



TECHNICAL DOCUMENT

**The pharmacist's role in
prevention, detection and
control of the arbovirus
infections from the community
pharmacy:
Dengue - Zika - Chikungunya
Yellow fever**

Dr. Cristina Fernández Barrantes

July 2018





ABOUT THE AUTHOR

Cristina Fernández Barrantes is a Doctor of Pharmacy (PharmD) from the University of Medical Sciences of Costa Rica and has a Master degree in Clinical Pharmacology from the Autonomous University of Barcelona. She currently works in the Drug Information Center of San Juan de Dios Hospital and she is a professor in the School of Pharmacy of the University of Costa Rica. Her study and interest area are pharmacovigilance, drug information and patient education, antibiotic therapy and drug interactions.



The contents of this publication are under a Creative Commons license protecting copyright. Its use allows its non-commercial remixing, retouching and creating, provided that credits are given to the author and the new creations are licensed under the same terms.

PHARMACEUTICAL FORUM OF THE AMERICAS

Executive Committee 2017-2018

President

Pharm. Gustavo Dodera Martínez (Argentina)

Vice-president

Pharm. Laura Raccagni (Argentina)

Treasurer

Pharm. Chem. Yolanda Zapata Bustamante (Ecuador)

Director of Pharmaceutical Education

Dr. Yajaira Quesada Rojas (Costa Rica)

Director of Pharmaceutical Practice

Dr. Nuria Montero Chinchilla (Costa Rica)

Technical Secretariat

Pharm. Chem. Carlos Lacava Fernández (Uruguay)

National member organizations

Confederación Farmacéutica Argentina (CoFA)
Argentinian Pharmaceutical Confederation

Conselho Federal de Farmácia do Brasil (CFF)
Federal Council of Pharmacy of Brazil

Colegio Nacional de Químicos Farmacéuticos de Colombia (CNQFC)
National College of Pharmaceutical Chemists of Colombia

Colegio de Farmacéuticos de Costa Rica (CoIFar)
College of Pharmacists of Costa Rica

Colegio de Químicos, Bioquímicos y Farmacéuticos de Pichincha, Ecuador (C.Q.B.F.P.)
College of Chemists, Biochemists and Pharmacists of Pichincha

Asociación de Químicos Farmacéuticos del Paraguay (AQUIMFARP)
Association of Pharmaceutical Chemists of Paraguay

Asociación de Química y Farmacia del Uruguay (AQFU)
Association of Chemistry and Pharmacy of Uruguay

American Pharmacists Association (APhA)

American Society of Health Pharmacists (ASHP)



Observing organizations

Pan-American Health Organization (PAHO)

International Pharmaceutical Federation (FIP)

Federación Panamericana de Farmacia (FEPAFAR)
Pan-American Pharmaceutical Federation

Federación Farmacéutica Sudamericana (FEFAS)
South American Pharmaceutical Federation

Federación Farmacéutica Centroamericana y del Caribe (FFCC)
Central American and Caribbean Pharmaceutical Federation

Consejo General de Colegios Oficiales de Farmacéuticos de España
General Board of Official Pharmaceutical Colleges of Spain



Organización
Panamericana
de la Salud



Organización
Mundial de la Salud
OFICINA REGIONAL PARA LAS Americas



International
Pharmaceutical
Federation



CONSEJO GENERAL
DE COLEGIOS OFICIALES
DE FARMACÉUTICOS



FEPAFAR
Federación Panamericana de Farmacia



Federación Farmacéutica
Sudamericana

Prologue

The region of the Americas is suffering from an important public health challenge due to infectious diseases transmitted by arbovirus. In February 2016, in the face of an increase of neonatal malformations and neurological disorders reports related to the disease caused by zika virus, the World Health Organization (WHO) declared a public health emergency of international concern. At the beginning of February of that year a Summit of Health Ministers of the Americas had been held in Montevideo, Uruguay under the sponsorship of the Pan-American Health Organization (PAHO) to consider the action plan related to this situation. The following month, in March, 2016, the Education and Research Foundation of the International Pharmaceutical Federation (FIP) provided financial support to the project *“Infectious diseases transmitted by Aedes aegypti mosquito, dengue, chikungunya and zika: a challenge for health systems. Supporting pharmacists to contribute to improve public health in the Americas population”*, proposed by the Pharmaceutical Forum of the Americas (PFA).

The pharmacists can develop a series of relevant activities at the primary health care level and contribute with their actions to the improvement of the public health, as long as they are well informed about what to do and there is a national and international collaboration framework. This is how this project was aligned with the good pharmaceutical practices promoted by FIP, WHO and PAHO, in accordance with the foundational goals of the PFA, which seek to improve health in the Americas through the development and improvement of pharmacy practice and pharmaceutical education; the execution of projects related to the practice of pharmacy and pharmaceutical education by pharmaceutical organizations of the Americas; the integration of FIP and PAHO/WHO policies regarding professional practice and the undergraduate, postgraduate and continuous educational programs; as well as the preparation and dissemination of statements and technical documents supporting the policies defined by the regional and international pharmacy organizations.

In the framework of the project execution, it is necessary to highlight that the main innovation was to promote a comprehensive approach which allowed estimating how the execution of actions aimed at the prevention of infectious diseases by the pharmacist, contributes to the improvement of the effectiveness of the health systems and the health of the population in the region of the Americas.

The technical document entitled: *The pharmacist's role in the prevention, detection and control of the arbovirus infections from the community pharmacy*, drafted by Dr. Cristina Fernández Barrantes, constitutes a fundamental contribution to the achievement of goals outlined in the execution plan of this project. In the first part of this document, a review of the epidemiology, pathophysiology, diagnosis, treatment and strategies for the prevention of the four arbovirus infections which currently constitute a health problem in the Americas is carried out: dengue, zika, chikungunya and yellow fever. In the second part, the main actions a pharmacist can develop for the detection, control and prevention of the diseases caused by the arbovirus infection are identified.

Cristina Fernández Barrantes is a young pharmacist from Costa Rica, who received the support from FIP Education and Research Foundation to participate in FIP World Pharmacy and Pharmaceutical Sciences Congress held in Dusseldorf, Germany in 2015. Since then, she has been associated to the activities developed by FIP and PFA.

On behalf of the Executive Committee of the Pharmaceutical Forum of the Americas, we thank the contribution of Dr. Cristina Fernández Barrantes. Equally important, we want to acknowledge all the people who collaborated with the revision of this document.

Dr. Nuria Montero Chinchilla
Director of Pharmaceutical Practice

Pharm. Gustavo Dodera Martínez
President

TABLE OF CONTENTS

I. Introduction	1
II. General considerations of arbovirus infection	3
III. Clinical description of arbovirus infections:	7
3.1 Dengue	7
3.1.1 Epidemiology	7
3.1.2 Pathophysiology	9
3.1.3 Clinical symptoms	11
3.1.4 Classification according to severity	16
3.1.5 Dengue in special populations	17
3.1.6 Diagnosis	19
3.1.7 Treatment of non-serious forms	20
3.1.8 Prevention strategies	20
3.2 Zika	21
3.2.1 Epidemiology	21
3.2.2 Pathophysiology	23
3.2.3 Clinical symptoms	25
3.2.4 Surveillance in neurological complications and special populations	27
3.2.5 Diagnosis	32
3.2.6 Treatment	32
3.2.7 Prevention strategies	33
3.3 Chikungunya	35
3.3.1 Epidemiology	36
3.3.2 Pathophysiology	38
3.3.3 Clinical symptoms	39
3.3.4 Chikungunya in special populations	41
3.3.5 Diagnosis	42
3.3.6 Treatment and prevention	42
3.4 Yellow fever	43
3.4.1 Epidemiology	43
3.4.2 Clinical symptoms	46
3.4.3 Yellow fever in special populations	49
3.4.4 Diagnosis	49
3.4.5 Treatment	50
3.4.6 Prevention strategies	51
3.5 Differences between dengue, chikungunya and zika	54
IV. Pharmacist's role in detection, control and prevention of arbovirus infections: patient education campaigns and public health strategies	57
4.1. Pharmacist's actions in detection and management of arbovirus infections in pharmacies	58
4.2 Vectors control	61
4.3 Dengue and yellow fever vaccination	69
4.4 Education: Education: preparation of information material, public health campaigns and presence in the media	71
V. Conclusions	90
VI. References	92

I. INTRODUCTION

Diseases produced by the arbovirus infection are a serious global public health problem, their surveillance and prevention not only imply the control of the viral disease but also the surveillance of the vectors. During the last year, a spread of the virus towards tropical and subtropical territories and even warm regions has been observed¹.

According to data from the World Health Organization (WHO) in 2016, diseases transmitted by vectors represent more than 17 % of all infectious diseases and, each year, they cause more than one million deaths¹.

Latin America is facing an epidemic of dengue, zika and chikungunya, viral infections transmitted by *Aedes* mosquito, mainly *Aedes aegypti*.

Dengue is the most common disease caused by arbovirus infection globally, nearly 2500 million people, in more than 100 countries are at risk of contracting dengue. It is estimated that 40 % of the world's population lives in areas of transmission of this virus. Approximately one of every 2000 dengue cases causes the death. It is estimated that the fatality rate of patients with serious dengue can be reduced from almost 10 % to less than 0.1 % if actions are taken promptly².

In view of the recent and quick spread of chikungunya virus at the end of 2013 and zika virus in 2014 in Latin American countries, the action of the pharmacist becomes necessary in the detection, prevention and control of these pathologies. The pharmacist is the healthcare professional most available to the population, so his active participation will directly impact the public health of the region.

Yellow fever is another arbovirus infection that has been present in the Americas and West Africa region. The term "yellow" refers to the jaundice that some patients have. Since the launching of the initiative against yellow fever by the WHO in 2006, major developments have been made in the fight against the disease. However, it is still a threat to public health.

The four arbovirus infections (dengue, zika, chikungunya and yellow fever) can produce a very similar clinical picture, mainly during the acute phase (first days of the disease), making it difficult for health personnel to make a clinical diagnosis and, thus, creating a problem for its proper management and occasionally triggering deadly events³.

The general objective of this technical document is to provide a bibliographical review regarding the epidemiology, the pathophysiology, the diagnosis and the treatment of the arbovirus infections: dengue, zika, chikungunya and yellow fever, which have a greater impact in the region of the Americas, as well as a review of the detection, control and prevention strategies in which the pharmacist can actively participate.

During 2016, the Pharmaceutical Forum of the Americas, through the “*Pharmacists United against Dengue, Chikungunya and Zika*” campaign, has established the following scope of action for the pharmaceutical professional⁴:

- To orient the population about the prevention and control of these diseases.
- To identify suspicious signs and symptoms and refer people to the health services for a diagnostic evaluation.
- To indicate, when relevant, proper therapies for the relief of signs and symptoms (over the counter medication).
- To monitor the patients under treatment and with a diagnosis to see if they achieve their therapeutic goals.

To mitigate the burden these diseases have on the public health, daily measures must be taken in every community. This is why the community pharmacist is encouraged to stay updated regarding this subject and to promote and develop the necessary strategies which will result in an improvement in the detection, management, prevention and control of dengue, zika, chikungunya, yellow fever and other arbovirus infections in the region.

II. General considerations of arbovirus infection

The term arbovirus infection refers to a heterogeneous group of viruses in the nature that are transmitted by hematophagous arthropods (vectors) to susceptible vertebrate hosts, generally wild animals. More than 500 viruses of this type are recognized and approximately 150 can cause the disease in humans. They are mainly divided in three families (figure No 1) and another way to classify them is according to the type of syndrome they cause in humans (figure No 2)^{2,5}.

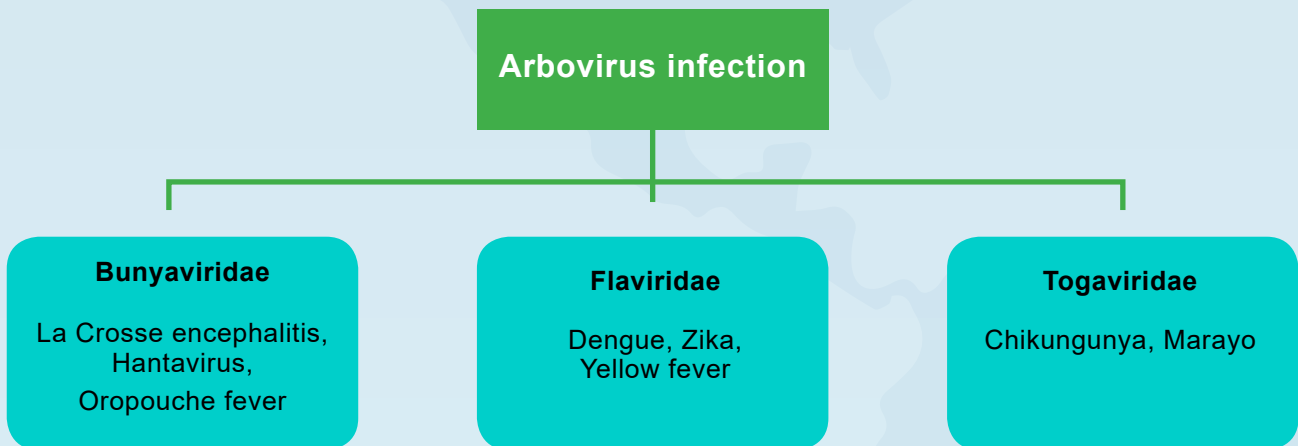


Figura N°1. Arbovirus infection group families
Adapted from: Acta Pediatr Mex. 2016 mar; 37(2): 111-131

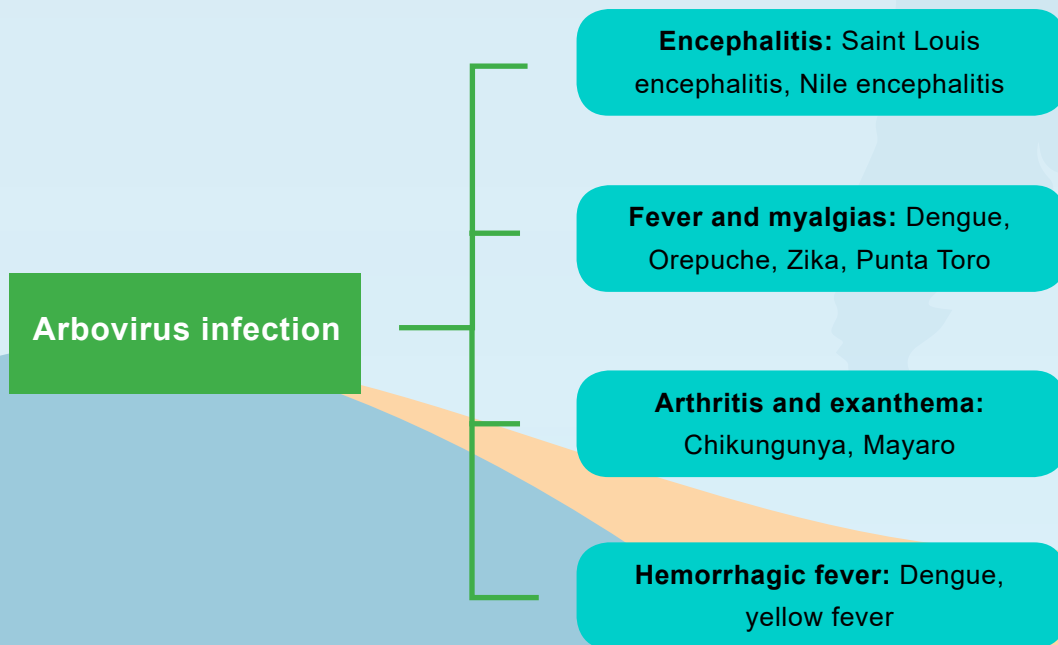


Figura N°2. Classification according to the syndrome it causes in humans
Adapted from: Acta Pediatr Mex. 2016 mar; 37(2): 111-131

There is a wide variety of vectors, such as mosquitoes, ticks, fleas; however, in this revision those which are transmitted by the *Aedes* mosquito (*Aedes aegypti*, *Aedes albopictus*, *Aedes polynesiensis*, among others) and affecting the Latin American territory will be addressed².

The maintenance cycles are those which allow the virus permanence in the nature. In general, these cycles take place in jungle or rural environments and they are usually responsible for the low levels of endemicity in certain regions. Ecological alterations or human modifications of the environment allow the increase of the vector insect's populations, vertebrates or in the level of virus circulation generating the so-called amplification cycles which, in general, trigger epidemic outbreaks⁵.

Normally, the arbovirus infections have little to no effect on the arthropod vectors, while the infection of vertebrate hosts can result in a significant morbidity and mortality⁵.

In this context, instead of a simple alternation within a single host-vector pair, the transmission of arbovirus infection is caused through high complexity transmission networks including several vertebrate hosts and vector insects. Particularly, humans are not necessarily the center of the transmission network and they can just be accidental hosts⁵.

Consequently, the surveillance of the arbovirus infections requires the control of vectors, which is why diseases caused by the arbovirus infection are hard to prevent and control².

It is believed that *Aedes aegypti* came from Africa to America with the arrival of the first Europeans to the American continent. The first outbreaks of the dengue disease in the Americas region date from 1635. The *Aedes albopictus* is also an arbovirus infection vector in South-East Asia and it appeared in the American continent for the first time in the United States in 1985. *Aedes albopictus* can act as a vector in urban and rural areas and it is not necessarily anthropophilic as *Aedes aegypti*. *Aedes aegypti* females are considered the most efficient mosquito vectors for its marked domestic habits which satisfy all their vital needs in the human habitation. The female requires human blood to keep its reproduction, it lays its eggs in clean or semi-clean water deposits, which is an important information for its control, as the viable breeding sites for the mosquito are all those objects serving as containers where rainwater is collected or objects where the water can remain stagnant, such as flowerpots².

In 1957, the Pan American Health Organization (PAHO) carried out an antivectorial campaign in Mexico for the elimination of Aedes, a goal that was reached in 1963. However, this situation could only be maintained for less than two decades. In 1978, a dengue case is documented, thus confirming its re-emergence².

Re-emerging diseases refer to those that rise after apparently having been eradicated or their incidence having been reduced, however, during the last years they became important under changing conditions of the nature and particular ecosystems, and they may appear in epidemic proportions constituting a health problem⁵.

It is believed that the re-emergence of the vectors lies in the social, economic and environmental factors which directly affect the evolution and adaptation mechanisms of these insects. Some of these factors are^{2,6}:

- **Climate change:** The increase in global temperature of 1 to 2 degrees can affect the extension of the geographical areas where the insects develop.
- **Demographic growth and distribution:** It is estimated that by the year 2020, 80 % of the population will be concentrated in the cities.
- **Deforestation and poor urbanization:** Lack of drinking water, which forces inhabitants to store water in badly covered containers or containers exposed to inclement weather.
- **Inadequate disposal of solid and liquid waste:** The inadequate waste disposal areas favor the emergence of potential transmitting mosquitoes breeding sites.
- **Migration and tourist trips:** The greater speed at which the population currently travels makes it possible for millions of people to cross borders every year favoring the virus circulation from the endemic areas to the disease-free areas. A publication from the "*Journal of Travel Medicine*" from 2013 presented the results from four prospective studies in which it is estimated that the incidence of dengue among those persons living in disease-free areas travelling to endemic areas is of 10.2 to 30 for every 1000 persons-month⁷. Although most of the infections are mild or even asymptomatic, a small proportion develops hemorrhagic dengue⁷.

A study carried out in two Mexican communities in 2012 evaluated the cultural dimensions that may favor or hinder dengue prevention. One of the communities had a greater historical experience with dengue than the other. A greater consensus was observed among the participants of the population with greater experience compared to the other population, which showed a more fragmented understanding. It was found that the information handled about the disease was confusing and insufficient, making other people and public bodies responsible for the prevention and excessively depending on fumigation as the only preventive measure, which makes cultural dimensions a hindrance to dengue prevention⁶. We will come back to the subject later, as they are an input to create public health interventions where the pharmacist can participate.

The arbovirus infections are not only causing problems in public health in Latin America. In the United States, they have an important impact with the introduction of dengue virus, mainly in the southern states, California, Florida and Hawaii, also in countries such as Puerto Rico and in the Caribbean islands as *Aedes* is spreading in those territories.

A study published in 2014 by “*Annals of Global Health*” Journal estimated the global economic burden dengue has. In the period between 2001 and 2010, \$950 million were invested annually in the medical treatment and vector control⁸.

III. Clinical description of infections caused by dengue, zika, chikungunya and yellow fever viruses

Following, a pathophysiology, clinical, diagnosis and treatment review of each of the arbovirus infections under study in this document will be carried out: dengue, zika, chikungunya and yellow fever. Then, a comparison between them will be made and finally, the differential diagnosis will be presented.

3.1 Dengue

3.1.1 Epidemiology of dengue

Dengue is a flavivirus with four related serotypes (DENV-1, DENV-2, DENV-3, DENV-4). Each of them generates an immune response to the unique infection in the host (they do not provide cross-immunity). They are distributed throughout the tropical and subtropical regions of the world and some warm regions of the United States, Europe, Africa and Middle East^{2,9}. These serotypes are genetically similar, they share approximately 65 % of its genome and they are communicable to primates (wild type) and humans (human type) mainly by *Aedes aegypti* mosquito^{2,12}.

The economic and social burden of dengue is important. It is estimated that 3,000 million people live in areas with risk of contracting dengue and there are 390 million infections (96 million of them are symptomatic) and 20,000 deaths each year. Dengue virus has a great spreading potential as *A. aegypti* can adapt to the urban life easily, so it can reach all the tropical and the subtropical areas. The *A. albopictus* is the second vector in importance related to dengue, which has also spread to different areas quickly in the last years^{9,12}.

In most cases, it appears as influenza or fever undifferentiated and in some 500,000 patients, as hemorrhagic dengue. In 1970, only nine countries had suffered hemorrhagic dengue epidemics, a number that had quadrupled by 1995. Currently, the disease is endemic in more than 100 countries from Africa, America, Eastern Mediterranean, South East Asia and Western Pacific. Before 1981, dengue was considered a public health problem of the Asian continent. This scenario changed as a result of the Cuban epidemic of that year, which was the first hemorrhagic dengue epidemic in America. Currently, it is the most important re-emerging disease in the American continent (Table No 1)^{2,9}.

Table No 1

Incidence of infections caused by dengue virus in America at the 52 week of the year 2016

Subregions	Dengue	Incidence rate x 100,000 inhabitants	Number of serious dengue cases	Deaths	Fatality rate
North America, Central America and México	286 895	57.7	1330	63	0.02
Andean	210 859	151.7	1379	275	0.13
Southern Cone	1 750 826	638.5	892	655	0.04
Hispanic Caribbean	80 272	313.8	670	39	0.05
English and French Caribbean	9 993	51.7	3	0	0.00
Total	2 338 849	244.8	4274	1032	0.04

Source: Number of cases of dengue and serious dengue reported in America, PAHO 2016¹³

The countries of the region with the four dengue circulating serotypes are: Mexico, Guatemala, Nicaragua, Colombia, Venezuela, French Guiana, Guadalupe, Brazil, Peru and Argentina².

Figure No 3, taken from the web page of the Center for Disease Control and Prevention of the United States (CDC) shows the global prevalence and presence of dengue according to the susceptibility of transmitting the infection. The blue colors in the map show the countries not susceptible to transmitting the infection or they are non-endemic regions. The regions in yellow color are those with no epidemiological information, the regions in orange color are those where it is probable to find the circulating virus and last, the regions in which the presence of the virus and the vector have been confirmed are in red.

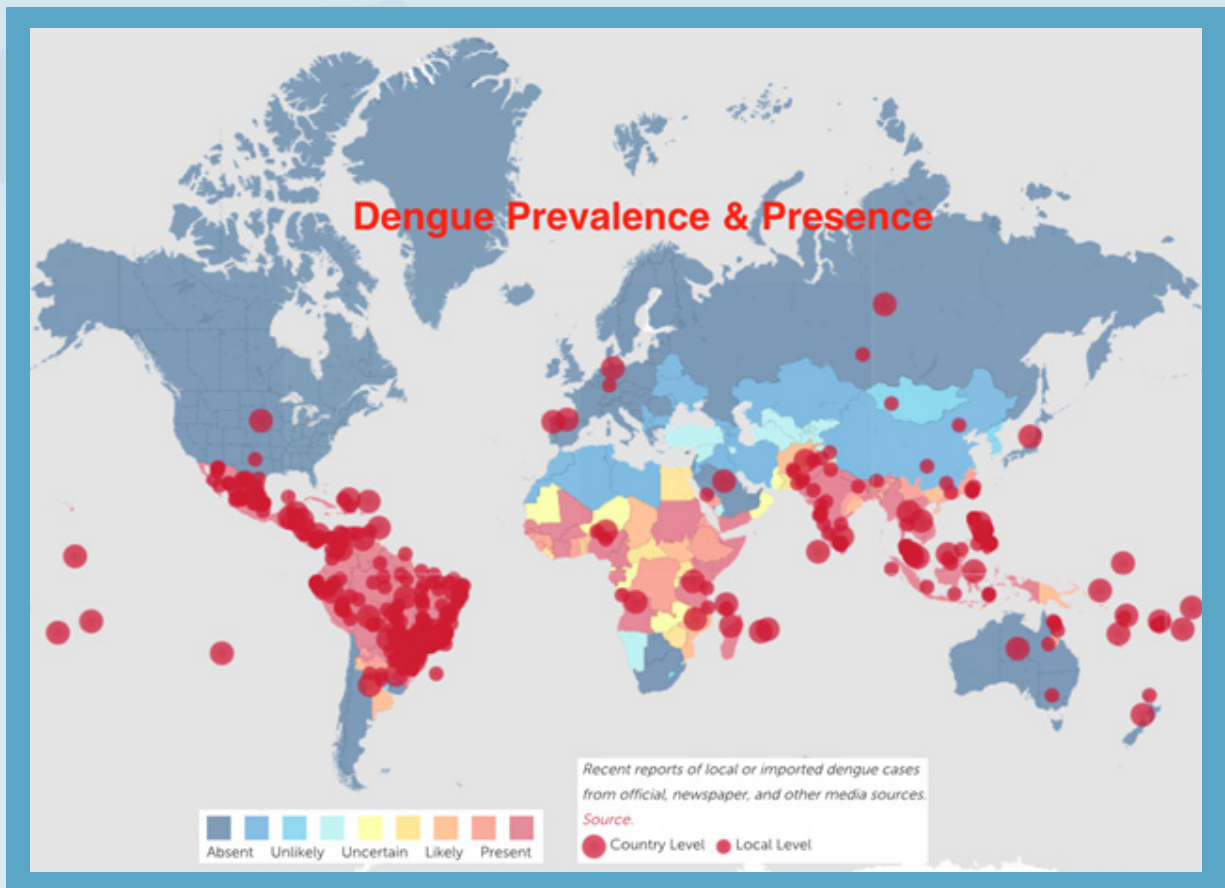


Figure No 3. Global distribution of dengue virus according to CDC¹⁵
 Source: Dengue World Map. <http://www.healthmap.org/dengue/es/>

3.1.2 Pathophysiology of dengue

Aedes females acquire the virus when biting a viremic vertebrate host. The virus infects the epithelial cells of the mosquito midgut, it spreads to the circulation and infects the salivary glands. This is where it establishes a persistent infection with an important replication in these cells. After biting the host, the female mosquito regurgitates saliva full of virus to the blood of the victim. The virus freely circulates in the plasma and comes into contact with the susceptible cells: endothelial cells, macrophages, monocytes and other cells from the mononuclear phagocyte system. (Figure No 4). The innate immune system is the first line of defense against the dengue virus and the infection triggers the expression of a wide variety of cytokines and inflammatory chemokines^{2,9}.

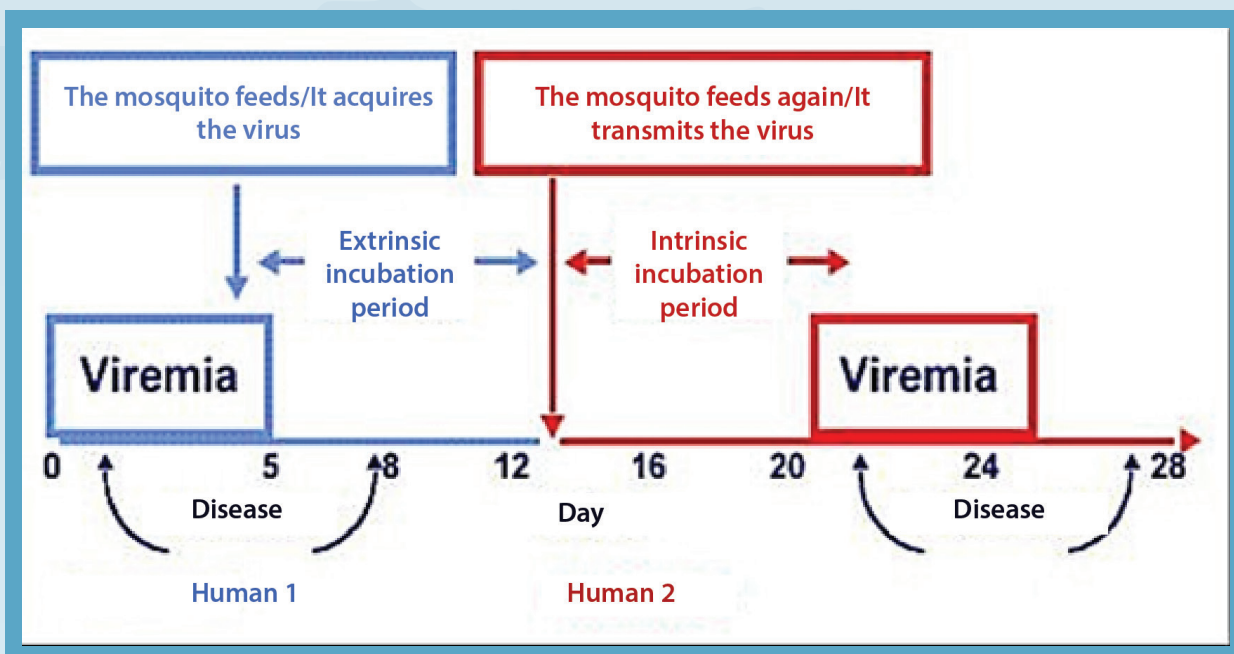


Figure No 4. Infection by the dengue virus in humans¹⁰
 Source: <http://epidemiologiaescobar.blogspot.com/2010/09/dengue-epidemiologiaescobar.html>

The infection can be asymptomatic or appear with a wide clinical spectrum which includes serious and non-serious symptoms, where four stages are recognized:

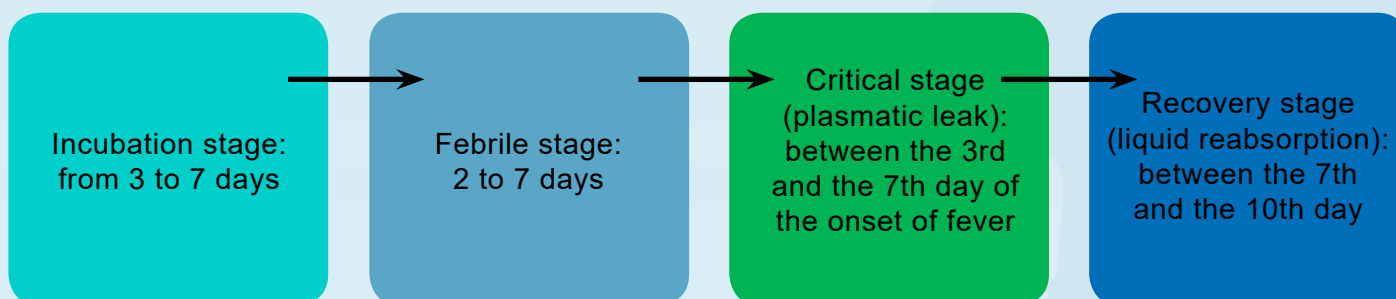


Figure No 5. Stages of the infection by dengue virus
 Source: Personal research

It has been documented that most frequently individuals suffering the serious forms have had a previous infection by a different serotype of the virus. This is because the antibodies of the primary infection bond to the virus of the secondary infection and form a complex that is phagocytized by the macrophages, a situation that causes that more cells result infected and greater amounts of cytokines and chemical mediators be released, which increases the vascular permeability^{2,8,9}.

The risk of hemorrhagic dengue (serious dengue) is greater in the case of the serotype DEN-2, followed by DEN-3, DEN-4 and DEN-1. The infected individual with a serotype keeps a prolonged immunological memory providing lifelong protection against the infecting serotypes (homotypic

protection), while the cross-protection against other serotypes (heterotypic protection) lasts an average of three months up to three years, after which they are completely susceptible to the infection with the other 3 serotypes^{2,9}.

3.1.3 Clinical symptoms of dengue

Dengue has several patterns of clinical presentation with progression and outcomes, from asymptomatic forms to serious bleeding and shock, resulting in death². The reinfection with a different serotype is associated to the serious clinical symptoms, due to a cross reaction by the antibodies^{2,9}. In the figure No 6, the course of the disease by dengue is shown.

After a period of incubation of three to seven days, the symptoms start suddenly. Normally the first clinical symptoms of dengue are the sudden establishment of the fever.

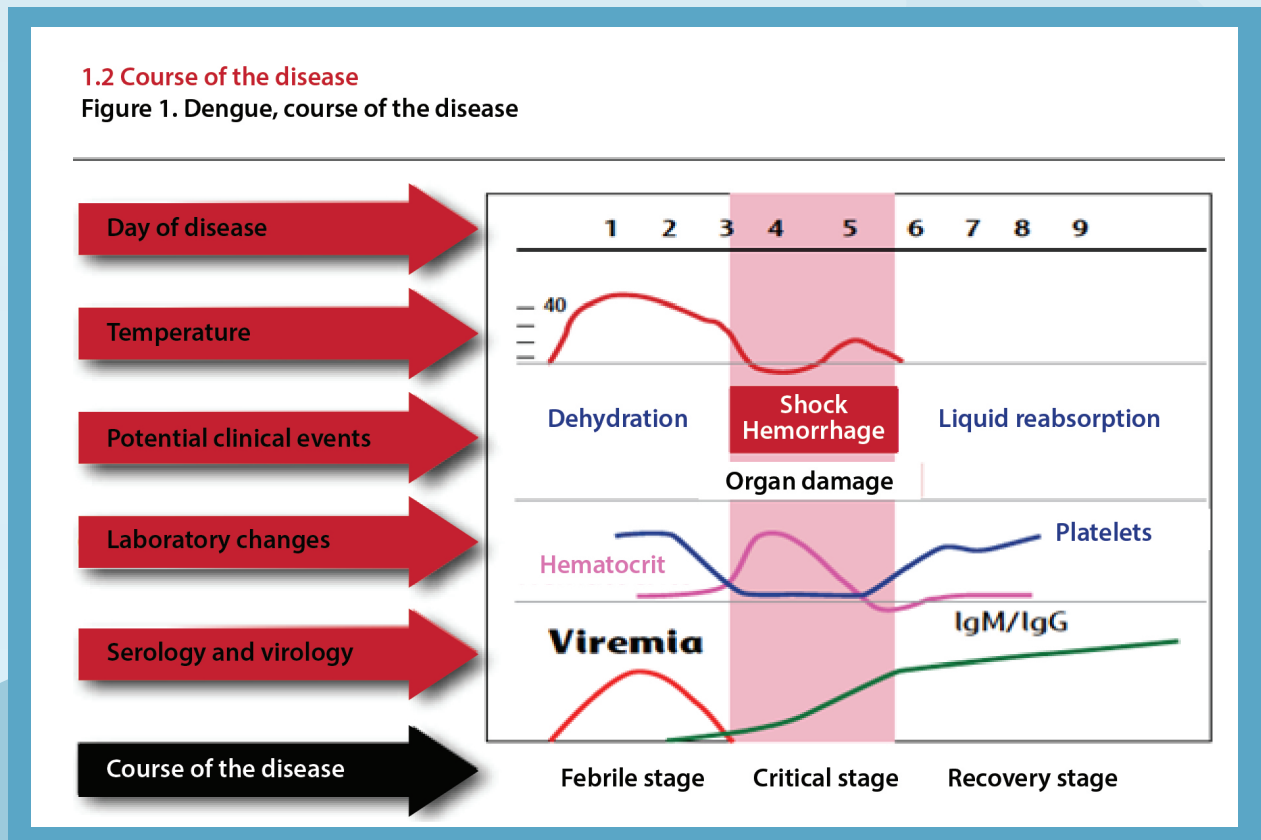


Figure No 6. Course of the dengue in humans
 Source: Dengue: guidelines for patient care in the Region of the Americas, WHO/PAHO, 2015.

Following, the three stages of the disease are described: febrile stage, critical stage and recovery stage:

1. Febrile stage:

Generally patients develop high and sudden fever which can be biphasic. Normally, the acute febrile stage produces temperatures of 39 to 40 °C and has a 2 to 7 day duration, normally accompanied by facial redness, erythema, generalized body pain, myalgia, arthralgia, headache, retro-orbital pain, pruritus and exanthema. Some patients may presentodynophagia and hyperemia in the pharynx and conjunctives. The gastrointestinal disorders (anorexia, nausea, vomits and liquid discharges) are common^{2,3,8,9}.

In the early febrile stage, it may be difficult to clinically distinguish dengue from other acute febrile diseases. Short after the onset of the disease, minor hemorrhagic symptoms may appear, such as petechial and skin ecchymosis. Also, there can be an increase of the size of the liver which can be painful on palpation^{2,3,8,9}.

The initial serious dengue symptoms are similar to the classic form, quickly followed by bleeding, hemodynamic instability and shock².

In the case of children, they usually have higher fever, but in general they experience less symptoms than adults during the febrile stage of the disease, which makes it even more difficult for the differential diagnosis⁹. The pediatric patients are more susceptible to develop shock because their microvasculature is much more permeable².

The most common lab findings are: mild to moderate thrombocytopenia (<150,000 platelets/mm³) in 90 % of patients and leukopenia (<4,000 leukocytes/mm³), normally with a moderate elevation of hepatic aminotransferases levels⁹.

This stage has a normal duration of 3 to 7 days, after which most of the patients recover without complications, however, it is possible that the patient does not recover and, if no improvement is observed, it must be suspected that the disease has not finish evolving and that a more serious stage can happen³.

Among the signs and symptoms that must be considered a warning in patients not recovering after 7 to 10 days of the disease are: intense abdominal pain, persistent vomits, sudden drop of temperature and alteration of the conscious state. Most of these signs and symptoms are the consequence of an increase in capillary permeability, so they mark the beginning of the critical stage^{2,3,8,9}.

The community pharmacist is the most available health personnel, thus, it is likely that the patient will resort to a pharmacy when the febrile stage starts or when the condition does not get better after several days with fever, thus, an effective communication and an evaluation of the condition of the patient will allow the advice about the health situation and, if necessary, refer the patient to the doctor. It must be emphasized that when there is a suspicion that a patient is initiating a critical stage of the disease, he must immediately go to the closest health service in his community. The serious forms of dengue are exclusively of medical management.

Figure No 7 summarizes the most important signs and symptoms of the febrile stage of dengue, as well as the warning signs and symptoms.

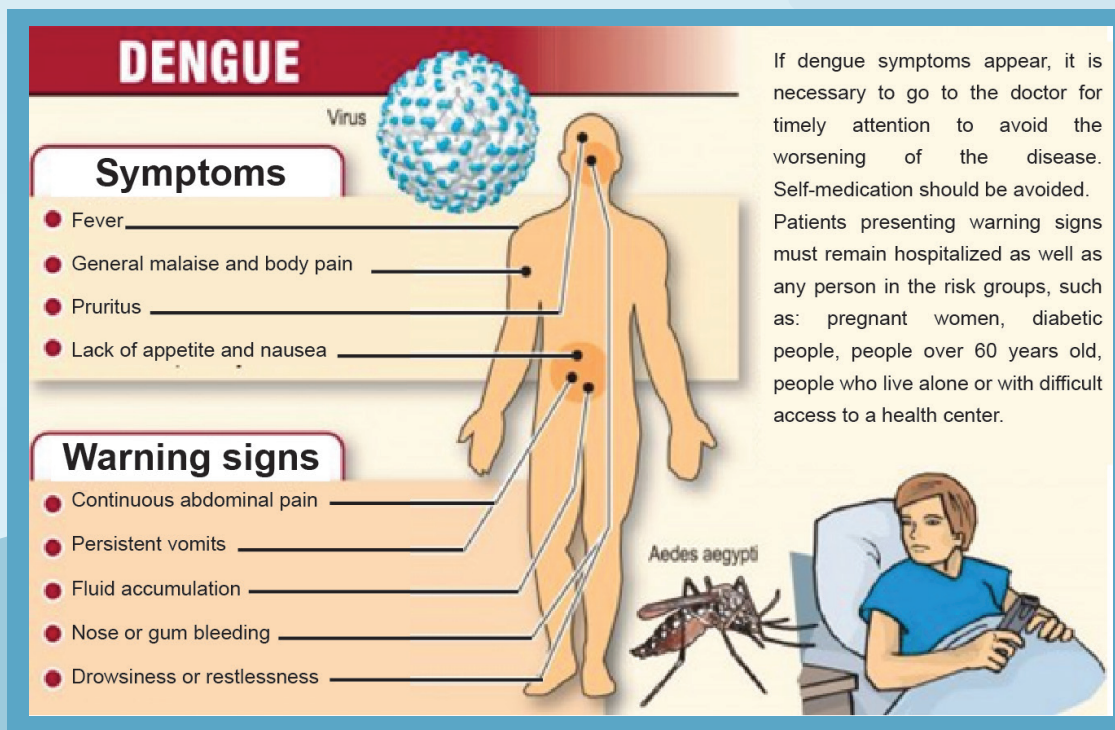


Figure No 7. Signs and symptoms of the febrile stage of dengue

Source11: <http://www.abc.com.py/edicion-impresa/locales/unos-19-pacientes-internados-en-el-ips-presentan-sintomas-de-dengue-80714.html>

2. Critical stage:

In some patients, in the first 3 to 7 days of the disease, the temperature drops and remains in 37.5 °C or less. In general, there can be a capillary permeability increase; in parallel, the hematocrits levels increase. This marks the beginning of the critical stage, that is, the stage of clinical symptoms due to the plasma extravasation that, in general, lasts 24 to 48 hours and can be associated with hemorrhage of the nasal mucosa (epistaxis) and the gums (gingivorrhage), as well as a transvaginal hemorrhage in women of childbearing age⁹.

The phenomenon of microvascular permeability and the thromboregulatory mechanisms are due to immunopathogenic causes which are not totally explained⁹.

The leukopenia with neutropenia and lymphocytosis with 15 % to 20 % of the atypical forms followed by a rapid decrease of the platelet count, usually precedes the plasma extravasation. At this point, patients without a great increase of the capillary permeability improve, while those with greater capillary permeability can get worse as a result of the loss of plasma volume and they may present warning signs. If the blood volume is not restored in a timely and correct manner “few hours later” those patients usually present clinical signs of tisular hypoperfusion and hypovolemic shock⁹. The shock occurs when a critical plasma volume is lost due to extravasation.

The signs and symptoms described before can lead to a serious hemorrhage which causes a reduction in hematocrits, leukocytosis and worsening of the state of shock. The hemorrhages in this stage mainly appear in the digestive system, but they can also affect the lungs, the central nervous system or any other organ.

The approach of the patient with dengue in the critical stage is exclusively of the medical doctor. The patient will require hospitalization and advanced care.

The pharmacist must refer all those patients with a suspected serious case to the health services.

3. Recovery stage:

When the patient survives the critical stage, it goes to the recovery stage. That is when the gradual reabsorption of the extravasated liquid takes place which returns from the extravascular to the intravascular compartment. This liquid reabsorption stage can last from 48 to 72 hours. In these cases, the general condition improves, appetite is recovered, the gastrointestinal symptoms improve, the hemodynamic status stabilizes and the diuresis increases. The hematocrit stabilizes or can be lower due to the dilution effect caused by the reabsorbed liquid, also, the number of white cells starts increasing with the increase of the neutrophils and the decrease of the lymphocytes. The number of circulating platelets rapidly increases^{2,3,8,9,12}.

There can be an onset of a skin rash and serious fatigue during several weeks after the recovery stage.⁹.

Table No 2 is part of the guidelines for dengue patient care in the Region of the Americas and it summarizes the clinical problems in the different stages of this disease. The pharmacist must be alert for the presence of dengue signs and symptoms, whether they are serious or not serious and refer the patient to the medical services, if necessary, in order to avoid complications that may have fatal consequences.

Table No 2

Clinical problems in the febrile stage, critical stage and recovery stage of dengue

Stage	Clinical problem
Febrile	Dehydration High fever can be associated to neurological disorders and seizures in children.
Critical	Shock due to plasma extravasation, serious hemorrhages, serious involvement of organs.
Recovery	Hypovolemia (if intravenous treatment with liquids has been excessive or has expanded in this stage)

Source: "Dengue: guidelines for patient care in the Region of the Americas" WHO/PAHO 2015⁹

It is also important to consider some of the differential dengue diagnosis, according to the disease stage, which are included in the following table:

Table No 3
Differential dengue diagnosis

Condition	Differential diagnosis
Conditions similar to dengue febrile stage	
Influenza-like illness	Influenza, measles, chikungunya, infectious mononucleosis, HIV seroconversion
Diseases with skin rash	Rubella, measles, chikungunya, zika
Diarrheal disease	Rotavirus, enteric infections
Diseases with neurological symptoms	Meningoencephalitis, febrile convulsions
Conditions similar to dengue critical stage	
Infections	Gastroenteritis, malaria, leptospirosis, typhoid fever, typhus, viral hepatitis, septic shock, yellow fever
Hemorrhagic fevers	Leptospirosis, Brazilian hemorrhagic fever, Argentine hemorrhagic fever, Bolivian hemorrhagic fever, mayaro
Other medical cases	Acute abdomen, diabetic ketoacidosis, lactic acidosis, leukopenia, thrombocytopenia, lupus erythematosus, hemolytic anemias

Adapted from: "Dengue: guidelines for patient care in the Region of the Americas", WHO/PAHO 2015⁹

3.1.4 Classification of dengue according to the severity⁹

Different bibliographical sources provide dengue classifications according to the clinical presentation; however, it must be considered that dengue is only one disease and that classifications help the actions of the medical personnel.

The current classification of the WHO dates from 2009 and considers two categories:

- Dengue
- Serious dengue

In the past, the dengue fever and dengue hemorrhagic fever classification with four severity degrees was used, however, this presented an important limitation for the epidemiological surveillance of the disease, as it suggested that the severity of the disease was directly related to the presence of

bleeding and not to the presence of other plasma extravasation symptoms which is when a patient that will develop a serious form of the disease can be timely taken care of⁹.

In figure No 8, the dengue severity classification characteristics according to the PAHO are described. The pharmacist must be aware that all forms of serious dengue and dengue with warning signs require strict observation and immediate medical intervention, thus, the patient must be referred to the closest community health center.

Dengue without warning signs	Dengue with warnings signs	Serious dengue
<p>A person who lives or has traveled in the last 14 days to areas with dengue transmission and presents fever from 2 to 7 days of evolution and 2 or more of the following symptoms:</p> <ul style="list-style-type: none">• Nausea/vomits• Headache/retro-orbital pain• Myalgia/arthritis• Petechias• Leukopenia	<p>Any dengue case that near the fever drop presents one or more of the following signs:</p> <ul style="list-style-type: none">• Abdominal pain• Persistent vomits• Fluid accumulation• Mucosae bleeding• Lethargy/irritability• Hepatomegaly• Progressive increase of hematocrit	<p>All dengue cases with one or more of the following symptoms:</p> <ul style="list-style-type: none">• Shock or respiratory difficulty• Serious bleeding• Serious organ compromise

Figure No 8. Dengue severity modified classification PAHO/WHO
Adapted from “Dengue: guidelines for patient care in the Region of the Americas” WHO/PAHO 2015⁹

3.1.5 Dengue in special populations⁹

3.1.5.1 Dengue and pregnancy: The pregnancy does not increase the risk of contracting dengue or predispose a different evolution of the disease, but the chances that it affects pregnant women are evident and the patients must be assisted with caution.

Some particularities of dengue in pregnant women are⁹:

- Maternal dead by dengue is very uncommon.
- Some pregnant women may have a threatened abortion, abortion or premature birth during the infection or up to a month after it.

- 4 % to 17 % of the cases will produce fetal growth retardation.
- The clinical symptoms, the treatment and the prognosis of dengue in pregnant women are similar to non-pregnant women, however, these are the most important considerations:
 - The physiological characteristics of the pregnancy may make dengue diagnosis difficult (leukocytosis, thrombocytopenia, hemodilution).
 - The most common clinical symptoms of dengue in pregnant women have been fever, myalgia, arthralgia, headache and retro-orbital pain.
 - In the first term of the pregnancy, a transvaginal bleeding related to dengue can erroneously be diagnosed as an abortion.
 - The pregnant woman can continue the normal course of the pregnancy, though fetal health will have to be controlled.
 - The abdominal pain, which constitutes one of the warning signs of dengue, can be similar to uterine contractions or be diagnosed as cholecystitis.
 - Among the differential diagnosis of dengue, we can find eclampsia and preeclampsia, the hemolysis syndrome, the elevation of the liver enzymes and a low platelet count.
 - Newborns of mothers who had dengue infection before or during the pregnancy have received maternal antibodies (Immunoglobulin G, IgG) against dengue or through the placenta and they have risk of contracting serious dengue if they are infected with a different virus serotype.

3.1.5.2 Dengue in newborns and nursing babies: Children under one year infected by dengue virus can present clinical symptoms which constitute a clinical picture of mild or moderate intensity and even a serious disease. In this group, mortality is higher. When vertical transmission of dengue infection takes place, the newborns can remain asymptomatic or can develop symptoms such as fever, exanthema, petechias, thrombocytopenia and hepatomegaly and evolve without complications; however, there is also a group which can develop serious symptoms⁹.

3.1.5.3 Dengue in older adults: Although the age does not imply a higher risk of contracting dengue, dengue infection in people over the age of 60 is associated to a higher risk of complications, compared to other age groups due to a higher incidence of concomitant diseases. Older adults are more susceptible to dehydration during the febrile stage of dengue. Normally, older adults are reluctant to seek medical attention and resort to traditional medicine or self-medication, which could add more complications⁹.

3.1.6 Diagnosis of dengue

There are different conventional laboratory techniques for dengue diagnosis: virus isolation, polymerase chain reaction and ELISA, which are described below (figures 9 y 10), which must be interpreted by the medical personnel; however, it is essential that the pharmacist knows about their existence and of the main developments in this field^{2,9,17,18}

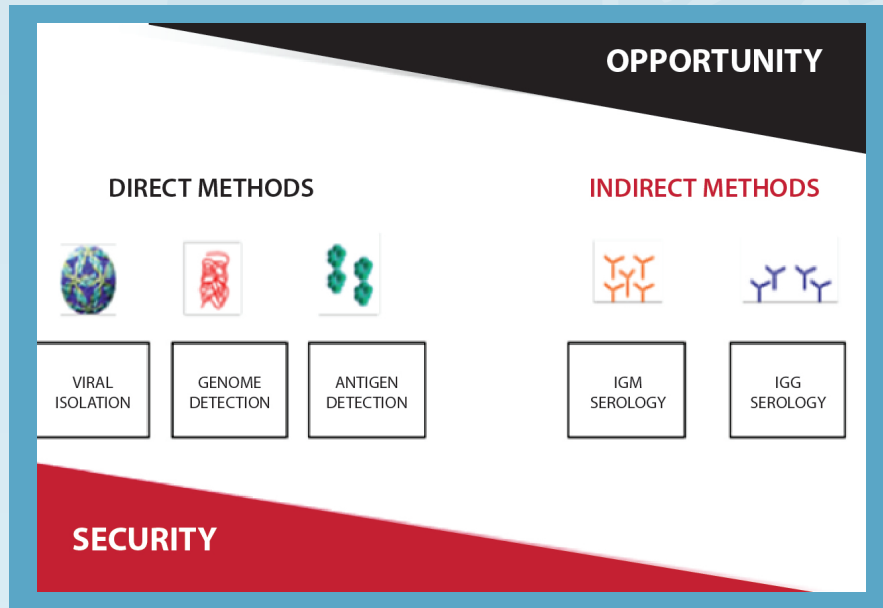


Figure No 9. Dengue diagnostic methods

Source: "Dengue: guidelines for patient care in the Region of the Americas" ⁹.

Virus isolation: Gold standard, limited use, expensive and requires specialized equipment.

Polymerase chain reaction: useful for the viral RNA detection in the first stages of infection. It is a quick and sensitive technique, though technical skills and a specialized laboratory are required. Patient's serum is used to make the determination.

ELISA: NS1 ELISA is the most useful alternative during the acute stage of the disease and ELISA specific for IgM is a good option during the convalescence period. Nonetheless, they are not adaptable to detection in real time, they require qualified personnel and they can be expensive.

Figure No 10. Diagnostic methods of dengue virus

Source: Personal research

3.1.7 Treatment of non-serious forms of dengue

There is no effective antiviral treatment for dengue. It is a symptomatic and support treatment and it includes the use of acetaminophen (paracetamol) for fever and pain relief. The use of non-steroidal anti-inflammatories is not recommended due to bleeding risk nor the use of acetylsalicylic acid due to the risk of developing Reye's syndrome in children under 12 years old^{2,3,9,11}.

Patients should be advised to drink, at least, five glasses of water of 250 mL a day in addition to the usual fluid intake to replenish the losses due to sweating, vomits, among others^{2,9}.

The critical and/or serious forms of the disease should be exclusively managed by a doctor.

Dengue vaccine (Dengvaxia[®]) has been recently approved for the marketing in several countries of the region such as: Argentina, Brazil, El Salvador, Costa Rica, Guatemala, Mexico, Paraguay and Peru. It is a live recombinant tetravalent vaccine developed by Sanofi Pasteur which is administered in three doses with six month intervals (at the beginning, at 6 and at 12 months.). It is said that it has a 64.7 % efficacy to prevent dengue, 80.3 % to prevent hospitalization and 95.5 % to prevent serious dengue cases^{2,17,18,21,22}.

On the other hand, the WHO recommends that the countries consider the possibility of introducing dengue vaccine only in geographical locations where epidemiological data indicate there is a great disease burden.⁹

3.1.8 Dengue prevention strategies¹⁸

The main prevention strategy is vector control. In the development of this technical document emphasis on this aspect will be done, as it is part of the education activities that the pharmacist can perform from the pharmaceutical services to the community. These are some of the strategies included:

- To avoid that mosquitoes find places to lay eggs through environmental management and modification.
- To dispose of solid waste adequately and avoid artificial habitats created by the man.
- To cover, empty and clean the containers where water for domestic use is stored weekly.
- To apply adequate insecticides to the containers where water exposed to weather is stored.

- To use personal protection at home, such as mosquito net in the windows, long-sleeved clothes, materials treated with insecticides, mosquito coil and vaporizers.
- To improve the community participation and mobilization to achieve the constant control of the vector.
- To fumigate with insecticides during epidemic outbreaks as one of the emergency antivectorial fighting measures.
- The active follow up and surveillance of vectors must be carried out to determine the efficacy of the control interventions.

3.2 Zika

3.2.1 Epidemiology of zika

Zika virus disease is an emerging disease caused by the virus with the same name. It is transmitted through *Aedes* mosquito bite such as *A. aegypti*, *A. albopictus*, *A. polynesiensis* and *A. hensilli*². It is an arbovirus infection of the Flaviviridae family which contains only one chain of RNA. Two main lineages have been identified: Asian and African. Its transmission is wild and urban and it is suggested that it can have non-human primate reservoirs^{2,3,23}.

The disease was identified in 1947 in a Rhesus monkey used as sentinel in the supervision of yellow fever in Zika forest, Uganda. In 1968, it was isolated for the first time in humans in Nigeria and from 1951 to 1981 cases in 13 countries of Africa and Asia were informed^{2,18,23}.

In 2013, a zika outbreak occurred in the Polynesia, which forced the Chilean government to monitor the Easter Island and in 2014, the first indigenous case was identified. During 2015, Brazil informed the indigenous transmission of zika virus in 18 states and three associated deaths; in that same year, countries such as Colombia, El Salvador, Guatemala, México, Paraguay, Surinam and Venezuela reported more indigenous cases^{2,3,19}. In September 2015, Brazilian investigators noted an increase in the birth of children with microcephaly, in the same areas where the presence of zika virus had been reported. By mid-February 2016, more than 4,300 cases of microcephaly had been reported. Retrospectively, investigators identified a growing number of fetal abnormalities in the French Polynesia after the outbreak occurred in that region^{23,24}.

In figure No 11, the countries with reports of zika virus infections in humans until March 2016 are shown.

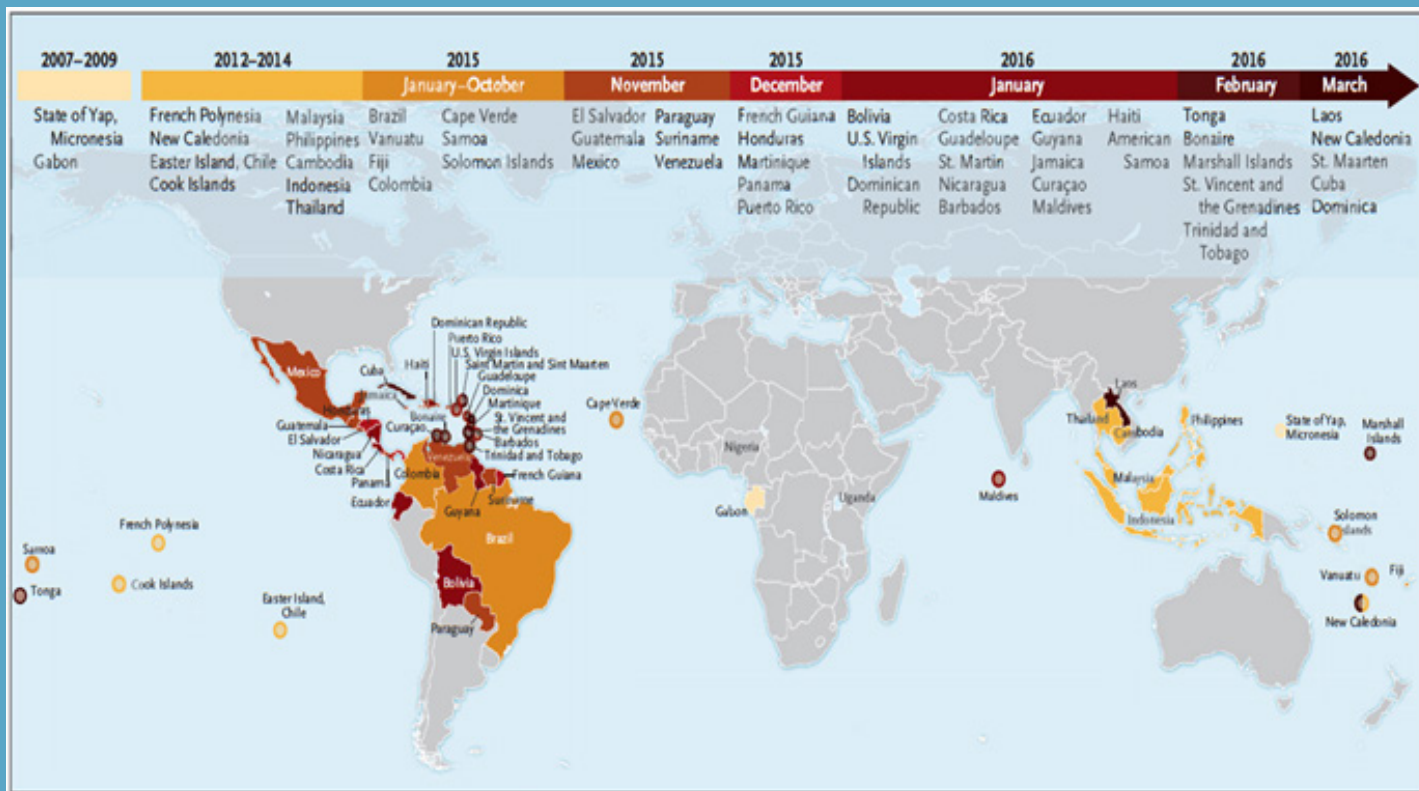


Figure No 11. Countries with reports of zika virus infections in humans until March 2016
Source: NEJM 374;16 Zika Virus²³

By March 2016, the virus had spread in at least 33 countries and territories of the Americas region²³. Table No 4 shows the number of zika cases reported in the Americas region according to data from the PAHO/WHO.

Table No 4

Incidence of infections caused by zika virus in America at the 52 week of the year 2016

Subregions	Indigenous cases+	Imported cases	Deaths	Cases of congenital zika	Population x 1000 inhabitants
North America	217	5018	0	40	360 476
Mexico and Central America	59 349	77	0	30	46 373
Andean	174 268	37	0	86	138 820
Brazil	321 366	0	9	2 289	209 568
Southern Cone	2 416	63	0	30	46 373
Hispanic Caribbean	126 517	41	5	73	37 759
English and French Caribbean	20 699	27	4	4	7364
Total	704 832	5263	18	2 846	552 733

+Number of suspected and confirmed cases

Source: Number of zika cases reported in America, PAHO 2016²⁵

3.2.2 2 Physiopathology of zika²³

In Africa, the transmission of zika virus takes place in a wild environment in which non-human primates and forest habitat *Aedes* mosquitoes are involved. On the other hand, in the urban and suburban environment, zika virus is transmitted through a human-mosquito-human cycle. The *A. aegypti* and *A. albopictus* species are those involved in the virus transmission in the Americas region.

There is significant evidence that zika virus can be transmitted from the mother to the fetus during pregnancy. The virus has been identified in the amniotic fluid of the mother whose fetuses presented brain abnormalities detected by ultrasound. See figure No 12 “Transmission cycle of zika virus in the urban environment.

Zika can be transmitted sexually by a person with the virus to the partner, even if the person infected does not present symptoms in that moment.

A person can transmit zika before the symptoms appear, when they already have the symptoms and once the symptoms disappear. The presence of zika virus in the semen and vaginal fluids has been determined and studies are being carried out to know how long the virus remains in the fluids. This is a worrying fact because there is an association between the virus infection and the presence of adverse results of the pregnancy.

According to a report published in 2016 by the CDC of the United States, cases of zika by transmission of the virus through blood transfusions have been confirmed. These cases have mainly appeared in Brazil^{24,25,26}.

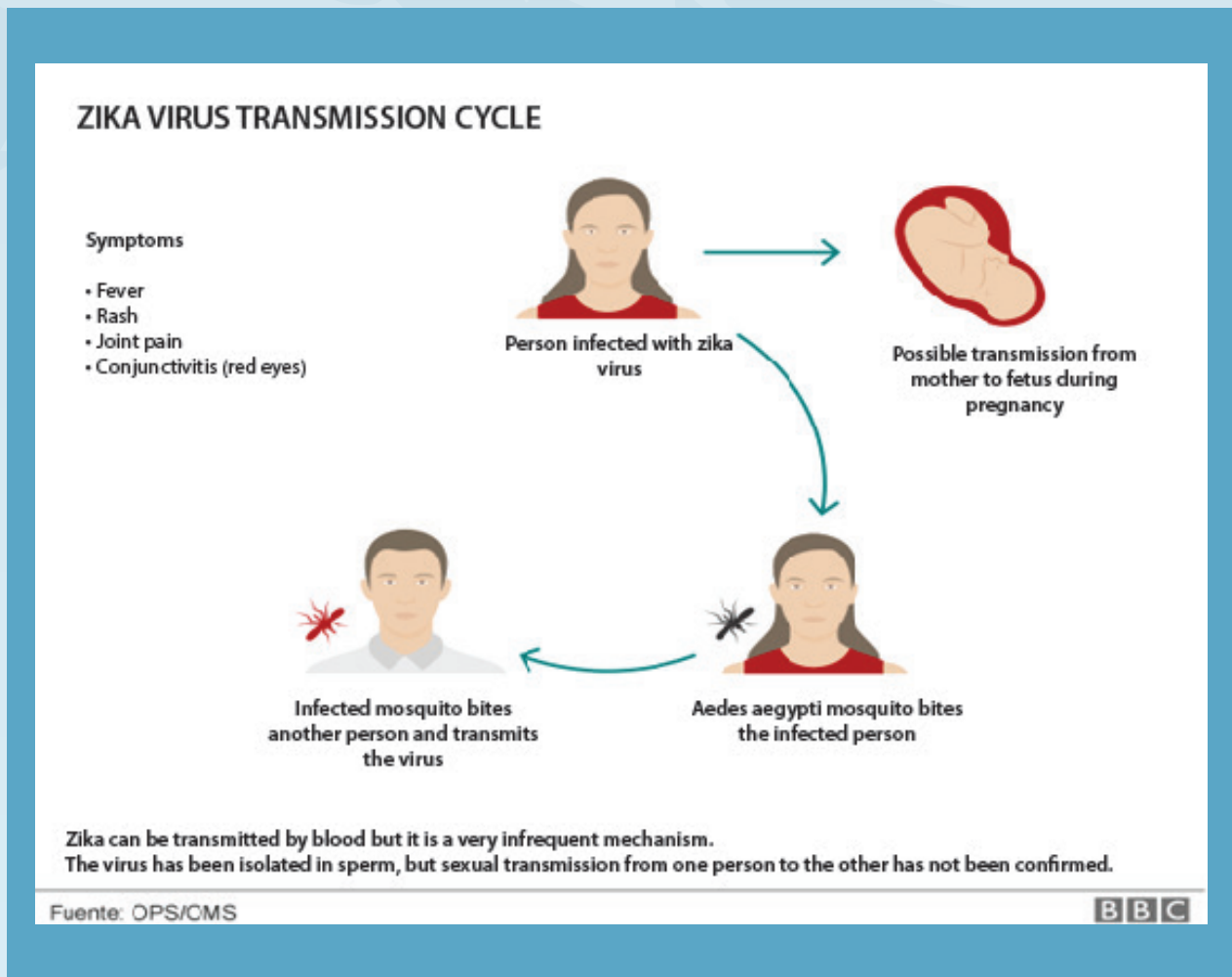


Figure No 12. Transmission cycle of zika virus in the urban environment¹⁹
http://www.bbc.com/mundo/noticias/2015/06/150611_salud_virus_zika_preguntas_respuestas_kv

3.2.3 Clinical symptoms of zika^{3,19,20,23,25,26}

The incubation period of zika virus is unknown, but it is known that it is similar to that of other arbovirus infections and it is estimated to be less than one week after the bite of the vector. The viremia is detected in the symptomatic stage but no after that.

It is estimated that four out of five patients are asymptomatic. The symptoms appear 3 to 12 days after the mosquito bite and the most common symptoms are:

- Mild fever (<38,5 °C)
- Exanthema, with cephalocaudal evolution (head, trunk and upper and lower limbs)
- Pruritus

- Non-purulent conjunctivitis
- Arthritis in feet and hands
- Myalgia
- Headache
- Retro-orbital pain
- Edema of lower limbs
- Vomits

Other symptoms include: dizziness, abdominal pain, diarrhea and vomits. The disease is generally mild and self-limited with a duration from two to seven days. Figure No 13 summarizes the most common signs and symptoms produced by zika virus.

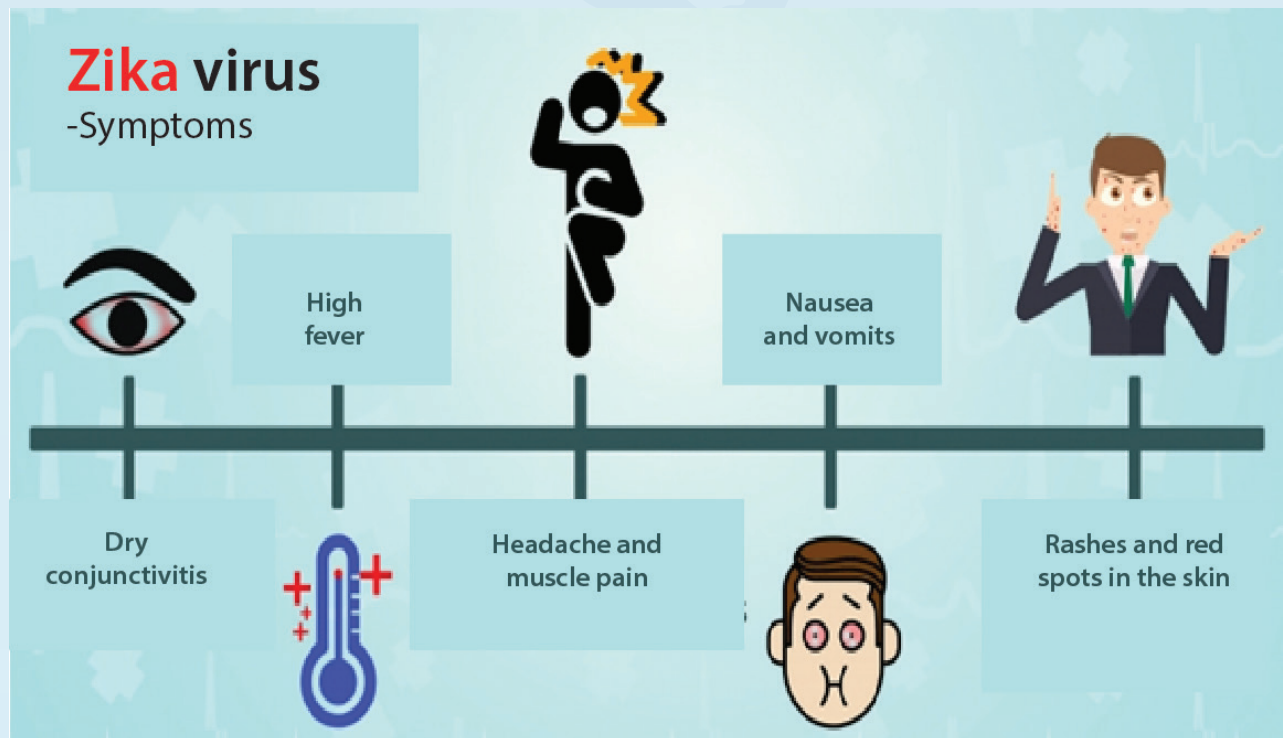


Figure No 13. Most important signs and symptoms of zika virus²⁰
 Source: https://twitter.com/prensa_libre/status/694238370923462657

It is not frequent that zika infection causes death, however, during the recent epidemic in Brazil, nine deaths have been described.

All the patients present exanthema and most of them present pruritus. Fever occurs in 75 % of the patients, but only in 25 % is higher than 39 °C for a period of one to eight days. The presence of hemorrhage, leukopenia, thrombocytopenia or hepatomegaly is not common. Instead, extremities edema and non-purulent conjunctivitis is frequent. During the convalescence stage a laminar peeling in hands and feet can be perceived.

Neurological complications: A time and geographical relationship has been observed between the neurological symptoms and the zika virus outbreaks in the Pacific in 2013 and 2014, as well as in the Americas. Guillain-Barre syndrome (GBS) is the most frequent neurological complication in its classic form or in some of its variants such as, for example, Miller-Fisher syndrome. Although they are less frequent, other symptoms are encephalitis, meningoencephalitis, cerebellitis, acute disseminated encephalomyelitis, inflammatory myelopathy and cranial nerves alterations.

Congenital syndrome related to zika: The full spectrum of the fetal symptoms consequence of the zika intrauterine infection has not been determined yet. Some evidence indicate that these symptoms are more serious if the pregnant woman contracted the infection in the first pregnancy term, but they can also appear if the infection was contracted during the second term or at the beginning of the third term of the pregnancy. Spontaneous abortions, fetal death, central nervous system alterations and joint alterations have been described. The central nervous system development alterations were characterized by a great variability in the symptoms. The most serious cases presented microcephaly (small head) with microencephaly (small brain) and hydrocephaly.

Differential diagnosis: In a patient with pruriginous exanthema, arthralgia, myalgia, periarticular edema and low fever, the most probable diagnosis would be zika infection as long as the epidemiological characteristics are compatible. Usually, infections by Mayaro virus, Nyong-nyong virus and other arbovirus infections causing arthritis do not affect the inhabitants of urban areas.

3.2.4 Surveillance of zika in neurological complications and special populations

In view of the increase of notifications of newborns with microcephaly in areas of zika virus and its possible relationship to this virus, the PAHO and the WHO issued epidemiological alerts on December 1, 2015. Such a warning recommends the member states to establish and maintain the capacity to detect and confirm zika virus infection cases; to prepare the health services in case of a possible additional demand in all the care levels, including the specialized levels for neurological syndromes, and to strengthen prenatal consultation and control activities.

The existing evidence about neurological complications associated to zika virus and the surveillance of microcephaly and congenital syndrome oriented to disease monitoring in pregnant women is summarized below. Also, the recommendations on the approach of the pharmacies in these situations are provided.

3.2.4.1 Surveillance of Guillain-Barre syndrome and other neurological complications^{25,27,28}

As was indicated before, the neurological symptoms can appear during the acute stage or in the convalescence of the zika virus infection. So far, Guillain-Barre syndrome (GBS) has been described as the most frequent neurological complication.

The GBS appears as ascending, progressive, symmetric, subacute muscle paralysis reaching its maximum level at four weeks and is accompanied by absence of reflexes. From the outbreak in the French Polynesia, the relationship between GBS and a previous zika virus infection could be documented and the information about the clinical and neurophysiological characteristics of the cases which mainly appeared as acute axonal motor neuropathy was obtained. Based on those results, it is estimated that the GBS risk is 0.24 for every 1,000 zika virus infections.

The WHO has defined two types of GBS cases related to zika virus:

Association suspicion

Patient with history of residence or trips to an area with presence of zika virus vectors or who has had sexual contact without protection with a person with history of residence or recent trips to an area of circulation of vectors for zika virus and presenting the following signs and symptoms:

- Bilateral weakness and sagging limbs
- Reduced or absent deep tendon reflexes
- Absence of an alternative cause justifying the weakness

Confirmed association

Suspected cases of GBS associated to zika virus infection, with laboratory confirmation of recent zika virus infection.

Source: Personal research, 2017

Normally, the suspicion of a neurological syndrome appears outside the viremia period; however, the disease approach guidelines recommend to detect the virus in serum or urine and also to detect immunoglobulin M antibodies (IgM) in serum by ELISA tests. In the following section, the diagnostic tests that will be carried out in the laboratory to confirm suspected cases of zika virus will be commented.

Every time a patient who resides or has travelled to areas with zika virus circulation presents a clinical condition affecting the central nervous system, the zika virus infection must be considered as a differential diagnosis, as in the case of traveler sexual partners who have had sexual relations without protection.

In the typical forms, the weakness begins distally in the lower limbs. Patients present a difficulty to walk, climb stairs or get up from a chair. Later, motor weakness can extend to the arms. Sensitivity alterations, such as paresthesia, dysesthesia or hypesthesia may appear. The presence of pain (neuropathic, radicular or musculoskeletal) is normal. Sometimes, it can progress and affect the facial nerves and produce bulbar and respiratory muscles compromise. An important percentage of patients may need an admission to an intensive care unit due to respiratory complications and dysautonomia (cardiac arrhythmias or changes in the blood pressure).

This is a very uncommon clinical picture in children, however, taking the measures indicated above is considered.

Although other neurological symptoms have been described in isolated clinical cases (encephalitis, meningoencephalitis, cerebellitis, acute disseminated encephalomyelitis, inflammatory myelopathy, and cranial nerve disorders), currently there is not enough epidemiological information about the real incidence of such medical conditions.

The pharmacist must guide the patient with this symptomatology to seek medical help since the GBS requires an approach by a specialist, possibly in a hospital. The pharmaceutical advice should be aimed at raising awareness among patients and/or their family about the severity of the clinical condition and an immediate action on the part of those involved.

It is important to consider that the GBS is a clinical diagnosis made by the specialist doctor through the analysis of cerebrospinal fluid when detecting the albuminocytologic dissociation, therefore, the pharmacist should not diagnose or recommend medication for cases of a suspected neurological complication by arbovirus infection, strictly speaking, by zika virus.

3.2.4.2 Surveillance of congenital syndrome associated to the zika virus infection

19,20,23,25,26,27,28,29

In October 2015, Brazil reported the detection of an unusual increase of newborns with microcephaly in the state of Pernambuco and according to the Brazilian Ministry of Health, cases of microcephaly increased by a factor of 20. This region was the most affected area by the indigenous outbreak of zika virus, which indicated a possible association between the congenital infection by this virus and the occurrence of microcephaly.

In November 2015, the relationship between microcephaly and zika virus is confirmed when the presence of this virus in blood and tissue samples of a newborn with microcephaly is found.

On February 1, 2016, the WHO issued an international alert: *WHO Statement on the first meeting of the International Health Regulations (2005) Emergency Committee on zika virus and observed increase in neurological disorders and neonatal malformations*. This committee recommended that it be declared that the recent cluster of microcephaly cases and other neurological disorders reported in Brazil constitute a public health emergency of international concern.

However, the characterization of congenital syndrome associated with zika virus infection is problematic, given the low specificity of the clinical picture of that infection, the gaps in knowledge about its clinical spectrum and the clinical evolution of the disease, as well as the definition of microcephaly among others. Figure No 14 shows newborns with normal-sized heads, with microcephaly and with severe microcephaly.

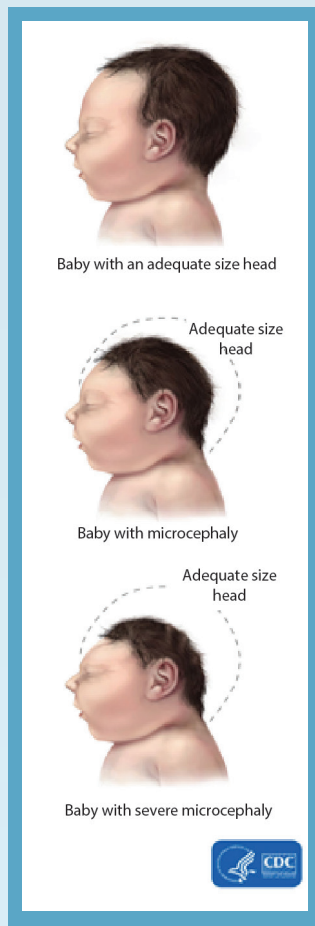


Figure No 14. Microcephaly

Microcephaly is defined by an occipitofrontal circumference below -2 standard deviations of the mean of the reference population according to age and sex.

In the image you can see the size relationship existing in a baby with an adequate size head with another baby with microcephaly and another with severe microcephaly.²⁴

Source: <https://www.cdc.gov/ncbddd/spanish/birthdefects/microcephaly.html>

The currently described syndrome includes the presence of microcephaly, with other signs such as craniofacial disproportion, as well as other anthropometric disproportions, redundant scalp with roughness, hypertonia or spasticity, irritability and epileptic seizures. Also, alterations of the central nervous system and joints such as twisted foot, hands and feet malformations.

An increase in the number of spontaneous abortions and fetal deaths that had other alterations associated with zika virus infection that are not yet understood, for example, pulmonary hypoplasia, has been reported.

No clinical differences have been described between a pregnant woman and another who is not pregnant. After the bite of the infected mosquito, the symptoms of the disease usually appear after an incubation period of three to twelve days. The infection can occur asymptotically in a significant proportion of cases (70-80 % of cases). The symptoms last from 4 to 7 days and tend to limit themselves.

As it is generally an asymptomatic infection and in the few symptomatic cases it is self-limiting, many times patients will not require treatment and they may even avoid consulting a health service.

The pharmacist should recognize the main symptoms of zika virus infection, which were described in section 3.2.3 (Clinical symptoms of zika virus), in order to correctly guide any pregnant woman who presents to them. If a zika virus infection is suspected, it must be referred to the doctor for its approach. It is important that the pharmacist provides information about the possible consequences derived from the congenital syndrome due to zika and the need to regularly attend prenatal consultations and to perform all the examinations indicated by the health team.

As a reminder, the following association of symptoms and signs (clinical or ultrasonographic) have been referred to as congenital zika syndrome and they are listed below:

Table No 5
Congenital zika syndrome

Placental calcification	Abnormalities of the brain with/without microcephaly
Oligoanhydramnios	Reduction/atrophy of brain volume
Abnormal flow in cerebral artery	Abnormal cortical development
Restriction of intrauterine growth	Hypoplasia of scalp
Arthrogryposis	Cerebral and brain calcifications
Redundant scalp skin	Cerebellar hypoplasia
Feet deformity	Subcortical calcification
Cataracts and ocular calcifications	Fetal death

Source: Provisional considerations for the care of pregnant women in scenarios with high zika circulation: document intended for health professionals, PAHO/WHO²⁸

From the surveillance of cases of congenital syndrome associated with zika virus infection, three case definitions are recognized:

Suspected case	Probable case	Confirmed case
<p>Live newborn presenting microcephaly or some congenital malformation of the central nervous system and whose mother has had history of residence or trips to an area with zika virus presence during the pregnancy or has had sexual relations without protection with a partner with history of residence or trips to an area with presence of zika virus vectors.</p>	<p>Live newborn meeting the criteria of congenital syndrome case suspected of being associated to zika virus infection and presenting intracranial morphological alterations diagnosed by any imaging method, excluding other possible known causes or whose mother has presented exanthema during the pregnancy.</p>	<p>Live newborn of any gestational age meeting the criteria of congenital syndrome case suspected of being associated to zika virus infection and whose zika virus infection has been confirmed by laboratory, regardless of the detection of other agents.</p>

Source: Personal research, 2017

Because there is no specific treatment against this infection, the preventive measures are still essential. Therefore, strategies should focus on educating pregnant women about the importance of follow-up of prenatal visits and the environmental and individual measures to reduce the risk of bites from mosquitoes transmitting zika. Zika virus prevention strategies are mentioned in more detail in section ^{3.2.7}.

3.2.5 Diagnosis of zika^{25,27,28}

In a large proportion of cases, the initial symptoms may go unnoticed or patients may consult late, which reduces the chances of taking biological samples, therefore, it is essential that the pharmacist pay attention to the symptoms of the patients who consult for fever, joint pain and exanthema since it could be a zika virus infection, and thus, timely referral of the patient to the medical doctor's office is considered a valid approach strategy that should be developed in pharmacies.

The diagnosis is mainly based on the detection of RNA in blood samples by polymerase chain reaction with reverse transcriptase or viral isolation in samples collected less than five days after the onset of symptoms^{2,23}. Although the period of viremia is not yet fully established, the virus has been detected in serum more frequently up to the fifth day after the onset of the symptoms and,

in some cases, up to the seventh day. On the other hand, in some cases it has been possible to detect high viral loads in urine during a long period of the acute stage.²⁵.

Serological tests are also widely used, however, the frequency of cross-reactions with other flaviviruses can make diagnosis difficult. In addition, in the early stage of infection, IgM and IgG levels can be very low, making diagnosis difficult to confirm³. Figure No 15 shows the different diagnostic techniques.

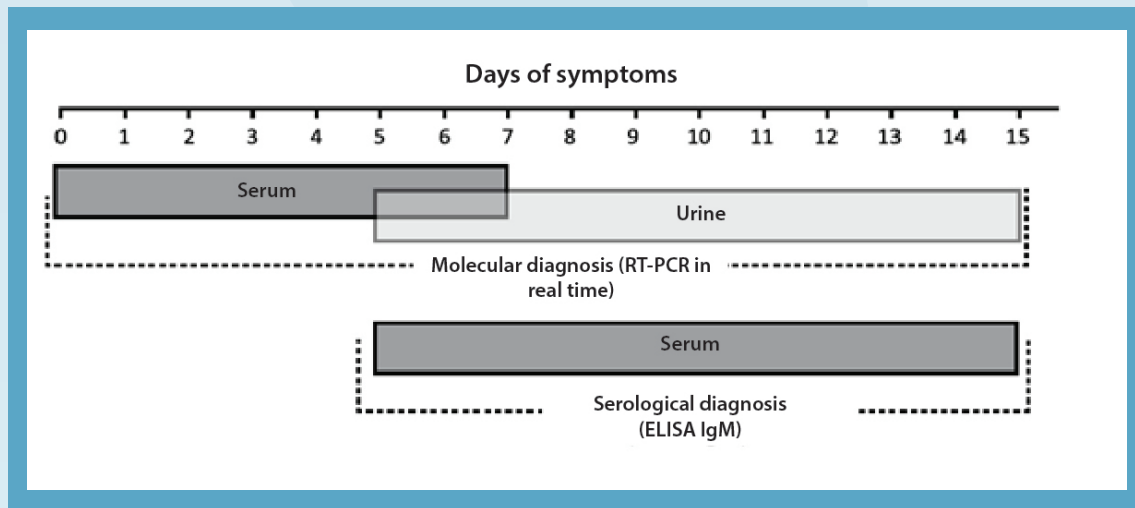


Figure No 15. Indications for diagnosis, according to day of onset of symptoms and type of sample
Source: Guidelines for the surveillance of zika virus disease and its complications, PAHO, 2016²⁵

3.2.6 Treatment of zika^{23,25,26}

As it is generally an asymptomatic infection and in the few symptomatic cases it is self-limiting, many times patients will not require treatment and they may even avoid consulting a health service. So far, there is no vaccine or specific treatment for zika virus infection. This is why the treatment is directed to the symptoms when they are bothersome.

The four pillars of zika virus treatment are described below, which can be recommended by the community pharmacist and also serve as an educational material for the general population. These treatment pillars apply to all people at risk of infection and mainly in those areas where the presence of the vector is documented, the main precautions that pregnant women and children should have, which were described by the WHO in 2016 in the document called *Provisional considerations for the care of pregnant women in scenarios with high zika circulation*.

Rest and isolation	Fever	Headache	Pruritus
<ul style="list-style-type: none"> In order to avoid the transmission to other persons, the contact of the patient infected by zika virus with Aedes genus mosquito must be avoided, at least during the first week of the disease (viremic stage). 	<ul style="list-style-type: none"> It is recommended to reduce fever with physical measures (damp wipes, little clothes, bath or shower with barely warm water). When physical measures are not effective, the use of antipyretic-analgesic is recommended: Acetaminophen / Paracetamol 	<p>Acetaminophen / paracetamol in the indicated doses for the treatment of fever will also be ordered.</p>	<ul style="list-style-type: none"> Topical use of calamine lotion or menthol-base aqueous cream. Also, the systemic treatment with type 1 antihistamines has a high security level, so they can be used in cases of intense pruritus.

Source: Personal research, 2017

Paracetamol (acetaminophen) dosing

In case of fever it is necessary to recommend the use of paracetamol (acetaminophen):

- Adults: 500 to 1000 mg every 6 hours, maximum daily dose of 4 g.
 - Children: 10 to 15 mg/kg/dose every 4 to 6 hours.
- Do not exceed 5 doses in 24 hours, maximum daily dose of 75 mg/kg/day, do not to exceed 4 g/day.

The use of acetylsalicylic acid is not recommended due to the risk of bleeding nor the use of non-steroidal anti-inflammatory (NSAIDs) because of their effect in the event that the infection corresponds to dengue or chikungunya.

Patients should be advised to drink, at least, 5 glasses (1,250 mL) of water per day to replace the depletion due to sweating, vomiting and other insensitve losses.

The approach of the patient with zika with suspected neurological complication or of the pregnant woman and children is exclusive of the doctor.

The pharmacist must refer the patients with suspected zika infection and which correspond to special populations to the health services.

3.2.7 Zika prevention strategies^{23,25,26}

As with the other arbovirus infections, the most effective preventive measures are to avoid vector bites, but other strategies focus on reducing sexual transmission and controlling the vector.

The preventive measures are applicable to the general population and the special populations (pregnant women and young children). Pharmacists should promote these measures in their communities:

Measures about the environment: They are collective measures and they are aimed at reducing the density of the vector. The control of the mosquito is the main measure that can achieve the interruption of the transmission of arbovirus infections. More than 90 % of the mosquito breeding sites are inside and in the immediate surroundings of the houses, therefore, the most important thing is to reduce the population of mosquitoes and the best way is to eliminate their breeding sites by preventing water from being deposited in containers outside the houses and their surroundings, tightly cover tanks or water tanks for domestic use; avoid accumulating garbage, deposit garbage in closed plastic bags, use closed containers and unclog drains so water does not get stagnant.

Personal protection measures: Use of appropriate clothes that minimize the skin exposure (pants and long shirts), use protective wire mesh in the doors and windows. Repellents authorized for human use can also be used, such as those containing N, N-diethyl-3-methylbenzamide (DEET), which can be applied to exposed skin or on the clothes and used in strict accordance with the instructions of the product label. There is no evidence of the restriction of use of these repellents in pregnant women, as long as they are used in accordance with the above indications.

The purpose of the isolation of patients is to prevent people infected during the viremic stage (first week) from being bitten by uninfected mosquitoes that could become new transmitters of the disease.

On the other hand, based on the growing evidence that zika virus can be transmitted sexually, the WHO recommends that all people with zika virus infection and their sexual partners, especially pregnant women, receive information on the risks of sexual transmission of the virus, contraceptive measures and safe sexual practices and whenever possible, be provided with condoms.

In those countries without indigenous cases of zika virus infection, it is recommended that pharmacists pay attention to the occurrence of cases of febrile exanthematous disease of unknown cause (in which dengue, chikungunya, measles, and rubella infection are ruled out) to provide recommendations for the management of the disease to patients. In case of suspected neurological complication, pregnancy or in newborn children, patients should be referred to the doctor immediately, since these are conditions that may require the management by specialists in a health center.

It is important to notify the health authorities according to the guidelines of each country for the benefit of the integrated surveillance of arbovirus infections.

The WHO is helping to model the development of the zika virus vaccine by creating an objective product profile for use in emergency situations. The profile specifies the desirable and minimum characteristics of these vaccines, for example, the administration of a single dose of the zika virus vaccine is preferable, but up to two doses are acceptable. The vaccine should give protection for, at least, one year in an emergency context, but protection for several years is preferable²⁵.

However, the development of the vaccine against zika virus is a complex task since many aspects of the disease are still unknown. Until January 2017, about 40 candidate vaccines against zika virus were in the development process. Five of them are entering, or are about to enter, phase I of trials, in which the safety of the vaccine and its efficacy to produce an immune response are evaluated. It is expected that in the next two to three years there will be a final product for application and approval of the regulatory authorities²⁵.

3.3 Chikungunya

3.3.1 Epidemiology of chikungunya

Chikungunya fever is an emerging disease transmitted by mosquitoes that since 2004 has caused major epidemics, causing considerable morbidity and suffering. The name chikungunya derives from a word in makonde (indigenous population in southeastern Tanzania) which means “hunched man” and describes the inclined posture of those suffering from this affliction and painful arthralgia^{2,32,33}.

Chikungunya is an RNA virus belonging to the genus Alphavirus of the Togaviridae family; there is only one serotype of the virus that apparently confers lifelong immunity to individuals recovering from infection^{2,32,33}.

Since 1770 epidemics of fever, skin rash and arthritis similar to chikungunya fever have been reported, however, the virus was not isolated from human serum or mosquitoes until an epidemic in Tanzania in 1952-1953. After the initial identification of the virus, other sporadic outbreaks occurred. However, in 2004, an outbreak originated in Kenya spread over two years to other African regions and other islands of the Indian Ocean^{2,32,33}.

In the Americas, the first cases date from December 2013 on San Martin Island and later, cases of indigenous transmission were reported in the Caribbean. The countries of America with the highest number of laboratory confirmed cases are: Mexico, Brazil and Ecuador. It should be considered that 3 to 38 % of the population has asymptomatic infection, which contributes significantly to the spread of the disease. Figure No 16 shows the origin, spread and distribution of chikungunya virus and its vectors in the world^{2,32,33}.

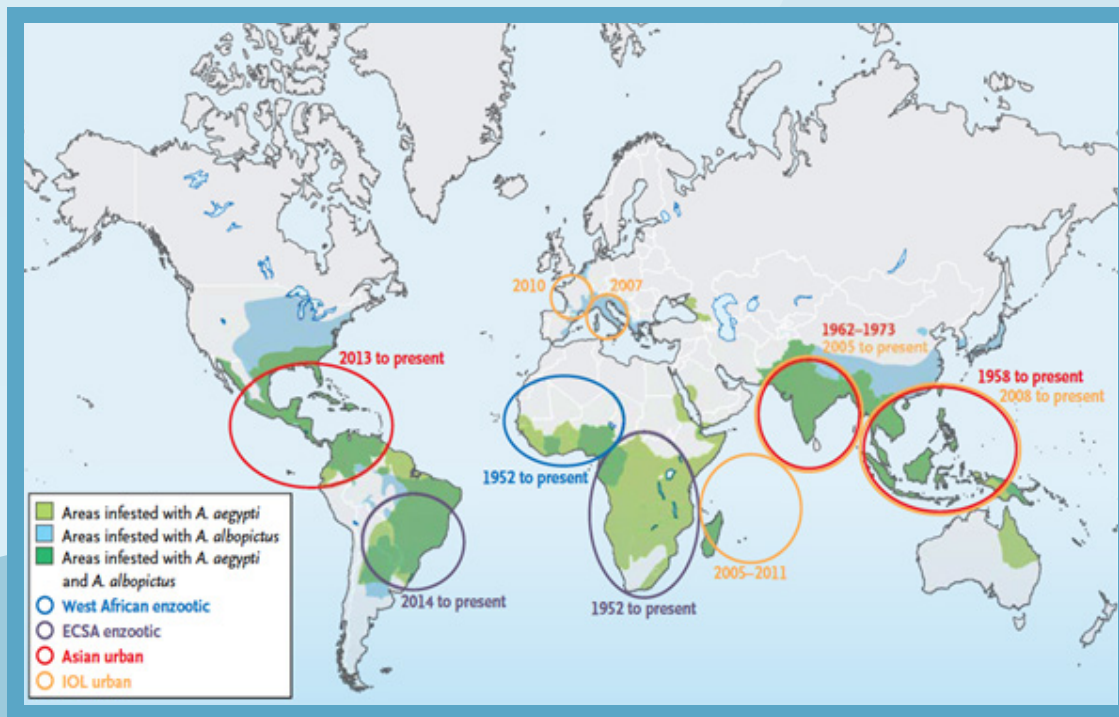


Figure No 16. Origin, spread and distribution of chikungunya virus and its vectors
Source: NEJM 2015; 372: 1231-9³²

There are two main vectors: *Aedes aegypti* and *Aedes albopictus*, given the wide distribution of these vectors in America, the entire region has been susceptible to the spread of the virus^{2,32,33}.

According to PAHO data, in the region of the Americas there were a total of 152,769 cases of chikungunya confirmed during 2016. Table No 6 shows the cases by region.

Table No 6

Incidence of infections caused by chikungunya virus in America at the 52 week of the year 2016

Subregions	Indigenous cases+	Imported cases	Incidence rate	Deaths	Population x 1000
North America, Central America, Mexico and the Hispanic Caribbean	36 469	169	77.74	1	573 240
Andean	47 664	6	34.34	12	138 820
Southern Cone	417 103	95	149.71	159	278 616
English and French Caribbean	2 867	0	39.07	0	7 339
Total	504 103	270	300.86	172	998 015

+Number of suspected and confirmed cases

Source: Number of reported cases of chikungunya in America, PAHO, 2016³⁵

3.3.2 Pathophysiology of chikungunya:

Mosquitoes acquire the virus from a viremic host. After an average incubation period of ten days, the mosquito is capable of transmitting the virus to a susceptible host. The virus is introduced into the skin where it replicates in the fibroblasts of the dermis and spreads through the bloodstream into multiple tissues. In infected humans, symptoms of disease usually appear after an incubation period of three to seven days (up to 12 days inclusive)^{2,32,33}.

Transmission of the virus can also be done transplacentally from a viremic mother to the newborn during delivery, and it is even suspected that it can cause abortions if it occurs in the first trimester of pregnancy. There is no evidence of transfer through breast milk^{2,24}.

Viral replication occurs mainly in target tissues such as muscles, joints, skin, liver, spleen and meninges in neonates and in patients with comorbidities².

The incubation period ends with the sudden onset of fever, which lasts no longer than a week, until the viremia ends. At this time, patients produce antiviral immunity of chikungunya².

Chronic chikungunya disease consists of persistent joint pain and relapses for weeks, months or years².

3.3.3 Clinical symptoms of chikungunya

Although chikungunya fever rarely endangers life, the symptoms can be disabling so that patients cannot go to work, generating very high costs in health systems^{2,32,33,34}.

Symptoms occur after an incubation period of three to seven days and up to 28 % of individuals can be asymptomatic^{32,33,34}.

The chikungunya virus can cause acute, subacute and chronic disease, while the acute stage usually lasts 5 to 10 days.^{2,3,32,33} Some studies even say that in up to 12 % of those infected, the chronic althralgic disease is established even after the elimination of the virus in the joints; this inflammatory process may persist for more than a year after the initial symptoms³³.

Acute disease: It is characterized by a sudden onset of fever above 39 °C and severe or disabling joint pain, which has been reported in 96.6 % of patients and differentiates it from dengue fever. Other signs and symptoms may include: headache, diffuse back pain, myalgia, nausea, vomits, polyarthritis, rashes and conjunctivitis^{2,32,33}. (Figure No 17)

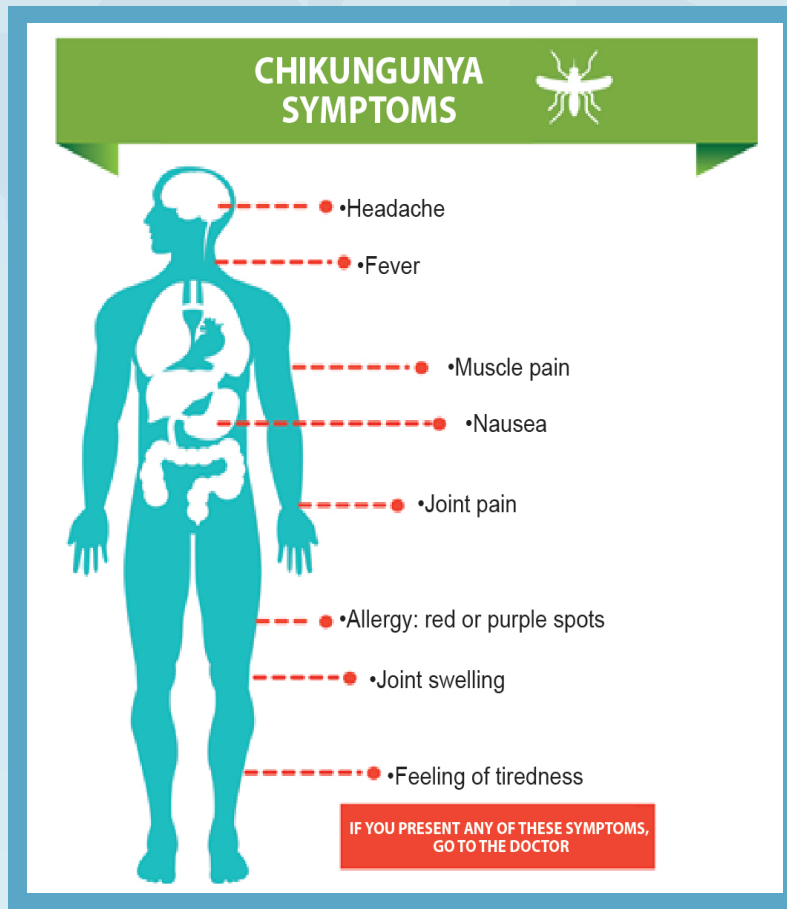


Figure No 17. Signs and symptoms of chikungunya virus disease
 Source: Blog Web Fight against dengue chikungunya
<https://prevencionhn.wordpress.com/category/chikungunya/>³⁴

The fever usually lasts a few days to a week, it can be continuous or intermittent, but a decrease in temperature is not associated with a worsening of symptoms. Joint symptoms are usually symmetrical and occur more frequently in the hands and feet, but may also affect more proximal joints^{2,32,33}.

Often adult patients are incapacitated by pain, sensitivity, inflammation and stiffness, however, it has been reported that arthralgia is milder in children^{2,3,17,32}.

The rash usually appears two to five days after the onset of fever in approximately 50% of patients. It is normally maculopapular and includes trunk and limbs, although it can also affect palms, soles and face. The hemorrhagic symptoms are rare, only in 1 to 7% appear as epistaxis or gingivorrhagy. Unlike other clinical symptoms, joint pain can persist and recur for weeks, months or even years, which is not observed in dengue either. The pain is usually located in the same affected joints during the acute stage; the time to cure the symptoms is uncertain^{2,3,32,33}.

Laboratory symptoms are similar to those of dengue except for less pronounced leukopenia and thrombocytopenia^{2,3,32,33}.

In the differential diagnosis, infectious diseases such as malaria, leptospirosis, post-infectious arthritis and juvenile rheumatoid arthritis should be considered^{2,3,32,33}.

Post-acute disease: From the fourth week to the end of the third month, the presence of multiform lesions and other associated lesions that are characterized by the presence of inflammatory symptoms, arthritis, synovitis, tenosynovitis or bursitis are observed. The evolution is produced continuously by inflammatory outbreaks frequently caused by the cold or intermittent periods may occur without symptoms. Intense asthenia and development of neuropsychological disorders may also appear³.

Chronic disease: As of the fourth month, it can last from a few months to several years. The same symptoms described in the post-acute stage have been observed and often the presence of painful relapses in the most used joints due to its inflammatory state after infection. In most chronic patients, there is a worsening of their quality of life during the first years after chikungunya infection^{3,32,33}.

3.3.4 Chikungunya in special populations

Patients with chronic diseases: The associated clinical symptoms are more frequent in patients with some underlying disease, for example, diabetes mellitus, cardiomyopathy, coronary disease, high blood pressure, chronic obstructive pulmonary disease and bronchial asthma³.

Children under one year, pregnant women and people over ⁶⁵: There is a higher risk of complications and they require follow-up by the doctor and in some cases, hospitalization may be necessary. In the case of affected children, they are more irritable and do not have great mobility; this sign has been described as “child in rubber doll”, they can also present skin lesions like exanthema, maculopapular erythema, among others³.

In the case of pregnant women, there are reports of spontaneous abortions and fetal deaths in the uterus in infected women before week 22 of pregnancy³. Among women in the viremia stage

during childbirth, an increase in the number of cesarean sections has been observed due to fetal distress, with an abnormal fetal heart rate³.

There is no evidence that chikungunya is transmitted through breast milk, therefore, breastfeeding should not be suspended in areas where the virus is circulating³².

3.3.5 Diagnosis of chikungunya

The diagnosis is based on clinical, epidemiological and laboratory criteria. From the clinical point of view, an abrupt onset of fever, together with severe arthralgia or arthritis that cannot be explained by any other medical cause. It is taken as a probable case if the patient lives or has visited any epidemic area or an area with reports of active transmission that coincides with the incubation period of the virus²⁴. However, laboratory confirmation is essential specially to differentiate the picture of different febrile diseases with similar clinical symptoms such as dengue or zika^{32,33}.

In general, three tests are used to diagnose this disease: viral isolation, polymerase chain reaction (PCR) and serology^{32,33}.

3.3.6 Treatment and prevention of chikungunya

To date, there are no specific drugs that act against chikungunya. In order to relieve symptoms, patients are usually treated with nonsteroidal anti-inflammatory drugs (NSAIDs) or medications to reduce fever and pain such as ibuprofen, naproxen, or acetaminophen^{32,33}.

Rest and hydration is also recommended². The use of acetylsalicylic acid is not advised due to the risk of bleeding and the development of Reye's syndrome in children under 12 years². The chronic symptoms of the disease are exclusively medical management².

Given the lack of a vaccine and an antiviral treatment, vector control represents the alternative to prevent the occurrence of outbreaks or epidemic events^{32,33}.

As protection during outbreaks, wearing clothes that minimize the exposure of the skin to the vectors is also recommended. Repellents can be applied to the skin or clothes, strictly respecting the instructions for use of the product. Repellents must contain DEET (N, N-diethyl-3-methylbenzamide), IR3535 (ethyl ester acid 3- [N-Acetyl-N-butyl] -aminopropionic) or icaridin (2-(2-hydroxyethyl) -1-methylpropyl ester of 1-piperidinocarboxylic acid) 1932,³³.

3.4 3.4 Yellow fever

3.4.1 Epidemiology of yellow fever

Yellow fever is a zoonosis typical of some tropical regions of South America and Africa (see figure No 18), which over time has caused numerous epidemics with high mortality rates³⁶. Its etiological agent is yellow fever virus, an arbovirus infection of the Flavivirus genus^{36,37}.

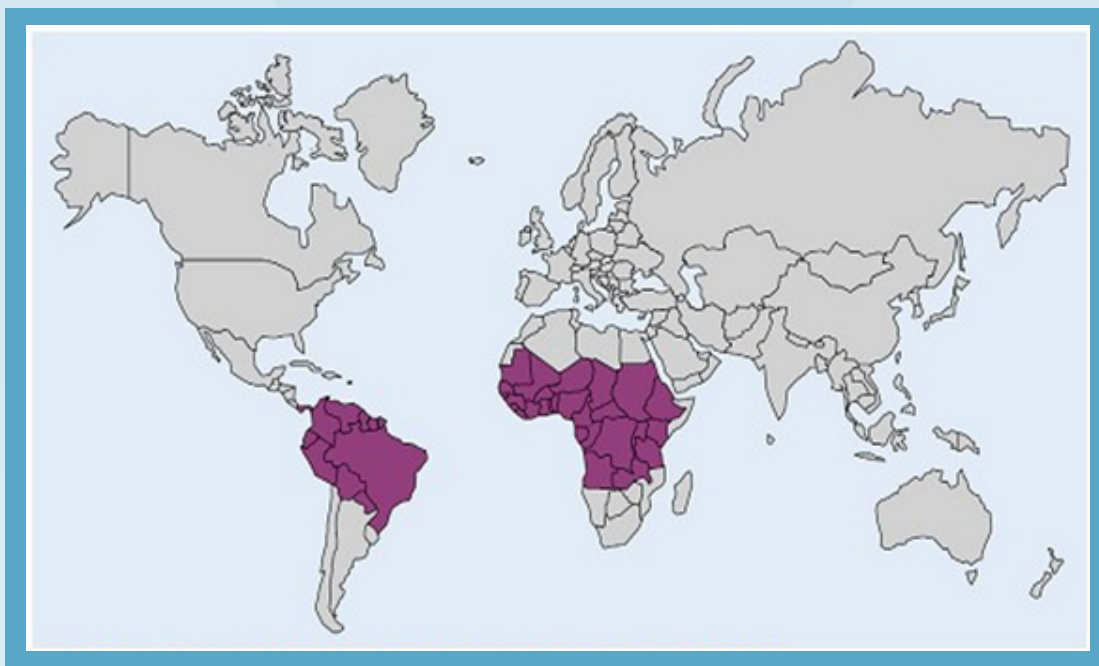


Figure No 18. Map showing countries affected by endemic yellow fever

Source: Yellow fever: It worth a review in the current epidemiological context.

http://scielo.sld.cu/scielo.php?script=sci_arttext&pid=S1727-897X2017000100010

With a model based on African data sources, it has been estimated that for 2013 there were between 84,000 and 170,000 severe cases and between 29,000 and 60,000 deaths³⁶.

The area of occurrence of cases of sylvan yellow fever remains restricted to the region of the South American continent and it includes French Guiana, Suriname, Guyana, Trinidad and Tobago, Venezuela, Colombia, Ecuador, Peru, Bolivia and the central-eastern region of Brazil^{36,37}.

The disease has cyclical characteristics, so its behavior varies during the different years²⁸. The largest number of cases was recorded in 1995 and it was due to an extensive outbreak in the western region of the Andean Area of Peru^{36,37}.

Occasionally, those who travel to countries where the disease is endemic can import it to countries where there is no yellow fever. To avoid these imported cases, many countries require a certificate of vaccination before issuing visas, especially when travelers come from endemic areas^{36,37}.

In the XVII to XIX centuries, the export of yellow fever to North America and Europe caused great outbreaks that disrupted the economy and the development and in some cases decimated the population^{36,37}.

There are two transmission cycles of yellow fever, wild and urban. In the wild cycle, the virus circulates among non-human primates and possibly among susceptible marsupials. The transmission is produced by the bite of some species of mosquitoes typical of the jungle. In the Americas region, the main vectors are *Haemagogus and Sabethes* mosquitoes. In this cycle, the human acquires the infection when, upon entering the jungle, he is bitten by mosquitoes infected by the yellow fever virus^{36,37}.

The urban cycle is characterized by the circulation of the virus among susceptible human beings. The virus is transmitted by the bite of the *Aedes aegypti* mosquito, a vector with domestic characteristics. The urban cycle begins when a person who has acquired the infection in the forest moves during the stage in which the virus circulates in their blood to urban centers with high density of *A. aegypti* and there, he is bitten by that vector which, in turn, transmits the virus to another susceptible person, thus establishing the chain of transmission of the disease in the urban environment^{36,37}.

Intermediate yellow fever is another type of transmission, in which semi-domestic mosquitoes that breed in the jungle and near houses infect both monkeys and humans. Increased contacts between people and infected mosquitoes increases transmission and there may be outbreaks simultaneously in many different towns in an area. This is the most frequent type of outbreak in Africa^{36,37}.

Table No 7 summarizes the epidemiological characteristics of yellow fever:

Table No 7
Epidemiological characteristics of yellow fever

Indicator	Description
Infectious agent	The yellow fever virus, an arbovirus infection of the Flavivirus genus, Flaviviridae family.
Reservoirs	In the wild cycle, mainly monkeys and mosquitoes of the jungle. In urban areas, the man and the <i>Aedes aegypti</i> mosquito.
Distribution	In its endemic form, in the tropical areas of Africa, South America and in Trinidad and Tobago in the Caribbean.
Transmission	By the bite of hematophagous mosquitoes. In the wild areas of the Americas, by mosquitoes of the <i>Haemagogus</i> and <i>Sabethes</i> genus. In urban areas by <i>A. aegypti</i> .
Incubation period	From 3 to 6 days after the mosquito bite.
Transmissibility period	The mosquito becomes infected when the patient is bitten during the viremia stage, which starts shortly before the fever starts and can last until the fifth day of the disease. <i>A. aegypti</i> can become infective after a period of 9 to 12 days after having bitten a viremic person (extrinsic incubation period).
Susceptibility/risk	All non-immune people who enter areas of transmission or with risk of transmission of the disease (tourists, farmers, fishermen, truckers or migrants, among others) or who live in them without being vaccinated.
Immunity	By the vaccine or by the natural infection. The immunity conferred by the vaccine will probably last a lifetime. The international health regulations require vaccination for travelers entering endemic areas of yellow fever.
Morbidity and mortality	Between 1993 and 2003, 2099 cases of wild yellow fever in the Americas region and 956 deaths were reported, with a lethality rate of 45 % for that period. The countries that have reported cases in that period were: Bolivia, Brazil, Colombia, Ecuador, French Guiana, Peru and Venezuela.

Source: Practical guide to control yellow fever, PAHO³⁶

Every community pharmacist who works in any of the following countries in the Americas region: Bolivia, Brazil, Colombia, Ecuador, Guyana, French Guiana, Peru, Trinidad and Tobago, Suriname and Venezuela and who treats a person presenting the following symptoms: fever, muscle pain, headache, nausea, vomits and yellowing of the skin and eyes should consider yellow fever infection as a first option, so it is their obligation to refer the case to a health center for prompt care.

On the other hand, if you have a patient with this symptomatology in any other country in the region, you should check if the patient was, at least, in any of the following countries in the last 6 or 7 days: Angola, Benin, Bolivia, Brazil, Burkina Faso, Cameroon, Colombia, Ecuador, Gabon, Gambia, Ghana, Guinea, Guyana, French Guiana, Liberia, Nigeria, Democratic Republic of the Congo, Sierra Leone, Sudan or Venezuela, since it could be a case of yellow fever.

According to the *Yellow Fever Epidemiological Update* published by the WHO on August 2, 2017 on its website, from epidemiological week 01 of 2016 to epidemiological week 30 of 2017, the countries of Brazil, Bolivia, Colombia, Ecuador, Peru and Suriname have reported suspected and confirmed cases of yellow fever³⁰. The number of cases is the following³⁸:

- Ecuador: confirmed cases (n=3)
- Suriname: confirmed case (n=1)
- Bolivia: confirmed cases (n=5)
- Colombia: confirmed and probable cases (n=18)
- Brazil: confirmed cases (n=798)
- Peru: confirmed and probable cases (n=82)

Next, the clinical symptoms of yellow fever are described in detail so that the community pharmacist can guide the patient.

3.4.2 Clinical symptoms of yellow fever

The term yellow fever refers to jaundice (yellowing of the skin and eyes) that some patients present. The clinical symptoms of infection by the yellow fever virus are very variable: from asymptomatic forms, passing through mild modalities with nonspecific symptoms, to classical hemorrhagic fever with high lethality^{36,37}.

The evolution of the disease can include three clinically evident periods:

- Period of infection
- Period of remission
- Period of intoxication

The incubation period varies from 3 to 6 days. Many cases are asymptomatic, but when there are symptoms, the most frequent are fever, muscle aches, especially on the back, headache, loss of appetite and nausea or vomits. In most cases the symptoms disappear in 3 or 4 days^{36,37}. However, a small percentage of patients enter a more toxic, second stage 24 hours after the initial remission. High fever returns and several organs are affected, usually the liver and kidneys. In this stage, jaundice, the dark color of urine and abdominal pain with vomits are frequent. There may be oral, nasal, ocular or gastric hemorrhages. Half of the patients who enter the toxic stage die within 7 to 10 days^{36,37}.

Figure No 19 summarizes the main signs and symptoms of yellow fever.

WHAT IS YELLOW FEVER?

Yellow fever is caused by a small virus transmitted by mosquito bites

Symptoms

- Arrhythmias, cardiac dysfunction
- Bleeding (can progress to hemorrhage)
- Coma
- Decreased urination
- Headaches
- Jaundice
- Muscle pain (myalgia)
- Red face, tongue and eyes
- Seizures
- Vomits

How it is transmitted?

It is transmitted through the insect bite

Treatment

There is no specific treatment for yellow fever. Symptoms treatment may include:

- Blood products for severe bleeding
- Dialysis for kidney failure
- Intravenous fluids

Fuente: Ministerio de Salud.

LA REPÚBLICA

Figure No 19. Main signs and symptoms of yellow fever³¹

Source: <http://misionesonline.net/2016/02/02/por-si-faltaba-algo-los-misioneros-deberan-volver-a-vacunarse-contra-la-fiebre-amarilla/>

Period of infection: Corresponds to the onset of symptoms and includes the viremia stage, it has an abrupt onset, with high fever ($>39\text{ }^{\circ}\text{C}$), chills, headache, nausea, dizziness, general malaise and muscle pain, especially in the lower back. In addition, it will present congestion of the conjunctive and the face. The laboratory results of a patient in this stage of yellow fever will present leukopenia with neutropenia, increased transaminases and albuminuria. The period of infection lasts approximately 3 to 6 days³⁶.

Remission period: It can last from 2 to 48 hours, in which the symptoms subside and the general condition of the patient improves. In mild forms, the patient begins the recovery stage, which lasts between 2 and 4 weeks. In general, cases of yellow fever are very difficult to diagnose when the disease has not progressed to the intoxication period. It is estimated that 15 % to 25 % of the cases the symptoms reappear in a more serious way³⁶.

Period of intoxication: Characterized by jaundice, epigastric pain, hemorrhagic symptoms, mainly epistaxis, gingival hemorrhage, hematemesis, melena and oliguria, followed by anuria, which indicates renal failure. Transaminases are very high. The lethality of the cases that evolve to the period of intoxication is approximately 50%. In the final stage, the patient presents hypotension, psychomotor agitation, stupor and coma. Death generally occurs between the seventh and the tenth day after the onset of symptoms³⁶.

As described above, it is necessary that, in case of a suspected case of yellow fever, the pharmacist refers the patient to the nearest health center since a significant proportion of cases (up to approximately 25 %) will progress to a stage of intoxication which has fatal consequences.

Likewise, the community pharmacist should bear in mind that the different clinical forms of yellow fever can also be identified in other febrile diseases that progress with jaundice, hemorrhagic symptoms or both. In the Americas region, the main diseases that must be considered in the differential diagnosis are³⁶:

- Leptospirosis
- Serious malaria
- Viral hepatitis
- Hemorrhagic fever due to the dengue virus
- Zika

3.4.3 Yellow fever in special populations³⁶

Pediatric population: They present the same symptomatology of adults, however, they are more likely to have a serious disease.

Pregnancy: When pregnant women become infected with the yellow fever virus, they can present various complications, both fetal and maternal, even leading to the death of the fetus and the mother. Congenital transmission has not been detected.

Older adults: They present the same symptomatology of young adults, however, they are more likely to have a serious disease.

3.4.4 Diagnosis of the yellow fever³⁷

As a reminder, the diagnosis of yellow fever is difficult, especially in the early stages. In the most serious cases, it can be confused with malaria, leptospirosis, viral hepatitis (especially fulminating forms), zika and other hemorrhagic fevers such as dengue, therefore, the conformation of the diagnosis through laboratory tests is essential to make the timely approach in a targeted manner.

The laboratory diagnosis is made by means of serological tests for the search for IgM antibodies and for the isolation of the virus in the blood³⁷.

In the early stages of the disease, the virus can sometimes be detected in the blood by the polymerase chain reaction with retrotranscriptase (molecular diagnosis).

Microorganism isolation is only possible when the sample is obtained in the acute stage, during the viremia period, that is, generally between the first and fifth days after the onset of symptoms^{36,37}.

In more advanced stages, it is necessary to resort to the detection of antibodies by ELISA tests or neutralization by plaque reduction (serological diagnosis)^{36,37}.

Serology is the most used procedure in the laboratory diagnosis of yellow fever. The detection of IgM by the ELISA method is currently the most widely used and disseminated technique because it presents high sensitivity and specificity and, above all, simplicity^{36,37}.

Figure No 20 shows a summary of the instructions for diagnosis according to the number of days from the onset of symptoms.

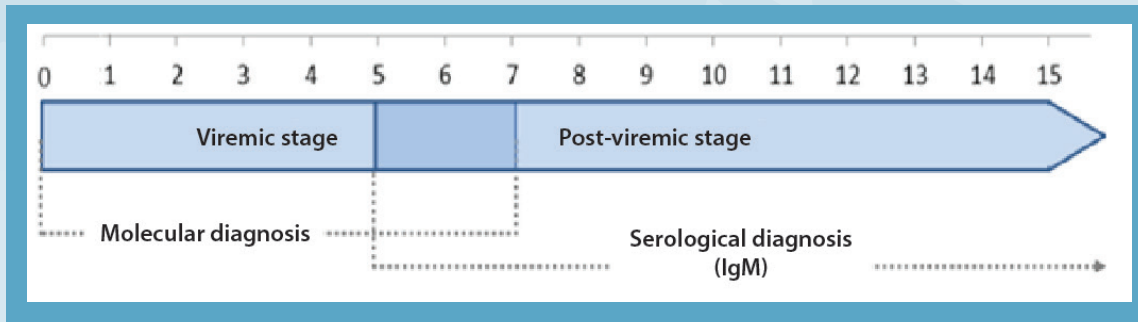


Figure No 20. Instructions for diagnosis according to the number of days from the onset of the symptoms

Source: Laboratory diagnosis of yellow fever virus infection, WHO, 2017³⁷

Other laboratory criteria for the diagnosis of cases are³⁷:

- Increase of IgG antibody levels against yellow fever virus (seroconversion) of, at least, four times.
- Histopathological lesions compatible with those of yellow fever or detection of viral antigens by the immunohistochemical method in tissue samples.

The community pharmacist should promote the visit to the medical centers in cases of suspected yellow fever in a patient in order to perform the laboratory tests that they consider pertinent. It must be remembered that the symptomatology of this disease is shared by other viral conditions so laboratory confirmation is necessary for the timely approach, mainly during the viremia stage when it is more likely that the virus will be isolated.

3.4.5 Treatment of yellow fever

There is no specific antiviral treatment for yellow fever, but the outcome improves with the treatment of dehydration, fever and liver and kidney failure. It is a disease that requires medical management exclusively; therefore, in case of suspected yellow fever, the patient should be referred to the nearest medical center^{36,37}. In mild cases, the treatment is symptomatic and acetylsalicylic acid should not be used since it can cause hemorrhages^{36,37}.

In case of suspected yellow fever the pharmacist should not recommend any medication, the patient should be instructed about the risks of self-medication indicating that the use of NSAIDs

should be avoided to prevent bleeding and refer the patient to the nearest medical center.

3.4.6 Yellow fever prevention strategies^{31,36}

Vaccination: The most important yellow fever preventive measure is vaccination. It provides effective immunity of 80 to 100 % of those vaccinated after 10 days and 99 % immunity after 30 days. Although the yellow fever vaccine is safe and rarely causes adverse effects, contraindications should be considered and safe immunization practices should be followed³⁶.

The vaccine contains live attenuated virus, is effective and has been used for more than 60 years for the active immunization of children and adults³⁶. A single dose is sufficient to confer protection for life, without the need for booster doses^{36,37}.

All current yellow fever vaccines are based on batches of seeds derived from the original attenuated 17D strain, developed in the late 1930s and early forties at the Rockefeller Foundation laboratories in New York and Rio de Janeiro³⁶.

In general, the yellow fever vaccine is considered one of the safest vaccines. The most frequent adverse reactions are: pain, redness at the application site and systemic reactions such as fever, headache, myalgia and general malaise²⁹. These reactions have been studied in, at least, 10 clinical trials and have been categorized as mild and self-limiting reactions that occur between the fifth and seventh days after application in a minority of vaccinated people³⁶.

Serious adverse reactions are very rare. Encephalitis has been documented after vaccination in children under 4 months. This is why the vaccine is contraindicated for children under 6 months. The application of the yellow fever vaccine is recommended after 12 months. In case of outbreaks, it can be applied after 6 months³⁶.

Very rare cases of a multisystemic disease similar to that produced by the natural infection of the wild yellow fever virus have also been reported³⁶.

People over 60 years old seem to be more likely to present adverse reactions, which is why they should be considered people requiring special monitoring. Vaccination of this population is

recommended in case of outbreaks or when they intend to visit a region at risk. The individual evaluation of the epidemiological risk of acquiring the disease against the risk of the appearance of an adverse event is recommended.

The International Health Regulations stipulate the vaccination against yellow fever requirement for people traveling to the geographical areas considered at risk. The competent health authority of each country must issue an International Certificate of Vaccination against Yellow Fever³⁶.

In case there are medical reasons for not administering the vaccine, these reasons must be certified by the competent authority³⁶.

People usually excluded from vaccination are:

- People with acute febrile diseases, with compromise of their general state of health.
- Children under 6 months, except during epidemics, a situation in which children of 6-9 months should also be vaccinated in areas with a high risk of infection.
- Pregnant women, except during outbreaks of yellow fever, when the risk of infection is high.
- People with a severe allergy to egg proteins.
- People with thymus disorders or severe immunodeficiencies due to symptomatic HIV/AIDS infection or other causes³⁶.

Vaccination is recommended for women who breastfeed living in endemic areas, since the risk of transmitting the vaccine virus to the child is less than the benefits of breastfeeding³⁶.

The yellow fever vaccine should be applied subcutaneously in a single dose in the upper arm. It can be administered simultaneously with any vaccine, even with other live virus vaccine (for example: measles, rubella, mumps and chicken pox), as long as they are applied in different sites³⁶.

If the yellow fever vaccine is not administered simultaneously with other injectable live virus vaccines, a minimum interval of four weeks between applications will be respected.

The instructions of the manufacturer of the vaccine included in the package insert must be followed.

All vaccines should be kept in cold chain between 2 °C and 8 °C.

Vaccination activities^{31,36}: The PAHO recommends vaccination against yellow fever to the residing population of countries with endemic areas and the progressive introduction of the vaccine in routine vaccination schemes. Table No 8 summarizes the vaccination activities according to the areas.

Table No 8
Summary of vaccination activities according to the areas

Areas	Routine vaccination in an immunization program	Vaccination of other age groups
Endemic areas and areas where migrations are originated	Introduction of vaccination in the regular scheme from 12 years, with a minimum coverage of 95%.	- Vaccination of 95 % of the population over one-year-old residing in the area (urban areas, rural areas or forest). - Vaccination of travelers entering the area
Non-endemic areas	- Vaccination of travelers entering endemic areas. - Creation of a national vaccine reserve for the control of outbreaks. - Massive vaccination in areas where there is an outbreak up to 95 % coverage. - The affected area must be reclassified as endemic area and the vaccination of the new cohorts must be maintained.	

Source: Practical guide to control yellow fever, PAHO³⁶

Other recommendations^{31,36}: Given the limitations on the availability of vaccines and in order to make a rational use of them, the WHO suggests:

- To carry out an evaluation of vaccination coverage against yellow fever in risk areas worldwide to guarantee, at least, 95 % coverage in the resident population of these areas.
- In case of facing an outbreak, indiscriminate vaccination campaigns should not be carried out. Priority should be given to the use of vaccines in the susceptible population and revaccination must be avoided.
- Ensure vaccination of all travelers to endemic areas, at least, 10 days before traveling.
- Having a small reserve stock according to availability of vaccines, allowing to respond in case of outbreaks is recommended.

The community pharmacist is an essential actor in the prevention of yellow fever, therefore, they should follow the vaccination guidelines mentioned above. They can also create prevention

campaigns and take advantage of vaccination scenarios, for example, the world vaccination week celebrated in April to raise awareness about the risks associated with yellow fever. In addition, he will promote vaccination in those who travel to endemic areas as established in the International Health Regulations.

Control of mosquitoes: The risk of yellow fever transmission in urban areas can be reduced by eliminating possible breeding sites for mosquitoes and applying larvicides to water containers and other places where there is stagnant water. The spraying of insecticides to kill adult mosquitoes during urban epidemics can contribute to reduce the number of mosquitoes and, consequently, the potential sources of yellow fever transmission³⁹.

The mosquito control campaigns have been successful in eliminating *Aedes aegypti*, the urban yellow fever vector, in most of Central and South America. Programs to control wild mosquitoes in forest areas are not practical to prevent the sylvan transmission of the disease³⁹.

3.5 Differences between dengue, chikungunya and zika

In Table No 9 and No 10, which are an adaptation of Charts 1 and 2 of the *Instrument for the diagnosis and care of patients with suspected arbovirus infection of the WHO*³ document, the signs and symptoms of the infections by dengue, chikungunya and zika are summarized, as well as the elements that justify the infection suspicion of these arbovirus infections.

Table No 9

Signs and symptoms of arbovirus infections: dengue, chikungunya and zika

Signs and symptoms	Dengue	Chikungunya	Zika
Most frequent reason for consultation	Fever, myalgia	Joint pain, fever	Exanthema or pruritus
Fever	Moderate Very frequent Duration: 5 to 7 days	Intense Very frequent Duration: 3 to 5 days	Mild Very rare Duration: 1 to 3 days
Exanthema	It appears from the 5° to the 7° day Not characteristic	It appears from the 2° to the 3° day Not characteristic	Normally from day 1 Maculopapular, cephalocaudal
Pruritus	Mild to intense	Mild to moderate	Moderate to intense
Conjunctivitis	Rare	Very rare	Very frequent
Neurological symptoms	Rare	Rare (it can be frequent and serious in newborns)	Possible and serious
Headache	Intense and frequent	Mild to moderate	Mild to moderate
Retroocular pain	Intense and frequent	Rare	Rare
Polyarthritis	Absent	Frequent	Frequent
Hand and feet edema	Rare	Frequent	Rare
Chronicity	No	Very frequent	Not described
Myalgia	Very frequent to intense	Frequent Moderate intensity	Rare
Hepatomegaly	Warning sign	Very rare	Very rare
Vomits	Warning sign	Very rare	Very rare
Diarrhea	Frequent	Very rare	Very rare
Intense abdominal pain	Warning sign	Not present	Not present
Skin bleeding	Frequent	Very rare	Very rare
Mucosae bleeding	Warning sign	Very rare (serious when it appears)	Very rare
Shock	Most frequent serious form	Rare	Unknown
Leukopenia	Moderate to intense	Mild to moderate	Mild to moderate
C-reactive protein	Normal	Elevated	Elevated
Elevated hematocrit	It is a warning sign	Rare	Rare
Platelet count	Normal to very low	Normal to low	Normal to low
Particular considerations	Risk of death	It can evolve to chronic arthropathy	Risk of congenital infection and Guillain Barre syndrome
Vaccine	Yes	No	No
Support treatment in mild forms	Acetaminophen (paracetamol) Hydration	Acetaminophen (paracetamol) Hydration	Acetaminophen (paracetamol) Hydration
Prevention		Use of repellents Vectors control	Use of repellents Vectors control

Source: Adaptation from Instrument for the diagnosis and care of patients with suspected arbovirus infection of the WHO, 2011⁶³

Table No 10

Elements that justify the suspicion of infection by dengue, chikungunya and zika viruses

Dengue	Chikungunya	Zika
<p>Person who lives or has traveled in the last 14 days to areas with dengue transmission and begins with high and sudden fever, usually with a duration of 2 to 7 days and two or more of the following symptoms:</p> <ul style="list-style-type: none"> • Nausea • Vomits • Myalgia • Arthralgia • Headache • Retro-orbital pain • Petechias • Leukopenia 	<p>Acute stage: Person who, during the two weeks prior to the onset of symptoms, has been in areas where chikungunya infection is epidemic or endemic and has fever >38.5 °C and arthralgia (usually disabling) or arthritis accompanied by severe, incapacitating pain that is not explained by other health conditions.</p> <p>Post-acute stage: Person whose joint symptoms (arthritis, arthralgias or joint edema) are maintained for more than 3 weeks until the end of the third month. There may be a continuous evolution from the onset of symptoms or intermittent periods without symptoms.</p> <p>Chronic stage (more than 3 months): Patients who had CHIKV disease and presented joint symptoms, such as pain, edema or joint stiffness for more than three months after the acute stage. They may also have chronic arthritis due to CHIKV, which must be studied and confirmed. Arthritis of another inflammatory etiology should be ruled out.</p>	<p>Person presenting acute onset exanthema (the reason for the consultation almost all the times and the first sign, usually pruritic, maculopapular and cephalocaudal), that has no other explanation and that during the two weeks prior to the onset of symptoms has been in areas where zika virus infection is epidemic or endemic and presents two or more of the following symptoms:</p> <ul style="list-style-type: none"> • Fever, generally <38,5 °C • Non-purulent conjunctivitis or conjunctival hyperemia • Arthralgia • Myalgia • Periarticular edema <p>Occasionally, neurological symptoms such as Guillain Barre can be present.</p>
<p>Any child coming from an area with dengue transmission or resident in that area, with acute febrile symptoms, usually with a duration of 2 to 7 days and without apparent etiology, can also be considered suspicious.</p>	<p>Acute cases: Occasionally they can be accompanied by non-joint symptoms, such as neurological, cardiovascular, dermatological, ophthalmological, hepatic, renal, respiratory and hematological, among others, or they can present dysfunction of, at least, one organ or system with vital risk.</p>	<p>In the case of newborns with a symptom of congenital infection, for example, microcephaly, the mother should be questioned to determine if she was in areas where the zika virus infection is epidemic or endemic during the first 3 months of pregnancy.</p>

Source: Adaptation from: Instrument for the diagnosis and care of patients with suspected arbovirus infection of the WHO, 2011⁶³

IV. PHARMACIST'S ROLE IN THE DETECTION, CONTROL AND PREVENTION OF ARBOVIRUS INFECTIONS: PATIENT EDUCATION CAMPAIGNS AND PUBLIC HEALTH STRATEGIES

Because of the geographical location of Latin America and the commercial exchange reflected in the migration phenomena with other countries, as well as the presence of mosquitoes as vectors, the emergence, reemergence and dissemination of arbovirus infections in our continent is inevitable, so that despite the development of new techniques, both diagnostic and treatment, as well as vaccines in cases of dengue and yellow fever, the pillar of arbovirus infections prevention should focus on the vectors control, since the moment when a new arbovirus infection will emerge is unknown^{2,3}.

Prevention focuses on reducing the number of mosquitoes by reducing the number of sites for egg storage (pots, tires, water reserves, among others) by drying them or treating them with insecticides^{2,3}.

Individual protection includes wearing long, brightly colored clothes, using mosquito repellents, and meshes for beds, doors and windows to avoid mosquito bites^{2,3}.

However, the ignorance of these diseases, the form of infection and especially the forms of control and prevention make the population increasingly vulnerable to arbovirus infections, which has generated an increase in cases with the consequent appearance of outbreaks and epidemics.

Pharmacists are the most accessible health professionals to the population and community pharmacies are usually the first places which patients come to when they have health problems. In recent years, the community pharmacy has focused its activity on ensuring an adequate use of medicines by patients, while it has been participating in numerous health education and prevention campaigns aimed at promoting better health and wellbeing of the citizens.

Other types of activities have also been carried out aimed at detecting pathologies that allow the patient to be treated early or to be referred to the doctor in a timely manner. The arbovirus infections should not be the exception to these initiatives, therefore, this section is intended to be a guide about the actions that the pharmacist can perform daily in the detection, approach, control and prevention of arbovirus infections.

A study conducted in the Philippines in 2013 evaluated the role of community pharmacists, doctors and nurses in the prevention of dengue and it was found that the population identifies the pharmacist as the person in charge of dispensing medication accompanied by the advice on the prevention of the disease. The results of this study allowed to provide recommendations to improve the participation of pharmacists in public health programs against dengue. The low participation of the pharmacist and the doctor in community activities was evidenced, even in the dissemination of information about dengue and the need to provide training to community pharmacists for the management of this arbovirus infection³⁹.

4.1 Actions of pharmacists in the detection and approach of arbovirus infections from pharmacies³⁹

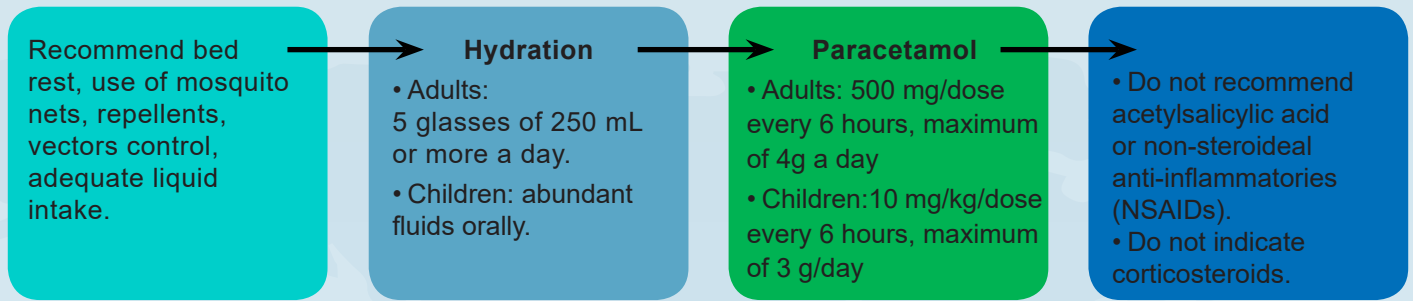
The following are a series of recommendations that the pharmacist could adopt in the presence of an alleged case of arbovirus infection in the community pharmacy.

All patients with suspected dengue, zika or chikungunya should be evaluated comprehensively and in case of presenting warning signs or severe forms of these diseases or the consultation of special populations (children, pregnant women, and elderly) should be referred to the doctor for its respective management.

Some serious symptoms or attention to special populations will require hospitalization and management of advanced support therapy, therefore, it is essential that the pharmacist recognizes the presence of warning signs and severity criteria of arbovirus infections for a responsible action in favor of public health of the community.

4.1.1 Patient approach without warning signs or severity, without comorbidities, who is not part of the special populations and tolerates the oral administration.

The patient should be interviewed about the symptoms presented, the duration and the intensity. Thus, it can be known if it is a serious case or vulnerable population. In case of diseases without warning signs or severity, the following is recommended:



Source: Personal research, 2017

Particularities of pharmacological treatment of non-serious forms of arbovirus infections^{2,3}:

The following is a summary of the pharmacological strategies for addressing the non-serious forms of arbovirus infections, which can be used as a recommendation to patients by the community pharmacist:

The first choice analgesic treatment is acetaminophen (paracetamol) for adults and children; the recommended doses are: 500 mg to 1 g every 6 hours and 15 to 20 mg/kg/doses respectively.

The use of aspirins or any other non-steroidal anti-inflammatory (NSAIDs) is not recommended particularly during the febrile stage and for 48 hours after the last febrile episode, due to the high risk of bleeding in patients with a possible infection or co-infection with dengue or yellow fever, or of developing Reye's syndrome in children under 12 years old.

In patients with serious joint pain that is not relieved with NSAIDs, narcotic analgesics or corticosteroids can be used in the short term after a risk-benefit evaluation of these treatments performed by a specialist.

In case of pruritus, type 1 topical or systemic antihistamines can be used.

Source: Personal research, 2017

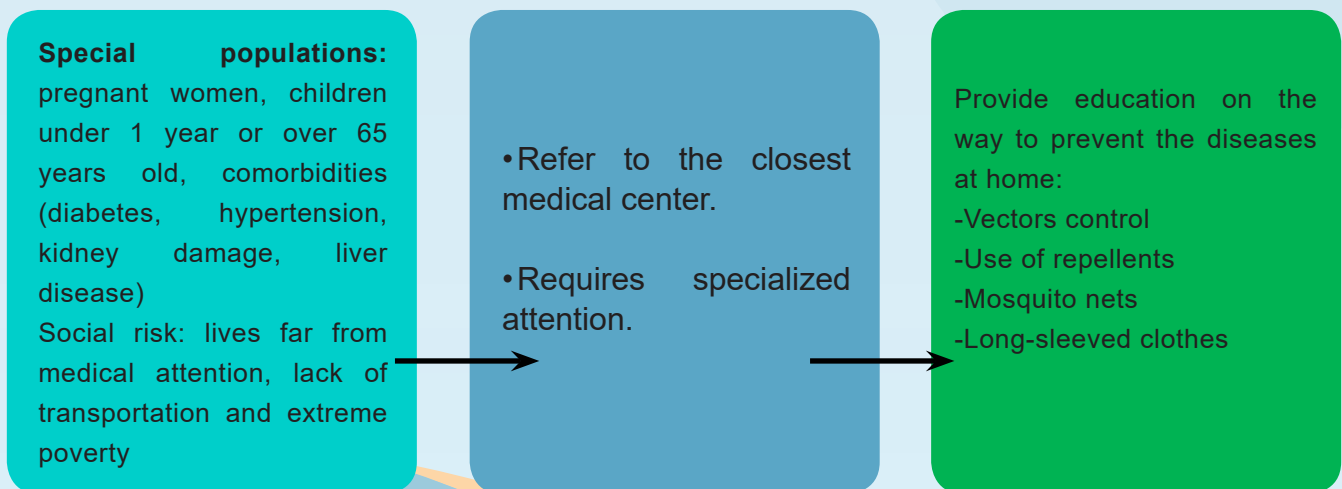
The patient should be informed that if there is no improvement or if there are severe signs and symptoms he/she should go to the doctor for an assessment since it may be a serious case that requires specialized care.

Following the dispensing of the medication, the patient should be educated about the management of vectors and disease prevention measures.

4.1.2 Approach of patients with warning signs or severity, special populations or social risk^{2,3}

The approach of severe forms of arbovirus infections and attention of special populations should be carried out by a medical professional. The pharmacist who addresses the case should guide the patient and educate him about the severity of the situation, motivate the patient to go to the nearest medical center as soon as possible.

In all cases, the pharmacist must educate the population to carry out prevention activities in the communities. The most important prevention strategy is vector control.



Source: Personal research, 2017

4.2 Vectors control

The prevention or reduction of the transmission of dengue, chikungunya, zika and yellow fever viruses depends entirely on controlling mosquito vectors or interrupting contact between them and humans. In order to control mosquito vectors, the WHO promotes a strategic approach, known as integrated vector control^{41,42}.

The integrated vector control is a *rational decision-making process to optimize the use of resources in the control of vectors*. Its objectives are the improvement of efficiency, profitability, ecological consistency and sustainability^{41,42}.

Among the main determinants linked to the increase in arbovirus infections are population growth, excessive or poorly planned urbanization, inadequate sanitary conditions, the deterioration of the health infrastructure and the emergence of more complex characteristics in the vector that transmits the virus⁶.

The activities to control transmission should focus on *A. aegypti* mosquitoes in immature stages (egg, larva and pupa) and in adult stage inside houses and adjacent spaces.

Other environments are also included where contact between human beings and vectors takes place, such as schools, hospitals and work centers^{41,42}.

4.2.1 Methods for vector control^{41,42}:

The *A. aegypti* mosquito uses a multitude of small spaces, both artificial and natural, as a breeding sites.

In some artificial containers large numbers of adult mosquitoes proliferate, while others are less productive. Therefore, efforts to control vectors should be directed to those habitats that are more productive and, consequently, more important from the epidemiological point of view, instead of targeting all types of containers, especially when there are notable resource limitations.

The vector transmission is reduced using one of the following three methods or several of them combined:

- Environmental management
- Chemical control
- Biological control

Pharmacies must promote the protection of people and houses through the following recommendations:

4.2.2 Protection of people and houses^{41,42}

- a. Reduction of infection sources in the houses and in the community at the initiative of its inhabitants, through the elimination of breeding sites (stagnant water in gardens, vases, tires, containers, among others).
- b. The use of clothing that reduces the amount of exposed skin at times of the day when mosquitoes are most active protects, to a certain extent, from vector bites and is a measure that is particularly recommended during outbreaks of the disease.
- c. Use of repellents on areas of exposed skin or on clothes. However, the instructions for use of the product must be strictly be complied with.
- d. Mosquito nets treated with insecticides are a good protection for people who sleep during the day (such as infants and people who need to stay in bed or work night shifts).
- e. In indoor environments, the use of household aerosol insecticides, mosquito coils or other insecticide sprays can also reduce the number of bites.
- f. Some elements of the house, such as metal racks for doors and windows or air conditioning, can reduce biting.

4.2.3. Safe use of insecticides^{41,42}

All pesticides are toxic to a certain extent, so when used, precautionary measures in particular must be respected, they must be handled with care, respect the occupational safety standards for those who use them and apply them in an appropriate manner. This strategy is reserved for health authorities that have trained personnel to manage and apply these insecticides.

4.2.4 WHO information campaigns: Action week against mosquitoes 2017

The information campaign “Action week against mosquitoes 2017” is an effort of the countries and territories of the Americas, promoted by PAHO to raise awareness and work with communities on the relationship between mosquitoes and the diseases they transmit, such as dengue, chikungunya, zika and yellow fever.

In 2016, the first Action week against mosquitoes in the Americas was held in the context of the health emergency caused by the outbreak of the zika virus. In the affected countries, media campaigns focused on mosquito removal and communication on personal protection measures, especially for pregnant women, supporting efforts to reduce the risks associated with zika virus disease. Of the 36 countries of the Americas and territories, 27 were involved in various promotion, communication and awareness actions at different levels.

Part of the educational material of these campaigns has been developed jointly with Ministries of health of countries of the region, among them the Argentine Ministry. Figures No 21 and No 22 show an example of educational material for the population related to the elimination of breeding sites in the home and in the community.



Figure No 21. Action campaign against mosquitoes 2017 of the PAHO, May 2017⁴²



Figure No 22. Action campaign against mosquitoes WHO/Government of Argentina, 2016⁴²

You can find the educational material to download on the PAHO and the Pharmaceutical Forum of the Americas websites. Videos, infographics and material to share on social networks are also attached. For more information visit: <http://www.paho.org/>, <http://www.forofarmacodeelasamericas.org>

4.2.5 Recommendations on the use of repellents against mosquitoes of the genus *Aedes*⁴³

The information that will be provided below is part of an educational material prepared by the Argentine Society of Pediatrics about the correct way to use repellents against *Aedes* genus mosquitoes. Community pharmacists should advise every patient acquiring a repellent on the correct way to use it in order to achieve the desired effectiveness and safety, as well as their rational use.

Insect repellents are substances that, because of their smell or nature, offer protection against insect bites. They are applied on the different exposed areas of the body by means of different systems: lotions, creams, vaporizers, roll-on, stick, gel or impregnated wipes, through which the active principles are deposited on the skin.

They generally ensure protection for 4 to 8 hours after use. They do not kill the insect, but they keep it away from the area where the insect repellent has been applied.

There are different types of insect repellents in the pharmaceutical market. One of the most widely used is N, N-diethyl-m-toluamide (DEET). The concentration of DEET may vary from one product to another and in different forms of presentation.

The duration of protection depends on the concentration. A product with 10 % DEET protects for approximately 2 to 3 hours, whereas 25 % DEET offers an average protection of 6 hours.

Due to the current epidemiological situation of arbovirus infections and other diseases transmitted by mosquitoes, the classic recommendations on the use of repellents have been modified, and extra care should be taken with children from 2 months, with repellents containing DEET.

It is considered that DEET offers the best protection against mosquito bites (predictable and prolonged protection), recommending a concentration of less than 30 % in children, although its use is not recommended in children under 2 months of age.

Citronella is less effective than DEET and in the current epidemiological context, its use is discouraged.

However, in a context not associated to a health contingency due to an outbreak of diseases, citronella is the choice for young children (under 2 years) and in pregnant women due to its low toxicity and high tolerance. Its action consists in producing an unpleasant effect on the nervous terminations and produces a blockage of the chemical perception of the insects. It drives insects away, but it neither kills them nor poisons the environment.

For the application of the repellents, the habits of biting activity of *Aedes aegypti* must be remembered: it is greater in the morning, several hours after dawn and in the afternoon, hours before dark. However, it sometimes feeds during the day in indoor areas or in nearby areas

protected from direct sunlight. Sometimes, it feeds indoors during the night if there are lights on.

It is important to take into account the following recommendations to avoid the appearance of adverse effects caused by the use of repellents:

- Check the product label to find information on how much DEET the repellent contains. Use products which concentrations do not exceed 30 %.
- Always follow the instructions on the product label.
- Do not apply the repellent under clothing.
- Do not apply the repellent on cuts, wounds or irritated skin.
- Do not spray products with DEET in closed areas.
- Do not spray products with DEET directly to the face. Spray the hands and then rub them carefully over the face, avoiding the eyes and mouth.
- Protect the baby's crib or stroller with mosquito nets when outside. When repellent is used on a child, the adult should apply it on their own hands and then spread it on the child's skin. Avoid applying it on the eyes and mouth of the child and use carefully around their ears.
- Do not apply the repellent on children's hands (children could put their hands in their mouths).
- Do not allow young children to apply the repellent themselves. Do not use repellents associated with sunscreens in the same formulation.

Since 2009, after the dengue epidemic, the use of silicone bracelets known as *repellent bracelets* has spread. These products are placed on the wrists or ankles and are impregnated with vegetable oil of citronella or eucalyptus that act as natural repellents. Such bracelet does not have a specific action on a particular type of insect and has a limited effectiveness because citronella is less effective than DEET and its use is discouraged in an epidemic situation.

Do not use:

- Bracelets that contain chemical repellents.
- Garlic or vitamin B1 taken by mouth.
- Ultrasonic devices that issue sound waves designed to repel insects.
- Houses for birds or bats.
- Garden devices that electrocute insects (in fact, they can attract insects to your garden).

During 2015, Argentina reported a growth in the demand and sale of repellents against mosquitoes of approximately 60 %, which generated a shortage of the product. For the manufacture of the

products that fight the mosquitoes, raw material is used that was not obtained in the country and was exported from Asia. In addition, there were few suppliers of repellents what generated an even greater impact on the availability of the product.

In view of the foregoing and motivated to prevent the shortage of repellents, the Pharmacists and Biochemist Association of the Capital City requested the authorization from the National Ministry of Health for pharmacies to perform the preparation of repellents against mosquitoes without a prescription. This is how the National Executive Power authorized pharmacies throughout Argentina to produce small-scale mosquito repellents in their authorized laboratories, at affordable prices to the population. In this way, the repellent shortage problem was mitigated and the population was given access to the simplest form of prevention of arbovirus infections, the use of repellent^{43,44,45}.

Two major initiatives in the field of repellent manufacture in pharmacies were proposed by the Pharmacists Association of the Province of Buenos Aires and the Pharmacists and Biochemists Association of the Capital City (Argentina)^{43,44,45}.

The Pharmacists Association of the Province of Buenos Aires (Argentina) carried out a prevention campaign against dengue in 2012. As part of this campaign, a technical document was made in which master formulations of repellents were included, which are mentioned below^{43,44,45,46,47,48}:

Citronella cream	Citronella lotion	N, N-diethyl-m-toluamide (DEET) lotion	N, N-diethyl-m-toluamide (DEET) gel
<p>Ingredients:</p> <ul style="list-style-type: none"> - Essence of citronella q.s. - Non-ionic hydrophilic base cream qsp 10 mg <p>Concentrations: 1.5 %, 3.0 % and 5.0 %</p> <p>Preparations: In a suitable container weigh the entire base cream and add citronella in portions and with homogenization. Pack and label</p> <p>Quality assurance:</p> <ul style="list-style-type: none"> - Aspect: homogeneous white or lightly yellowish cream. - 10 % pH in water: between 4 and 7 - Content control and sealing of the closure. <p>Conservation: At a temperature not exceeding 40 °C</p> <p>Expiration: 3 months.</p>	<p>Ingredients:</p> <ul style="list-style-type: none"> - Essence of citronella q.s - Vehicle with enough quantity (qsp) for 1000 mL: isopropyl myristate 5 g, polyethylene glycol 400 15 g, isopropanol qsp 100 mL <p>Concentrations: 1.5 %, 3.0 % and 5.0 %</p> <p>Preparation: In a suitable container weigh the citronella and add the vehicle and shake until you have a clear solution, bring to volume and filter if necessary. Pack and label. It can be used as a spray lotion.</p> <p>Quality assurance:</p> <ul style="list-style-type: none"> - Aspect: colorless or slightly yellowish liquid, free of foreign elements - Content control and sealing of the closure. <p>Conservation: At a temperature not exceeding 40 °C</p> <p>Expiration: 3 months.</p>	<p>Ingredients:</p> <ul style="list-style-type: none"> - DEET q.s. - Glycerin 20 g - Ethanol 70° qsp 100 g <p>Concentration: Up to 25 % w/w</p> <p>Preparation: In a suitable container weigh the DEET and the glycerin. Dissolve with ethanol 70°. Glycerin and DEET are not soluble between them, but alcohol solubilizes both. Filter if necessary. Pack and label. A plastic container of medium or high density polyethylene is recommended, due to the solvent effect of DEET.</p> <p>Quality assurance:</p> <ul style="list-style-type: none"> - Aspect: colorless or slightly yellowish liquid, free of foreign elements - Content control and sealing of the closure. <p>Conservation: At a temperature not exceeding 40 °C</p> <p>Expiration: 12 months.</p>	<p>Ingredients:</p> <ul style="list-style-type: none"> - DEET q.s. - Carbomer 0.50 g - Glycerin 20.0 g - Triethanolamide (TEA) 50 % q.s. - Ethanol 70° qsp 100 g <p>Concentrations: Up to 25 % w/w</p> <p>Preparation: A. In a suitable container weigh the carbomer and glycerin. Homogenize and leave until the next day. A very viscous homogeneous material is left. B. Place the DEET in another container and mix it with 50 g of 70° ethanol. Incorporate B over A with agitation. A bit viscous, homogeneous liquid is obtained. Neutralize with 50 % TEA by dripping and stirring until pH 6-7. Bring weight with 70° ethanol and homogenize. Pack and label. A plastic container of medium or high density polyethylene is recommended, due to the solvent effect of DEET.</p> <p>Quality assurance:</p> <ul style="list-style-type: none"> - Aspect: homogeneous white or lightly yellowish cream. - 10 % pH in water: between 4 and 7 - Content control and sealing of the closure. <p>Conservation: At a temperature not exceeding 40 °C</p> <p>Expiration: 12 months.</p>

On the other hand, the Pharmacists and Biochemists Association of the Capital City (Argentina) carried out a course of elaboration of four repellent master formulas against these vectors in March 2016. The video explaining the preparation of the formulas is called Preparation of formulas: repellents against dengue and is available on YouTube at the following link³⁶: https://www.youtube.com/watch?v=UU30EUSn_jU

4.3 Dengue and yellow fever vaccination^{20,21,30,49}

The community pharmacist can recommend the use of dengue vaccine in endemic areas. Therefore, it is recommended that the pharmacist knows the following:

4.3.1 Dengue vaccine: Dengvaxia® is the name of the vaccine developed by Sanofi-Pasteur Laboratories to prevent dengue caused by serotypes 1, 2, 3 and 4 of the dengue virus in people aged 9 to 45 years living in endemic areas.

The vaccination scheme consists of three doses that must be administered at 6-month intervals, both for adults and for the pediatric population.

It is administered subcutaneously.

It is contraindicated in:

- Patients with congenital or acquired immunodeficiency that impair cell-mediated immunity including immunosuppressive therapies such as chemotherapy or high doses of systemic corticosteroids.
- People with symptomatic HIV infection.
- Pregnant women.
- Women in breastfeeding period.

Like any vaccine, it may not protect 100 % of people vaccinated. Personal protection measures against mosquito bites after vaccination are recommended.

It should not be mixed with any other vaccine or injectable medication. After reconstitution, it should be used immediately.

Regarding their safety profile, the most frequent adverse reactions are: reaction at the injection site (erythema, bruising, swelling, pruritus), headache, myalgia, general malaise, asthenia and fever.

However, in April 2018, the WHO issued a statement related to the safety associated with the application of the dengue vaccine, in which it is indicated that the injection may have to be given only to people who have already suffered the disease^{50,51}.

The result of this alert is derived from a long-term follow-up investigation of the product and it is also known that since November 2017 Sanofi Pasteur reported that people who have never been ill with dengue were at risk of developing a more serious disease if they were vaccinated, which was confirmed by the WHO vaccines group through the pronouncement issued^{50,51}.

La vacuna se puede ofrecer a individuos con infección por VIH asintomática con recuentos de CD4+ ≥ 200 células/mm³ que requieran vacunación.

4.3.2 Yellow fever vaccine: In the case of the yellow fever vaccine, it is known to be safe and affordable, it provides effective immunity against the disease to 80-100 % of those vaccinated after 10 days and an immunity of 99 % after 30 days. A single dose is sufficient to confer immunity and protection for life, without the need for booster doses. The individual evaluation of the epidemiological risk of acquiring the disease against the risk of the appearance of an adverse event is recommended.

The vaccine can be offered to individuals with asymptomatic HIV infection with CD4 counts ≥ 200 cells/mm³ who require vaccination.

Pregnant women should be vaccinated in an epidemiological emergency situation and following the express recommendations of the health authorities.

Vaccination is recommended for women who breastfeed living in endemic areas, since the risk of transmitting the vaccine virus to the child is less than the benefits of breastfeeding.

For pregnant women or breastfeeding women traveling to areas with yellow fever transmission, vaccination is recommended when the trip cannot be postponed or avoided. They should receive

advice on the potential benefits and risks of vaccination to make an informed decision.

The vaccine is applied from the year of age. In case of outbreak it can be applied to children from 6 months of age and older.

People over 60 years are more likely to have adverse reactions associated with the vaccine, so it is suggested to establish the risk-benefit ratio.

All people traveling to endemic areas should be vaccinated against yellow fever according to the International Health Regulations. In turn, the competent health authority must issue an International Certificate of Vaccination against Yellow Fever to the person vaccinated. It is recommended to apply the vaccine, at least, 10 days before the trip.

For the other arbovirus infections, chikungunya and zika, vaccines have not yet been developed.

4.4 Education: preparation of information material, public health campaigns and presence in the media

Education should be the central strategy in the control and prevention of arbovirus infections, therefore, table No 11 shows, by way of example, different campaigns and educational material disseminated in countries of the region, as well as other information resources available for the training of the pharmacy professionals.

Likewise, the presence of pharmacists in the media is identified, which is a way of informing the population about the subject. The available resources consist of posters, videos, technical documents with the regulations of each country, among others.

4.4.1 Material informativo y educativo

Informative and educational material

Table No 11

Examples of some informational and educational campaigns on dengue, zika, chikungunya and yellow fever in the Americas

País/Región	Description of the campaign/educational material	Links
Argentina ^{47,48,49}	<p>Dengue, chikungunya and zika campaign: Informative campaign of the Ministry of Health of Argentina in which informative posters, videos, news and technical documents are available.</p> <p>Pharmacists for the Quality of Life: Pharmacists Association of the Province of Buenos Aires program.</p> <p>Yellow fever vaccination campaign. Informative material about the symptoms of the disease and how to prevent it.</p>	<p>http://www.msal.gob.ar http://www.msal.gob.ar/vivamoslibresdemosquitos/</p> <p>http://farcavi.blogspot.com/p/campanas-farcavi.html https://www.argentina.gob.ar/salud/vacunas/febreamarilla</p>
Brazil ^{52,53}	<p>Pharmacist in Action campaign: Informative campaign for pharmacists made by the Conselho Federal de Farmacia in which information material such as posters and videos are available.</p> <p>Brazilian Society of Dengue and Arbovirus Infection: It offers multiple informative and educational resources, as well as training resources.</p>	<p>http://campanhacff.wixsite.com/farmaceuticoemacao</p> <p>http://www.sbd-a.org</p>
Chile ⁵⁴	<p>Recommendations for dengue, zika, chikungunya: Informative campaign of the Ministry of Health of Chile in which the generalities of the diseases and the situation in that country are explained.</p>	<p>http://web.minsal.cl/virus-zika/</p>
Colombia ⁵⁵	<p>Prevention of communicable diseases: Educational space of the Colombian Ministry of Health for patients.</p>	<p>https://www.minsalud.gov.co/salud/publica/PET/Paginas/Enfermedades-transmisibles.aspx</p>
Costa Rica ^{56,57}	<p>Dengue, chikungunya and zika campaign: Prepared by the Pharmacists Association with the collaboration of the Pharmaceutical Forum of the Americas and the FIP.</p> <p>Virtual platform of the Association of Pharmacists of Costa Rica: Virtual course "Pharmaceutical approach to diseases caused by dengue, chikungunya and zika viruses".</p> <p>Informative and didactic material of the Ministry of Health: Directed to patients and health professionals.</p>	<p>http://www.colfar.com</p> <p>http://www.colfar2.com</p> <p>https://www.ministeriodesalud.go.cr/index.php/centro-de-informacion/material-educativo/mi-comunidad-sin-dengue</p>

Country/ Region	Description of the campaign/educational material	Links
El Salvador ⁵⁸	Dengue, chikungunya and zika campaign: Prepared by the Ministry of Health, focused on patients and on the presentation of videos, radio clips, reports of vector eradication campaigns, news and technical documents.	http://w2.salud.gob.sv/novedades/noticias/noticias-ciudadanosas/56-anuncios-en-portada-de-ciudadanoa/307-campana-contra-el-dengue-chikungunya-y-zika.html
Guatemala ⁵⁹	Scouts of Guatemala , they organize a campaign to prevent diseases transmitted by the <i>A. aegypti</i> mosquito.	http://www.scouts.org.gt/oficial/avisos/3167
México ⁶⁰	Avoid zika, chikungunya and dengue: Campaign of the Government of Mexico with educational material for patients and professionals (technical documents), multimedia material, news among others.	https://www.gob.mx/chikungunya-dengue
Perú ^{61,62}	Health prevention campaigns: In charge of the Ministry of Health of Peru. Health and prevention: Social Security of Peru, provides information on yellow fever	http://www.minsa.gob.pe/index.asp?op=2#Prevención%20para%20la%20Salud http://www.essalud.gob.pe/salud-y-prevencion/
Paraguay ⁶³	General direction of health promotion: Educational material, posters for patients.	http://www.mspbs.gov.py/promociondelasalud/herramientas/materiales-educativos/
Uruguay ⁶⁴	Campaign against the mosquito of <i>A. aegypti</i>: Carried out by the Ministry of Public Health with the support of PAHO/WHO. It is a communication campaign to help Uruguay remain free of indigenous cases of these diseases.	http://www.paho.org/uru/index.php?option=com_content&view=article&id=1153:ningun-caso-registrado-de-dengue-zika-o-chikungunya&Itemid=243
Pharmaceutical Forum of the Americas ⁶⁵	Pharmacists United against Dengue, Chikungunya and Zika: Informative campaign with posters, bulletins for patients, material for professionals and videos.	http://forofarmaceticodelasamericas.org/colegas-informense-como-recibir-evaluar-y-cuidar/
Pan-American Health Organization ⁶⁶	Informative resources: Health issues, summaries of the epidemiological situation of these diseases and resources on ways to control and prevent these diseases. Resources available on the WHO and PAHO webpages.	http://www.who.int/denguecontrol/es/
PAHO Virtual Campus ⁶⁷	Self-learning courses: Two courses are available in Spanish, one on zika disease and the other on chikungunya disease. - <i>Zika: clinical approach in basic care.</i> - - <i>Virtual course on chikungunya.</i>	https://www.campusvirtualesp.org/?q=es/cursos/auto-aprendizaje

The following are examples of posters, infographics or educational material prepared in different countries of the region:

4.4.2 Informative and educational material

ARGENTINA

Dengue, chikungunya y zika se pueden prevenir.



Cualquier recipiente con una mínima cantidad de agua puede ser un criadero:



- Botellas
- Latas y macetas vacías
- Tanques de agua sin tapa
- Cubiertas

- Bebederos de animales
- Floreros
- Tapitas de bebidas

NO LE HAGAS LUGAR EN TU CASA AL MOSQUITO

0800-222-1002
msal.gob.ar





El calor y las lluvias favorecen la multiplicación del mosquito *Aedes Aegypti*, transmisor de

DENGUE, ZIKA Y CHIKUNGUNYA

Para prevenir los criaderos de mosquitos


Tapá depósitos de agua


Mantené boca abajo los recipientes que no estén en uso


Cambiá el agua de floreros y bebederos de animales cada tres días


Tirá latas, botellas, neumáticos y otros objetos en desuso que acumulen agua


Limpiá y sacá las malezas del patio

Si tenés estos síntomas no te automediquéis y consultá al médico.


Fiebre


Dolor de cabeza y detrás de los ojos


Fuerte dolor muscular y en las articulaciones


Vómito o dolor abdominal


Sarpullido

También debés protegerte de las picaduras

Aplicá repelentes contra insectos en la piel expuesta y sobre la ropa



Colocá mosquiteros en la casa



No le des lugar en tu casa al mosquito. Evitemos que el virus se propague.

MENDOZA
NUEVO GOBIERNO



BOLIVIA

Lo que debe conocer sobre la vacuna contra la **fiebre amarilla**

- Estos son los aspectos básicos sobre la inmunización contra esta enfermedad endémica.

El virus de la fiebre amarilla mata al causar insuficiencia hepática y renal.

El vector

Sus vectores son los mosquitos *Aedes Aegypti* y el *Aemagogus*.



Síntomas

- Fiebre
- Dolor muscular
- Hemorragia

La vacuna es gratuita, incluye: el biológico, atención, la jeringa.

- No tiene refuerzos. Sólo requiere **una dosis** para toda la vida.
- Vacunan en hospitales, policlínicos y centros de salud, según cronograma del SEDES.
- Debe vacunarse **10 días** antes de ingresar a una zona tropical.
- Si perdió su carnet de vacunación puede firmar un formulario para que le renueven.

En viajes al exterior es necesario canjear el carnet nacional por el internacional.

Puede vacunarse a partir de los 13 meses de vida.



Fuente: Servicio Departamental de Salud de La Paz, elaboración
Página Siete / Gráfico: Rubén A. /
Página Siete

VACÚNATE CONTRA LA

**Fiebre
Amarilla**



BRASIL

FARMACÊUTICOS EM AÇÃO

Todos contra o *Aedes aegypti*



FARMACÊUTICO

19 MARÇO

DIA NACIONAL DE MOBILIZAÇÃO

Participe!

Realização:



ALERTA POR CASOS FIEBRE AMARILLA



La Secretaría de Salud federal alertó sobre casos confirmados de fiebre amarilla en Brasil, Colombia y Perú.



En Sao Paulo, Brasil, se confirmaron la muerte de seis personas aparentemente por fiebre amarilla en lo que va de este 2017

Decoloración amarillenta de ojos



Si se presentan síntomas se debe solicitar atención médica inmediata.

Este mes se enviaron a Sao Paulo 400 mil dosis más de vacunas.



Saludiarío

CHILE

Si viaja a localidades con casos de

ZIKA DENGUE CHIKUNGUNYA



protéjase de la picadura del mosquito Aedes, siguiendo las siguientes recomendaciones:



Use ropa de color claro que cubra la mayor parte del cuerpo.



Use repelentes en las zonas expuestas (con 30% de sustancia activa DEET o picaridina), de acuerdo a instrucciones del producto.



Use aire acondicionado o malla mosquitera al dormir. En su defecto, mantenga ventanas y puertas con mallas que impidan el acceso del mosquito.



Refuerce precauciones en el periodo de mayor actividad del mosquito, que es durante las primeras horas de la mañana y el atardecer.

 minsal.cl

LLAME A SALUD RESPONDE
600-360-7777
PROFESIONALES DE LA SALUD ATENDIENDO SUS DUDAS LAS 24 HORAS,
LOS 7 DÍAS DE LA SEMANA

PÓNGASE MOSCA CONTRA EL DENGUE



Siga estas sencillas recomendaciones:

1 Ordene los recipientes que puedan acumular agua; póngalos boca abajo, o tápelos bien.



2 Revise todas las áreas, jardín o cualquier espacio abierto de la vivienda, evitando que por su forma, tanto plantas o troncos, se conviertan en recipientes de agua de lluvia.



3 Revise si en los recipientes donde hay agua estancada existen larvas. Si se detectan, hay que eliminarlas, procediendo de la siguiente manera:

- a. Lave y cepille fuertemente una vez a la semana los recipientes en donde se almacena agua: baldes, palanganas, tanques, etc.
- b. Tápelos sin dejar pequeñas aberturas para evitar que los mosquitos entren a dejar sus huevos.
- c. Se pueden criar peces en los depósitos donde el agua se acumula, para que se alimenten de las larvas.



4 Perfore la base de las macetas para el drenaje del agua.



5 Si hay floreros dentro o fuera de la casa, se debe cambiar el agua cada tres días.



6 Deposite el larvicida recomendado por la Secretaría de Salud en los recipientes donde se acumule agua.

7 Corte periódicamente el pasto del jardín.



8 Destruya los desechos que puedan servir de criaderos (triturar los cascarones de huevos, perforar latas vacías, enterrar llantas).



Donde hay
agua estancada,
hay mosquitos.



COLOMBIA

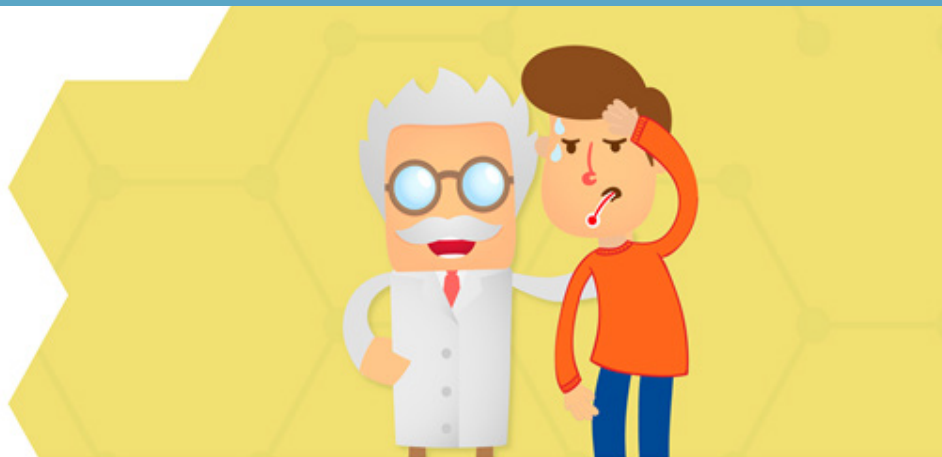
Jornada de vacunación contra **fiebre amarilla**



Para menores a partir de los 18 meses y adultos hasta los 59 años, 11 meses y 29 días

Sábado 1 de abril de 8:00 am a 4:00 pm en todos nuestros puntos de atención

También tendremos disponibles las demás vacunas del esquema PAI



HABLEMOS DE **FIEBRE AMARILLA**



FIEBRE AMARILLA SINTOMATOLOGÍA

- Fiebre
- Dolor Muscular
- Dolor de Cabeza
- Escalofríos
- Pérdida de Apetito
- Vómitos con Sangre
- Sangrado (Hemorragia)



COSTA RICA



**ESTE ES
MI ENEMIGO
¡YO LO ELIMINO ANTES
DE QUE NAZCA!**

Limpie



**pilas, canoas,
estañones,
bebederos de
animales u otros
recipientes útiles
que puedan
acumular agua.**

Todos contra el zancudo que produce Dengue, Chikungunya y Zika













**Detectar
los síntomas
puede salvar
la vida de otros
o la suya**










**ZIKA
CHIKUNGUNYA
DENGUE**

¡infórmese!

Los pacientes con zika, chikungunya y dengue pueden ser asintomáticos. El conjunto y la intensidad de signos y síntomas de las tres condiciones son variables.

COSTA RICA

SIGNOS Y SÍNTOMAS		ZIKA 	CHIKUNGUNYA 	DENGUE 
FIEBRE 		Si está presente, usualmente es baja	Casi siempre presente. Alta y de inicio inmediato	Siempre presente. Alta y de inicio inmediato
DOLORES EN LAS ARTICULACIONES 		Si están presentes, son leves	Presentes e intensos en la mayoría de los casos	Casi siempre presentes y moderados
SARPULLIDO / MANCHAS ROJAS EN LA PIEL 		Casi siempre presentes, usualmente aparecen en las primeras 24h	Pueden presentarse en muchos casos, después del 3r día del inicio de la enfermedad	Pueden estar presentes
PICOR/COMEZÓN/PURITO 		Puede estar presente y ser de leve a grave	Ocurre en casi la mitad de los casos. Pueden ocurrir lesiones con burbujas/ ampollas/ vesículas	Puede estar presente y es leve
ENROJECIMIENTO DE LOS OJOS 		Puede estar presente	Puede estar presente	Raro, pero el dolor alrededor de los ojos es muy frecuente
MANIFESTACIONES HEMORRÁGICAS 		Ausentes	Poco comunes	Pueden estar presentes
OTRAS MANIFESTACIONES 		Dolor de cabeza, dolor muscular y malestar general	Dolor de cabeza, dolor muscular, constipación y dolor del estómago	Dolores de cabeza, detrás de los ojos y musculares intensos

IMPORTANTE         

Para que un mosquito transmita estas enfermedades, debe haberse infectado previamente al picar a una persona enferma.

Tiende a picar durante el día, siendo su mayor actividad a primera hora de la mañana y al final de la tarde.

Recuerde no conservar agua en recipientes desatados, lavar tanques, no acumular basura, deshechar desechos, y utilizar mosquitos en ventanas y puertas.

Acuda a su farmacéutico o a un servicio de salud.

EL SALVADOR



¡QUÉ BUENO!

Que la gente
hace la untadita
en pilas y barriles
¡ASÍ EVITAMOS EL DENGUE!

Recuerde que
es cada 5 días

Ministerio de Salud
EL SALVADOR

Si usted tiene alguna duda, marque el
Teléfono Amigo del Ministerio de Salud.
2221-1001
www.salud.gob.sv

PRESIDENCIA
FUNE
BUENO
CAMBIO

HONDURAS



Estamos en emergencia todos contra el zancudo que transmite el Zika.
SI NO HAY ZANCUDO NO HAY ZIKA



El Zika puede causar daño cerebral a tu bebé y parálisis a adultos y niños



Use repelentes, mosquiteros y tape los depósitos de agua para acabar con el zancudo que transmite el Zika



MÉXICO

EL MOSCO DEL DENGUE

VIVE EN TU CASA

Los criaderos están donde menos te imaginas **¡ELIMÍNALOS!**

Tapa bien los recipientes donde almacenes agua: garrafones, jarras.

Voltea las cubetas y envases que no se estén utilizando.

Cambia el agua de las plantas cada tercer día

Mantén sin agua tu batea cuando no la uses

Cambia el agua de tus mascotas cada tercer día

Mantén la basura perfectamente tapada o sellada.

Elimina todo lo que almacene agua de lluvia: tambores, lantás, latas.

SERVICIO NACIONAL DE SALUD (SEMAR)

INSTITUTO MEXICANO DEL SEGURO SOCIAL (IMSS)

SALUD

SERENA

Servicios de Salud de Yucatán

PERÚ

#VamosaPrevenir

LOS SÍNTOMAS DEL DENGUE, CHIKUNGUNYA Y ZIKA SON SIMILARES



Fiebre



Malestar general



Sarpullido



Si presentas uno de estos síntomas acude al establecimiento de salud más cercano.

¡NO TE AUTOMEDIQUES!



¿ESTÁS PRONTO A VIAJAR?

EL ZANCUDO DEL DENGUE Y LA CHIKUNGUNYA, TAMBIÉN TRANSMITE EL ZIKA

SUS SÍNTOMAS SON SIMILARES



Aedes aegypti



EL ZIKA EN CASO DE EMBARAZO PODRÍA CAUSAR COMPLICACIONES EN EL DESARROLLO DEL BEBÉ

Hecho el depósito legal en la Biblioteca Nacional del Perú N° 2015-08635 / WPMGA. Av. Salaverry N° 801 - Jesús María
Impreso: 2015 OPPSET INDUSTRY S.R.L. / Av. Los Cañales 574-048 - Barrancón, La Victoria / diciembre 2015

Para mayor información, llama gratis a
INFOSALUD: ☎ 0800-10828



PARAGUAY



URUGUAY



URUGUAY CONTRA EL AEDES AEGYPTI

EVITEMOS QUE SE PROPAGUE EN NUESTRO PAÍS EL MOSQUITO QUE TRANSMITE EL DENGUE, LA FIEBRE CHIKUNGUNYA Y EL VIRUS ZIKA.

MEDIDAS DE PREVENCIÓN

- Dar vuelta recipientes con agua: latas, botellas, cubiertas en desuso, etc.
- Tapar los tanques de agua.
- Utilizar mosquiteros en las aberturas del hogar.
- Usar repelente siempre.
- Eliminar adecuadamente la basura.
- Consultar al médico ante fuerte fiebre y dolor articular.



SÍNTOMAS:

Dengue: Fuerte fiebre. Dolor articular.

Virus Zika: Fiebre leve. Dolores de cabeza y articulaciones. Conjuntivitis. Erupciones.

Fiebre Chikungunya: Fuerte fiebre. Dolor en articulaciones, cabeza y músculos. Erupciones. Vómitos. Malestar general.



¡AHORA MÁS QUE NUNCA!
URUGUAY CONTRA EL AEDES AEGYPTI.



ARGENTINA

Domingo 28 de Febrero de 2016 ● Santafe

Los farmacéuticos, protagonistas en la campaña contra el dengue

El Colegio que nuclea a estos profesionales en la Primera Circunscripción de la provincia de Santa Fe busca asumir un rol activo en materia de prevención de las enfermedades transmitidas por el mosquito.

Agencia NOVA
Noticias de la Provincia de Buenos Aires

AMD
Asociación de Médicos Digitales
Provincia de Buenos Aires

Google Búsqueda Buscar

11 de febrero de 2016
Última actualización: 11:29
Lectores: 53017

14°C
21 km/h

Inicio Secciones ▾ Institucional Staff Medios abonados Contacto Newsletter

Exhibirán material preparado por el ministerio

Farmacias de la provincia se suman a la campaña contra Dengue, Chikungunya y Zika

COSTA RICA

Realizan campaña educativa contra dengue, chikungunya y zika

MARZO 30, 2017 5:12 AM | JACQUELINE OTEY ✉



La iniciativa es organizada por el Colegio de Farmacéuticos de Costa Rica. Foto de archivo para efectos ilustrativos.

Desde el lunes 27 y hasta el viernes 31 de marzo, en las 1.100 farmacias que hay en el país, se realizará una **campaña educativa-informativa** sobre las **enfermedades dengue, chikungunya y zika**.

La iniciativa es organizada por el Colegio de Farmacéuticos de Costa Rica y **tendrá a los farmacéuticos regentes como sus principales protagonistas**.

La idea es que los profesionales en farmacia **entreguen información relevante sobre cada una de las enfermedades**, sus factores de riesgo, signos, síntomas, consecuencias, precauciones.

Los facultativos **atenderán consultas de las personas sobre estos padecimientos y realizarán actividades especiales** para motivar a los costarricenses a tener un mayor conocimiento sobre ellas.

"Los meses de marzo y abril son los que se presentan uno de los picos epidemiológicos del año en relación con el dengue, el chikungunya y el zika. Y, si a esto le sumamos que muchísimos costarricenses

Dominican Republic

Farmacia El Sol con campaña contra enfermedades

📁 Categoría: Infectología

📅 Publicación: 29 Febrero 2016 | ⌚ 06:43 am



La Vega.- Farmacia El Sol, de La Vega, desarrolla una campaña educativa de prevención contra el Zika-virus, dengue y chikungunya con apoyo de la Dirección Provincial de Salud y El laboratorio Ibero Fármacos.

El objetivo de esta actividad es promover espacios de educación en los Centros Educativos María Montessori y San Martín de Porres.

En la misma se proporcionó información sobre la prevención y eliminación de los criaderos del mosquito que transmite el Zika, dengue y chikungunya.

V. CONCLUSIONS

Arbovirus infections are a complex public health problem that require multiple approaches and efforts on the part of health professionals as well as political authorities and citizens. The geographical location of Latin America, the commercial exchange, tourism and migrations, as well as the presence of mosquitoes highly adaptable as vectors, makes the emergence and reemergence of these diseases inevitable.

These diseases have the potential to generate significant burdens on health and work systems translated into missed days of work disabilities and costs for direct care, which directly affects the economy of the countries in the region.

The pharmacist has a strong strategic position since he is the health professional most accessible in the communities, which enables him to actively participate in the detection, approach, control and prevention of arbovirus infections.

The strategic activities that pharmacists can develop are focused on:

- Participating and/or developing activities of health promotion, prevention and education directed to individuals and the community to contribute to the interruption of the chain of transmission of diseases.
- Guiding the individual and the population in general about the prevention measures and control of diseases, including the administration of vaccines.
- Identifying suspicious signs and symptoms and referring people to the various health services for a diagnostic and a clinical evaluation.
- Recommending, when applicable, appropriate OTC medications for the relief of signs and symptoms, as well as protective measures, including the use of repellents.
- Following up with patients with diagnosis, treatment or at risk for these diseases so they can achieve their health goals.

To achieve these objectives, the governments of the region through their ministries of health or the specific initiatives from the professional pharmacy organizations, have developed information campaigns with educational materials ready to be reproduced, which can be used in community pharmacies.

Finally, the presence of pharmacists in the media and social networks is a very useful tool to inform the communities about the impact of arbovirus infections, but above all, about how to prevent them.

The pharmacist contributes to improving public health by informing and educating the population about necessary and current health issues such as those with arbovirus infections.

VI. BIBLIOGRAPHIC REFERENCES

1. Enfermedades transmitidas por vectores, Organización Mundial de la Salud, Centro de Prensa, Nota descriptiva número 387.
<http://www.who.int/mediacentre/factsheets/fs387/es/>. Visitado junio 2017
2. Arredondo-García JL, Méndez Herrera A, Medina-Cortina H. Arbovirosis en Latinoamérica. *Acta Pediatr Mex.* 2016 mar;37(2): 111-131
3. Organización Panamericana de la Salud. Instrumento para el diagnóstico y la atención a pacientes con sospecha de arbovirosis. Washington D.C. 2016
4. Foro Farmacéutico de las Américas
<http://forofarmaceticodelasamericas.org/colegas-informense-como-recibir-evaluar-y-cuidar/>. Visitado junio 2017
5. Contreras-Gutiérrez M, Uribe, S. Arbovirus y virus específicos de insectos: flebotómíneos un caso de interés. *Boletín del museo entomológico Francisco Luis Gallego.* Volumen 6, Número 4, diciembre 2014
6. Torres T, Guerrero J, Salazar G. Dimensiones culturales del dengue que favorecen o dificultan su prevención en México. *Rev Panam Salud Pública* 31(3), 2012
7. Ratman I, Leder K, Black, J, Torresi J. Dengue Fever and International Travel. *International Society of Travel Medicine, Journal of Travel Medicine* 2013; Volume 20 (Issue 6): 384-393
8. Fredericks A, Fernandez-Sesma A. The burden of dengue and chikungunya worldwide: implications for the Southern United States and California. *Annals of Global Health* 2014; 80:466-475
9. Organización Panamericana de la Salud. Dengue: Guías para la atención de enfermos en la región de las Américas. Segunda edición 2015. Washington D.C 2015
10. Infección por el virus del Dengue en el humano:
<http://epidemiologiaescobar.blogspot.com/2010/09/dengueepidemiologiaescoba.html>. Visitado julio 2017
11. Signos y síntomas de la fase febril del dengue: <http://www.abc.com.py/edicion-impresalocales/unos-19-pacientes-internados-en-el-ips-presentan-sintomas-de-dengue-80714.html> Visitado julio 2017
12. Simmons C, Farrar J, Van Vinh Chay N. Current Concepts Dengue. *N Engl J Med* 2012
13. Organización Panamericana de la Salud. Número de casos reportado por dengue y dengue grave en América, OPS 2016
14. http://www.paho.org/hq/index.php?option=com_docman&task=doc_view&Itemid=270&gid=37782&lang=en. Visitado julio 2017
15. Dengue world map: <http://www.healthmap.org/dengue/es/>. Visitado Julio 2017
16. Oliveira M, Terzian A, Rodrigues M, Estofolete C, Lacerda M. Mosquito-transmitted virus-the great Brazilian challenge. *Brazilian Journal of Microbiology* 47S (2016) 38-50
17. Síntomas de la fase febril del dengue: <http://www.abc.com.py/edicion-impresalocales/unos-19-pacientes-internados-en-el-ips-presentan-sintomas-de-dengue-80714.html>. Visitado junio 2017

18. Organización Panamericana de la Salud, OMS oficina regional para las Américas. Últimos adelantos técnicos en la prevención y el control del dengue en la región de las Américas. Informe de reunión mayo 2014. Washington, D.C.
19. Ciclo de transmisión del virus zika en el ambiente urbano.
http://www.bbc.com/mundo/noticias/2015/06/150611_salud_virus_zika_preguntas_respuestas_kv.
Visitado setiembre 2017
20. Signos y Síntomas del Virus del Zika:
https://twitter.com/prensa_libre/status/694238370923462657. Visitado setiembre 2017
21. <http://www.sanofipasteur.com/es/articles/mexico-inicia-la-vacunacion-contr-el-dengue.aspx>. Visitado setiembre 2017
22. Preguntas y respuestas sobre las vacunas contra el dengue OMS.
http://www.who.int/immunization/research/development/dengue_q_and_a/es/. Visitado junio 2017
23. Petersen L, Jamieson D, Powers A, Honein M. Zika Virus. N Engl J Med 2016; 374:1552-63
24. <https://www.cdc.gov/ncbddd/spanish/birthdefects/microcephaly.html>. Visitado setiembre 2017
25. Organización Panamericana de la Salud, oficina regional de la OMS para las Américas. Guía para la vigilancia de la enfermedad por el virus del Zika y sus complicaciones. 2016, Washington, D.C.
26. República de Costa Rica. Protocolo de vigilancia de enfermedad por virus Zika y sus principales complicaciones. Versión 1/2016. Diciembre 2016, San José, Costa Rica
27. Ministerio de Salud/INCIENSA/Caja Costarricense de Seguro Social. Protocolo de vigilancia de microcefalia y síndrome congénito asociado a virus del zika en Costa Rica. Diciembre 2016, San José, Costa Rica
28. Organización Panamericana de la Salud, OMS oficina regional para las Américas. Consideraciones provisionales para la atención de mujeres gestantes en escenarios con alta circulación del virus Zika: documento destinado a profesionales de la salud. Mayo 2016, Washington, D.C.
29. Organización Mundial de la Salud. Prevención de la transmisión sexual del virus del zika. Actualización de las orientaciones provisionales. Junio 2016
30. “Fiebre amarilla: vale la pena una revisión en el contexto epidemiológico actual”
http://scielo.sld.cu/scielo.php?script=sci_arttext&pid=S1727-897X2017000100010. Visitado Setiembre 2017
31. Principales signos y síntomas de la fiebre amarilla.
<http://misionesonline.net/2016/02/02/por-si-faltaba-algo-los-misioneros-deberan-volver-a-vacunarse-contr-la-fiebre-amarilla/>. Visitado Setiembre 2017
32. Weaver S, Lecuit M. Chikungunya Virus and the Global Spread of a Mosquito- Borne Disease. N Engl J Med 2015; 372:1231-9
33. Corrales-Aguilar E, Troyo A, Calderón-Arguedas O. Chikungunya: un virus que nos acecha. Acta méd costarric Vol 57 (1), enero-marzo 2015
34. Lucha contra el dengue y la chikungunya
<https://preveccionhn.wordpress.com/category/chikungunya/>. Visitado junio 2017

35. Número de casos reportados por chikungunya, OPS 2016
http://www.paho.org/hq/index.php?option=com_docman&task=doc_view&Itemid=270&gid=37782&lang=en. Visitado julio 2017
36. Organización Panamericana de la Salud. Guía práctica- Control de la fiebre amarilla. Washington 2005
37. Organización Panamericana de la Salud. Diagnóstico por laboratorio de la infección por Virus de la Fiebre Amarilla. Washington 2017
38. Organización Panamericana de la Salud. Actualización Epidemiológica. Fiebre Amarilla. Washington, agosto 2017
39. Solidum J. The roles of pharmacists in relation to medical doctors, nurses and BHWs in preventing dengue. Journal of Life Sciences and Technologies Vol 1, No 1, March 2013
40. Ministerio de Salud de Costa Rica, INCIENSA y Caja Costarricense de Seguro Social. Protocolo de Vigilancia y Manejo Clínico de la Chikungunya. Julia 2014
41. Organización Mundial de la Salud. Estrategias de lucha antivectorial.
http://www.who.int/denguecontrol/control_strategies/es/. Visitado junio 2017
42. Organización Panamericana de la Salud. Campaña contra mosquitos.
http://www.paho.org/hq/index.php?option=com_content&view=article&id=12355&Itemid=42087&lang=es. Visitado junio 2017
43. Sociedad Argentina de Pediatría. Recomendaciones sobre el uso de repelentes.
http://www.sap.org.ar/docs/profesionales/consensos/recomendaciones_sap_repelentes.pdf. Visitado julio 2017
44. Colegio Oficial de Farmacéuticos y Bioquímicos de la Capital Federal-Argentina. Preparación de fórmulas: repelentes contra el dengue.
https://www.youtube.com/watch?v=UU30EUSn_jU. Visitado julio 2017
45. Formulaciones oficinales en dengue.
<http://www.colfarma.org.ar/Cient%C3%ADfca/Documentos%20compartidos/Guia%20de%20Actualización%20en%20Dengue.pdf>. Visitado julio 2017
46. Comisión Federal para la protección contra riesgos sanitarios: Dengvaxia.
<https://www.gob.mx/cms/uploads/attachment/file/207525/401M2015.pdf>
Visitado junio 2017
47. Ministerio de Salud de Argentina. <http://www.msal.gob.ar>. Visitado junio 2017
48. Colegio de Farmacéuticos de la Provincia de Buenos Aires-Farmacéuticos por la vida
<http://farcavi.blogspot.com/p/campanas-farcavi.html>. Visitado junio 2017
49. Campaña de vacunación contra la Fiebre Amarilla. Ministerio de Salud Argentino.
<https://www.argentina.gob.ar/salud/vacunas/fiebreamarilla>. Visitado Setiembre 2017
50. Periódico La Nación, Costa Rica <https://www.nacion.com/ciencia/salud/oms-pide-aplicar-vacuna-contra-dengue-solo-a-gente/DPWY5ZFAKJGFJNQJKGSZBGQRMU/story/>. Visitado julio 2018
51. World Health Organization. Revised SAGE recommendation on use of dengue vaccine. http://www.who.int/immunization/diseases/dengue/revised_SAGE_recommendations_dengue_vaccines_apr2018/en/. Visitado Julio 2018

52. Conselho Federal de Farmacia Brasil.
<http://campanhacff.wixsite.com/farmaceuticoemacao>. Visitado junio 2017
53. Sociedad Brasileira de Dengue y Arbovirosis. www.sbd-a.org. Visitado setiembre 2017
54. Ministerio de Salud de Chile. <http://www.minsal.cl/virus-zika/> Visitado junio 2017
55. Ministerio de Salud Colombiano.
<https://www.minsalud.gov.co/salud/publica/PET/Paginas/Enfermedades-transmisibles.aspx>. Visitado junio 2017
56. Colegio de Farmacéuticos de Costa Rica. <http://www.cofar.com>. Visitado junio 2017
57. Ministerio de Salud de Costa Rica.
<https://www.ministeriodesalud.go.cr/index.php/centro-de-informacion/material-educativo/mi-comunidad-sin-dengue>. Visitado julio 2017
58. Ministerio de Salud de El Salvador. www.salud.gob.sv. Visitado junio 2017
59. Guías Scouts de Guatemala. <http://www.scouts.org.gt>. Visitado junio 2017
60. Oficina del Gobierno Mexicano. <https://www.gob.mx>. Visitado junio 2017
61. Ministerio de Salud de Perú. <http://www.minsa.gob.pe>. Visitado junio 2017
62. Salud y Prevención. Seguro Social de Perú. <http://www.essalud.gob.pe/salud-y-prevencion/>. Visitado octubre 2017
63. Dirección General de Promoción de la Salud de Paraguay.
<http://www.mspbs.gov.py>. Visitado julio 2017
64. Organización Panamericana de la Salud oficina Uruguay. <http://www.paho.org/uru>. Visitado julio 2017
65. Recursos informativos de la Organización Panamericana de la Salud.
http://www.paho.org/hq/index.php?option=com_topics&view=article&id=1&Itemid=40734&lang=es. Visitado julio 2017
66. Foro Farmacéutico de las Américas.
<http://forofarmaceticodelasamericas.org/colegas-informense-como-recibir-evaluar-y-cuidar/>. Visitado julio 2017
67. Campus Virtual de Salud Pública, OPS. Cursos de autotrendizaje.
<https://www.campusvirtualesp.org/?q=es/cursos/auto-aprendizaje>. Visitado junio 2018

