Dengue
Diagnosis and clinical management

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CDC

Disclaimer

The findings and conclusions of this report are those of the authors and do not necessarily represent the oficial position of the Centers for Disease Control and Prevention

Basic Concepts

Aedes aegypti

- Four dengue viruses (DENV 1-4)
- Long-term homotypic immunity, short-term heterotypic immunity
- Mainly transmitted by mosquitoes, other routes of transmission possible
- Most dengue infections are asymptomatic
- Most symptomatic cases are mild

Why should we care about dengue?

- Outbreaks and incidence continue to increase globally
- Most common cause of fever among travelers returning from Asia and Latin America
- Around 5% of patients progress to severe disease
- Older and frequent travelers: additional risks for severe disease
- Unrecognized disease is a common cause of death
- Early suspicion, and timely and judicious IV fluids replacement can significantly decrease mortality

Dengue Clinical Classification – WHO (2009)

Dengue

Probable Dengue
Live in/travel to endemic area within the last 14 days
Fever and **two** of the following criteria:

- Nausea/vomiting
- Rash
- Aches and pains (headache, retro-orbital pain, myalgia, arthralgia)
- Tourniquet test positive/petechiae
- Leukopenia

Dengue with warning signs

One or more of the following warning signs:

- Abdominal pain or tenderness
- Persistent vomiting (≥3/h, or ≥4/6 h)
- Clinical fluid accumulation (ascites, pleural effusion)
- Mucosal bleeding
- Lethargy, restlessness
- Postural hypotension
- Liver enlargement >2 cm
- Progressive increase in hematocrit

Severe dengue

One or more of the following manifestations:

- Severe plasma leakage leading to
  - Shock
  - Respiratory distress
- Severe bleeding
- Severe organ involvement
  - Liver (AST or ALT >1,000)
  - Brain
  - Heart

AST: Aspartate Aminotransferase
ALT: Alanine Aminotransferase

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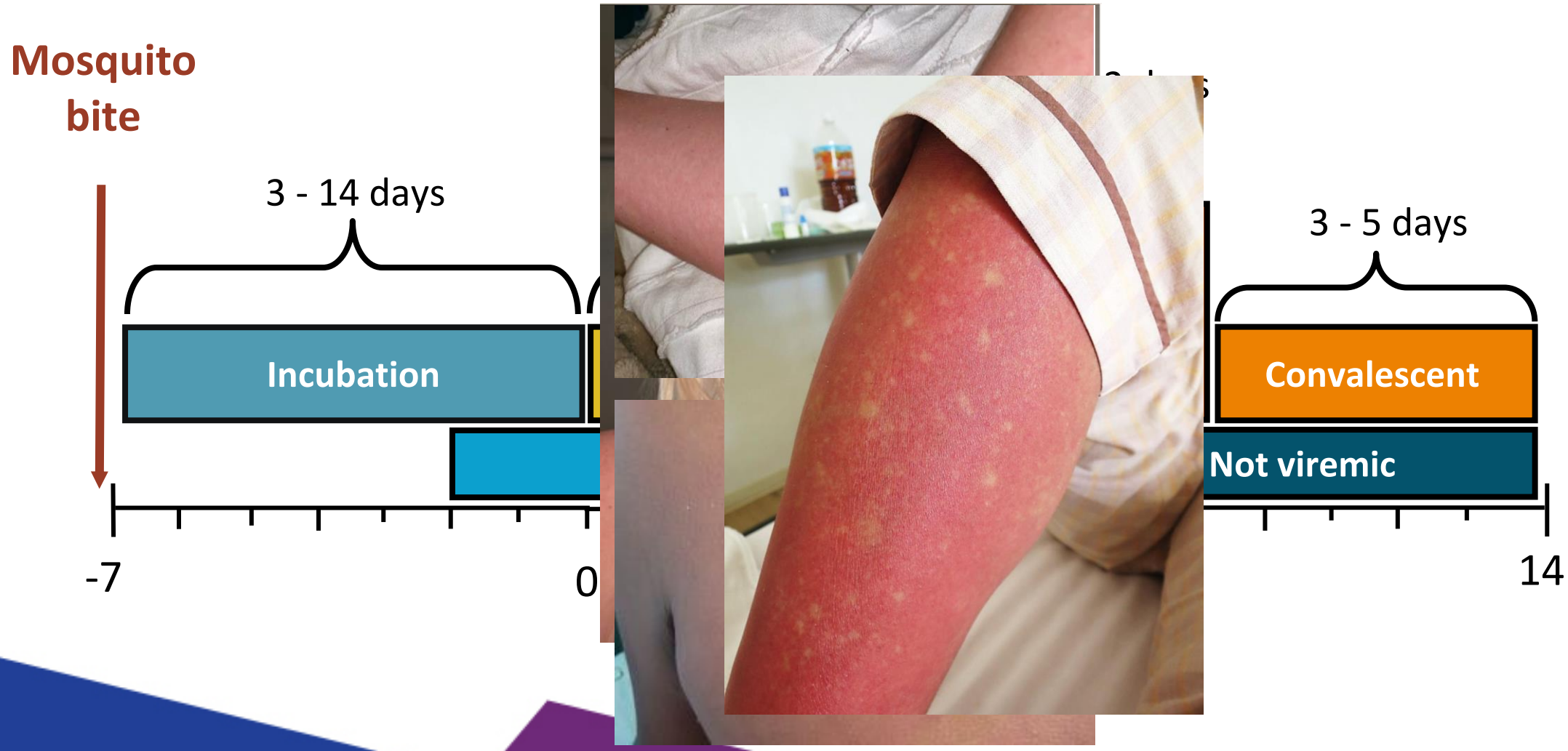
Dengue Clinical Course

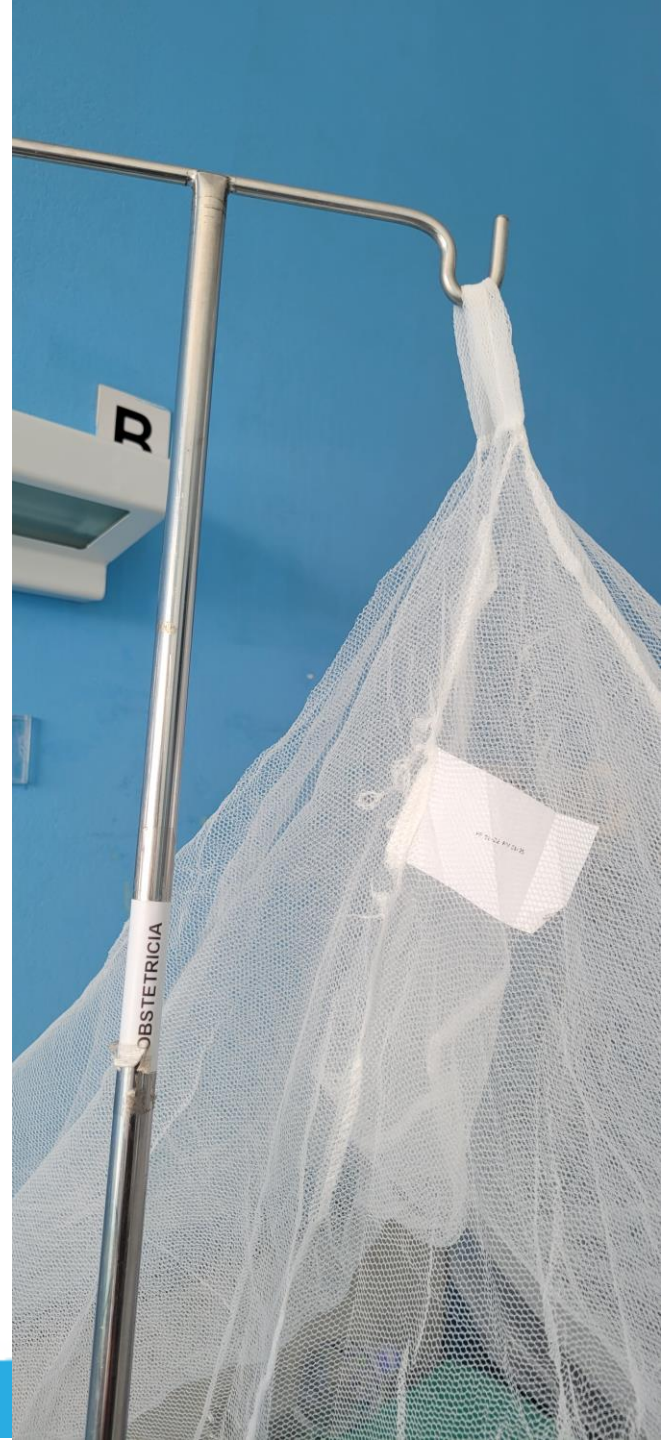


Dengue Clinical Course

- Presentation can change quickly
  - Identify and monitor warning signs
- Plasma leakage and progression to severe dengue usually occur in the critical phase
  - Defervescence, warning signs, hemoconcentration, fluid accumulation
- **Hypovolemic shock** is the main manifestation of severe dengue
  - Early signs of shock: narrowing pulse pressure, tachycardia, delayed capillary refill

Risk factors for severe disease

- Obesity, asthma, hypertension/heart disease, diabetes, kidney disease, chronic liver disease, coagulopathies, hemolytic diseases
- Pregnancy, infancy, elderly patients
- Secondary infection
  - Higher risk in secondary infection, compared to 1st, 3rd, and 4th
  - Dengue can progress to severe disease with any infection

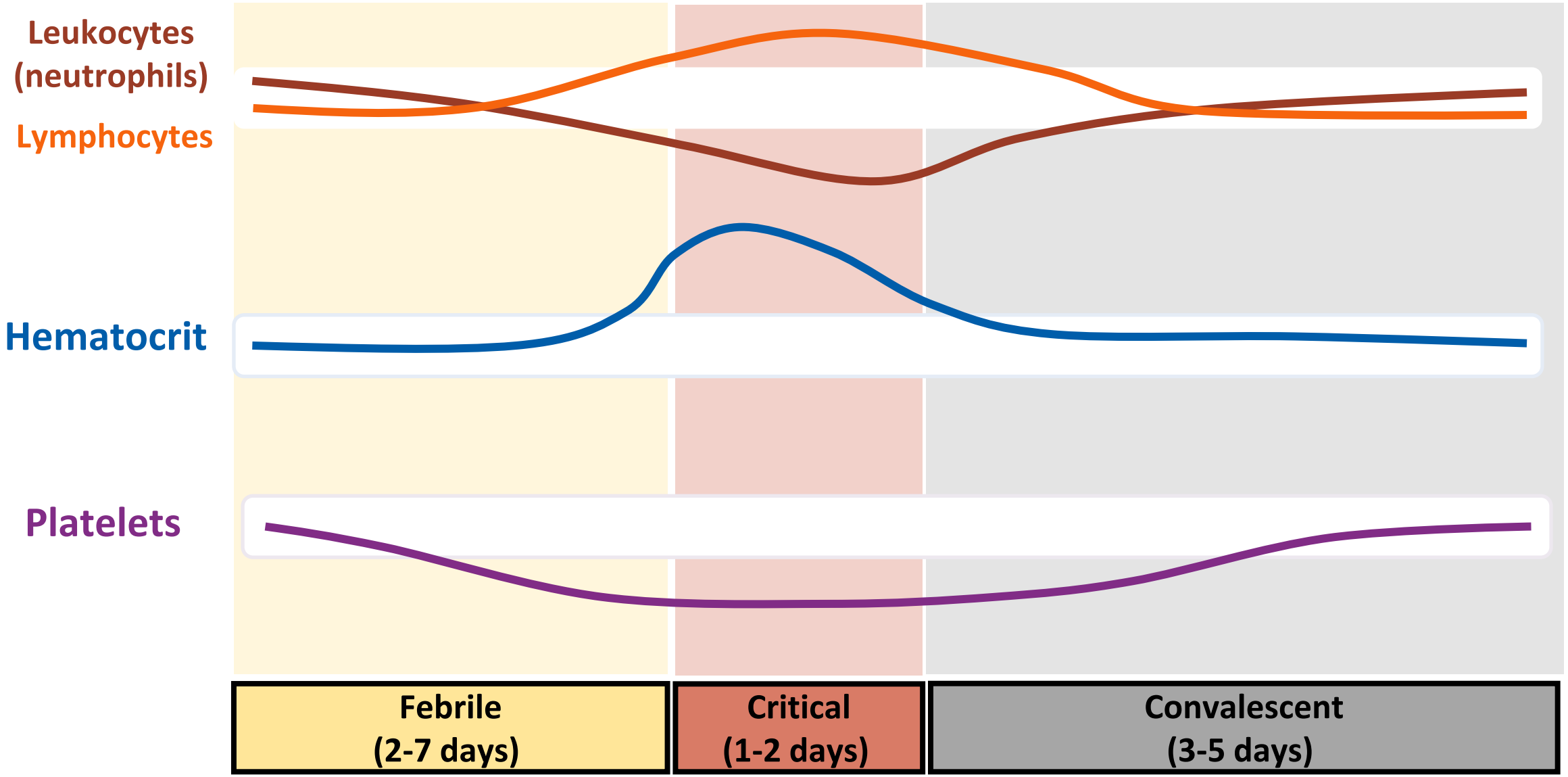


Acute management of dengue should be based on clinical evaluation and NOT on lab confirmation

Diagnostic testing

- Dengue is a nationally notifiable disease
- Rapid diagnostic tests are NOT widely available
- Testing can be arranged through the arboviral surveillance team at the State/Local Health Department
- Some commercial laboratories offer DENV RT-PCR, NS1, and DENV IgM

Common laboratory findings



Dengue Case Management

ASSESSMENT

Presumptive Diagnosis

Live in / travel to endemic area plus fever and two of the following:

- Nausea and vomiting
- Rash
- Aches and pains (headache, eye pain, muscle ache or joint pain)
- Warning signs
- Tourniquet test positive
- Leukopenia

Warning Signs

- Severe abdominal pain or tenderness
- Persistent vomiting
- Mucosal bleed
- Liver enlargement >2cm
- Clinical fluid accumulation
- Lethargy; restlessness
- Increase in HCT concurrent with rapid decrease in platelet count

No warning signs

Group A
Outpatient management

For patients with warning signs of severe dengue OR co-existing conditions

- Pregnancy
- Infancy
- Diabetes mellitus
- Poor social situation
- Old age
- Renal failure

Group B
Inpatient management

For patients with any of

- Severe plasma leakage with shock and/or fluid accumulation with respiratory distress
- Severe bleeding
- Severe organ impairment

Group C
Inpatient management

Centers for Disease Control and Prevention
National Center for Emerging and Zoonotic Infectious Diseases

CS261232-A

Clinical management

https://www.cdc.gov/dengue/healthcare-providers/treatment.html

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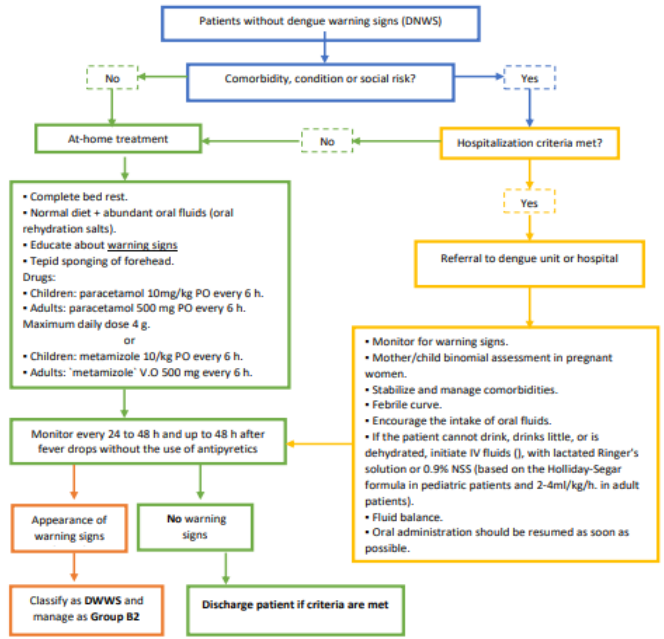
Algorithm for the Management of Dengue Patients Without Warning Signs (DNWS) – Groups A and B1



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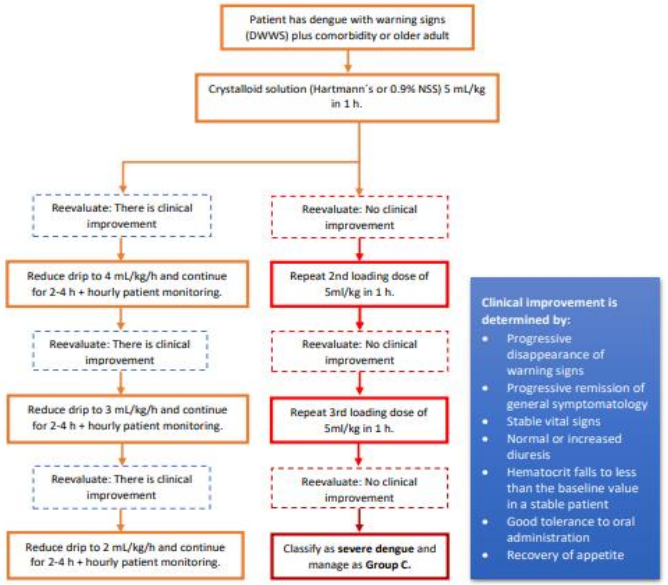
Algorithm for Intravenous Fluid Management in Patients with DWWS plus Comorbidity or Older Adult – Group B2



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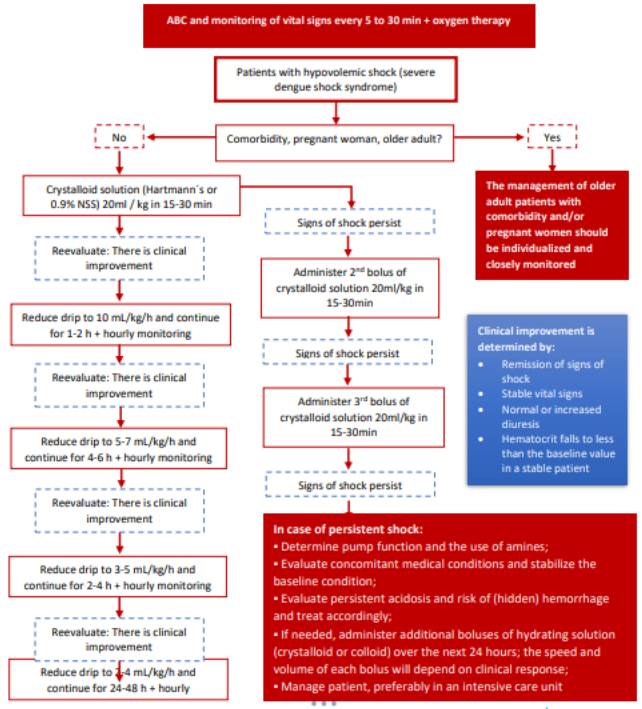
Algorithm for Intravenous Fluid Management in Patients with Hypovolemic Shock (Severe Dengue Shock Syndrome) – Group C



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https://www.paho.org/en/documents/algorithms-clinical-management-dengue-patients

Group A – Outpatient Follow-up

Patients with:

- No warning signs, *and*
- Ability to drink sufficiently, *and*
- Normal urine output

- **Should be assessed daily**
  - Daily CDB/Hct (until out of critical phase)
- **Monitor for:**
  - Signs of dehydration in febrile phase
  - Disease progression and defervescence
  - Warning signs
- **Recommendations**
  - Mosquito bites prevention, bed rest, **oral fluids**, paracetamol

Inpatient management

Group B - Patients with any:

- Warning signs
- Co-existing conditions (pregnancy, renal failure, coagulopathy)
- Other chronic conditions
- Infants, >65 years old
- Social circumstances

Group C - Patients with any:

- Shock – Compensated and decompensated
- Fluid accumulation with respiratory distress
- Severe bleeding
- Severe organ involvement

Guiding principles of fluid management

- Limit IV fluids in febrile phase
- IV fluids usually needed for only 24–48 hr
- Give only isotonic solutions
- **Give minimum IV fluids required to restore intravascular volume, maintain good perfusion and urine output of at least 0.5 ml/kg/hr**
- Monitor signs of fluid response – **REASSESS**
- Use ideal body weight to calculate maintenance fluids in overweight/obese patients

Dengue management don’ts

- Do not use NSAIDS
- Do not give intramuscular injections

- Do not use corticosteroids
- Do not give prophylactic platelet transfusions

Dengue vaccines

Dengvaxia

US ACIP recommends **3 doses** (six months apart) for the prevention of dengue in:

- People **9–16** years old <u>with</u>
  - laboratory confirmation of previous dengue virus infection <u>and</u>
  - living in endemic areas

Dengue vaccines

Qdenga (TAK-003)

WHO-SAGE has recommended **2 doses** (three months apart) in

- People **6–16** years old
  - Settings with high dengue disease burden and high transmission intensity
  - Introduced 1-2 years prior to age-specific peak incidence of hospitalizations
- Authorized by the European Medicine Agency, approved in several countries (UK, Argentina, Indonesia, Thailand, Brasil)
- FDA application was voluntarily withdrawn in the United States

There are currently no dengue vaccines recommended for **travelers** in the United States

Takeaways

- In the US, most dengue cases are travel-associated
  - Occurrence expected to increase
- Suspect dengue in all febrile travelers coming from endemic areas within 14 days
- No therapeutics are currently available to treat dengue
- No dengue vaccines are currently available for travelers in the United States
- Contact local/state Health Department for notification and confirmatory testing

Takeaways

- If dengue is suspected:
  - Determine phase of the disease (febrile, critical, convalescent)
  - Determine severity of the disease (without/with warning signs, severe)
  - Assess comorbidities and other risk factors
  - Determine clinical management requirements based on group classification (A,B1, B2,C)

- Main severe dengue presentation is shock, not bleeding

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