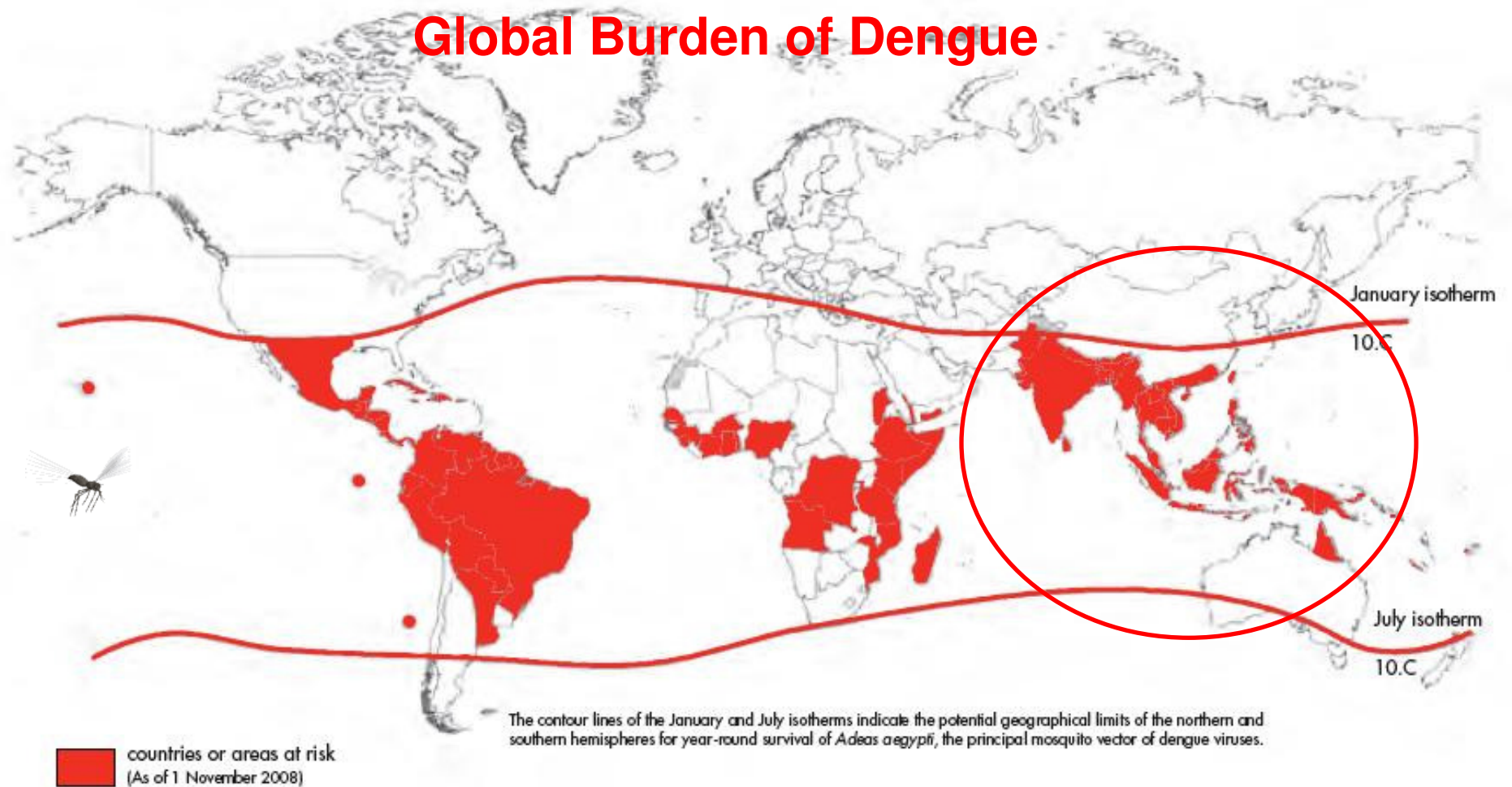




# **Dengue Update: WHO 2009 Guideline**

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## Global Burden of Dengue



1.8 Billion or >70% of the population at risk for dengue worldwide live in the Southeast Asia and Western Pacific Region

**DENGUE**  
GUIDELINES FOR DIAGNOSIS,  
TREATMENT, PREVENTION AND CONTROL



New edition  
2009



For research on  
diseases of poverty  
UNICEF - UNDP - World Bank - WHO



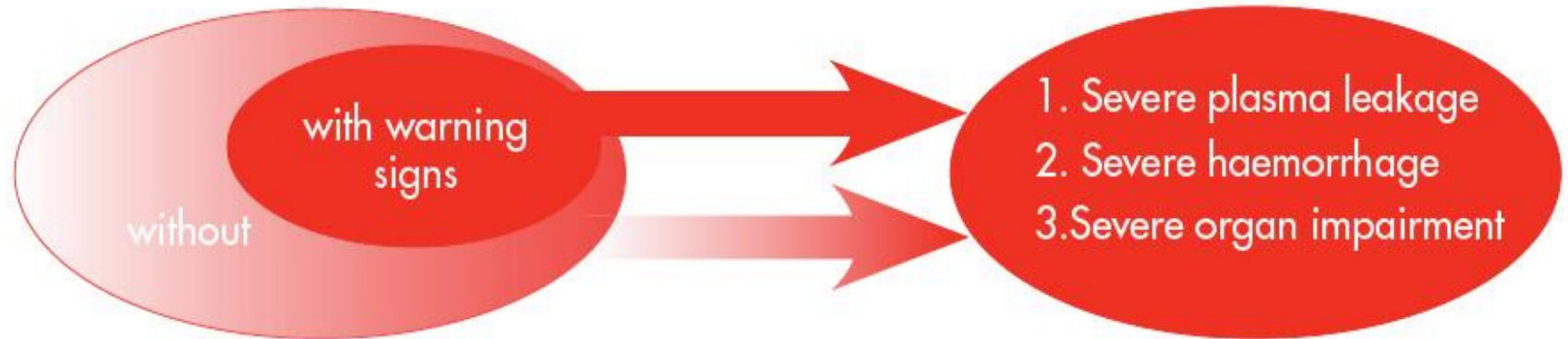
World Health  
Organization

- Chapter 1 Epidemiology, burden of disease and transmission
- **Chapter 2 Clinical management and delivery of clinical services**
- Chapter 3 Vector management and delivery of vector control services
- Chapter 4 Laboratory diagnosis and diagnostic tests
- Chapter 5 Surveillance, emergency preparedness and response
- Chapter 6 New avenues

# Dengue Case Classification and Levels of Severity

## DENGUE ± WARNING SIGNS

## SEVERE DENGUE



### CRITERIA FOR DENGUE ± WARNING SIGNS

#### Probable dengue

live in /travel to dengue endemic area.

Fever and 2 of the following criteria:

- Nausea, vomiting
- Rash
- Aches and pains
- Tourniquet test positive
- Leukopenia
- Any warning sign

#### Laboratory-confirmed dengue

(important when no sign of plasma leakage)

#### Warning signs\*

- Abdominal pain or tenderness
- Persistent vomiting
- Clinical fluid accumulation
- Mucosal bleed
- Lethargy, restlessness
- Liver enlargement >2 cm
- Laboratory: increase in HCT concurrent with rapid decrease in platelet count

\*(requiring strict observation and medical intervention)

### CRITERIA FOR SEVERE DENGUE

#### Severe plasma leakage

leading to:

- Shock (DSS)
- Fluid accumulation with respiratory distress

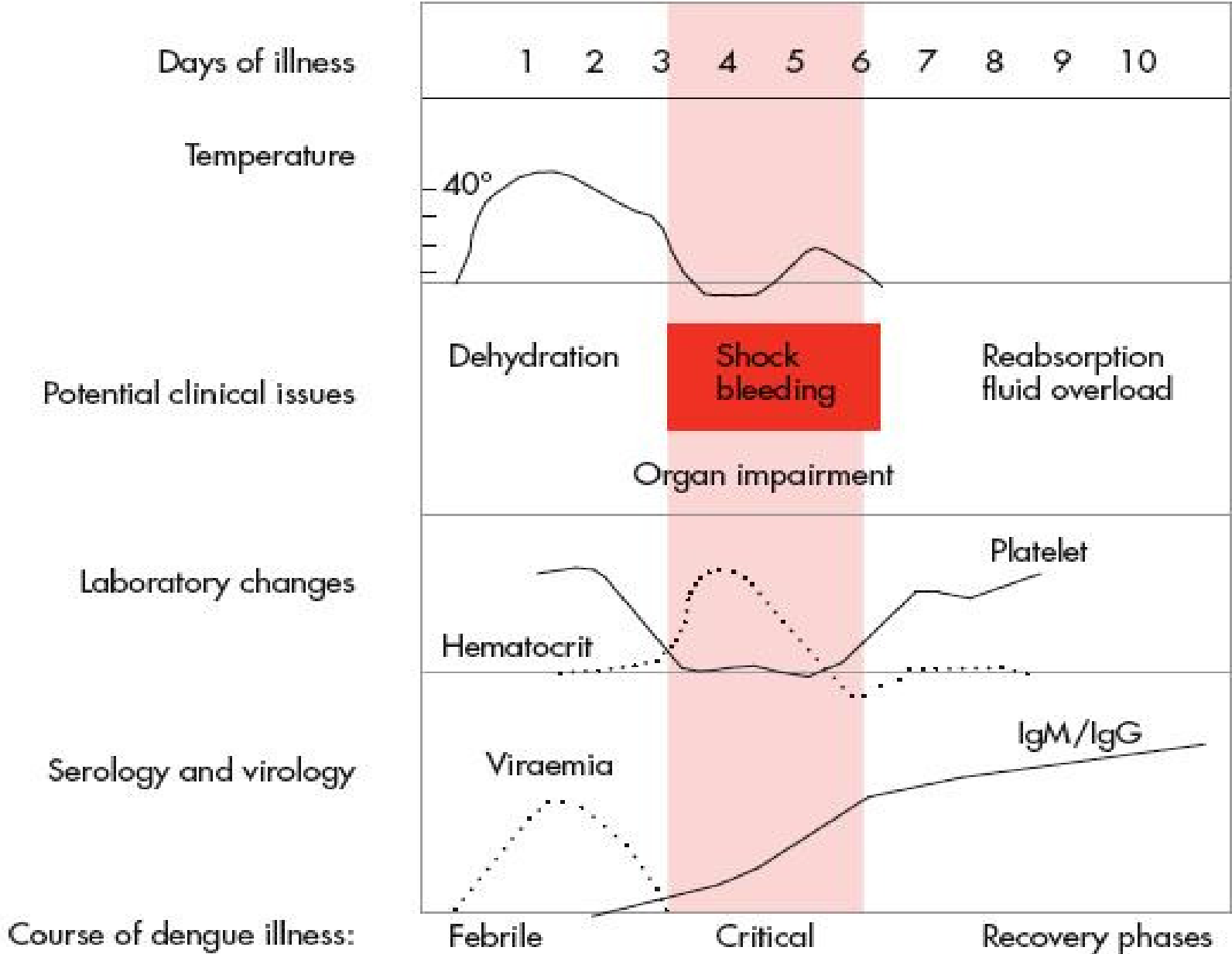
#### Severe bleeding

as evaluated by clinician

#### Severe organ involvement

- Liver: AST or ALT  $\geq 1000$
- CNS: Impaired consciousness
- Heart and other organs

# The Course of Dengue Illness



## Clinical Problems During the Different Phases of Dengue

1	Febrile phase	Dehydration; high fever may cause neurological disturbances and febrile seizures in young children
2	Critical phase	Shock from plasma leakage; severe haemorrhage; organ impairment
3	Recovery phase	Hypervolaemia (excessive IVF therapy)

## Differential Diagnosis of Dengue Fever

### Conditions that mimic the febrile phase of dengue infection

Flu-like syndromes

Influenza, measles,  
Chikungunya, infectious  
mononucleosis , HIV  
seroconversion illness

Illnesses with a rash

Rubella, measles, scarlet fever,  
meningococcal infection,  
Chikungunya, drug reactions

Diarrhoeal diseases

Rotavirus, other enteric infections

Illnesses with neurological  
manifestations

Meningo/encephalitis febrile  
seizures

## Differential Diagnosis of Dengue Fever

### Conditions that mimic the critical phase of dengue infection

Infectious	Acute gastroenteritis, malaria, leptospirosis, typhoid, viral hepatitis, acute HIV seroconversion illness, bacterial sepsis, septic shock
Malignancies	Acute leukemia and other malignancies
Other clinical pictures	Acute abdomen – acute appendicitis, cholecystitis, perforated viscus Diabetic ketoacidosis Lactic acidosis Leukopenia and thrombocytopaenia ± bleeding Platelet disorders Renal failure Respiratory distress (Kussmaul's breathing) Systemic Lupus Erythematosus



# A Stepwise Approach to the Management of Dengue

## Step I. Overall assessment

- I.1 History, including information on symptoms, past medical and family history
- I.2 Physical examination, including full physical and mental assessment
- I.3 Investigation, including routine laboratory and dengue-specific laboratory

## Step II. Diagnosis, assessment of disease phase and severity

## Step III. Management

### III.1 Disease notification

III.2 Management decisions. Depending on the clinical manifestations and other circumstances,

patients may:

- be sent home (Group A);
- be referred for in-hospital management (Group B);
- require emergency treatment and urgent referral (Group C).

# A Stepwise Approach to the Management of Dengue

## Step I—Overall assessment

### History

The history should include:

- date of onset of fever/illness;
- quantity of oral intake;
- assessment for warning signs
- diarrhoea;
- change in mental state/seizure/dizziness;
- urine output (frequency, volume and time of last voiding);
- other important relevant histories, such as family or neighbourhood dengue, travel to dengue endemic areas, co-existing conditions, jungle trekking and swimming in waterfall, recent unprotected sex or drug abuse (consider acute HIV seroconversion illness).

## Physical Examination

- assessment of mental state;
- assessment of hydration status;
- assessment of haemodynamic status
- checking for tachypnoea/acidotic breathing/pleural effusion;
- checking for abdominal tenderness/hepatomegaly/ascites;
- examination for rash and bleeding manifestations;
- tourniquet test (repeat if previously negative or if there is no bleeding manifestation).

## Investigation

A full blood count should be done at the first visit. A hct test in the early febrile phase establishes the patient's own baseline hct. A decreasing white blood cell count makes dengue very likely. A rapid decrease in platelet count in parallel with a rising hct is suggestive of progress to the plasma leakage/critical phase. In the absence of the patient's baseline, age-specific population hct levels could be used as a surrogate during the critical phase.

## **Step II—Diagnosis, assessment of disease phase and severity**

## **Step III—Management**

### **Disease notification**

In dengue-endemic countries, cases of suspected, probable and confirmed dengue should be notified for appropriate public health measures. Suggested criteria for early notification of suspected cases are that the patient lives in or has travelled to a dengue-endemic area, has fever for three days or more, has low or decreasing white cell counts, and/or has thrombocytopenia  $\pm$  positive tourniquet test. In dengue-endemic countries, the later the notification, the more difficult it is to prevent dengue transmission.

### **Management decisions**

Patient may *be sent* home (Group A), be referred for in-hospital management (Group B), or require emergency treatment and urgent referral (Group C).

# DENGUE CASE MANAGEMENT

## ASSESSMENT

### PRESUMPTIVE DIAGNOSIS

- Live in/travel to dengue endemic area.  
Fever and two of the following criteria:
- Anorexia and nausea
  - Rash
  - Aches and pains
  - Warning signs
  - Leukopenia
  - Tourniquet test positive

Laboratory confirmed dengue  
(Important when no sign of plasma leakage)

### WARNING SIGNS\*

- Abdominal pain or tenderness
- Persistent vomiting
- Clinical fluid accumulation
- Mucosal bleed
- Lethargy, restlessness
- Liver enlargement >2 cm
- Laboratory: Increase in HCT concurrent with rapid decrease in platelet count

\*[requiring strict observation and medical intervention]

## CLASSIFICATION

**NEGATIVE**

Co-existing conditions  
Social circumstances

**POSITIVE**

**NEGATIVE**

**POSITIVE**

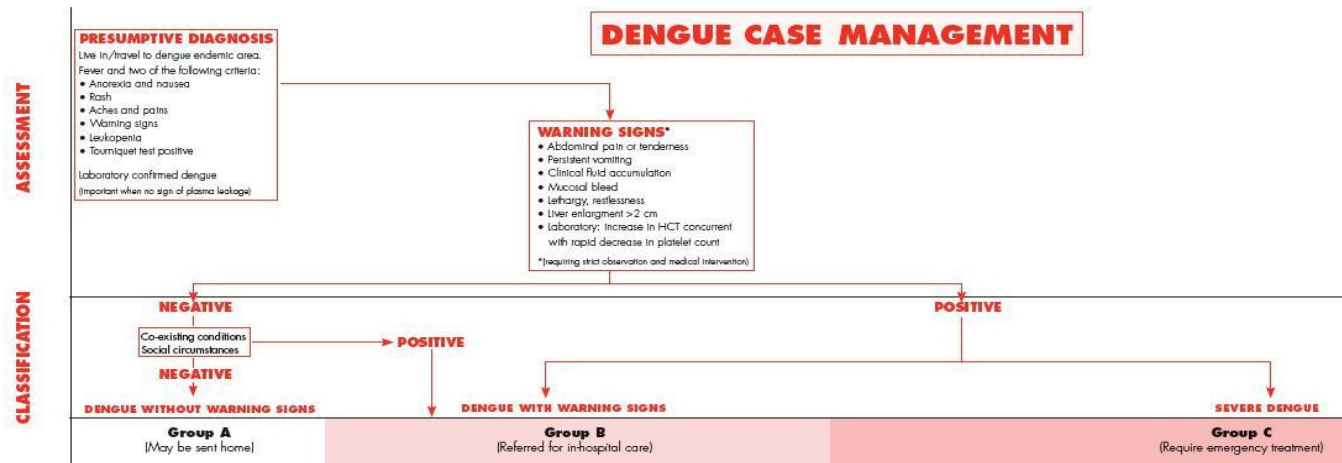
**DENGUE WITHOUT WARNING SIGNS**

**DENGUE WITH WARNING SIGNS**

**SEVERE DENGUE**

## MANAGEMENT

<b>Group A</b> (May be sent home)	<b>Group B</b> (Referred for in-hospital care)	<b>Group C</b> (Require emergency treatment)
<p><b>Group criteria</b> Patients who do not have warning signs <b>AND</b> who are able:</p> <ul style="list-style-type: none"> <li>• to tolerate adequate volumes of oral fluids</li> <li>• to pass urine at least once every 6 hours</li> </ul> <p><b>Laboratory tests</b></p>	<p><b>Group criteria</b> Patients with any of the following features:</p> <ul style="list-style-type: none"> <li>• co-existing conditions such as pregnancy, infancy, old age, diabetes mellitus, renal failure</li> <li>• social circumstances such as living alone, living far from hospital</li> </ul> <p><b>Laboratory tests</b></p> <ul style="list-style-type: none"> <li>• full blood count (FBC)</li> </ul> <p><b>OR:</b> Existing warning signs</p> <p><b>Laboratory tests</b></p> <ul style="list-style-type: none"> <li>• full blood count (FBC)</li> <li>• haematocrit (HCT)</li> </ul> <p><b>Treatment</b> Obtain reference HCT before fluid therapy. Give isotonic solutions such as 0.9% saline, Ringer's Lactate. Start with 5–7 ml/kg/hr for</p>	<p><b>Group criteria</b> Patients with any of the following features:</p> <ul style="list-style-type: none"> <li>• severe plasma leakage with shock and/or fluid accumulation with respiratory distress</li> <li>• severe bleeding</li> <li>• severe organ impairment</li> </ul> <p><b>Laboratory tests</b></p> <ul style="list-style-type: none"> <li>• full blood count (FBC)</li> <li>• haematocrit (HCT)</li> <li>• other organ function tests as indicated</li> </ul>



## Group A

(May be sent home)

### Group criteria

Patients who do not have warning signs

AND

who are able:

- to tolerate adequate volumes of oral fluids
- to pass urine at least once every 6 hours

### Laboratory tests

- full blood count (FBC)
- haematocrit (HCT)

## Treatment

Advice for:

- adequate bed rest
- adequate fluid intake
- Paracetamol

Patients with stable HCT

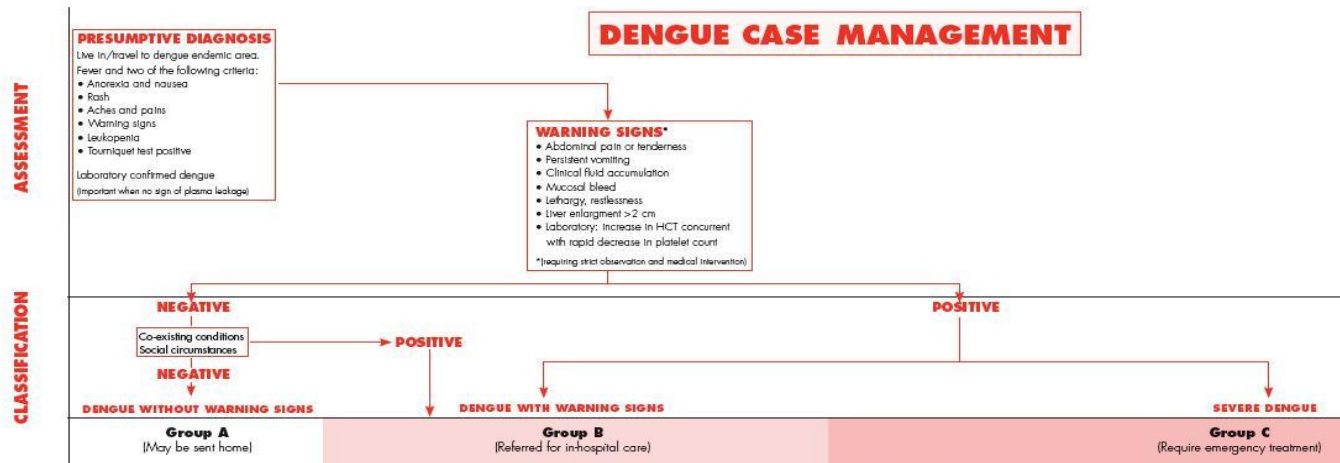
## Monitor

Daily review for disease progression:

- decreasing white blood cell count
- defervescence
- warning signs (until out of critical period).

Advice for immediate return to hospital if development of any warning signs, and

- written advice for management (e.g. home care card for dengue)



## Group B

**positive for co-existing conditions**

(Referred for in-hospital care)

### Group criteria

Patients with any of the following features:

- pregnancy, infancy, old age, diabetes mellitus, renal failure
- social circumstances such as living alone, living far from hospital

### Laboratory tests

- full blood count (FBC)
- haematocrit (HCT)

### Treatment

- Encouragement for oral fluids. If not tolerated, start IV therapy 0,9% saline or Ringer's Lactate at maintenance rate.

### Monitor

- temperature pattern
- volume of fluid intake and losses
- urine output (volume and frequency)
- warning signs

## Group B

### With existing warning signs

(Referred for in-hospital care)

OR: Existing warning signs

### Laboratory tests

- full blood count (FBC)
- haematocrit (HCT)

### Treatment

Give isotonic solutions such as 0.9 % saline, Ringer's Lactate. Start with 5–7 ml/kg/hr for 1–2 hours, then reduce to 3–5 ml/kg/hr for 2–4 hr, and then reduce to 2–3 ml/kg/hr or less according to clinical response.

### Reassess clinical status and repeat HCT:

- if HCT remains the same or rises only minimally -> continue with 2–3 ml/kg/hr for another 2–4 hours;
- if worsening of vital signs and rapidly rising HCT -> increase rate to 5–10 ml/kg/hr for 1–2 hours.

### Reassess clinical status, repeat HCT and review fluid infusion rates accordingly:

- reduce IVF gradually when the rate of plasma leakage decreases towards the end of the critical phase. This is indicated by:
  - adequate urine output and/or fluid intake
  - HCT decreases below the baseline value in a stable patient.

### Monitor

- V/S and peripheral perfusion (1–4 hourly until patient is out of critical phase)
- urine output (4–6 hourly)
- HCT (before and after fluid replacement, then 6–12 hourly)
- blood glucose
- other organ functions (renal profile, liver profile, coagulation profile, as indicated).



## Calculations for normal maintenance of intravenous fluid infusion

Normal maintenance fluid per hour can be calculated on the basis of the following formula\*  
(equivalent to Holliday-Segar formula):

4 mL/kg/h for first 10 kg body weight

+ 2 mL/kg/h for next 10 kg body weight

+ 1 mL/kg/h for subsequent kg body weight

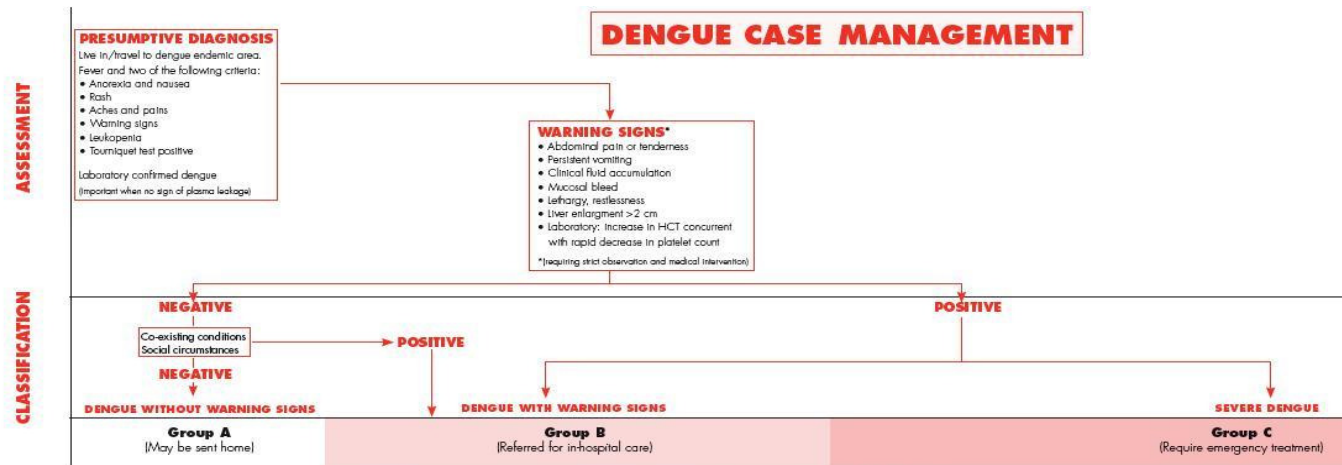
*\*For overweight/obese patients calculate normal maintenance fluid based on ideal body weight (IBW)  
(Adapted from reference 16)*

IBW for overweight/obese adults can be estimated on the basis of the following formula

Female:  $45.5 \text{ kg} + 0.91(\text{height} - 152.4) \text{ cm}$

Male:  $50.0 \text{ kg} + 0.91(\text{height} - 152.4) \text{ cm}$

(17)



## Group C

### SEVERE DENGUE

(Require emergency treatment)

#### Group criteria

Patients with any of the following features:

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

#### Laboratory tests

- full blood count (FBC)
- haematocrit (HCT)
- other organ function tests as indicated

#### Treatment of compensated shock

Start IVF resuscitation with isotonic crystalloid solutions at 5–10 ml/kg/hr over 1 hour. Reassess patients' condition.

#### If patient improves:

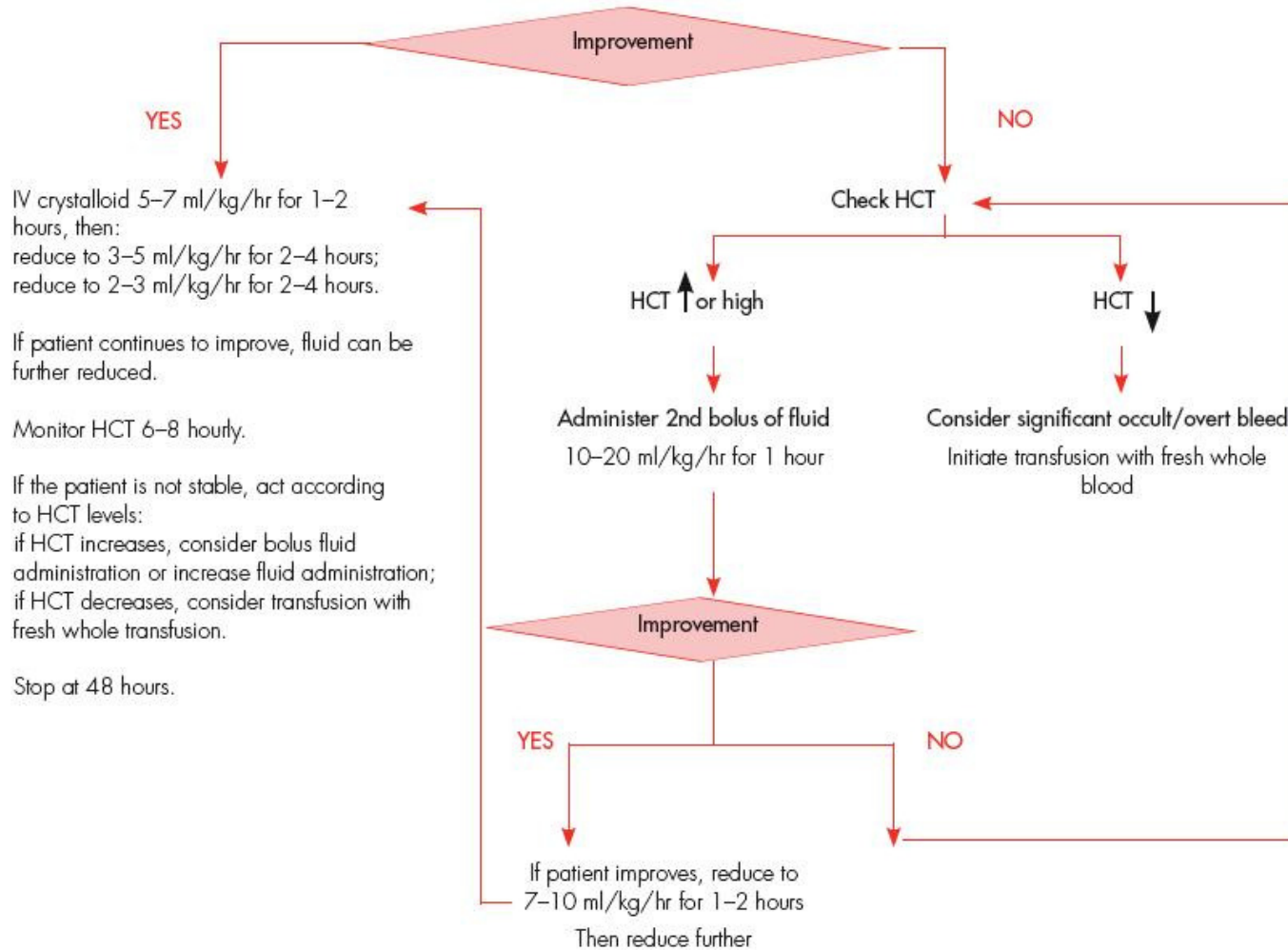
- IVF should be reduced gradually to 5–7 ml/kg/hr for 1–2 hours, then to 3–5 ml/kg/hr for 2–4 hours, then to 2–3 ml/kg/hr for 2–4 hours and then reduced further depending on haemodynamic status;
- IVF can be maintained for up to 24–48 hours.

#### If patient is still unstable:

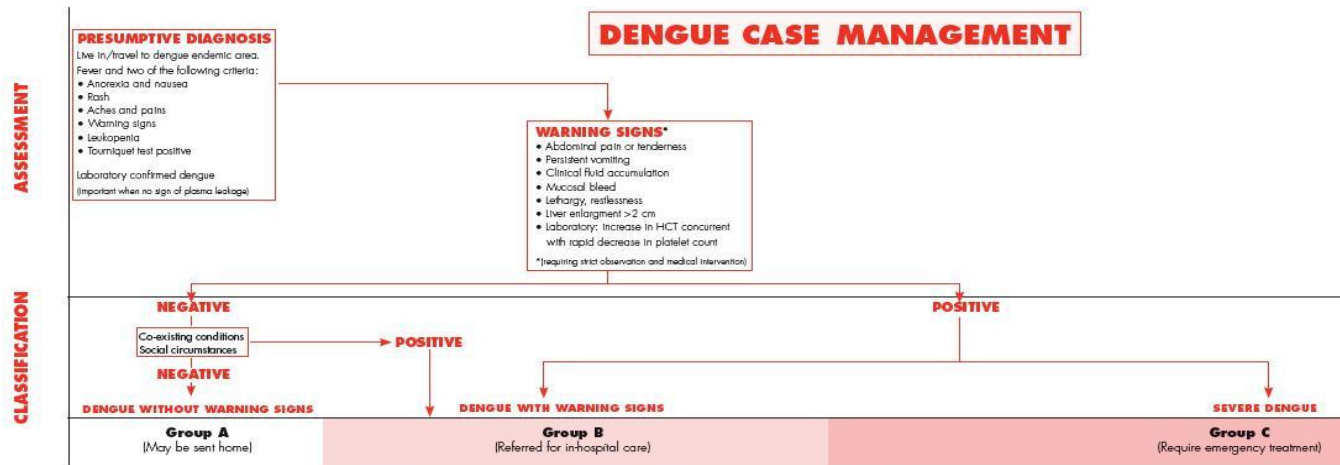
- check HCT after first bolus;
- if HCT increases/still high (>50%), repeat a second bolus of crystalloid solution at 10–20 ml/kg/hr for 1 hour;
- if there is improvement after second bolus, reduce rate to 7–10 ml/kg/hr for 1–2 hours and continue to reduce as above;
- if HCT decreases, this indicates bleeding and need to cross-match and transfuse blood as soon as possible.

# Algorithm for fluid management in compensated shock

Compensated shock (systolic pressure maintained but has signs of reduced perfusion)  
Fluid resuscitation with isotonic crystalloid  
5–10 ml/kg/hr over 1 hour



HCT = haematocrit



## Group C

### SEVERE DENGUE

(Require emergency treatment)

#### Treatment of hypotensive shock

Initiate IVF resuscitation with crystalloid or colloid solution at 20 ml/kg as a bolus for 15 minutes.

#### If patient improves:

- give a crystalloid/colloid solution of 10 ml/kg/hr for 1 hour, then reduce gradually.

#### If patient is still unstable:

- review the HCT taken before the first bolus;
- if HCT was low <40%, this indicates bleeding, the need to cross-match and transfuse
- if HCT was high compared to baseline value, change to IV colloids at 10–20 ml/kg as a second bolus over 30 minutes to 1 hour; reassess after second bolus.

- If patient is improving reduce the rate to 7–10ml/kg/hr for 1–2 hours, then back to IV crystalloids and reduce rate
- if patient's still unstable, repeat HCT after second bolus.
- If HCT decreases, this indicates bleeding
- if HCT increases/remains high (>50%), continue colloid infusion at 10–20 ml/kg as a third bolus over 1 hour, then reduce to 7–10 ml/kg/h 1–2 hours, then change back to crystalloid solution and reduce rat.

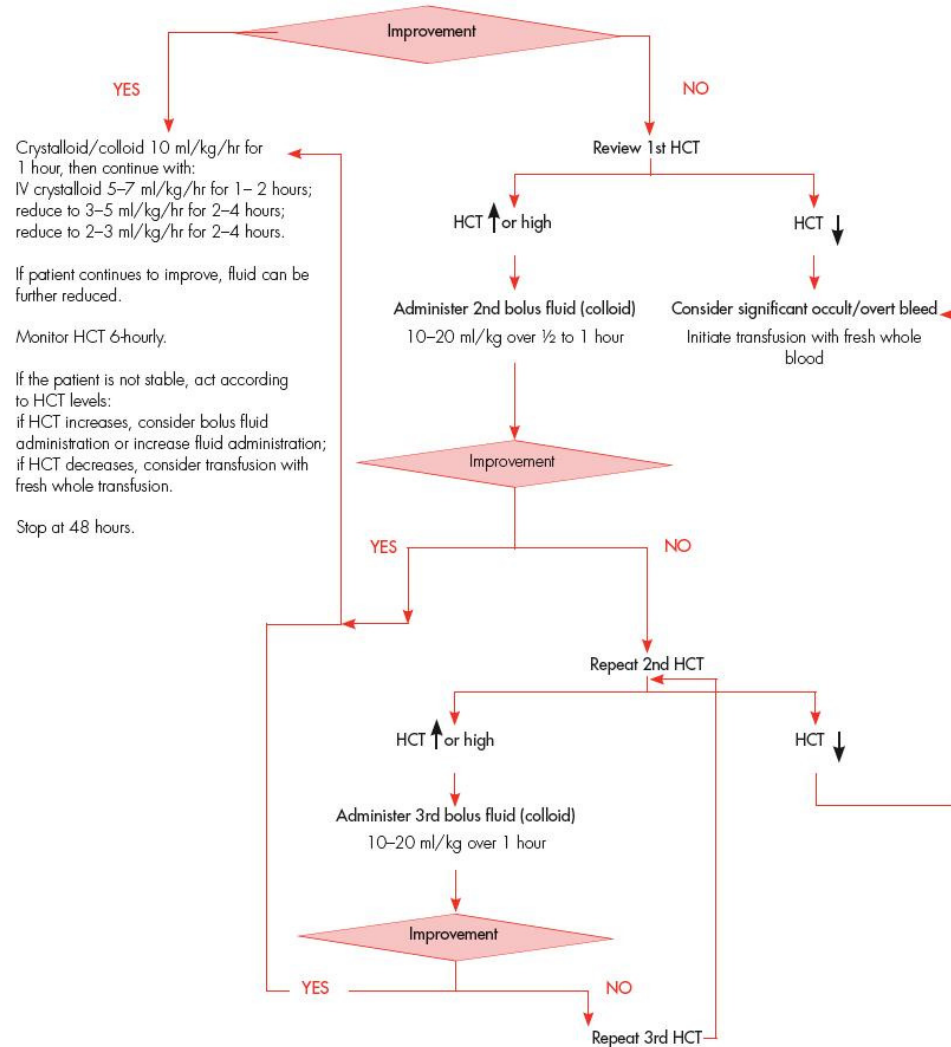
#### Treatment of haemorrhagic complications

Give 5–10 ml/kg of fresh packed red cells or 10–20 ml/kg of fresh whole blood.

# Algorithm for fluid management in Hypotensive shock

## Hypotensive shock

Fluid resuscitation with 20 ml/kg isotonic crystalloid or colloid over 15 minutes  
 Try to obtain a HCT level before fluid resuscitation



# Treatment of complications and other areas of treatment

## Fluid overload

Large pleural effusions and ascites is a common cause of acute respiratory distress and failure in severe dengue.

Causes of fluid overload are:

- excessive and/or too rapid IVFs;
- incorrect use of hypotonic rather than isotonic crystalloid solutions;
- inappropriate use of large volumes of IVFs in patients with unrecognized severe bleeding;
- inappropriate transfusion of fresh-frozen plasma, platelet concentrates and cryoprecipitates;
- continuation of IVFs after plasma leakage has resolved (24–48 hours from defervescence);
- co-morbid conditions such as congenital or ischaemic heart disease, chronic lung and renal diseases.

## **Early clinical features of fluid overload**

- respiratory distress, difficulty in breathing;
- rapid breathing;
- chest wall in-drawing;
- wheezing (rather than crepitations);
- large pleural effusions;
- tense ascites;
- increased jugular venous pressure (JVP).

## **Late Clinical Features**

- pulmonary oedema (cough with pink or frothy sputum  $\pm$  crepitations, cyanosis);
- irreversible shock (heart failure, often in combination with ongoing hypovolaemia).

## **Additional Investigations**

- Chest x-ray shows cardiomegaly, pleural effusion, upward displacement of the diaphragm by the ascites and varying degrees of “bat’s wings” appearance ± Kerley B lines suggestive of fluid overload and pulmonary oedema;
- ECG to exclude ischaemic changes and arrhythmia;
- ABG;
- Echocardiogram for assessment of left ventricular function,
- Cardiac enzymes.



**The management of fluid overload varies according to the **phase of the disease and the patient's haemodynamic status.****

- Stable haemodynamic status and is out of the critical phase (more than 24–48 hours of defervescence), stop IVF but continue close monitoring. If necessary, give oral or IV furosemide 0.1–0.5 mg/kg/dose once or twice daily, or a continuous infusion of furosemide 0.1 mg/kg/hour.

- Monitor serum potassium and correct the ensuing hypokalaemia.

- Stable haemodynamic status but is still within the critical phase, reduce the intravenous fluid accordingly.

- Avoid diuretics during the plasma leakage phase because they may lead to intravascular volume depletion.

- In shock with low or normal haematocrit levels but show signs of fluid overload, consider occult haemorrhage.

- Fresh whole blood transfusion should be initiated as soon as possible.

- If the patient remains in shock and the haematocrit is elevated, repeated small boluses of a colloid solution may help.

## Treatment of Fluid Overload

- Oxygen therapy should be given immediately.
- Stop IVF therapy during the recovery phase will allow fluid in the pleural and peritoneal cavities to return to the intravascular compartment.
- IVF should be discontinued or reduced to the minimum rate when the following signs are present:
  - signs of cessation of plasma leakage;
  - stable blood pressure, pulse and peripheral perfusion;
  - HCT decreases in the presence of a good pulse volume;
  - afebrile for more than 24–48 days (without the use of antipyretics);
  - resolving bowel/abdominal symptoms;
  - improving urine output.

**Recognizing when to decrease or stop IVF is key to preventing fluid overload.**

## Other complications of dengue

- Hyperglycaemia and hypoglycaemia, even in the absence of diabetes mellitus and/or hypoglycaemic agents.
- Electrolyte and acid-base imbalances are probably related to gastrointestinal losses. Hyponatraemia, hypokalaemia, hyperkalaemia, serum calcium imbalances and metabolic acidosis (sodium bicarbonate for metabolic acidosis is not recommended for  $\text{pH} \geq 7.15$ ) can occur.
- Co-infections and nosocomial infections.

## **Discharge criteria**

**(all of the following conditions must be present)**

<b>Clinical</b>	No fever for 48 hours. Improvement in clinical status (general well-being, appetite, haemodynamic status, urine output, no respiratory distress).
<b>Laboratory</b>	Increasing trend of platelet count. Stable haematocrit without intravenous fluids.

