Algorithms for the Clinical Management of Dengue Patients

Regional Arboviral Disease Program
Algorithms for the Clinical Management of Dengue Patients

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Introduction

Dengue is an infectious disease caused by a flavivirus called dengue virus (DENV), which has four known distinct serotypes (DENV-1, DENV-2, DENV-3, and DENV-4). This disease represents a threat to global public health, with an estimated 390 million infections occurring annually. In the Americas, dengue is the most common arboviral disease. Since its reintroduction in the early 1980s, the number of cases has increased exponentially, with epidemics occurring every three to five years. The most recent epidemic, with more than 3.1 million cases, was reported in 2019 and has continued into 2020, with 1.7 million cases (3,677 of them severe) and 613 deaths as of mid-June. The four DENV serotypes are circulating in the Americas and in many countries they are occurring simultaneously, thus increasing the risk of epidemics and serious forms of the disease.

Added to the complex situation that dengue represents in the Americas is the simultaneous circulation of two other arboviral diseases: chikungunya and Zika. These arboviral diseases can cause infections with clinical manifestations very similar to those caused by DENV, which makes a correct clinical diagnosis difficult and results in the improper clinical management of cases. To address this situation, the Pan American Health Organization/World Health Organization (PAHO/WHO) has developed and published materials on the diagnosis and clinical management of dengue and other arboviral diseases. The most recent are Dengue: guidelines for patient care in the Region of the Americas, 2nd edition, and the Tool for the diagnosis and care of patients with suspected arboviral diseases. It should also be noted that work is currently underway on the first edition of Guidelines for the care of patients with arboviral diseases in the Region of the Americas, which should be published by the end of 2020.

This document gives the user summary information on the clinical management of suspected dengue cases, which is fully illustrated in tables and algorithms. The objective is to provide a quick reference guide on the definition of a suspected case of dengue, its severity, clinical management according to intervention groups, and criteria for the hospitalization and discharge of dengue patients. This document is intended to give the health workers responsible for treating dengue cases an additional tool for proper patient management, in order to prevent deaths caused by this disease.
Methodology

The information contained in this document is based on the publications *Dengue: guidelines for patient care in the Region of the Americas* (second edition) and the *Tool for the diagnosis and care of patients with suspected arboviral diseases*, both produced by PAHO. It includes up-to-date information on the criteria for hospitalizing dengue patients and the use of metamizole to control fever in these cases. This information was updated based on the results of a systematic review and meta-analysis conducted by PAHO in 2019, as part of the GRADE methodology for developing the first edition of the *Guidelines for the care of patients with arboviral diseases in the Region of the Americas*. The work was carried out in three virtual meetings held in June 2020.

Working group: The preparation and review of this document was the responsibility of the technical staff of the PAHO/WHO Regional Arboviral Disease Program and clinicians in the Americas who are members of PAHO’s international technical group of experts on arboviral disease (international GT-arbovirus).
Acknowledgements

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The review and final editing of this document was the responsibility of Dr. Gamaliel Gutiérrez at PAHO/WHO.
### Abbreviations and Acronyms

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>DENV</td>
<td>Dengue virus</td>
</tr>
<tr>
<td>DNWS</td>
<td>Dengue without warning signs</td>
</tr>
<tr>
<td>DWWS</td>
<td>Dengue with warning signs</td>
</tr>
<tr>
<td>g</td>
<td>Gram / grams</td>
</tr>
<tr>
<td>GT-arbovirus</td>
<td>Technical group of experts on arboviral disease</td>
</tr>
<tr>
<td>h</td>
<td>Hour / hours</td>
</tr>
<tr>
<td>ICU</td>
<td>Intensive care unit</td>
</tr>
<tr>
<td>IV</td>
<td>Intravenous</td>
</tr>
<tr>
<td>kg</td>
<td>Kilogram / kilograms</td>
</tr>
<tr>
<td>mg</td>
<td>Milligram / milligrams</td>
</tr>
<tr>
<td>min</td>
<td>Minute / minutes</td>
</tr>
<tr>
<td>ml</td>
<td>Milliliter / milliliters</td>
</tr>
<tr>
<td>NSS</td>
<td>Normal saline solution</td>
</tr>
<tr>
<td>PAHO</td>
<td>Pan American Health Organization</td>
</tr>
<tr>
<td>PO</td>
<td>Orally</td>
</tr>
<tr>
<td>SD</td>
<td>Severe dengue</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organization</td>
</tr>
</tbody>
</table>
Definition of a Suspected Dengue Case

A person who lives in or has traveled to areas with dengue transmission in the last 14 days and presents acute fever, usually from 2 to 7 days duration, and two or more of the following manifestations: nausea/vomiting, rash, headache/retro-orbital pain, myalgia and arthralgia, petechiae or positive tourniquet test (+), leukopenia, with or without any warning sign or sign of severity.

Any child who resides or has traveled in the last 14 days to an area with dengue transmission that presents acute fever, usually from 2 to 7 days duration, with no apparent focus of infection, is also considered a suspected case.
## Classification of Dengue Severity

<table>
<thead>
<tr>
<th>Dengue without warning signs (DNWS)</th>
<th>Dengue with warning signs (DWWS)</th>
<th>Severe dengue (SD)</th>
</tr>
</thead>
</table>
| Person who lives or has traveled to areas with dengue transmission in the last 14 days and presents fever, usually of 2 to 7 days duration, and at least 2 of the following criteria:  
1. Nausea / vomiting  
2. Exanthema  
3. Headache / retro-orbital pain  
4. Myalgia / arthralgia  
5. Petechiae or tourniquet test (+)  
6. Leukopenia | Every dengue case that, near and preferably at defervescence, presents one or more of the following signs:  
1. Intense abdominal pain or tenderness  
2. Persistent vomiting  
3. Fluid accumulation  
4. Mucosal bleed  
5. Lethargy/restlessness  
6. Postural hypotension (lipothyemia)  
7. Liver enlargement >2 cm  
8. Progressive increase in hematocrit | Every dengue case that has one or more of the following manifestations:  
1. Shock or respiratory distress due to severe plasma leakage.  
2. Severe bleeding: based on evaluation by the attending physician  
3. Severe organ involvement (liver impairment, myocarditis, etc.) |

### First level Ambulatory management
- Admit to hospital or dengue units

### Hospitalize in ICU
- Requires strict monitoring and immediate medical intervention
Algorithm for the Treatment of Suspected Cases of Dengue

Define case

Does the patient meet the definition of a suspected case of dengue?

Yes

Answer the following questions:

- In what phase of dengue is the patient? (febrile/critical/recovery)
- Does the patient have warning signs?
- What is their hemodynamic and hydration state? Is the patient in shock?
- Does the patient have an associated disease or condition or social risk?
- Does the patient require hospitalization?

Classify based on dengue severity

Dengue without warning signs

- Group A: At-home treatment. Management at first level of care

Dengue with warning signs

- Group B1: Possible referral to dengue unit for observation and treatment of associated infection or disorders
- Group B2: Referral to hospital or dengue units for administration of intravenous fluids

Severe dengue

- Group C: Emergency treatment during transfer and emergency referral to a more complex hospital

Perform differential diagnosis *

Suspected:
- COVID-19
- Zika
- Influenza
- Measles
- Rubella
- Chikungunya
- Rickettsiosis
- Malaria
- Leptospirosis
- Typhoid fever
- Viral hepatitis
- Yellow fever
- Leukemia
- Hantavirus

*The local epidemiological context should be taken into account.
## Intervention Groups

<table>
<thead>
<tr>
<th>Severity classification</th>
<th>Group A</th>
<th>Group B1</th>
<th>Group B2</th>
<th>Group C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dengue without warning signs (DNWS)</td>
<td>Dengue without warning signs (DNWS)</td>
<td>Dengue with warning signs (DWWS)</td>
<td>Severe dengue (SD)</td>
<td></td>
</tr>
</tbody>
</table>
| Group criteria | Tolerate sufficient volumes of oral fluids | Presence of associated diseases or conditions:  
  - Pregnancy  
  - ≤ 1 years old  
  - ≥ 65 years old  
  - Morbid obesity  
  - Hypertension  
  - Diabetes mellitus  
  - Asthma  
  - Renal damage  
  - Hemolytic diseases  
  - Chronic hepatomegaly  
  - Peptic ulcer disease or gastritis of any etiology  
  - Being treated with anticoagulants  
  - Other or,  
  Presence of social risk:  
  - The patient lives alone or far from where they can receive medical care  
  - Does not have transportation  
  - Lives in extreme poverty | Every dengue case that, near and preferably at defervescence, presents one or more of the following signs:  
  1. Intense abdominal pain or tenderness  
  2. Persistent vomiting  
  3. Fluid accumulation  
  4. Mucosal bleed  
  5. Lethargy/restlessness  
  6. Postural hypotension (lipohypotymia)  
  7. Liver enlargement >2 cm  
  8. Progressive increase in hematocrit | Every dengue case that has one or more of the following manifestations:  
  - Shock or respiratory distress due to severe plasma leakage.  
  - Severe bleeding: based on evaluation by the attending physician  
  - Severe organ involvement (liver impairment, myocarditis, etc.) |
| Management level of care | First level. At-home treatment | Possible referral to hospital or dengue units. Requires observation and treatment of their associated infection or condition. | Hospital or dengue units. Requires IV fluid administration. | Intensive Care Unit. Requires emergency treatment |
Criteria for the Hospitalization of Dengue Patients

The following hospitalization criteria are based on a systematic review and meta-analysis conducted in 2019. A total of 217 studies were identified that included 237,191 patients with a dengue diagnosis in whom the relationship between different potential prognostic factors and progression to severe disease was evaluated.

<table>
<thead>
<tr>
<th>Criteria for the hospitalization of dengue patients</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patients with dengue and any of the following symptoms should be hospitalized:</strong></td>
</tr>
<tr>
<td>• Dengue with warning signs</td>
</tr>
<tr>
<td>• Severe dengue</td>
</tr>
<tr>
<td>• Intolerance to oral administration of fluids</td>
</tr>
<tr>
<td>• Respiratory distress</td>
</tr>
<tr>
<td>• Narrowed pulse pressure</td>
</tr>
<tr>
<td>• Prolonged capillary perfusion (more than 2 seconds)</td>
</tr>
<tr>
<td>• Hypotension</td>
</tr>
<tr>
<td>• Acute renal failure</td>
</tr>
<tr>
<td>• Pregnancy</td>
</tr>
<tr>
<td>• Coagulopathy</td>
</tr>
</tbody>
</table>

**Additional considerations:** Other factors that may determine the need to hospitalize dengue patients include the presence of comorbidities, very young and very old age, social and/or environmental conditions. The decision to admit patients with these conditions should be individualized.

Criteria for the Discharge of Dengue Patients

<table>
<thead>
<tr>
<th>Criteria for discharge of dengue patients</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical criteria</strong></td>
</tr>
<tr>
<td>• Absence of fever for 48 hours without administration of antipyretics</td>
</tr>
<tr>
<td>• Improvement of clinical status (general well-being, good appetite, normal hemodynamic status, normal or increased diuresis, no respiratory distress or evidence of bleeding)</td>
</tr>
<tr>
<td><strong>Laboratory criteria</strong></td>
</tr>
<tr>
<td>• Increasing trend for platelet count</td>
</tr>
<tr>
<td>• Stable hematocrit, without intravenous fluids</td>
</tr>
</tbody>
</table>
Algorithm for the Management of Dengue Patients Without Warning Signs (DNWS) – Groups A and B1

Patients without dengue warning signs (DNWS)

Comorbidity, condition or social risk?

No

At-home treatment

- Complete bed rest.
- Normal diet + abundant oral fluids (oral rehydration salts).
- Educate about warning signs
- Tepid sponging of forehead.

Drugs:
- Children: paracetamol 10mg/kg PO every 6 h.
- Adults: paracetamol 500 mg PO every 6 h. Maximum daily dose 4 g.
  or
- Children: metamizole 10/kg PO every 6 h.
- Adults: `metamizole` V.O 500 mg every 6 h.

Monitor every 24 to 48 h and up to 48 h after fever drops without the use of antipyretics

Appearance of warning signs

No warning signs

Classify as DWWS and manage as Group B2

Yes

Hospitalization criteria met?

No

At-home treatment

- Complete bed rest.
- Normal diet + abundant oral fluids (oral rehydration salts).
- Educate about warning signs
- Tepid sponging of forehead.

Drugs:
- Children: paracetamol 10mg/kg PO every 6 h.
- Adults: paracetamol 500 mg PO every 6 h. Maximum daily dose 4 g.
  or
- Children: metamizole 10/kg PO every 6 h.
- Adults: `metamizole` V.O 500 mg every 6 h.

Monitor every 24 to 48 h and up to 48 h after fever drops without the use of antipyretics

Appearance of warning signs

No warning signs

Classify as DWWS and manage as Group B2

Discharge patient if criteria are met

Yes

Referral to dengue unit or hospital

- Monitor for warning signs.
- Mother/child binomial assessment in pregnant women.
- Stabilize and manage comorbidities.
- Febrile curve.
- Encourage the intake of oral fluids.
- If the patient cannot drink, drinks little, or is dehydrated, initiate IV fluids (I, with lactated Ringer’s solution or 0.9% NSS (based on the Holliday-Segar formula in pediatric patients and 2-4ml/kg/h. in adult patients).
- Fluid balance.
- Oral administration should be resumed as soon as possible.
Algorithm for Intravenous Fluid Management in Dengue Patients with Warning Signs (DWWS) – Group B2

Patient has dengue with warning signs (DWWS)

Comorbidity or adult older?

No

10ml / kg crystalloid solution (Hartmann’s or 0.9% NSS) in 1 h.

Reevaluate: There is clinical improvement

Reduce drip to 5 to 7 mL/kg/h and continue for 2-4 h + hourly patient monitoring.

Reevaluate: There is clinical improvement

Reduce drip to 3-5 mL/kg/h and continue for 2-4 h + hourly patient monitoring.

Reevaluate: There is clinical improvement

Reduce drip to 2 to 4 mL/kg/h and continue for 24-48 h + hourly patient monitoring.

Yes

See algorithm for DWWS plus comorbidity or older adult

Reevaluate: No clinical improvement

Repeat 2nd loading dose of 10ml/kg in 1 h.

Reevaluate: No clinical improvement

Repeat 3rd loading dose of 10ml/kg in 1 h.

Reevaluate: No clinical improvement

Classify as severe dengue and manage as Group C.

Clinical improvement is determined by:

- Progressive disappearance of warning signs
- Progressive remission of general symptomatology
- Stable vital signs
- Normal or increased diuresis
- Hematocrit falls to less than the baseline value in a stable patient
- Good tolerance to oral administration
- Recovery of appetite
Algorithm for Intravenous Fluid Management in Patients with DWWS plus Comorbidity or Older Adult – Group B2

Patient has dengue with warning signs (DWWS) plus comorbidity or older adult

Crystalloid solution (Hartmann’s or 0.9% NSS) 5 mL/kg in 1 h.

Reevaluate: There is clinical improvement

- Reduce drip to 4 mL/kg/h and continue for 2-4 h + hourly patient monitoring.

Reevaluate: No clinical improvement

- Repeat 2nd loading dose of 5 mL/kg in 1 h.

- Repeat 3rd loading dose of 5 mL/kg in 1 h.

- Classify as severe dengue and manage as Group C.

Reevaluate: No clinical improvement

- Reduce drip to 3 mL/kg/h and continue for 2-4 h + hourly patient monitoring.

- Reevaluate: No clinical improvement

- Reduce drip to 2 mL/kg/h and continue for 2-4 h + hourly patient monitoring.

Clinical improvement is determined by:

- Progressive disappearance of warning signs
- Progressive remission of general symptomatology
- Stable vital signs
- Normal or increased diuresis
- Hematocrit falls to less than the baseline value in a stable patient
- Good tolerance to oral administration
- Recovery of appetite
Algorithm for Intravenous Fluid Management in Patients with Hypovolemic Shock (Severe Dengue Shock Syndrome) – Group C

ABC and monitoring of vital signs every 5 to 30 min + oxygen therapy

Patients with hypovolemic shock (severe dengue shock syndrome)

No

Comorbidity, pregnant woman, older adult?

Yes

The management of older adult patients with comorbidities and/or pregnant women should be individualized and closely monitored

Crystalloid solution (Hartmann’s or 0.9% NSS) 20ml / kg in 15-30 min

Reevaluate: There is clinical improvement

Signs of shock persist

Administer 2nd bolus of crystalloid solution 20ml/kg in 15-30min

Reevaluate: There is clinical improvement

Administer 3rd bolus of crystalloid solution 20ml/kg in 15-30min

Signs of shock persist

In case of persistent shock:

▪ Determine pump function and the use of amines;
▪ Evaluate concomitant medical conditions and stabilize the baseline condition;
▪ Evaluate persistent acidosis and risk of (hidden) hemorrhage and treat accordingly;
▪ If needed, administer additional boluses of hydrating solution (crystalloid or colloid) over the next 24 hours; the speed and volume of each bolus will depend on clinical response;
▪ Manage patient, preferably in an intensive care unit

Clinical improvement is determined by:

▪ Remission of signs of shock
▪ Stable vital signs
▪ Normal or increased diuresis
▪ Hematocrit falls to less than the baseline value in a stable patient

Reduce drip to 10 mL/kg/h and continue for 1-2 h + hourly monitoring

Reduce drip to 5-7 mL/kg/h and continue for 4-6 h + hourly monitoring

Reduce drip to 3-5 mL/kg/h and continue for 2-4 h + hourly monitoring

Reduce drip to 1-4 mL/kg/h and continue for 24-48 h + hourly monitoring

Reduce drip to 10 mL/kg/h and continue for 1-2 h + hourly monitoring

Reduce drip to 5-7 mL/kg/h and continue for 4-6 h + hourly monitoring

Reduce drip to 3-5 mL/kg/h and continue for 2-4 h + hourly monitoring

Reduce drip to 1-4 mL/kg/h and continue for 24-48 h + hourly monitoring
References


2. Pan American Health Organization. Tool for the diagnosis and care of patients with suspected arboviral diseases. Available at: https://iris.paho.org/handle/10665.2/33895

