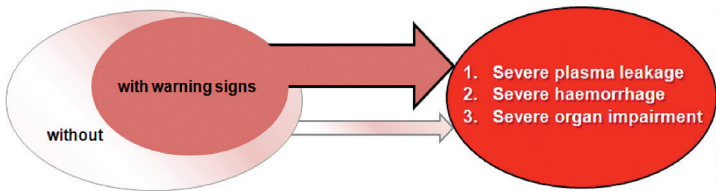


# MANAGEMENT OF DENGUE INFECTION IN ADULTS (THIRD EDITION) 2015



DENGUE ± WARNING SIGNS

SEVERE DENGUE



## KEY MESSAGES

1. Dengue infection is a **systemic** and **dynamic** disease with clinical, haematological and serological profiles changing from day to day.
2. Clinical deterioration may occur in the critical phase and is marked by plasma leakage and rising haematocrit (HCT).
3. Look out for warning signs which may indicate severe dengue.
4. Recognition of shock in its early stage and prompt fluid therapy with close monitoring of fluid adjustment may give a good clinical outcome.

### DENGUE CASES NOTIFICATION

- All suspected dengue cases must be notified (telephone/fax/e-notification) to the nearest health office within 24 hours of diagnosis, followed by the written standard notification format.
- Update the notification when there is change in disease severity or dengue death.

### LABORATORY INTERPRETATION

- The median HCT level among Malaysian population is taken as:
  - male  $\leq$  60 years – 46%
  - male  $>$  60 years – 42%
  - female (all age groups) – 40%
- In the absence of baseline HCT, a HCT value higher than the above should raise the suspicion of plasma leakage.
- Usually, leucopaenia precedes thrombocytopaenia.

### DENGUE SEROLOGY TESTS

- Rapid combo test (dengue NS1 antigen/dengue IgM/IgG antibodies) should be done as a screening tool in suspected dengue infection and results can be obtained within 15-20 minutes.
- Dengue non-structural protein-1 (NS1 Antigen) is helpful in early phase ( $<$  day 5) of dengue infection and usually becomes undetectable in the convalescence phase.
- Real time reverse transcriptase polymerase chain reaction (RT-PCR) should be done in clinically suspected seronegative patients and also in seropositive severe dengue infection (serotyping).

### DENGUE CLASSIFICATION & LEVEL OF SEVERITY

#### CRITERIA FOR DENGUE $\pm$ WARNING SIGNS

##### Probable dengue

- Live in/travel to dengue endemic/hotspot/outbreak area
- Fever and 2 of the following criteria:
  - Nausea, vomiting
  - Rash
  - Aches and pains
  - Leucopaenia
  - Any warning sign

##### Laboratory-confirmed dengue

(important when no sign of plasma leakage)

##### Warning signs\*

- Abdominal pain or tenderness
- Persistent vomiting ( $\geq$ 3 times per day)
- Persistent diarrhoea ( $\geq$ 3 times per day)
- Clinical fluid accumulation
- Mucosal bleed
- Lethargy, confusion, restlessness
- Tender liver
- Laboratory: increase in HCT concurrent with rapid decrease in platelet count

\* (requiring strict observation & 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

## APPROACH TO OUTPATIENT EVALUATION OF DENGUE INFECTION

### Overall assessment

1. History
  - Date of onset of fever/illness
  - Oral intake
  - Assess for warning signs
  - Change in mental state/seizure/dizziness
  - Urine output (frequency, volume and time of last voiding)
  - Other important relevant histories:
    - Pregnancy
    - Co-morbidities
2. Physical examination
  - i. Assess mental state and GCS score
  - ii. Assess hydration status
  - iii. Assess haemodynamic status
    - Skin colour (C), capillary filling time (normal <2 seconds) (C), cold/warm extremities (T), pulse volume (V) and rate (R) - **CCTVR**
    - Blood pressure and pulse pressure
  - iv. Look out for tachypnoea/acidotic breathing/pleural effusion
  - v. Check for abdominal tenderness/tender liver/ascites
  - vi. Examine for bleeding manifestation
3. Investigation
  - i. FBC and HCT
  - ii. Point of care test for dengue infection (RCT or NS1 antigen)

### Diagnosis, disease staging and severity assessment

Based on evaluations in history, physical examination ± FBC, HCT and point of care test, the clinicians should be able to determine:

1. Likelihood of dengue infection
2. The phase of dengue infection (febrile/critical/recovery)
3. Severity of the illness

### Plan of management

1. Dengue assessment checklist must be filled
2. Notify the district health office followed by disease notification form
3. If admission is indicated
  - Stabilise the patient at primary care before transfer
  - Communicate with the receiving hospital/Emergency Department (ED) before transfer
  - At ED, dengue patients with deteriorating vital signs must be uptriaged accordingly
  - All dengue patients requiring admission should be immediately started on an appropriate fluid therapy (oral or IV)
  - Chest X-ray and ultrasound (where available) are required in patients suspected to have vascular leakage.
4. If admission is not indicated
  - Daily follow up is necessary until the patient remains afebrile for at least 24 - 48 hours
  - Provide patient with Outpatient Dengue Monitoring Record and Home Care Advice Leaflet for Dengue Patients

## DISEASE MONITORING PARAMETERS

Parameters for monitoring	Frequency of monitoring		
	Febrile phase	Critical phase	Reabsorption phase
<b>Clinical Parameters</b>			
General well being Appetite / oral intake Warning signs	Daily or more frequently towards late febrile phase	At least twice a day and more frequently as indicated	Daily or more frequently as indicated
Haemodynamic status • CCTVR • BP • Pulse pressure Respiratory status • RR • SpO <sub>2</sub> Neurological Status • Conscious level • Restlessness • Seizures	4-6 hourly depending on clinical status	2-4 hourly depending on clinical status  <b>In shock</b> Every 15-30 minutes till stable then 1-2 hourly	4-6 hourly
Urine output	4 hourly	2-4 hourly <b>In shock</b> : Hourly	4-6 hourly
Parameters for monitoring	Frequency of monitoring		
	Febrile phase	Critical phase	Reabsorption phase
<b>Laboratory Parameters and Imaging</b>			
<b>All investigations done at ED must be reviewed immediately upon ward admission</b>			
FBC	Daily or more frequently as indicated	4-12 hourly depending on clinical status <b>In shock</b> Repeated before and after each fluid resuscitation and as indicated	Daily
BUSE/Creatinine LFT + AST RBS Creatine Kinase	As clinically indicated	At least daily or more frequently as indicated <b>In shock</b> Crucial to monitor ABG and lactate closely	As clinically indicated
ABG, lactate Coagulation profile Troponin or CKMB CRP, Fibrinogen, LDH, Ferritin, Triglyceride ECG, Echocardiogram Ultrasound	As clinically indicated	As clinically indicated	As clinically indicated

## COMMON PITFALLS IN FLUID THERAPY

- Treating patients with unnecessary fluid boluses based on raised HCT or warning signs as the sole parameter without considering other clinical parameters.
- Excessive and prolonged fixed fluid regime in stable patients.
- Infrequent monitoring and adjustment of infusion rate.
- Continuation of intravenous fluid during the recovery phase.
- Excessive fluid therapy in patients with co-morbidities (such as heart disease and renal disease).

**FLUID THERAPY IN NON-SHOCK PATIENTS (DENGUE FEVER WITH WARNING SIGNS)**

- In dengue patients without co-morbidities who can tolerate orally, adequate oral fluid intake of two to three litres daily should be encouraged (often 1.2-1.5 times the normal maintenance will be required during the critical phase).
- Frequent adjustment of maintenance fluid regime is needed during the critical phase.
- In patients with persistent warning signs with increasing or persistently high HCT, the graded fluid bolus may be initiated with caution.

**CALCULATION FOR ROUTINE MAINTENANCE INTRAVENOUS FLUID****Non-obese patients**

- 1.2 to 1.5 ml/kg/hour

**Obese patients (BMI  $\geq 27.5$  kg/m<sup>2</sup>)**

- **Routine maintenance fluid can be calculated based on adjusted body weight (ABW).**
  - $ABW = IBW + 0.4 (\text{actual weight} - IBW)$
  - **Ideal bodyweight (IBW) can be estimated based on the following formula.**
    - Female:  $45.5 \text{ kg} + 0.91(\text{height in cm} - 152)$
    - Male:  $50.0 \text{ kg} + 0.91(\text{height in cm} - 152)$

**CAUTION :** Fluid intake and urine output must be reviewed and adjusted according to clinical response.

**GRADED FLUID BOLUS REGIME IN NON-SHOCK PATIENTS (DF with Warning Signs)**

- Obtain a baseline HCT before fluid therapy.
- Give crystalloids solution (such as 0.9% saline).
- Start with 5 ml/kg/hour for 1–2 hours, then reduce to 3 ml/kg/hr for 2–4 hours, and then reduce to 2 ml/kg/hr or less according to the clinical response.
- If the clinical parameters are worsening and HCT is rising, increase the rate of infusion.
- Reassess the clinical status, repeat the HCT and review fluid infusion rates accordingly.

**WHEN TO SUSPECT SIGNIFICANT OCCULT BLEEDING****Suspect significant occult bleeding in the following situations:**

- HCT not as high as expected for the degree of shock to be explained by plasma leakage alone.
- A drop in HCT without clinical improvement despite adequate fluid replacement (40-60 ml/kg).
- Severe metabolic acidosis and end-organ dysfunction despite adequate fluid replacement.

**MANAGEMENT OF SIGNIFICANT BLEEDING**

- Transfuse blood (5–10ml/kg of packed red cells) and observe the clinical response. Consider blood components if required.
- Consider repeating the blood transfusion if there is further blood loss or no appropriate rise in HCT after blood transfusion.
- Endoscopy by trained surgeon or gastroenterologist is indicated if these patients have persistent bleeding despite optimum medical therapy.

**DENGUE INFECTION IN PREGNANCY**

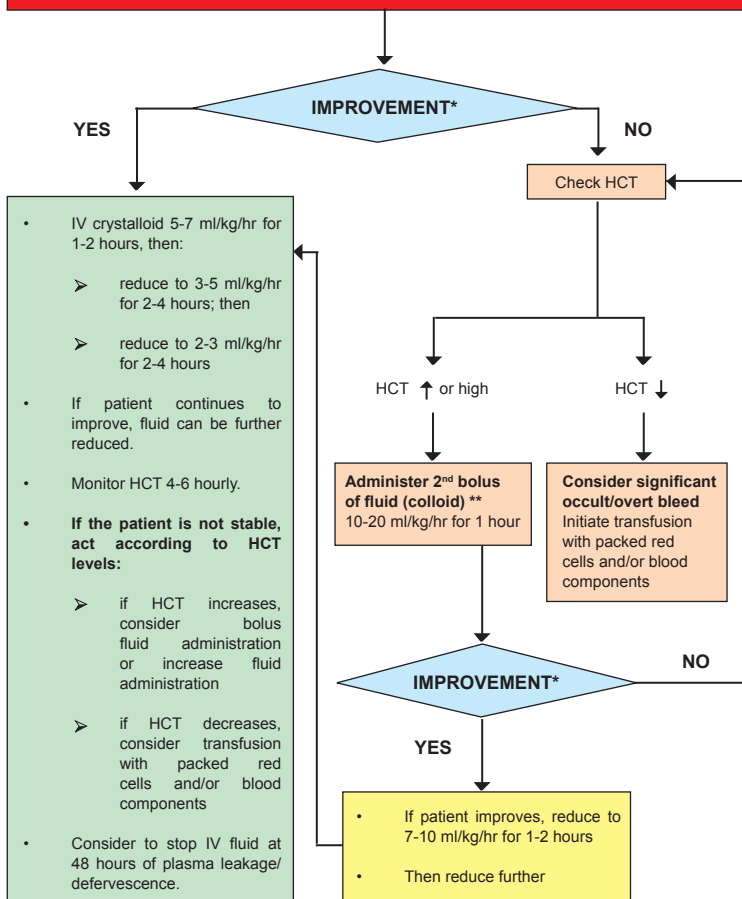
- All pregnant mothers with dengue infection should be managed in hospitals by a multidisciplinary team (physician, anaesthetist and obstetrician) due to a higher risk of morbidity and mortality.
- Spontaneous vaginal delivery is the preferred mode of delivery.
- Group and cross match (GXM) must be done. Blood and blood products transfusion to be given only when indicated or when instrumental/operative delivery is decided
- Serology test (Dengue IgM and NS1 antigen) or real time RT-PCR should be performed in neonates when congenital dengue infection is suspected.

## ALGORITHM A - 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 for 1 hour
- Obtain FBC, HCT, RP, LFT, RBS, PT/APTT, CK, Lactate/HCO<sub>3</sub>, GXM<sup>1</sup> before fluid resuscitation.



\* Reassess the patient's clinical condition, vital signs, pulse volume, capillary refill time, urine output and temperature of extremities.

\*\* Colloid is preferable if the patient has already received previous bolus of crystalloid

IV = intravenous ; HCT = haematocrit

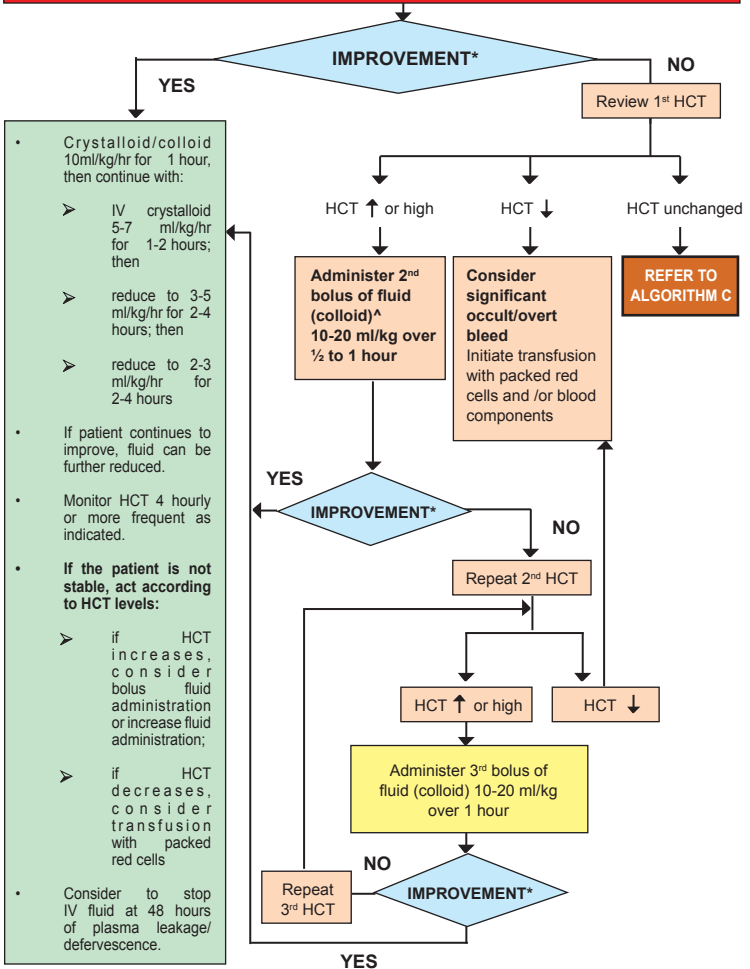
↑ = increased ; ↓ = decreased

<sup>1</sup>GXM: emergency cross-match

**ALGORITHM B - FLUID MANAGEMENT IN DECOMPENSATED SHOCK**

**DECOMPENSATED SHOCK**

- Fluid resuscitation with 20 ml/kg colloid / crystalloid within 15 - 30 minutes
- Obtain HCT/FBC, RP, LFT, RBS, PT/APTT, CK, Lactate/HCO<sub>3</sub>, GXM<sup>1</sup> before fluid resuscitation.

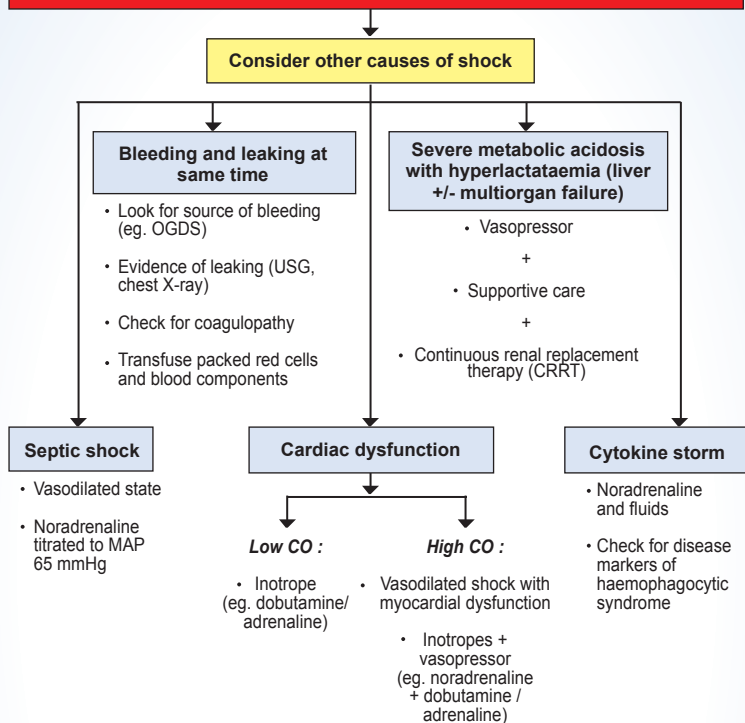


\* Reassess the patient's clinical condition, vital signs, pulse volume, capillary refill time and temperature of extremities.  
 ^ Colloid is preferable if the patient has already received previous bolus of crystalloid.

IV = intravenous ; HCT = haematocrit  
 ↑ = increased ; ↓ = decreased  
<sup>1</sup>GXM: emergency cross-match

**ALGORITHM C - FLUID MANAGEMENT IN DECOMPENSATED SHOCK  
(WITH PRESENCE OF BLEEDING & LEAKING OR OTHER CAUSES OF SHOCK)**

**HAEMATOCRIT REMAIN UNCHANGED AFTER FIRST FLUID RESUSCITATION**



All the above types of shocks need to be supported by echocardiography and non-invasive cardiac output monitoring and treatments tailor to each patient.

HCT = haematocrit ; MAP = mean arterial pressure ; CO = cardiac output;  
OGDS = oesophagogastroduodenoscopy ; USG = ultrasonography

This Quick Reference provides key messages and a summary of the main recommendations in the Clinical Practice Guidelines (CPG) Management of Dengue Infection in Adults 2015 (Third Edition).

Details of the evidence supporting these recommendations can be found in the above CPG, available on the following websites:

Ministry of Health Malaysia: [www.moh.gov.my](http://www.moh.gov.my)

Academy of Medicine Malaysia: [www.acadmed.org.my](http://www.acadmed.org.my)