# 7. MANAGEMENT OF DENGUE INFECTION

## 7.1 Introduction

There is no currently available anti viral medication against the dengue virus after the host invasion. The mainstay of dengue infection management stays symptomatic and supportive. A stepwise approach as suggested in Table 4 can be useful. Dengue is a dynamic disease and management issues vary according to the three phases of the clinical course (**section 7.4**). It is crucial to recognize plasma leakage & shock at an early stage, to guard against severe organ impairment. This can only be achieved through frequent clinical and laboratory monitoring.

Dengue patients who are managed in the outpatient setting should be provided with an OPD form (**DEAG Form O, Appendix 3a**) to ensure that all relevant information stays available to all the concerned health care providers.

Primary care providers with no immediate hematocrit facilities should refer patient to the nearest health care facility where hematocrit measurement facility is available for further management.

### Table 4: A Stepwise Approach in Evaluation of Dengue Fever

It is important to evaluate every patient in a stepwise manner - as follows:

***Step 1: Overall assessment***

1. **History**

- Date of onset of fever/ illness
- Oral intake of fluids (estimated)
- Assess for warning signs – Table 5
- Diarrhea
- Bleeding
- Change in mental state/seizure/dizziness
- Urine output (frequency, volume and time of last voiding)
- Other important relevant points in history:
  - History of dengue in the family or the neighborhood
  - Jogging/walks in the park and swimming in waterparks

- H/O recent travel to the endemic zones (inside or overseas destinations)

- Recent unprotected sexual or drug use behavior (consider acute HIV seroconversion illness)

-Co-morbidities (consider sepsis particularly in patients with diabetes mellitus)

**2. Physical examination**

i. Assess mental state and record Glasgow Coma Scale (GCS) score

ii. Assess hydration status

iii. Assess hemodynamic status

-Skin color

-Cold/ warm extremities

-Capillary refill time (normal <2 seconds)

-Pulse rate

-Pulse volume

-Blood pressure

-Pulse pressure

iv. **Resp. Sys:** Look out for tachypnea/ acidotic breathing/ pleural effusion

v. **G.I Sys:** Check for abdominal tenderness/ hepatomegaly/ ascites

vi. Examine for manifest bleeding

vii. Tourniquet test (Repeat at 6 hourly interval – 3 times - if previously negative)

**3. Investigations**

1: CBC and HCT

2: Dengue serology

OPD form (Appendix 3a) is useful for screening febrile patients with suspected and probable dengue. Elucidating details in history and examination as above will be required in admitted patients (Appendix 3b – Form I)

Once the diagnosis is made it is important to recognize the stage of the disease and the presence of any warning signs. Further management will depend on the preceding information.

### *Step 2: Diagnosis, disease staging and severity assessment*

Based on evaluations from history, physical examination +/- CBC and HCT, the clinicians should be able to determine:

1. Diagnosis of Dengue Fever (suspected, probable or confirmed)
2. The phase of illness (febrile/critical/convalescent or recovery)
3. The hydration and hemodynamic status of patient
4. Whether the patient requires admission

### *Step 3: Plan of management*

1. Notify the EDO health
   - via phone of all the probable cases of dengue - followed by a written notification on **DEAG-"Form R" (Appendix 4a)**
   - In **confirmed cases** use disease notification form. (**Appendix 4b**)
2. **If admission is indicated** - **refer to admission criteria** 7.3.1:
   - Stabilize the patient (**Algorithm A or B as appropriate - page 45, 46**)
   - Communicate with the receiving hospital/ Emergency & Trauma Department/HDU before transfer
3. If admission is not indicated (**Table 6 - page 33**):
   - Daily or more frequent follow up is necessary especially from day 3 of illness onwards until the patient becomes afebrile for at least 24 - 48 hours without antipyretics
   - Refer to Home Care Advice Leaflet for Dengue Patients (**Appendix 9**)

Adapted from[3, 8, 9]

**Table 5:** Warning signs [13, 14]

| Signs & Symptoms | Laboratory Findings |
|---|---|
| Abdominal pain or tenderness | Increasing HCT with falling platelets |
| Persistent vomiting | Free fluid in pleura or peritoneum on ultrasonography |
| Pleural effusion, ascites | |
| Significant manifest bleed | |
| Restlessness/ lethargy/ Irritability in infants | |
| Tender enlarged liver | |
| Decreased urine output | |

Patients who are not in critical phase and hemodynamically stable can be treated at home with close follow-up as required

**Table 6:** Clinical and Laboratory Criteria for Patients Who Can be Treated at Home

1. Tolerating orally, adequate urine output
2. Absence of significant manifest bleed
3. Absence of clinical alarm signals (**refer Table 5**)

**Physical examination defining hemodynamic stability:**

| | |
|---|---|
| Pink, warm extremities | Normal capillary refill time (normal <2 seconds) |
| Good pulse volume | Stable blood pressure |
| Normal pulse pressure (> 30mmHg) | Absence of disproportionate tachycardia |
| No tachypnea or acidotic breathing | Absent hepatomegaly or abdominal tenderness |
| No bleeding manifestation | No sign of pleural effusion/ ascites |
| No alterations in mental state and full GCS score | |

**Table 6: Investigation defining hematological stability stable state:**

- Stable serial HCT
- In the absence of a baseline HCT level, a HCT value sustained at >40% in female adults and >46% in male adults should be safe enough for the patient to be discharged [81, 82]

Adapted from [83, 81, 82]

## 7.2 Triaging the Patient at Accident & Emergency / Outpatient Department

As usual the purpose of triaging patients in A&E department is to identify those patients who would require urgent medical attention. This is to avoid critically ill patients being ignored while less critical patients are being attended to.[84, 83, 85, 86]

Triage the patient according to warning signs already given (**Table 5**)

## 7.3 CRITERIA FOR HOSPITAL REFERRAL / ADMISSION

### 7.3.1 Referral from primary care providers to hospital

The decision for referral and admission must not be based on a single clinical parameter but should depend upon the overall assessment of the patient, taking history, physical examination and labs into consideration.

**Referral from primary care providers to hospital**

**1. Symptoms**

- Presence of warning signals (**Table 5**)
- Inability to tolerate oral fluids
- Inadequate urine output (less than 25ml/hour or 0.5ml/kg/hour in children)
- Seizure

**2. Signs**

- Clinical signs of dehydration
- Shock (Table 1)
- End organ failure

**3. Special Situations for early referral to the hospital**

- Patients with co-morbidity e.g. Diabetes, Hypertension, Ischemic Heart Disease, Coagulopathies, Morbid Obesity, Renal Failure, Chronic Liver disease, COPD
- Infants < 1 year of age and elderly > 65 years of age
- Pregnancy
- Social factors that limit follow-up e.g. living far from health facility, no transport, patient living alone, etc

**4. Laboratory Criteria**

- Rising HCT accompanied by reducing platelet count

### 7.3.2 Referral from basic health units / hospitals without specialist to the hospitals with requisite expertise

All the doctors are encouraged to talk to the DEAG expert for on-line advice. Early consultation with the nearest expert should be initiated for all DHF patients, irrespective of the complications, end organ dysfunction or bleeding.

**Prerequisites for transfer**

1. All efforts must be made to optimize the patient's condition before and during transfer.
2. The Emergency Department and/or Medical Department of the receiving hospital must be informed prior to transfer.
3. Adequate and essential information must be sent together with the patients that includes fluid chart, monitoring chart and investigation results.

# 7.4 DISEASE MONITORING

## 7.4.1 Principles of Disease Monitoring

1. As discussed previously, dengue is a systemic and dynamic disease. Therefore disease monitoring would vary dynamically in different phases of the disease.

2. During the critical phase (plasma leakage) which may last for 24-48 hours, monitoring needs to be intensified and frequent adjustments in the fluid regime may be required.

3. Recognition of onset of convalescent phase is also important because intravenous fluid regime needs to be progressively reduced/ discontinued at this stage.

## 7.4.2 Outpatient Disease Monitoring

Every patient, who presents in outpatient or A & E department and is suspected to be suffering from dengue, should be assessed in stepwise manner as recommended in **Table 4**. Daily or more frequent follow up is necessary especially from day 3 of illness, until the patient becomes afebrile for at least 24- 48 hours without antipyretics. An outpatient assessment and advice form (Form O; **Appendix 3a**) is recommended for use for outpatient care (**Appendix 3a**).

## 7.4.3 Inpatient Disease Monitoring

Once admitted, every patient with suspected dengue should be reviewed thoroughly in the shortest possible time (Form I, **Appendix 3b**). In addition to the routine history, physical examination a stepwise approach (**Table 4**) should be employed to record the relevant data. The plan of management and monitoring cannot be static and should be based on the phase of the disease and the hemodynamic status of the patient. **Table 8 summarizes the recommendations regarding the parameters and frequency of monitoring according to the different phases of the illness.**

| Phase of Illness | Key Points |
|---|---|
| Febrile | - Differentiation of dengue illness from other febrile illness<br>- Not possible to differentiate DF from DHF |
| Critical | - Plasma leakage occurs as patient progress to late febrile phase or as temperature begins to defervesce (T < 38.0 $^{o}$C)<br>- Clinical deterioration occurs during this phase due to plasma leakage<br>- Plasma leakage results in hemoconcentration and hypovolemic / shock.<br>- Excessive intravenous fluids may increase plasma leakage in pleural space and contribute to respiratory distress<br>- Bleeding can be precipitated by prolonged shock and shock can be perpetuated by bleeding.<br>- May mimic acute abdomen of other causes<br>- May be confused with septic shock or other forms of shock. |
| Reabsorption | - Cessation of plasma leakage<br>- Reabsorption of fluid from extravascular compartment<br>- Hemodiluation occurs following fluid reabsorption.<br>- Hypervolemia and pulmonary edema if intravenous fluid therapy is continued |

**Table 7:** Key points in different phases of Dengue Fever

| Parameters of monitoring | Frequency of monitoring | | |
|---|---|---|---|
| | **Febrile phase** | **Critical phase** | **Convalescent Phase** |
| **Monitoring charts to use** | Use "Monitoring Chart I"- Appendix 2a" | Use "Monitoring Chart II & III" -Appendix 2b & 2c" | Use "Monitoring Chart I"- Appendix 2a" |
| **Clinical parameters** | | | |
| General well-being, appetite / oral intake, warning signs & symptoms, neurological / mental state | 4 – 6 hourly | hourly | 4-6 hourly |
| Signs of **bleeding, abdominal tenderness, ascites and pleural effusion** | Daily or more frequently towards late febrile phase | At least twice a day and more frequently as indicated | Daily or more frequently as indicated |
| **Hemodynamic status:**<br>• Pink/ cyanosis<br>• Extremities(cold/warm)<br>• Capillary refill time<br>• Pulse Rate & volume,<br>• BP, Pulse pressure<br>**Respiratory status:**<br>• Respiratory Rate<br>• $SpO_2$ | 4 – 6 hourly depending on clinical status | Hourly<br>**During Shock:**<br>Every 15 minutes till stable then 1 – 2 hourly | 4 – 6 hourly |
| **Urine output** | 4 – 6 hourly | Hourly<br>**During shock:**<br>Every 15 minutes | 4 – 6 hourly |
| **FBC + HCT** | Daily or more frequently if indicated | 4 – 12 hourly depending on clinical status<br>**During shock:**<br>Repeated before and after each bolus of fluid during resuscitation and as indicated | Daily |
| BUSE/Creatinine<br>LFT<br>RBS<br>Coagulation profile<br>$HCO_3$/$TCO_2$/Lactate | As indicated | At least daily or more frequently as indicated<br>**During shock:**<br>It is crucial to monitor acid-base balance / ABG closely | As indicated |

**Table 8:** Parameters and frequency of monitoring according to different phases of dengue Illness.

Adapted from [3, 83]

## 7.5 FLUID MANAGEMENT

### 7.5.1 Dengue with Warning Signs (Table 5)

Presence of warning signs usually heralds the onset of plasma leak in critical phase. All such patients should be admitted and monitored in a health care facility.

Common pitfalls in fluid therapy:

1. Treating patient with unnecessary fluid bolus basing decision solely on HCT
2. Excessive and prolonged fixed fluid regime in stable patients. Failure to adjust rate of fluid administration in accordance with the rate of plasma leak which can be assessed with appropriate monitoring
3. Continuation of intravenous fluid during the convalescent phase

At least some of patients exhibiting warning signs of dengue would recover with early intravenous rehydration without ever going into shock. However, some cases would deteriorate to severe dengue shock syndrome. If the patient has dengue fever with warning signs, the recommended action plan is depicted in **Table 9a.**

**Table 9a: Action Plan for Patient who has Dengue Fever with Warning Signs (without shock)**

**Recommendations**

- Admit the patient. If stable may be given fluid quota(7.5.5) orally
- IV fluid is indicated in patients who are vomiting or unable to tolerate oral fluids. 9b: section 7.5.2
- IV fluid is also indicated in patients with increasing HCT (indicating on-going plasma leakage) despite increased oral intake.
- Crystalloid (0.9% Saline) is the fluid of choice

As mentioned above, if patient is unable or is non-tolerant of oral fluids; IV fluids may be started according to table 9b: section 7.5.2

### 7.5.2 Patients in Critical Phase without Shock

There are no studies that have looked at fluid therapy in non-shock dengue patients. Appropriate (as per quota) oral fluid intake may be sufficient in some patients who are hemodynamically stable and not vomiting. However IV fluid (0.9% saline is recommended) is indicated in patients with serially increasing HCT (indicating on-going plasma leakage) despite appropriate oral intake. Intravenous fluid therapy should also be considered in patients who are vomiting and not tolerating orally.[87, 83]

The normal maintenance requirement for IV fluid therapy in such patients could be calculated based on the formula (M+5% - 7.5.5). Frequent adjustment of maintenance fluid regime is often needed during the critical phase. Often 1.2-1.5 times the normal maintenance will be required during the critical phase. Fluid infusion rate should be reviewed regularly to match the rate of infusion with estimated rate of plasma leak.

A rising HCT AND/ OR hemodynamic instability indicates on-going plasma leakage and will require an increase in the IV fluid infusion rate. If patients deteriorate and progress to shock, a more aggressive fluid resuscitation is indicated (section 7.5.3).[87, 83]

Reduce or consider discontinuation of IV fluid therapy when patients begin to show signs of recovery (usually after 24-48 hours of beginning of critical phase) or the HCT drops in a hemodynamically stable patient.

**Table 9b - IV Fluid management during critical phase without shock**

- Obtain a baseline HCT before fluid therapy
- Use crystalloids solution (such as 0.9% saline).
- Start with 1.5 - 7 ml/kg/hour for 1 hour. Subsequent rate should be adjusted according to the pulse pressure (≥30 mm) and urine output (≥ 0.5 ml/kg/hr or 25ml/hr in adults).
- 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

### 7.5.3 Dengue Shock Syndrome (DSS) (Compensated and Decompensated - Refer to Algorithms A and B)

Dengue shock syndrome is a medical emergency. Recognition of shock in its early (compensated) stage and prompt fluid resuscitation will ensure a good clinical outcome.[88] (Refer to **Table 1** for details). Consequences of failure to recognize the compensated shock phase may be drastic. As the compensated phase leads to decompensated phase the disease outcome becomes less certain with increasing chance of a more complicated course. **Pulse pressure of < 20 mmHg and severe oliguria are late signs of shock**

All patients with dengue shock should be managed in high dependency intensive care units. Fluid resuscitation, however, must be initiated promptly and should not be delayed while waiting for admission to ICU or high dependency unit.

In spite of successful initial resuscitation the patient may experience recurrent episodes of shock because of continuing capillary leakage which can last for 24-48 hours.

Intravenous fluid therapy is the mainstay of treatment for dengue shock. [3, 88, 89] To date, only three randomized controlled trials studying different types of fluid regime in DSS in children aged from 5 to 15 years of age are available.[88, 89, 90] Because of this paucity of studies in the adult population, **our recommendations are extrapolated from these studies.** These studies showed no clear advantage of using any of the colloids over crystalloids in terms of the overall outcome. However, colloids may be preferable as the fluid of choice in patients with intractable shock after crystalloid resuscitation. Colloids seem to restore the cardiac index and reduce the level of HCT faster than crystalloids in patients with intractable shock. [89] The choice of colloids includes dextran 40, gelatin solution (e.g. Hemaxel) and hetastarch solution (e.g. Hespan, Hextend).

### Principles for fluid resuscitation

The volume of initial and subsequent fluid resuscitation depends on the degree of shock Initial fluid bolus can be 10 or 20 ml/kg ideal body weight in compensated and decompensated shock respectively. The volume and rate of fluid replacement should be carefully titrated to the clinical response to maintain an effective circulation while avoiding an over replacement.

Improvement in the following parameters indicates adequate fluid resuscitation:

**Clinical parameters indicating adequacy of fluid resuscitation:**

| | |
|---|---|
| • Improvement in general well-being | • Improving pulse pressure |
| • Good orientation &mental state | • Reduction in tachycardia or normalization of heart rate |
| • Warm peripheries | • Increase in urine output |
| • Capillary refill time ≤ 2sec | • Reducing tachypnea or normalization of respiratory rate |
| • Stable BP | |

**Laboratory parameters indicating adequacy of fluid resuscitation:**

- Decrease in HCT (in face of hemodynamic stability)
- Improvement in metabolic acidosis

If the initial cycles of fluid resuscitation with crystalloids (30 ml/ kg in total - refer to Algorithms A & B) fail to establish a stable hemodynamic state and HCT remains high, colloids should be considered [3, 83]

If the repeat HCT drops after fluid resuscitation and the patient remains in shock, one should suspect significant bleed (often occult) and blood transfusion should be instituted as soon as possible (refer to Algorithm for fluid management for DSS).

**7.5.4 Persistent Shock** (Refer to Algorithms **A** and **B**)

Consider persistent shock in patients who fail to improve with adequate fluid resuscitation

**Following causes of persistent shock must be considered and managed:**

**Significant bleeding:** (Often occult).

- *Treat with Packed cells (5ml/kg) or whole blood (10ml/kg) may be used. This is expected to increase the HCT by 5%. If HCT is >45% it must be decreased by giving iv fluids before using blood; even if bleeding is likely*

**Hypocalcemia:**

*Treat with IV (10%) calcium gluconate @ 1 ml/kg (max 10mls diluted in equal volume of saline) as slow bolus over 10 minutes with cardiac monitoring (may be repeated 6 hourly). Empiric treatment with calcium may be given if patient fails to improve or deteriorates despite fluid resuscitation.* [91]

**Acidosis:**

*If the arterial blood bicarbonate ($HCO_3$) falls below 15 meq/l in the patients with decompensated shock, treat with NaHCO3 (8.4%) with an empiric dose of 1ml/kg, diluted in equal volume of saline in a slow infusion. (A bolus of not more than 10 ml /dose – maximum up to 5 doses). Shift the patient to HDU under expert supervision* [91]

**Hypoglycemia:**

*Treat with intravenous dextrose after bed side glucose measurement*

If patient's is still in state of persistent shock despite all the above measures consider sepsis and cardiogenic shock

- Treat with I/V antibiotics: Use intravenous antibiotics as oral administration may worsen vomiting and result in erratic absorption. Choice of antibiotics should be sufficiently broad to provide cover for Gram+, Gram- and anaerobic organisms in keeping with the prevailing culture sensitivity pattern. Choice may later be reviewed in light of blood C/S result of the patient.
- Consider inotropic support

Fluid therapy has to be judiciously controlled to avoid fluid overload which could result in massive pleural effusion, pulmonary edema or ascites. [3, 83]

### 7.5.5 Calculation of Fluid Quota for Adults

Fluid quota in adults is based on the maximum lean mass of 50kg in adults. Irrespective of the real weight of an adult - (even if he weighs more than 50 kg) - he still would have the same amount of circulatory volume as that in a 50 kg adult. For adults weighing less than 50 kgs, the actual weight may be used for calculating fluid quota (Section 11). The following discussion explains fluid calculation for adults weighing ≥ 50 kgs. The formula is referred to as M+5%. This refers to a sum of maintenance fluids PLUS 5% losses. The entire fluid quota is given over 48 hours (the duration of the critical phase). For patients presenting in shock the quota may be given over 24 hours. Such a patient may have been leaking for a considerable length of time and may well be in the latter half of the critical phase.

**Calculation of total fluids during critical phase in adult (50 kg)**

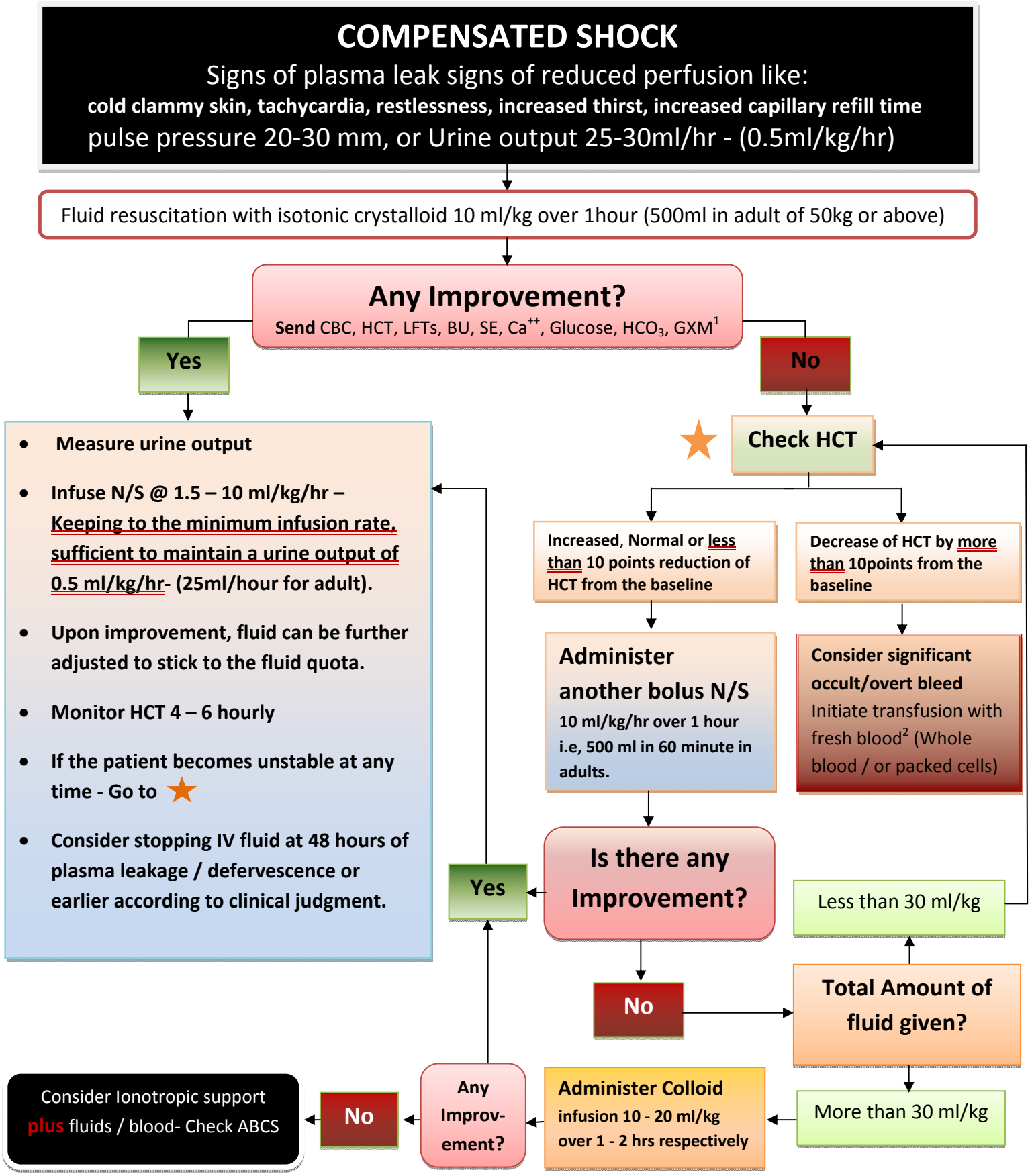
| | | |
|---|---|---|
| **M (Maintenance)** | 100ml/kg for 1st 10 kg | 1000 |
| | +50 ml/kg for next 10 kg | + 500 |
| | +20 ml/kg for balance wt | + 600 |
| | Total Maintenance | 2100 |

**5% of body weight =** 50ml x body wt. (kg) 50 kg x 50 mls = 2500 mls

M + 5% = 4600 mls

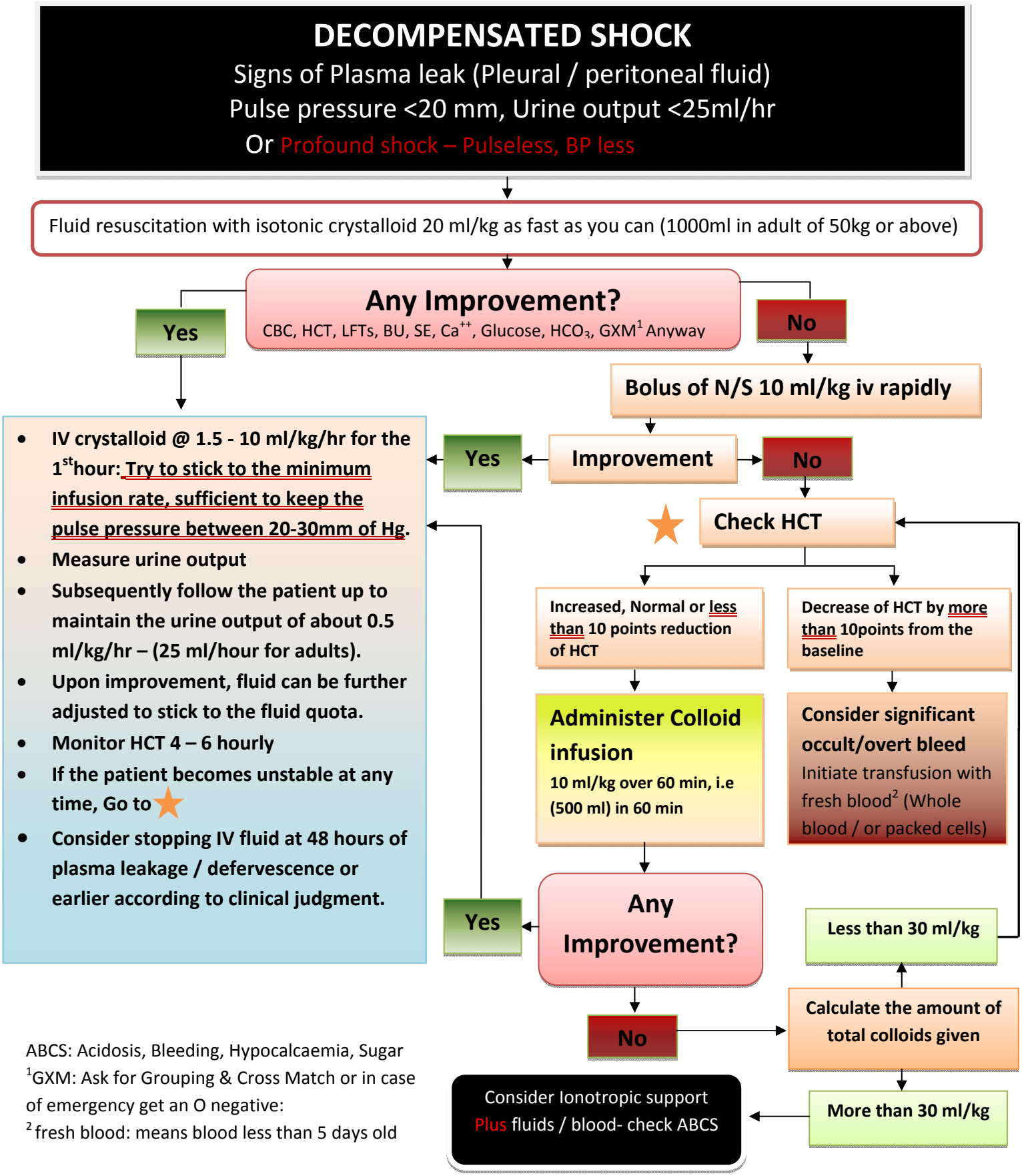
It is important to note that if the patient is taking oral fluids, this oral intake should also be included in the total fluid quota which also would include any fluid given in the form of boluses.

## Algorithm A – Fluid Management in Compensated Shock




ABCS: Acidosis, Bleeding, Hypocalcaemia, Sugar: [1]GXM: Ask for Grouping & Cross Match or in case of emergency get an O negative: [2] fresh blood: Means blood less than 5 days old

## Algorithm: B – Fluid Management in Decompensated Shock




ABCS: Acidosis, Bleeding, Hypocalcaemia, Sugar

[1]GXM: Ask for Grouping & Cross Match or in case of emergency get an O negative:

[2] fresh blood: means blood less than 5 days old

# 7.6 MANAGEMENT OF BLEEDING/HAEMOSTASIS

## 7.6.1 Hemostatic Abnormalities in Dengue Infection

The hemostatic changes that occur in dengue infection are considered to be the result of endothelial activation.[92, 93] This process may aggravate thrombocytopenia in addition to the activation of coagulation pathways which are an inherent part of the disease.[92, 93, 94] However, thrombocytopenia and coagulation abnormalities would not reliably predict bleeding in dengue infection. [47, 48]

Markers of endothelial activation such as elevated levels of thrombomodulin, tissue factor and Von Willebrand factor are more often seen in severe dengue fever.[95, 96] Increased levels of these proteins may indicate microvascular thrombosis and end-organ damage.[97]

## 7.6.2 How to Recognize Significant Occult Bleeding?

Bleeding is considered significant when it results in hemodynamic instability. Bleeding from the gums or per vagina, epistaxis and petechiae are common but will usually cease spontaneously and are often not significant.[3] Significant bleeding can a consequence of disseminated intravascular coagulation which usually occurs following prolonged shock and acidosis.[46]

**Suspect significant occult bleeding in the following situations:**

1. Hematocrit not as high as expected, for the degree of shock to be explained by plasma leakage alone. [46]
2. A drop in hematocrit, without clinical improvement, despite adequate fluid replacement [46, 81]
3. Severe metabolic acidosis and end-organ dysfunction despite adequate fluid replacement.[46]

### 7.6.3 Management of Bleeding in Dengue

Mild bleeding such as from the gums, per vagina, epistaxis or petechiae, usually cease spontaneously and do not require blood transfusion.[3] Transfusion of blood and blood components in dengue is indicated when there is evidence of significant bleeding.[46]

Transfusion of blood in patients with significant bleeding

- Transfuse 5 ml/kg of fresh-packed red cells or 10 ml/kg of fresh whole blood at an appropriate rate and observe the clinical response.
- Repeat blood transfusion if there is further blood loss or HCT fails to rise appropriately after blood transfusion.

**Recommendations**

- Patients with mild bleeding such as from the gums or per vagina, epistaxis and petechiae do not require blood transfusion.
- Blood transfusion with whole blood or packed cell (preferably less than 1 week) is indicated in significant bleeding.

### 7.6.4 Management of Upper Gastrointestinal Bleeding

There is no study to our knowledge that has looked at the use of proton pump inhibitor in upper GIT bleeding in dengue setting. Endoscopy and endoscopic injection therapy in upper GIT hemorrhage increases the risk of bleeding and must be avoided.[98]

Generally, most of the GIT bleed will improve after 48-72 hours of the defervescence. Any bleed that persists beyond this time will require further investigation.

**Recommendations**

- Endoscopy and endoscopic injection therapy in upper GIT hemorrhage should be avoided.
- Blood transfusion with whole blood or packed cell (as fresh as is available, preferably less than one week old) is indicated in significant bleeding.

## 7.6.5 The Role of Prophylactic Transfusions in Dengue

Prophylactic transfusion with platelets and fresh frozen plasma does not produce sustained changes in the coagulation status and platelet count in patients with DHF/DSS.[99, 100] Prophylactic transfusion with platelets and fresh frozen plasma does not change or reduce the bleeding outcome in DHF. [50, 99, 100]

Inappropriate transfusion of blood components increases the risk of pulmonary edema and respiratory embarrassment.[99]

**Recommendation**

There is no role for prophylactic transfusion with platelets and fresh frozen plasma to prevent bleeding in the dengue patients.

## 7.6.6 The Role of Adjunctive Therapy in Dengue

There is insufficient evidence to support the use of recombinant activated factor VII in dengue patients with significant bleeding.[101, 102] The coagulation system seems to be over-activated in dengue and infusion of activated factor concentrates may increase the risk of thrombosis.[103]

There is insufficient evidence to support the use of intravenous immunoglobulin[104] and steroids[105] in the management of dengue patients. Likewise, there appears to be no role for the use of Vitamin K and tranexamic acid. However there are anecdotal reports, [106] that demonstrated a dramatic response when pulse methylprednisolone and high dose immunoglobulin G (lgG) was used in the early phase of haemophagocytic syndrome. .

## 7.7 MANAGEMENT IN HIGH DEPENDENCY UNIT (HDU)

The management DSS in high dependency unit (HDU) follows the general principles of management of any critically ill patient in the HDU. However, there are certain aspects which are of particular relevance to the management of DSS. There are several indications for referring these patients for care in HDU. These are listed in the box below. [15, 107, 108]

**Indications for referral to HDU:**

1. Any patient with significant plasma leak – (Patients falling in Algorithm A&B)
    - Pulse Pressure < 30 mm of Hg, Urine output of < 25ml/hour
2. Requirement for respiratory support (non-invasive and invasive ventilation)
3. Significant bleeding
4. Encephalopathy or other complications

### 7.7.1 Indications for respiratory support (non-invasive and invasive ventilation)

The main objectives of respiratory support are to support pulmonary gas exchange and to reduce the metabolic cost of breathing. There is some evidence that respiratory support should be considered early in a patient's course of illness and should not be delayed unnecessarily.[109]

In patients with metabolic acidosis, respiratory support may be considered early despite the preservation of relatively normal arterial blood pH. When PaCO2 is higher than what is expected to compensate for the acidosis, the patient should be promptly intubated.

Formula to calculate the expected PaCO2 = 1.5 x [HCO3-] + 8±2 mmHg

In patients with encephalopathy and GCS of < 9, intubation is often required to protect the airway.[110, 111]

**Indications for mechanical ventilation:**

- Respiratory failure
- Severe metabolic acidosis
- Encephalopathy with GCS < 9

## 7.7.2 Indications for Hemodynamic Support

In dengue, hypotension is usually due to plasma leakage or internal bleeding. Fluid resuscitation is crucial and should be initiated first. However, vasopressor (e.g. dopamine, noradrenaline) **may be considered** when a mean arterial pressure is persistently <60 mmHg **despite adequate fluid resuscitation**. [112]

**CAUTION: While vasopressors increase the blood pressure, tissue hypoxia may be further compromised by the vasoconstriction. Instituting inotropic support without fluid repletion may be detrimental.**

Formula: MAP (Mean Arterial Pressure) = DBP + 1/3 (SBP - DBP)

DBP = diastolic blood pressure; SBP = systolic blood pressure

Volume overload, seen towards the end of the critical phase and subsequently, provokes an important patho-physiological consideration.

It can be argued that in the face of normal cardiac & renal function, it is difficult to overhydrate a person to an extent that pulmonary edema results. Kidneys are very efficient in getting rid of extra volume. Volume over load in the recovery phase of dengue theoretically may be explained by the following:

- Renal status in dengue related volume overload is akin to that of post-surgery patient with poor volume handling.
- Extravasated fluid is protein rich and exerts its own colloidal osmotic pressure thereby retaining fluid in the third space, only to be resorbed through lymphatics. Balance between extravasation and reabsorption may be critical in determining the circulatory volume.

## 7.7.3 Safety and risk – a guideline for invasive procedures

### a. Central venous catheter (CVC) insertion

Volume resuscitation alone would not be a justification for CVC if adequate peripheral intravenous access can be obtained (e.g. 14 – or 16-gauge intravenous catheters). Assuming that the diameter stays equal, peripheral intravenous catheter may provide a better flow rate because of a shorter length.[113]

There are no studies that would, specifically, address the (bleeding) risks of invasive procedures in dengue patients. In general, thrombocytopenia and other bleeding diathesis are relative contraindications for placement of CVC. A high femoral, low internal jugular and subclavian venous punctures are difficult to compress and thereby, confer an increased risk of uncontrolled bleeding. However, studies have shown that there are significant variations (0 - 15.5%) in the risk of bleeding in patients with different coagulopathy.[114, 115, 116, 117, 118]

When CVC is indicated in dengue patients (e.g. poor peripheral venous access, requirement of vasopressors, monitoring of CVP in critically ill and surgical patients) it should be inserted by an experienced operator and under ultrasound guidance if available.[119, 120]

There are multiple insertion sites to choose from: femoral vein, external jugular vein, internal jugular vein, subclavian vein, brachial vein and cephalic vein. However, because the subclavian vein and artery are not accessible to direct compression, the subclavian site is least appropriate for a patient with a bleeding diathesis[121, 122]

**Recommendation**

- Volume resuscitation does not require a central venous catherization (CVC) if sufficient peripheral intravenous access can be obtained.
- When CVC is indicated, it should be inserted by a skilled operator, preferably under ultrasound guidance if available.
- Subclavian vein cannulation should be avoided as far as possible.

### b. Arterial catheter insertion

Intra-arterial cannulation provides additional advantage of continuous arterial pressure monitoring and repeated arterial blood gas sampling. It has a very low incidence of bleeding (1.8 – 2.6%) [123]

**Recommendation**

An arterial catheter should be inserted in DSS patients who require intensive monitoring and frequent blood taking for investigations.

### c. Gastric tube

It is hard to imagine a reason for NG tube in dengue; but if a NG tube is required, the nasogastric route should be avoided. Consider orogastric tube as this is less traumatic.

### d. Pleural tap and chest drain

Intercostal drainage of pleural effusions should be avoided as it can lead to severe hemorrhage and sudden circulatory collapse.[124]

**Recommendation**

Intercostal drainage for pleural effusion is not indicated to relieve respiratory distress. Mechanical ventilation should be considered.