Dengue Treatment Guidelines

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Ministry of Health and Wellness
MAURITIUS

Approval Form

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DENGUE TREATMENT GUIDELINES			
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This document is mostly contextualized material taken directly from UpToDate, the World Health Organization and US Centers for Disease Control – see the references for details.

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Treatment Guidelines for Dengue

Introduction[1]

There are four dengue virus (DENV) types (DENV-1, DENV-2, DENV-3, and DENV-4), all of which are capable of inducing severe disease (dengue hemorrhagic fever [DHF] / dengue shock syndrome [DSS]).

Treatment of dengue patients poses a unique challenge as there is no specific antiviral therapy; thus, supportive care becomes paramount. The disease manifests in a spectrum, from asymptomatic or mild illness to severe forms which are life-threatening. Effective treatment strategies focus on managing symptoms, preventing complications, and early recognition of progression to severe dengue.

The likelihood for development of severe dengue is highest among individuals who are infected a second time by a different DENV type from the first infection (known as secondary or heterotypic infection).

Clinical classification of dengue[2, 5]

In 2009, the WHO introduced a revised classification scheme consisting of the following categories:

1. Dengue without warning signs — A presumptive diagnosis of dengue infection may be made in the setting of residence in or travel to an endemic area plus fever and two of the following:
    a. Nausea/vomiting
    b. Rash
    c. Headache, eye pain, muscle ache, or joint pain
    d. Leukopenia
    e. Positive tourniquet test
2. Dengue with warning signs — Dengue with warning signs of severe infection includes dengue infection as defined above in addition to any of the following:
    a. Abdominal pain or tenderness (especially at the end of the febrile phase)
    b. Persistent vomiting
        i. More than three times over the last 6-24h
        ii. Three or more episodes in one hour
    c. Clinical fluid accumulation (ascites, pleural effusion)
    d. Mucosal bleeding
        i. Gingivorrhagia, epistaxis, vaginal bleeding not associated with menstruation or more menstrual bleeding than usual, and hematuria
    e. Lethargy or restlessness
    f. Hepatomegaly >2 cm (below the coastal margin)
    g. Increase in hematocrit concurrent with rapid decrease in platelet count
        i. Hematocrit > 46 in males ≤ 60y old

ii. Hematocrit > 42 in males > 60y old

iii. Hematocrit > 40 in females

iv. Any increment of ≥ 20% from baseline hematocrit is considered hemoconcentration

v. Platelets < 100,000 if normal baseline

3. Severe dengue — Severe DENV infection includes infection with at least one of the following:

    a. Severe plasma leakage leading to:

        i. Shock

            1. Pulse pressure ≤ 20 mmHg

            2. Systolic blood pressure < 90mmHg

            3. Mean arterial pressure < 60mmHg

            4. Heart rate > systolic blood pressure

        ii. Fluid accumulation with respiratory distress

    b. Severe bleeding (as evaluated by a clinician)

    c. Severe organ involvement:

        i. Aspartate aminotransferase (AST) or alanine aminotransferase (ALT) ≥1000 units/L

        ii. Impaired consciousness

        iii. Organ failure

            1. Encephalopathy / seizures

            2. No urine output > 4 h

            3. Myocardial injury

            4. Liver failure

            5. Respiratory failure

Phases of dengue infection[2]

There are three phases that can be seen in the setting of DENV infection: a febrile phase, a critical phase, and a recovery phase; however, the critical phase is not seen in all categories of infection:

1. The febrile phase of DENV infection is characterized by sudden high-grade fever (≥38.5°C) accompanied by headache, vomiting, myalgia, arthralgia, and a transient macular rash in some cases.

    a. The febrile phase lasts for three to seven days, after which most patients recover without complications.

b. Retroorbital pain, gastrointestinal symptoms (including anorexia, nausea, vomiting, abdominal pain, and diarrhea) and respiratory tract symptoms (cough, sore throat, and nasal congestion) are additional manifestations.

c. Physical examination may demonstrate conjunctival injection, pharyngeal erythema, lymphadenopathy, and hepatomegaly. Facial puffiness, petechiae (on the skin and/or palate), and bruising (particularly at venipuncture sites) may be observed.

d. A tourniquet test can be performed by inflating a blood pressure cuff on the arm to midway between systolic and diastolic blood pressures for five minutes. The skin below the cuff is examined for petechiae one to two minutes after deflating the cuff; presence of 10 or more new petechiae in one square inch area is considered a positive test.

e. Leukopenia and thrombocytopenia (≤100,000 cells/mm^3) are common. Serum aspartate transaminase (AST) levels are frequently elevated; the elevations are usually modest (2 to 5 times the upper limit of normal values), but marked elevations (5 to 15 times the upper limit of normal) occasionally occur.

f. Between days 3 and 7 of the illness, the clinician must watch for signs of vascular leakage. Significant vascular leakage reduces intravascular volume and decreases organ perfusion. Corresponding clinical manifestations may include persistent vomiting, increasingly severe abdominal pain, tender hepatomegaly, development of pleural effusions and/or ascites, mucosal bleeding, and lethargy or restlessness; laboratory findings may include a high or increasing hematocrit level (≥20 percent from baseline) concurrent with a rapid decrease in the platelet count.

2. The vast majority of infections that progress to a critical phase result from second DENV infections that occur more than 18 months after a resolved first infection. However, a subset of critical infections occurs in children less than one year of age, at the time maternal antibody is below protective levels and the child experiences a primary wild type infection. In addition, severe DENV infection may occur after primary infection in individuals with significant medical comorbidities.

    a. The critical phase lasts for 24 to 48 hours.

    b. Initially, adequate circulation may be maintained by physiological compensation, resulting in pulse pressure narrowing (systolic pressure minus diastolic pressure ≤20 mmHg).

    c. Once hypotension develops, systolic pressure falls rapidly and irreversible shock may follow despite aggressive attempts at resuscitation.

    d. Hemorrhagic manifestations may be observed in the febrile phase and/or critical phase. Major skin and/or mucosal bleeding (gastrointestinal or vaginal) may occur in adults with no obvious precipitating factors and only minor plasma leakage.

    e. Other less frequent manifestations included hematemesis, heavy menstrual bleeding, melena, epistaxis or hematuria.

    f. Imaging modalities for detection of plasma leakage include ultrasonography (of the chest and abdomen) and chest radiography to help identify ascites and pleural effusion.

3. During the recovery phase, plasma leakage and hemorrhage resolve, vital signs stabilize, and accumulated fluids are resorbed.

a. An additional rash (a confluent, erythematous eruption with small islands of unaffected skin that is often pruritic) may appear during the recovery phase (within one to two days of defervescence and lasting one to five days).

b. The recovery phase typically lasts two to four days; adults may have profound fatigue for days to weeks after recovery.

Clinical diagnosis of dengue[2]

The diagnosis of DENV infection should be suspected in febrile individuals with typical clinical manifestations and relevant epidemiologic exposure.

During the first week of illness, the diagnosis of DENV infection may be established via detection of viral nucleic acid in serum by means of reverse-transcriptase polymerase chain reaction assay (typically positive during the first five days of illness) or via detection of viral antigen nonstructural protein 1 (NS1; typically positive during the first seven days of illness).

Detection of IgM in a single specimen obtained from a patient with a clinical syndrome consistent with dengue is widely used to establish a presumptive diagnosis.

Triage of dengue patients[3, 4, 5]

1. History taking should assess:
    a. Date of onset of fever/illness
    b. Quantity of oral fluid intake
    c. Presence of diarrhoea / vomiting
    d. Urine output (frequency, volume and time of last voiding)
    e. Assessment of warning signs
    f. Change in mental state/seizure/dizziness
    g. Other important relevant history, such as family or neighbourhood dengue, travel to dengue-endemic areas and co-existing conditions (e.g. infancy, pregnancy, obesity, diabetes mellitus, hypertension)
    h. Past history of dengue infection
2. Findings during physical examination can include:
    a. Conjunctival injection
    b. Pharyngeal erythema
    c. Lymphadenopathy
    d. Hepatomegaly
    e. Facial puffiness
    f. Petechiae
    g. Ecchymosis

Therefore, physical examination should evaluate the mental state, hydration status, hemodynamic status, tachypnea / acidotic breathing / pleural effusion, abdominal tenderness / hepatomegaly / ascites, rash and bleeding manifestations. The tourniquet test can also be performed.

3. Laboratory findings, especially during the febrile phase, are:
    a. Leukopenia
    b. Thrombocytopenia
    c. Elevated AST
    d. Elevated aPTT or decreased fibrinogen levels
    e. Increased hematocrit by ≥ 20% from baseline
4. Imaging studies during the critical phase may demonstrate:
    a. CXR shows pleural effusions
    b. Abdominal ultrasound shows ascites and gallbladder thickening

Risk factors for severe disease[4, 5]

- Infants and children (age < 10 years) especially with malnutrition
- Elderly (age > 65 years)
- Obesity (Body Mass Index > 30)
- Pregnant women or females who have abnormal vaginal bleeding
- Hemolytic diseases such as glucose-6-phosphatase dehydrogenase deficiency, thalassemia and other hemoglobinopathies
- Peptic ulcer disease
- Congenital heart disease
- Poorly controlled chronic diseases such as diabetes mellitus, hypertension, obstructive lung diseases, cardiovascular diseases, chronic renal failure, and chronic liver disease
- Patients on long-term steroids, anticoagulants, immunosuppressants or NSAID treatment

Admission criteria[6]

The following patients should be admitted:

— Dengue with warning signs

— Dengue with criteria of severe disease

— Oral intolerance

— Difficulty breathing

— Narrowing pulse pressure

— Arterial hypotension

— Acute renal failure

— Prolonged capillary refill time

— Pregnancy

— Coagulopathy

Clinical management of dengue[1]

Mild dengue (i.e., dengue without warning signs) can be treated at home. Moderate dengue (i.e., dengue with warning signs) or patients who have risk factors for severe dengue should be admitted to a ward for close monitoring and medical treatment. Severe dengue requires admission to the ICU setting.

1. Outpatient management is appropriate for patients with presumptive diagnosis of dengue infection in the absence of warning signs or coexisting conditions (pregnancy, infancy, old age, diabetes, renal failure, underlying hemolytic disease, obesity, or poor social situation).

    a. Such patients should be able to tolerate oral fluids, urinate at least once every six hours, and have near normal blood counts.

    b. Patients should be instructed regarding the warning signs of severe dengue infection and the critical phase that follows defervescence (which lasts for 24 to 48 hours); during this period, patients may deteriorate rapidly.

    c. During the febrile phase (lasting two to seven days) and the subsequent critical phase (lasting one to two days), the patient should be evaluated daily till the end of the critical phase for signs of dehydration and other warning signs of severe dengue.

    d. Serial blood counts should be followed to evaluate for interval increases in hematocrit concurrent with rapid decrease in platelet count, indicating presence of plasma leakage and increased risk of bleeding complications.

    e. Fever may be controlled with acetaminophen; nonsteroidal anti-inflammatory drugs and aspirin-based products should be avoided out of concern for their effect on platelet function and the potential increased risk for bleeding.

        i. Fever and myalgias should be managed with acetaminophen (maximum 60 mg/kg/day in children; 4 g/day in adults).

    f. Patients should be instructed to take plenty of fluids and watch for signs of dehydration (decrease in urination, few or no tears, dry mouth or lips, sunken eyes, listlessness or confusion, cold or clammy extremities, sunken fontanel in an infant); these findings warrant prompt clinical evaluation.

    g. As fever declines (three to eight days after onset of symptoms), patients should be instructed to seek prompt attention for any of the following: severe abdominal pain, persistent vomiting, skin rash, bleeding from nose or gums, vomiting blood, dark stools, drowsiness or irritability, pale or cool skin, and difficulty breathing.

2. Inpatient management is warranted for patients with dengue and warning signs of severe infection, severe dengue infection, or dengue infection with coexisting conditions.

a. The period of maximum risk for shock is between the third and seventh day of illness, which typically coincides with resolution of fever.

b. In general, plasma leakage first becomes evident between 24 hours before and 24 hours after defervescence.

c. An elevated hematocrit is an indication that plasma leakage has already occurred and that fluid repletion is required.

d. Most patients who present for medical attention before profound shock develops and who receive appropriate fluid therapy recover quickly.

e. Specific algorithms are annexed for the management of shock.

f. Blood transfusion is appropriate in patients with significant bleeding or low hematocrit and failure to improve with fluid resuscitation. In complex cases, it can be challenging to distinguish whether a decrease in hematocrit reflects volume repletion or blood loss.

    i. Gastrointestinal bleeding, epistaxis, or heavy menstrual bleeding may be severe enough to warrant blood transfusion.

    ii. Platelet transfusion has not been shown to be effective at preventing or controlling hemorrhage but may be warranted in patients with severe thrombocytopenia (<10,000/mm3) and active bleeding. In general, the preponderance of data does not support a role for prophylactic platelet transfusion in patients with severe thrombocytopenia in the absence of active bleeding.

    iii. Administration of intravenous vitamin K is warranted for patients with severe liver dysfunction or prolonged prothrombin time

g. Once hemodynamic stability has been restored, intravenous fluids should be continued with gradual reduction of the infusion rate over the next 24 to 48 hours.

    i. Fluid lost into potential spaces (pleura, peritoneum) during the period of plasma leakage is reabsorbed rapidly. Therefore, intravenous fluid supplementation should be discontinued following the period of increased vascular permeability; excessive fluid administration after this point can precipitate hypervolemia and pulmonary edema.

Discharge criteria[1]

Discharge from the treating specialist's service is appropriate when patients have been afebrile for at least 24 hours or have passed two days after an episode of shock, are clinically well, and have normal appetite, urine output, and hematocrit.

However, seek the advice of the Public Health Department to see whether the patient needs to have a negative dengue PCR in his / her serum prior to discharge.

Complications of dengue[2]

1. Liver failure has been described due to hypotension or hypoxia.

2. Neurologic manifestations associated with DENV infection include encephalopathy and seizures. Other neurologic syndromes that have been reported to be potentially associated with DENV

infection include stroke, acute pure motor weakness, mononeuropathies, polyneuropathies, Guillain-Barré syndrome, and transverse myelitis.

3. Cardiovascular manifestations (including myocardial impairment, arrhythmias, and, occasionally, fulminant myocarditis) have been described in patients with DENV infection.
4. Mechanisms of acute kidney injury may include shock, rhabdomyolysis, glomerulonephritis, and acute tubular necrosis.
5. Retinal vasculitis and hemophagocytic lymphohistiocytosis have been described in association with DENV infection.
6. Bacterial coinfection with or following DENV infection occurs but is rare.

Differential diagnosis

The differential diagnosis of dengue fever in Mauritius includes malaria, acute HIV, influenza, measles, leptospirosis, chikungunya, COVID-19 and hepatitis.

Specific international evidence-based guidelines for the management of dengue[6]

The updated Pan American Health Organization makes the following recommendations:

1. *In patients diagnosed with dengue infection, should an intense oral hydration scheme be used?*
    a. It is recommended to use an intense oral hydration scheme in dengue patients to decrease the progression to severe forms and the appearance of disease complications.

    Quality of evidence: LOW

    Strength of recommendation: STRONG

2. *In dengue patients with warning signs, should parenteral hydration be indicated?*
    a. It is recommended to start parenteral hydration in dengue patients with at least one warning sign.

    Quality of evidence: VERY LOW

    Strength of recommendation: STRONG

3. *In patients with dengue infection who receive parenteral hydration, should resuscitation with crystalloids or colloids be initiated?*
    a. It is recommended to use crystalloids instead of colloids in the initial management of patients with dengue shock.

    Quality of evidence: LOW

    Strength of recommendation: STRONG

4. *In dengue patients with thrombocytopenia, should the transfusion of blood components (platelet concentrate or fresh frozen plasma) be indicated?*
    a. It is recommended not to transfuse blood components (platelet concentrate, fresh frozen plasma) to dengue patients with thrombocytopenia.

b. The recommendation applies to all patients with dengue and thrombocytopenia, regardless of platelet count.

c. The recommendation does not apply to patients with bleeding or additional conditions that predispose a person to bleeding (e.g., pregnancy). In these situations, the indication for the transfusion of blood components should be considered.

d. Thrombocytopenia in infections can be due to consumption (instead of platelets loss); hence, transfusion is of limited help.

Quality of evidence: VERY LOW

Strength of recommendation: STRONG

5. *In patients with dengue infection, what pharmacological interventions may be indicated to manage symptoms?*

a. Paracetamol (acetaminophen) is suggested instead of nonsteroidal anti-inflammatory drugs, antihistamines, or steroids for initial symptomatic management in patients with dengue infection.

b. Nonsteroidal anti-inflammatory drugs may increase the risk of hemorrhage in dengue patients.

c. However, some studies suggest that ibuprofen may be safe in mild disease.[7]

Quality of evidence: VERY LOW

Strength of recommendation: CONDITIONAL

6. *In patients with severe dengue infection, should treatment with systemic steroids be indicated?*

a. It is suggested not to administer systemic steroids to patients with dengue shock.

Quality of evidence: VERY LOW

Strength of recommendation: CONDITIONAL

Special populations

1. Pregnancy:[8, 9]

a. The potential for vertical transmission should be considered for mothers with dengue who are symptomatic late in pregnancy or at delivery.

b. Dengue can have harmful effects, including death of the fetus, low birth weight, and premature birth.

c. Newborns usually develop symptoms within 14 days of birth (commonly within the first week), but most babies are asymptomatic.

d. Decision to deliver should be made by experienced obstetricians. Consideration should be given to maternal status, severity of the disease, fetal status and gestation age.

e. Dengue during pregnancy can triple the risk of maternal death.

2. AIDS patients:[10]
    a. Patients who are severely immunosuppressed may have up to 5 times higher risk of developing severe disease.
    b. Presentation and management of dengue tends to be the same in these patients.
    c. Monitor such patients closely.
3. Children:[11]
    a. Doses of medications and intravenous fluids have to be adjusted according to age and weight.
    b. Normal values for laboratory parameters can vary by age.
    c. Any increase of ≥20% from baseline hematocrit is considered hemoconcentration.
    d. Symptomatic and supportive treatment under close observation is the mainstay of treatment in neonates with dengue infection.
    e. In general, dengue in infants is due to primary infection but the manifestations could be severe as infants might have received dengue antibodies transplacentally from their mother.
    f. Infants tend to present with symptoms of upper respiratory tract infection or with gastrointestinal symptoms.
4. Thalassemia and sickle-cell disease:[11]
    a. Hemolysis can be triggered during acute dengue illness. This manifests in both early and late febrile stages of thalassemia.
    b. Hemoconcentration during plasma leakage may be missed in anemic patients with dengue due to low baseline HCT level.

The annexed pocket guide from the US Centers for Disease Control summarizes the steps to take when managing dengue patients.[12]

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11 November 2024

Dengue Case Management

Presumptive Diagnosis

Live in / travel to (in the last 14 days) endemic area plus fever and two of the following:

- Nausea and vomiting
- Rash
- Aches and pains (headache, eye pain, muscle ache or joint pain)
- Any warning signs
- Positive tourniquet test
- Leukopenia

Warning Signs

- Intense continuous abdominal pain or pain when palpating abdomen
- Persistent vomiting (≥3 episodes in 1 hr or ≥4 in 6 hrs)
- Fluid accumulation (pleural effusion, ascites, or pericardial effusion)
- Mucosal bleeding (gums, nose, vagina [metrorrhagia or hypermenorrhea], kidney [macroscopic hematuria])
- Altered mental status (irritability, drowsiness, Glasgow Coma Scale score <15)
- Hepatomegaly (≥2cm below costal margin)
- Progressive increase of the hematocrit (in at least 2 consecutive measurements taken 6 hours apart)

No warning signs

Group A
Outpatient management

For patients with warning signs of severe dengue OR any of the following:

- Pregnancy
- Acute renal failure
- Coagulopathy
- Shortness of breath
- Not tolerating oral fluids
- Co-existing conditions and social risk on a case-by-case basis*

Group B
Inpatient management

For patients with any of the following:

- Shock or respiratory distress due to plasma leakage
- Clinically significant bleeding
- Severe organ impairment (myocarditis, hepatitis [ALT or AST>1000 IU] encephalitis)

Group C
Inpatient management

*For co-existing conditions and social risk see page 6, item #9.

Dengue Management DO's and DON'Ts

✗ **DON'T use corticosteroids routinely.** They are not routinely indicated and can increase the risk of GI bleeding, hyperglycemia, and immunosuppression.

✗ **DON'T give prophylactic platelet transfusions or for a low platelet count.** Platelet transfusions do not decrease the risk of severe bleeding and may instead lead to fluid overload and prolonged hospitalization.

✗ **DON'T give half normal (0.45%) saline.** It leaks into third spaces and may worsen ascites and pleural or pericardial effusions.

✗ **DON'T assume that IV fluids are necessary.** First check if the patient can take fluids orally. Use only the minimum amount of IV fluid to keep the patient well-perfused. Decrease IV fluid rate as hemodynamic status improves or urine output increases.

✓ **DO tell outpatients when to return.** Teach them about warning signs and their timing, and the critical phase that follows defervescence.

✓ **DO recognize the critical phase.** The critical phase begins with defervescence or an increasing hematocrit and lasts for 24-48 hours. During this phase some patient may deteriorate within hours and require close monitoring.

✓ **DO closely monitor fluid intake and output, vital signs, and hematocrit levels.** Intake and output should be monitored according to hemodynamic status and severity of clinical presentation as outlined in the treatment algorithms.

✓ **DO recognize and treat early shock.** Early shock (also known as compensated or normotensive shock) is characterized by narrowing pulse pressure (systolic minus diastolic BP $\leq$ 20 mmHg), increasing heart rate, and delayed capillary refill or cool extremities.

✓ **DO administer colloids (such as albumin) for refractory shock.** Patients who do not respond to 2–3 boluses of isotonic saline should be given colloids instead of more saline.

✓ **DO give pRBCs or whole blood for clinically significant bleeding.** If hematocrit is dropping with unstable vital signs or significant bleeding is apparent, immediately transfuse blood.

Group A

Outpatient Management

Patients without warning signs, coexisting conditions or social risk (see page 6)

During the febrile phase (2–7 days) and subsequent critical phase (1–2 days) you should evaluate your patients daily

- » Order and review complete blood cell counts
- » Monitor for dehydration, warning signs, and defervescence (indicating the beginning of the critical phase)

Advise patient or their family to do the following

Control the fever

- Give acetaminophen at 6 hour intervals if the patient is febrile (no more than 4 doses per day). Do not give ibuprofen or aspirin-containing drugs.
- Sponge patient's skin with tepid water when temperature is high.

Prevent dehydration which occurs when a person loses too much fluid (from high fever, vomiting, or poor oral intake). Give plenty of fluids (not only water) and watch for signs of dehydration. Bring patient to clinic or emergency room if any of the following signs develop:

- Decrease in urination (check number of wet diapers or trips to the bathroom)
- Few or no tears when child cries
- Dry mouth, tongue or lips
- Sunken eyes
- Listlessness, agitation, or confusion
- Fast heartbeat (>100/min)
- Cold or clammy fingers and toes
- Sunken fontanel in an infant

Prevent spread of dengue within your house

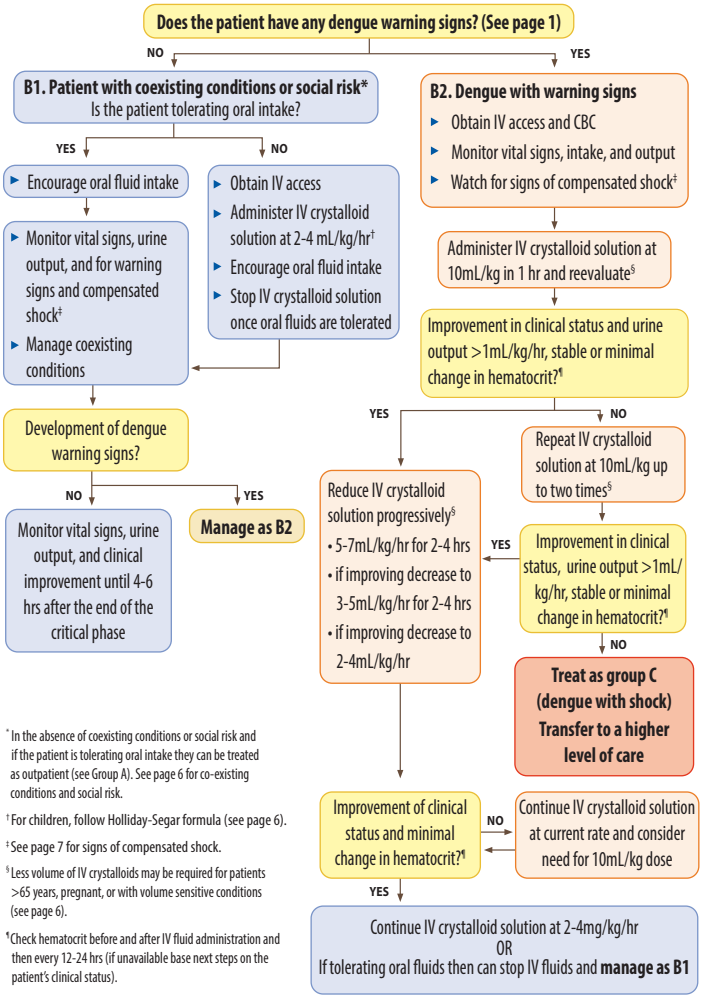
- The patient should sleep under a bed net. Everyone in the house should use registered insect repellent.
- Empty and scrub containers that hold water in and around the home.
- Place screens on windows and doors to prevent mosquitoes from entering the home.

Fever usually lasts 2-7 days and warning signs commonly appear as the fever starts to decline.

Return **immediately** to clinic or emergency department if any of the following warning signs appear:

- Severe abdominal pain or persistent vomiting
- Bleeding from nose or gums
- Abnormal vaginal bleeding
- Vomiting blood
- Black, tarry stools
- Drowsiness or irritability
- Pale, cold, or clammy skin
- Difficulty breathing

Group B
Inpatient Management



* In the absence of coexisting conditions or social risk and if the patient is tolerating oral intake they can be treated as outpatient (see Group A). See page 6 for co-existing conditions and social risk.

† For children, follow Holliday-Segar formula (see page 6).

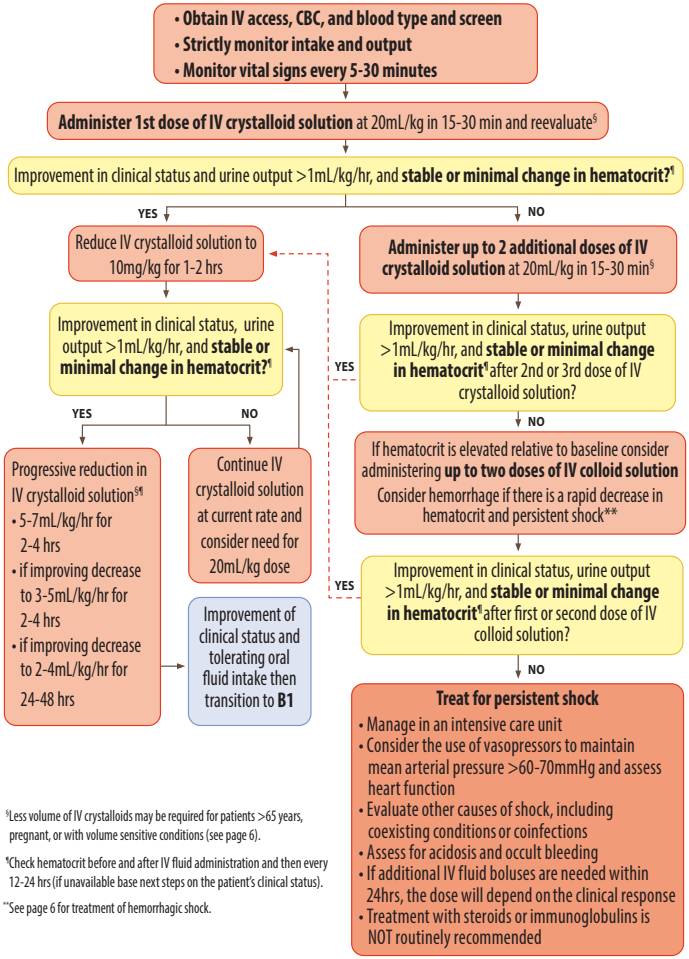
‡ See page 7 for signs of compensated shock.

§ Less volume of IV crystalloids may be required for patients >65 years, pregnant, or with volume sensitive conditions (see page 6).

¶ Check hematocrit before and after IV fluid administration and then every 12-24 hrs (if unavailable base next steps on the patient's clinical status).

Group C

Inpatient Management for Patients with Compensated or Hypotensive Shock



§Less volume of IV crystalloids may be required for patients >65 years, pregnant, or with volume sensitive conditions (see page 6).

¶Check hematocrit before and after IV fluid administration and then every 12-24 hrs (if unavailable base next steps on the patient's clinical status).

**See page 6 for treatment of hemorrhagic shock.

Clinical Criteria for Hospitalization and Discharge, and Recommendations for Fluid Management and Hemorrhagic Shock

Criteria for Hospitalization

- **Presence of any warning sign**
- **Shortness of breath**
- **Pregnancy, acute renal failure or coagulopathy**
- **Compensated or hypotensive shock (see pg7)**
- **Signs and symptoms of plasma leakage:**
  - Pleural or pericardiac effusions
  - Ascites or gallbladder wall edema
- **Severe hemorrhage or spontaneous bleeding**
- **Organ dysfunction**
  - Hepatitis (AST or ALT ≥1000 IU) or painful hepatomegaly
  - Altered mental status
  - Myocarditis
- **Co-infection requiring inpatient management**
- **Co-existing conditions or social risk (on a case-by-case basis):**
  - Conditions: hypertension, diabetes, asthma, chronic kidney disease, chronic liver disease, peptic ulcer disease or other gastritis, body-mass index ≥30kg/m^2, receiving anticoagulation medications
  - Social risk: Age <1 year or >65 years, living alone or has poor access to healthcare facilities, lack of transportation, unstable housing, extreme poverty

Clinical Improvement Criteria

- Progressive waning of warning signs and general symptoms
- Stable vital signs
- Normal urine output (>0.5 – 1.5 mL/kg/hr)
- Adequate oral intake
- Increase in appetite

Discharge Criteria for Groups B1, B2, and C

All clinical and laboratory criteria must be met.

Clinical criteria:

- Absence of fever for 48 hrs without administering antipyretics
- Improved appetite
- Vital signs within normal range
- Urine output 0.5 – 1.5mL/kg/hr
- Normal work of breathing
- No evidence of bleeding

Laboratory criteria:

- Increasing trend in platelet counts
- Stable hematocrit without administration of intravenous fluids

Oral Fluid Management

Basal fluid requirements

- **Adults:**
  - 18—65 years: 30-35 mL/kg
  - >65 years: 25 mL/kg
- **Children:**
  - 1—10 years: 100–150 mL/kg or
  - 11—18 years: 1,000mL + 50mL for every kg over 10kg
- Account for increases in oral fluid requirements due to diarrhea, vomiting, sweating, fever (basal needs increase by 13% for every degree over 38.0°C), and dehydration

Choice of Initial Intravenous Fluid

Crystalloids

- Lactated Ringers — contains 131mmol/L sodium and 115mmol/L chlorine; avoid in patients with severe hyponatremia
- 0.9% Normal Saline — large volumes can exacerbate acidosis; contains elevated sodium and chlorine levels (154mmol/L each); avoid when chlorine levels exceed 105 mmol/L

Colloids

- Use with up to two doses is recommended only in refractory shock after crystalloid solutions have been administered
- Dependent on local availability
- Dextrans can exacerbate hemorrhage

Maintenance fluid rates (Holliday & Segar formula)

Use ideal body weight (IBW) in patients who are overweight

- 4ml/kg/hr for the first 10kg of IBW
- 2ml/kg/hr for the next 10kg of IBW
- 1ml/kg/hr for every additional kg of IBW
- Lower IV fluid rates than those recommended may be used for patients who are >65 years, pregnant, or have volume-sensitive conditions such as heart failure, chronic liver disease, and end-stage renal disease

Treatment of Hemorrhagic Shock

- **5-10mL/kg packed red blood cells**
- **10-20mL/kg of whole blood**
- **Transfusion of platelets or fresh frozen plasma is not recommended**

Normal Vital Signs

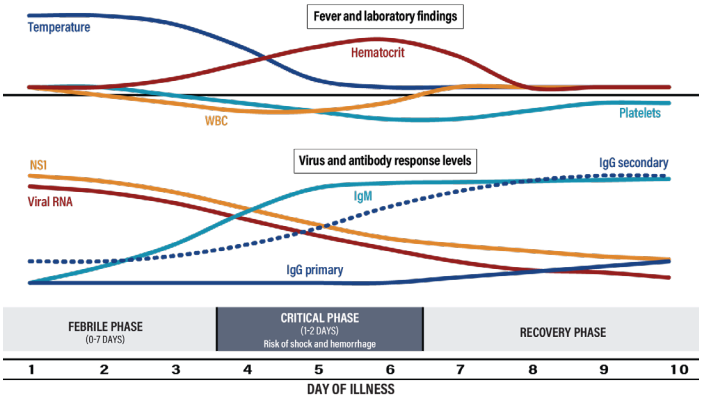
Age	Estimated Weight	Normal Heart Rate Range	Average HR	Normal Respiratory Rate Range	Hypotension Level (Systolic BP)
1 month	4 kg	110-180	145	40-60	<70
6 months	8 kg	110-170	135	25-40	<70
12 months	10 kg	110-170	135	22-30	<72
2 years	12 kg	90-150	120	22-30	<74
3 years	14 kg	75-135	120	22-30	<76
4 years	16 kg	75-135	110	22-24	<78
5 years	18 kg	65-135	110	20-24	<80
6 years	20 kg	60-130	100	20-24	<82
8 years	26 kg	60-130	100	18-24	<86
10 years	32 kg	60-110	85	16-22	<90
12 years	42 kg	60-110	85	16-22	<90
14 years	50 kg	60-110	85	14-22	<90
≥15 years		60-100	80	12-18	<90

Hemodynamic Assessment

Hemodynamic Parameters	Stable Circulation	Compensated Shock	Hypotensive Shock
Conscious level	Clear and lucid	Clear and lucid	Restless, combative
Capillary refill	Brisk (≤2 sec)	Prolonged (>2 sec)	Very prolonged, mottled skin
Extremities	Warm and pink	Cool peripheries	Cold, clammy
Peripheral pulse volume	Good volume	Weak and thready	Feeble or absent
Heart rate	Normal heart rate for age	Tachycardia for age	Severe tachycardia or bradycardia in late shock
Blood pressure	▶ Normal blood pressure for age ▶ Normal pulse pressure for age	▶ Normal systolic pressure, but rising diastolic pressure ▶ Narrowing pulse pressure ▶ Postural hypotension	▶ Narrow pulse pressure (≤ 20 mmHg) ▶ Hypotension ▶ Unrecordable blood pressure
Respiratory rate	Normal respiratory rate for age	Tachypnea	Hyperpnea or Kussmaul's breathing (metabolic acidosis)
Urine output	Normal	Reducing trend	Oliguria or anuria

Clinical signs and symptoms and laboratory findings to differentiate dengue, Zika, and chikungunya

Certainty of the evidence	Signs and Symptoms		
	Dengue	**Chikungunya**	**Zika**
HIGH (findings that differentiate them)	- Thrombocytopenia - Progressive increase in hematocrit - Leukopenia	Arthralgias	Pruritus
MODERATE (findings that probably differentiate them)	- Anorexia or hyporexia - Vomiting - Abdominal pain - Chills - Hemorrhages (includes bleeding on the skin, mucous membranes, or both)	Rash Conjunctivitis Arthritis Myalgias or bone pain	Rash Conjunctivitis
LOW (findings that may differentiate them)	- Retro-ocular pain - Hepatomegaly - Headache - Diarrhea - Dysgeusia - Cough - Elevated transaminases - Positive tourniquet test	Hemorrhages (includes bleeding on the skin, mucous membranes, or both)	Adenopathies Pharyngitis or odynophagia



Paz-Bailey G, Adams LE, Deen J, Anderson KB, Katzelnick LC. Dengue. Lancet. 2024;403(10427):667-682. doi:10.1016/S0140-6736(23)02576-X