal trends and the spread of the virus to detect the introduction into new areas;

- Determine the emergence of neurological and autoimmune complications, as well as their impact on public health;

- Identify risk factors for Zika virus infection, and

- Identify circulating Zika virus lineages, whenever feasible.

Once the introduction of the virus has been documented, ongoing surveillance should be maintained to monitor epidemiological and entomological changes that might affect Zika virus transmission. Any changes detected by the surveillance system should be promptly communicated to national prevention and control authorities, in order to ensure timely and appropriate decisions.

Below is a provisional[31] case definition for Zika virus infection.

Suspected case. Patient with rash or elevated body temperature (> 37.2 °C) with one or more of the following symptoms (not explained by other medical conditions): arthralgia or myalgia; non-purulent conjunctivitis or conjunctival hyperemia, and headache or malaise.

Confirmed case is a suspected case with positive laboratory result for the specific detection of Zika virus (see algorithm for laboratory diagnosis).

Available at: http://www.paho.org/hq/index.php?option=com_docman&task=doc_download&Itemid=&gid=30176&lang=en.

Neurological and Autoimmune Complications

Considering that neurological and autoimmune complications have been reported during some Zika virus and dengue outbreaks, it is recommended that Member States establish or strengthen surveillance of neurological syndromes for all age groups, particularly in situations of possible Zika virus circulation.

Surveillance of neurological syndromes is aimed at increasing awareness of health care professionals, so that they may provide adequate clinical management to those cases presenting neurological complications; also, to contribute to finding the possible relationship between neurological complications, Zika virus infection, and previous infection with other agents.

Congenital Anomalies

PAHO/WHO recommends analyzing live birth databases, specifically regarding malformations/neurological disorders, in order to detect any unusual increase in frequency.

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[31] This case definition is based on the definition used during the outbreak in French Polynesia, 2013-2014 (Direction de la Santé BdVs, Polynesie Francaise. Surveillance de la dengue et du zika en Polynésie Française, 2013-2014. Available at: http://www.hygiene-publique.gov.pf/spip.php?article120). It has been adapted to the clinical description available after the introduction of the Zika virus in the Region of the Americas, and may be subject to further modifications as new knowledge and information on the disease and the etiological agent becomes available.

Surveillance of neurological anomalies must be part of the surveillance of congenital anomalies. It should be ongoing to better determine the magnitude and burden due to said conditions.

Event-based surveillance is a useful tool in this situation. For this reason, healthcare professionals involved in antenatal care, as well as child care, should be encouraged to report all unusual events.

Microcephaly is defined as a head circumference of 2 standard deviations (SD) below the mean for age and sex, or approximately below the second percentile. There are no absolute values to define microcephaly given that it varies by race, sex, and gestational age.

Any increase of microcephaly or other neurological congenital disorders must be assessed, investigated, and reported to pertinent public health authorities.

Laboratory Diagnosis

During the first 5 days following the definition of the clinical situation (viremic period), viral ribonucleic acid (RNA) can be detected in serum by molecular techniques (conventional or RT-PCR). RT-PCR for dengue as the main differential diagnosis should be negative. In addition, a generic assay for flavivirus, followed by genetic sequencing to establish the specific etiology could be used as well.

When a case is clinically suggestive of infection, and negative for dengue, further tests for other flaviviruses, including Zika virus, should be performed.

Serological tests (ELISA or immunofluorescence) to detect specific IgM or IgG antibodies against Zika virus may be positive after 5 or 6 days, following the onset of symptoms. It is necessary to show an increased antibody titer in paired samples, with an interval of about two weeks. However, confirmation of positive results with plaque reduction neutralization test (PRNT), showing at least a four-fold increase in the titer of neutralizing antibodies to Zika virus, is recommended. There can be cross-reactivity with other flaviviruses, especially dengue and yellow fever or, less frequently, with West Nile virus. Hence, a fourfold rise or more of the neutralizing antibody titer against dengue in a patient infected with Zika virus, particularly if the patient has previously had dengue, could be detected. Given this cross-reactivity of flavivirus, serology results should be interpreted with caution.

International Reporting

Because of the recent introduction of Zika virus in the Americas, and to contribute to integrated arbovirus surveillance, national public health authorities are encouraged to inform PAHO/WHO through established IHR channels, any laboratory- confirmed cases of Zika virus infection reported in the countries and territories of the Region.

Additionally, in order to contribute to the knowledge of Zika virus infection complications, PAHO/WHO urged Member States to report any increase in cases of neurological and autoimmune syndromes (in adults and children), or congenital malformations in newborns that cannot be explained by other known causes.

Case Management and Treatment

Because Zika virus outbreaks could generate additional burden at all levels of the health care system, it is necessary to develop and implement institutional protocols for the triage and rehabilitation of patients.

- There is no vaccine or specific treatment for Zika virus infection.

- Treatment is mainly symptomatic and supportive; it includes rest, and the administration of acetaminophen for fever relief. Antihistamines to control pruritus, usually associated with maculopapular rash, could be prescribed.

- Aspirin is not advised, due to the risk of bleeding and developing Reye's syndrome in children younger than 12 years of age. The use of other nonsteroidal anti-inflammatory drugs is not advised either, since the clinical symptoms may be caused by dengue or chikungunya, diseases in which their use is contraindicated.

- Patients should be advised to drink plenty of fluids to replenish those lost from sweating, vomiting and other losses.

Differential Diagnosis

It is important to differentiate Zika virus infection from dengue due to severe clinical outcomes of dengue. In addition, co-infection (Zika and dengue) could affect the same patient. Compared with dengue, the clinical picture of Zika virus infection is milder or more moderate, the onset of fever is more acute and shorter in duration; in addition, no shock or severe bleeding has been observed.

Patient Isolation

To prevent the spread infection, a Zika virus-infected patient should avoid *Aedes* mosquito bites during the first week of illness (viremic phase). Resting under a bed net – whether it is insecticide-treated (IT) or not – or remaining in a place with intact window/door screens is highly recommended. Physicians or health care workers who take care of Zika virus-infected patients should protect against mosquito bites by using insect repellent (IR3535 or Icaridin), and wearing long sleeves and pants.

Prevention and Control Measures

Vector prevention and control

Vector prevention and control measures to reduce vector density are crucial, and, if effective, can prevent transmission of this and other mosquito-borne viruses.

An effective and operational Integrated Management Strategy for the Prevention and Control of Dengue (IMS –Dengue) provides the basic preparedness for Zika virus. In the current situation, the intensification of comprehensive prevention and control measures based on IMS-dengue is recommended. Because of the relevance of vector control measures, key elements of a vector control program for guiding the response are listed below.

Integrated Vector Management (IVM)

An effective and operational dengue and chikungunya vector control program provides the basis for adequate preparation against Zika virus. Therefore, the recommendation is to apply and intensify surveillance and vector control measures developed for dengue and chikungunya, as part of the integrated vector management component.

To ensure success, it is imperative to include intersectoral participation and collaboration at all levels of government, including health, education, environment, social, development and tourism sectors, among others. IVM also relies on support of non-governmental and private organizations. Communication channels must remain open, and community participation must be mobilized. It is important to provide clear and trustworthy information to the public about these diseases via communication campaigns.

Given the broad distribution of *Ae. aegypti* and *Ae. albopictus* in the Americas, prevention and control measures should be aimed at reducing vector density, and obtaining the acceptance and collaboration of communities in adopting such measures. Hence, national authorities should strive to:

◖ Strengthen environmental management to prevent or minimize vector propagation, and human contact with the mosquito, by eliminating vector breeding sites in each household and in common areas of districts and cities (e.g., parks, schools, cemeteries, etc.).

◖ Organize mass sanitation campaigns to eliminate breeding sites, specifically in areas where routine garbage collection has been interrupted.

◖ Implement breeding site control measures by physical, biological and chemical methods, while actively involving families and communities.

◖ Identify areas of high risk of transmission (risk stratification), and prioritize those where people are concentrated (e.g., schools, transport terminals, hospitals, health centers, etc.). Mosquitoes should be removed from a radius of at least 400 meter around these facilities.

◖ In areas where autochthonous or imported cases of dengue, chikungunya, and/or Zika virus are detected, the use of insecticide (adult) treatment is suggested (primarily through spraying) to remove infected mosquitos and interrupt transmission. It is important to take into account that this is an exceptional measure, which is only effective when carried out by adequately trained personnel, following internationally accepted technical guidelines, and when implemented together with other proposed measures, as described above. Spraying is the primary way to intensively interrupt transmission, and to gain time to consolidate the removal of larval breeding sites.

◖ Select the appropriate insecticides (in accordance with PAHO/WHO recommendations), verifying the product's label and formula, and considering the susceptibility of mosquito populations to the selected insecticide.

◖ Use and maintain spraying equipment appropriately, and maintain stockpiles of insecticides.

◖ Ensure intensified monitoring (e.g., quality control) of fieldwork operators, both during larval control and adult insecticide treatments (fumigation).

Integrated (simultaneous or coordinated) vector control activities in space and time (e.g., insecticide and larval control by trained personnel, coupled with sanitation and the promotion of community participation) are essential to achieve the greatest impact in the shortest time frame.

It is crucial that personnel involved in chemical control use, without exception, appropriate personal protection equipment for this activity. It is the responsibility of vector control programs to supply this equipment to staff, to audit its use, and to have sufficient stockpiles under appropriate conditions.

Personal Prevention Measures

It is important for patients infected with dengue, chikungunya, or Zika virus to minimize contact with the vector. This measure helps prevent the spread of the virus and, therefore, the disease. Patients, their household members, and the community must be educated about the risk of transmission to others, and of the ways to minimize the risk by reducing vector populations and human-vector contact.

The following measures are recommended to minimize vector-patient contact:

◖ Patients should rest under mosquito nets (bed-nets), with or without insecticide.

◖ Patients and other members of the household should wear clothes that cover the extremities.

◖ Apply repellents containing DEET, IR3535 or Icaridin to exposed skin or clothing; its use must strictly follow the instructions printed on the product's label.

◖ Use wire-mesh screens on doors and windows.

Personal prevention measures are also effective in preventing transmission of the virus to healthy people.

Travelers

Prior to departure, health authorities should advise travelers heading to any country with documented circulation of dengue, chikungunya, and/or Zika virus to take the necessary measures to protect themselves from mosquito bites. It is also important to inform travelers of the symptoms of dengue, chikungunya, and Zika virus, in order to assist them in identifying those infections promptly while on travel. This advice could be relayed through travel medicine services, clinics, travel health web pages of the Ministry of Health, or other relevant government web pages.

While visiting places with dengue, chikungunya, and/or Zika virus transmission, travelers should be advised to:

◖ Take appropriate measures to protect themselves from mosquito bites through the use of repellents or appropriate clothing that minimizes skin exposure.

◖ Avoid mosquito-infested areas.

◖ Use nets and/or insecticide.

◖ Recognize symptoms of dengue, chikungunya, and Zika virus and seek professional health care if any of the symptoms develop.

Upon returning, travelers should be advised that if they suspect they have dengue, chikungunya, or Zika virus infection, they should contact their health care provider.

Specific Recommendations Regarding Microcephaly

The following recommendations on surveillance, case management, and prevention and control measures for microcephaly will be reviewed and updated as new evidence on the disease becomes available. These recommendations emphasize those of preceding paragraphs regarding Zika virus infection.

In order to contribute to the further understanding of the etiology of this event, PAHO/WHO urged Member States to report any increase in the number of cases of microcephaly or other neurological disorders in newborns that cannot be explained by known causes.

Surveillance and Investigation

PAHO/WHO recommends analyzing live birth databases, specifically in relation to malformations and neurological disorders, in order to detect any unusual increase in their frequency. Surveillance of microcephaly must be integrated into the monitoring of congenital anomalies. This surveillance should be continuous to help determine the disorder's magnitude and burden.

Any increase in the number of cases of microcephaly or other congenital neurological disorder should be analyzed and investigated.

There are no absolute values to define microcephaly, given that the cranial circumference varies by race, sex, and gestational age. For this reason, the WHO child growth standards tables on head circumference-for-age, with percentiles, and expanded tables for constructing national health tables are available at: http://www.who.int/childgrowth/standards/hc_for_age/en/.

Clinical Manifestations and Case Management

Infants with microcephaly often have other concurrent disabilities. Different symptoms and signs associated with microcephaly (very small head, difficulty feeding, high pitched crying, seizures, spasticity of arms and legs, developmental delays and disabilities, among others) have been described. Infants with suspected microcephaly must always be evaluated by a healthcare professional. In addition to the clinical evaluation, neuroimaging tests to evaluate possible structural damage are generally required.

There is no specific treatment for microcephaly. Infants with the condition who show developmental delay might benefit from early intervention programs or developmental, physical, and occupational therapy, as well as from interdisciplinary programs.

Pregnant Women and Newborn Follow-up

It is important to ensure antenatal care for pregnant women, including basic clinical assessment and paraclinical tests, according to established national protocols.

In areas where the Zika virus is circulating, pregnant women should be emphatically advised to take personal precautions to avoid contact with the vector (see recommendations under personal prevention measures).

Newborns with congenital malformations must be monitored to determine any neurodevelopmental outcomes. The evaluation of newborns with congenital anomalies requires the participation of multidisciplinary teams, including neuro-pediatricians, geneticist, rehabilitation therapists, psychologists, and social service providers, among others.

Parents or guardians should be properly informed of the fetus or newborn conditions, especially if there is a risk of unfavorable outcomes. They should be made aware of the importance of follow-up appointments, and of following health and disease prevention measures.

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