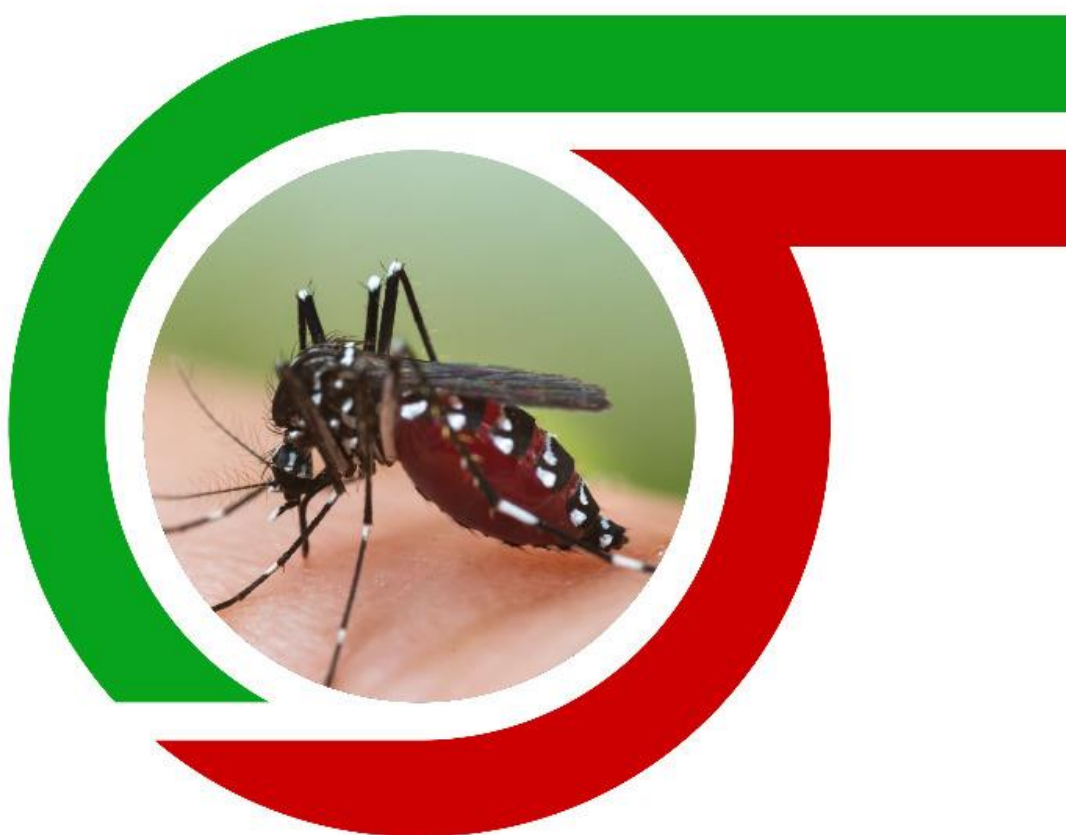




**MINISTRY OF
HEALTH DEVELOPMENT**



National Guidelines

**GUIDELINES ON MANAGEMENT OF DENGUE FEVER &
DENGUE HAEMORRHAGIC FEVER**

October 2022

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Foreword

Recent trends on morbidity and mortality of Dengue illness have caught the attention of people of various walks of life. The in-ward and the outpatient departments of the hospitals of Somaliland are receiving increasing numbers of patients with dengue illness.

This new national guideline on management of dengue fever and dengue hemorrhagic fever in adults, developed by the Case management committee of the Ministry of Health Development is expected to further improve existing knowledge and bridge any gaps on the above topic.

This is intended to reach all levels of the health care services which would lead to reduction in morbidity and prevention of mortality due to dengue illness. I extend my gratitude to each and every one who contributed towards the creation of this guideline.

Special thanks go to D. Mustafa Mohamed Ahmed, Dr. Nasra Yusuf Ahmed and Dr. Abdiaziz Omer Muse for their contribution and development of this guidelines and also deeply appreciates to the Save the Children International (SCI) for their support in the printout of the guideline documents and the following cascade training to health workers across the country.

I hope that this document would have a positive influence on the management of patients with dengue illness.

Director General
Ministry of Health Development

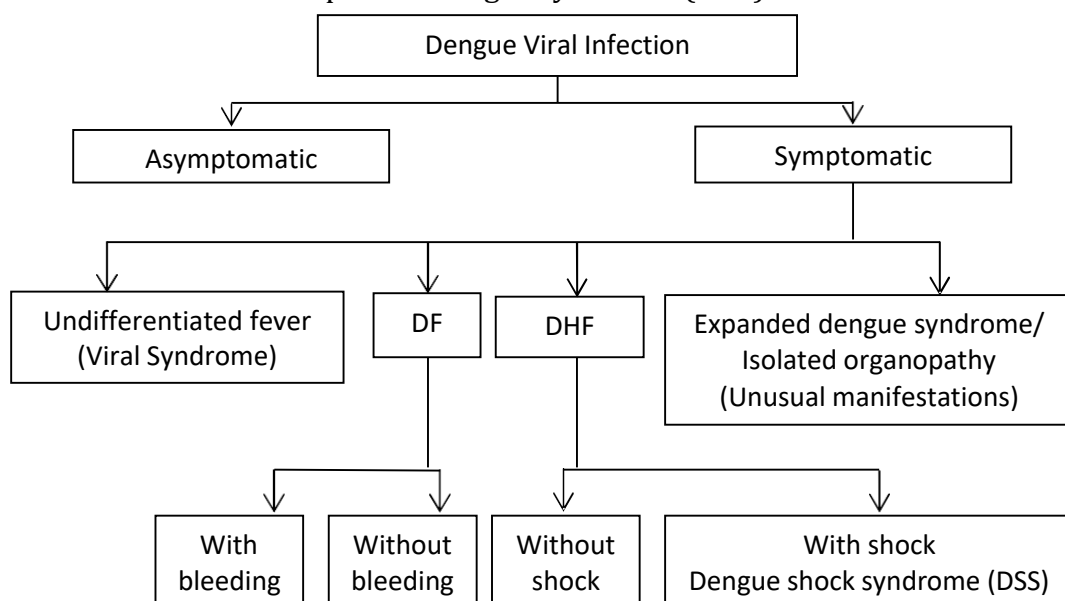
1. Introduction

The clinical course of dengue infection varies from individual to individual and even in the same individual from time to time. This guideline includes new concepts, based on scientific evidence, on the management of Dengue Fever (DF) and Dengue Haemorrhagic Fever (DHF). It emphasizes the importance of early detection of beginning and end of plasma leakage; prevention, early detection and treatment of shock and other complications. Management of special situations such as Dengue in pregnancy and the place for adjunctive treatment in Dengue are also discussed.

2. The Natural Course of the Illness

Many patients infected with dengue virus remain asymptomatic. Others, after an incubation period of 4-7 (range 3-14) days, develop a febrile illness which could turn out to be one of the following.

- Undifferentiated fever
- DF
- DHF
- Expanded dengue syndrome (rare)



Courtesy: comprehensive guidelines for prevention and control of dengue and dengue haemorrhagic fever. Revised and expanded edition. (SEARO Technical Publication Series No. 60) 2011

2.1. Undifferentiated fever

Those who have been infected with dengue virus, especially for the first time (i.e. primary dengue infection), may develop a simple fever indistinguishable from other viral infections.

2.2. Dengue fever (DF)

It is generally an acute febrile illness, with severe headache, myalgia, arthralgia and rashes. Leucopenia and thrombocytopenia may also be observed. Although DF may be benign, it could be an incapacitating disease with severe headache, muscle and joint and bone pains (break- bone fever). Occasionally unusual haemorrhage such as gastrointestinal bleeding, hypermenorrhea and massive epistaxis may occur.

Undifferentiated febrile illness and classical dengue fever can be managed as any other viral fever with symptomatic treatment. However, often it is difficult to differentiate DF from DHF in the early phase (febrile phase) of the illness.

2.3. Dengue haemorrhagic fever (DHF)

DHF is characterized by the acute onset of high fever and is associated with signs and symptoms similar to DF in the early febrile phase. Plasma leakage is the hallmark of DHF which occurs soon after the end of the febrile phase. There is a tendency to develop hypovolemic shock (dengue shock syndrome) due to plasma leakage.

Therefore suspected DF and DHF patients should be closely monitored to identify patients with DHF.

For efficient management of DHF it is important to understand its natural history and its dynamic nature. Clinical course of DHF is stereotypic and consists of three stages

- Febrile phase
- Critical phase (leakage phase)
- Convalescent phase

2.3.1. Febrile phase

Febrile phase is characterized by continuing high fever lasting for 2-7 days. Other features seen in the febrile phase include facial flushing/diffuse blanching erythema of the skin, myalgia, arthralgia, headache, nausea and vomiting. Some patients may have sore throat, injected pharynx, conjunctival injection and diarrhoea. Mild haemorrhagic manifestations can occur. Leucopenia ($WBC < 5000 \text{ mm}^3$) and mild thrombocytopenia ($< 150,000 / \text{mm}^3$) are common in the late febrile phase. Above features are usually indistinguishable between DF and DHF during the febrile phase. However, the presence of tender hepatomegaly favours the diagnosis of DHF.

2.3.2. Critical phase (leakage phase)

The critical phase is heralded by the onset of plasma leakage. This usually occurs towards the late febrile phase, often after the 3rd day of fever, usually around the 5th or 6th day of illness with defervescence (settling of fever). However some patients may enter the critical phase while having high fever.

Plasma leakage is due to increased capillary permeability. **Plasma leakage in DHF is selective and transient and usually lasts for 24-48 hours.** Increased capillary permeability is the result of immune mediators and is not a result of destruction of capillaries. Though the disease is systemic, plasma leakage occurs selectively into the peritoneal and pleural spaces. Pericardial effusion, if there is any, is rather minimal. Generalized or facial oedema, if seen, is more likely to be due to fluid overload rather than due to plasma leakage.

With the leakage of plasma there will be haemo-concentration which will manifest as an increase in HCT. A 20% rise of HCT from the baseline is indicative of significant plasma leakage. (A smaller rise in HCT which may be seen in the early phase of the disease is usually due to dehydration). A rise in HCT less than 20% can be found in patients who received excess oral/I.V. fluids or in patients with bleeding.

Other evidence of plasma leakage are a decrease in serum albumin ($<3.5\text{g/dl}$) and non-fasting serum cholesterol ($<100\text{ mg/dl}$).

The degree and the rate of plasma leakage in DHF can vary. It can be minimal in some patients while in others it can be very significant.

The leak usually starts slowly, increases gradually, slows down and then ceases altogether at the end of leakage phase (usually within 48 hours from the onset).

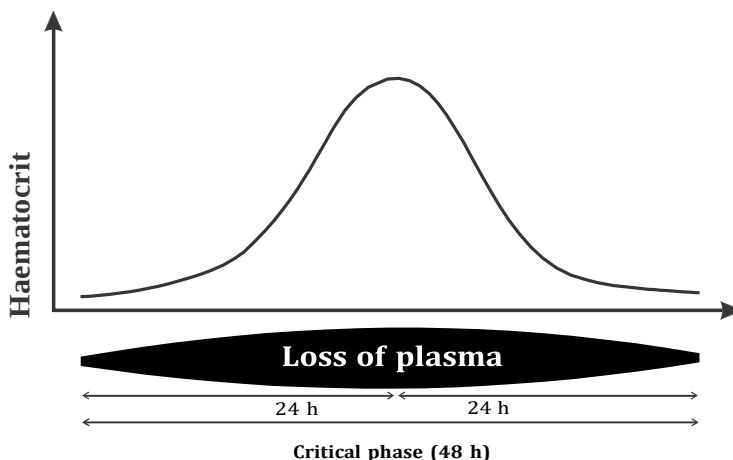


Figure: Fluid leakage in the critical phase

Those who have severe leakage may develop shock when a critical volume of plasma is lost. If the shock is prolonged consequent organ hypo-perfusion will result in progressive organ impairment, metabolic acidosis and disseminated intravascular coagulation (DIC) which often lead to massive bleeding.

Therefore early detection of critical period (onset of plasma leakage) and appropriate fluid management is of paramount importance.

Haemorrhagic manifestations are not essential for the diagnosis of DHF in the presence of objective evidence of plasma leakage (refer page 09). However the term “DHF” is retained because these patients may develop overt or concealed bleeding during the course of illness.

2.3.3. Convalescent phase (recovery phase)

This starts after the end of the critical phase and usually lasts 2-5 days. There will be reabsorption of extravasated fluid during this period.

Features which would suggest that the patient has reached the convalescent phase are:

- Improved general wellbeing and improved appetite
- Appearance of convalescent rash
- Generalized itching (more intense in palms and soles)
- Haemodynamic stability
- Bradycardia (seen in some patients)
- Diuresis
- Stabilization of Haematocrit (HCT) may even be lower than baseline due to reabsorption of extravasated fluid)
- Rise in white cell count followed by a rise in the platelet count.

However, if excessive amounts of intravenous (IV) fluids have been used in the critical phase there could be signs of fluid overload such as respiratory distress due to pulmonary oedema or large pleural effusions.

2.4. Expanded dengue syndrome/ Isolated organopathy (unusual manifestations)

Patients with dengue illness can sometimes develop unusual manifestations such as involvement of liver, kidneys, brain or heart with or without evidence of fluid leakage and therefore do not necessarily fall into the category of DHF. These conditions are very rare and management is symptomatic. Such unusual manifestations may be associated with co-infections and comorbidities. However, these manifestations if seen in DHF patients are mostly a result of prolonged shock leading to organ failure.

3. Diagnosis at OPD Level & by the Primary Care Physician

In the present hyper-endemic setting in Sri Lanka, dengue illness (DF and DHF) should be considered in the differential diagnosis of patients presenting with acute onset of fever **with the following**:

- Headache, especially retro-orbital pain
- Myalgia /Arthralgia
- Rash (diffuse, erythematous, macular)
- Haemorrhagic manifestations (petechiae, positive tourniquet test etc.)
- Leukopenia ($< 5000 /\text{mm}^3$)
- Rising haematocrit of 5 - 10 %
- Platelet count $\leq 150,000 /\text{mm}^3$

4. Criteria for Admission

The first contact physician may decide to admit a patient on clinical judgment. However it is essential to admit patients:

- With a platelet count of $\leq 100,000/\text{mm}^3$
(Platelet count above $100,000/\text{mm}^3$ but below $150,000/\text{mm}^3$ and dropping rapidly may be admitted depending on the circumstances)
- With the following warning signs after day 3 of fever/illness:
 - Abdominal pain or tenderness
 - Persistent vomiting
 - Clinical signs of plasma leakage: pleural effusion, ascites
 - Mucosal bleeding
 - Lethargy, restlessness
 - Liver enlargement $>2\text{ cm}$
 - Increase in HCT concurrent with rapid decrease in platelet count

Other patients who may need admission even without the above criteria are:

- Pregnant mothers
- Elderly patients
- Obese patients
- Patients with co-morbid conditions like diabetes, chronic renal failure, ischaemic heart disease, thalassaemia and other haemoglobinopathies and other major medical problems
- Patients with adverse social circumstances- e.g. living alone, living far from health facility without reliable means of transport.

5. Management of those who do not need Admission

Following treatment measures are recommended:

- Ensure adequate oral fluid intake of around 2500 ml for 24 hours (if the body weight is less than 50kg give fluids as 50ml/kg for 24 hours). This should consist of oral rehydration fluid, king coconut water, other fruit juices, kanji or soup rather than plain water. Exclude red and brown drinks which could cause confusion with haematemesis or coffee ground vomitus.
- Adequate physical rest
- Tepid sponging for fever
- Paracetamol not exceeding 2 tablets six hourly (reduce dose for patients with lower body weights). Warn the patient that the fever may not fully settle with paracetamol and advice not to take excess.
- Anti-emetics and H₂ receptor blockers if necessary
- **Avoid all NSAIDS and steroids**
- Withhold Aspirin, Clopidogrel & Dipyridamole in patients who take these on long term basis

Review daily with Full Blood Count (FBC). **First FBC** should be done at least on the **third day of fever/illness** and daily thereafter if the platelet count is $>150,000/\text{mm}^3$. FBC should be done twice daily if the platelet count is $<150,000/\text{mm}^3$. (However a FBC should be done on the first day of fever in pregnant patients and in patients with co-morbidities).

Note: A normal full blood count or a count suggestive of bacterial infection on the first day of illness does not exclude Dengue illness. Therefore follow up FBCs are essential.

Advise **immediate return** for review if any of the following occur:

- Clinical deterioration with settling of fever
- Inability to tolerate oral fluids
- Severe abdominal pain
- Cold and clammy extremities
- Lethargy or irritability/restlessness
- Bleeding tendency including inter-menstrual bleeding or menorrhagia
- Not passing urine for more than 6 hours

6. In-ward Patients

6.1 Introduction

In-ward patients include patients with DF and patients with DHF. Differentiation between these two is difficult during the initial few days (first three to four days of fever).

The hallmark of DHF is plasma leakage. This is not present in DF. Plasma leakage is the main cause for shock, subsequent bleeding, organ failure and death.

The only way of diagnosing a patient with DHF clinically is the detection of plasma leakage. Therefore the mainstay of in-ward care is:

- **Early detection of plasma leakage (onset of critical phase)**
- **Judicious fluid management to prevent shock and fluid overload**

6.2 Detection of critical phase (onset of plasma leakage)

A white cell count of 5000/mm³ or less with predominance of lymphocytes and a platelet count less than 100,000/mm³ indicate that the patient may enter the critical phase within the next 24 to 48 hours if behaves as DHF. Plasma leakage begins around the transition from the febrile to the afebrile phase. However, some patients may continue to have fever even during the critical phase.

A progressively rising HCT even before reaching a rise of 20%, with other features such as tender hepatomegaly may indicate that the patient is entering the critical period.

Presence of **pleural effusion and ascites** indicates that the patient is already in the critical phase. Pleural effusion detected clinically may not be obvious in a Chest X Ray (CXR)-PA, but may be seen only in a CXR right lateral decubitus film. **Use of a focused ultra sound scan (USS) will help to identify clinically undetectable Pleural effusion and Ascites** (Gall bladder wall oedema may be seen by USS in both DF and DHF. Though it may also be the earliest sign of leaking in DHF; if pericholecystic oedema is not progressing in subsequent USS such patients are likely to have only DF). If appropriate interventions are not adopted early, the patient may progress to develop shock.

6.3 Early detection of shock

- In a patient with features of Dengue haemorrhagic fever **Compensated shock** is defined as circulatory failure manifested by narrow pulse pressure (less than or equal to 20mmHg).
- If there is hypotension (SBP <90mmHg or reduction of SBP by >20% or mean BP <60mmHg) the patient is in **Decompensated shock**. If the blood pressure and pulse is un-detectable the patient is in **Profound shock**.

It is important to detect the patient before going into shock status (During **Pre-shock stage**). If an abnormality is detected even in one vital parameter mentioned in 6.4.3 (eg: Tachycardia, prolong capillary refill time or pulse pressure less than 25mmHg) this might indicate that the patient is progressing towards shock. Therefore, close monitoring, proper assessment and appropriate timely action is essential.

Prevention or early treatment of shock is essential if complications are to be avoided. To detect shock early, observation for following symptoms and signs is important. Hence maintenance of monitoring charts, which help to detect early symptoms and signs of shock, is important in the management of DF/DHF. Please refer to annexure I-III for the monitoring charts.

Symptoms suggestive of Pre-shock/Shock (from 3rd day of illness)

- Sweating
- Abdominal pain
- Persistent vomiting
- Restlessness / altered conscious level
- Postural dizziness
- Decreased urine output (OUP) (<0.5 ml/kg/hour)
- Calculate the urine output in ml/kg/hr, using the same weight used for fluid calculation.

Signs suggestive of Pre-shock/Shock (from 3rd day of illness)

- Cold extremities
- Prolonged capillary refill time >2 seconds
- Unexplained tachycardia
- Increasing diastolic pressure
- Narrowing of pulse pressure ≤ 20 mmHg
- Postural drop ≥ 20 mmHg of systolic blood pressure
- Hypotension (< 20% from patient's baseline or SBP <90mmHg if baseline not known or mean BP 60mmHg)
- Increased respiratory rate

6.4 Monitoring patients during hospital stay

6.4.1 *If the patient is clinically stable on admission and DF/DHF is suspected*

- Chart temperature 4 hourly
- Assess vital signs
- Watch for evidence of bleeding specially malena or bleeding pervagina and quantify.
- Maintain an intake and output chart (annexure I). Fluid balance should be calculated, documented and assessed 6 hourly.
Calculate the urine output in ml/kg/hr, using the same weight used for fluid calculation.
- Do a full blood count on admission and then daily

6.4.2 *When platelet count drops below 130,000/mm³*

Start monitoring using the monitoring chart annexure II.

➤ **The purpose of this monitoring is to detect entry into the critical phase.**

Monitor ;

- General condition, appetite, vomiting, bleeding and other signs and symptoms as in page 10.
- Temperature four hourly
- Vital parameters- pulse, blood pressure (both systolic and diastolic), respiratory rate, and capillary refill time - **three hourly**
- Detailed fluid balance (Annexure I) with:
 - Intake with type and route of fluid
 - Output - urine/vomit/diarrhoea/bleeding (quantify)Fluid balance should be calculated, documented and assessed 6 hourly.
- FBC twice daily
- HCT 6 hourly

6.4.3 *When the patient enters into the critical phase (leakage phase)*

Start monitoring using the monitoring chart annexure III.

➤ **The purpose of maintaining this monitoring chart is for accurate fluid management and early detection of shock.**

Entry into the Critical phase is indicated by evidence of plasma leakage and more frequent monitoring is now necessary.

Monitor,

- Vital parameters- hourly
- Fluid balance chart- assess three hourly
 - Consider introducing an indwelling urinary catheter in*
 - All high risk patients during critical phase
 - Patients in shock
- HCT - three hourly or more frequently

In addition to these, monitor other parameters mentioned in 6.4.2.

6.4.4 If there is evidence of shock (compensated/decompensated)

Vital parameters should be checked every 15 minutes till the patient is haemo-dynamically stable. During intense fluid resuscitation HCT should be checked immediately before and 15 minutes after each fluid bolus and then at least two to three hourly.

If the shock is prolonged (not responding to initial fluid bolus) an indwelling urinary catheter should be inserted and urine output should be measured hourly. Due to fluid extravasation leading to a relative reduction in intravascular volume, the urine output (UOP) is likely to be less than normal. Hence, a UOP of 0.5 ml to 1 ml/kg body weight / hour is adequate during this period. **Overenthusiastic fluid replacement to achieve a higher UOP may lead to fluid overload.**

Liver profile, blood sugar, serum calcium, serum electrolytes, serum creatinine, clotting profile and venous blood gases should be done in complicated cases such as prolonged shock, not responding to adequate fluid resuscitation, liver failure and renal failure.

6.4.5 In convalescent phase

Look for features of improvement (Refer page 05). Watch for symptoms and signs of fluid overload such as periorbital oedema, cough, wheeze and tachypnoea, rise of both systolic and diastolic blood pressures with widening of pulse pressure, basal crepitations and rhonchi. Urine output is usually high during this phase. Some patients may develop bradycardia which is usually asymptomatic and transient. Therefore, continue to monitor vital signs and maintain intake and output chart.

6.5 Management of in-ward patients

6.5.1 Febrile phase with platelet count more than 100,000/mm³

Management of this phase is essentially similar to outpatient management except for the addition of intravenous fluids. IV fluids may be indicated in patients who are unable to take adequate oral fluids, or in patients with diarrhoea or vomiting.

Type of I.V. fluid should be Normal Saline or Hartmann's solution. The total amount of fluid (both I.V. and oral) should be limited to 2500 ml for 24 hours for an average adult (2 ml/Kg/hr upto a maximum of 50 Kg of weight). However, if there is vomiting or diarrhoea this amount should be increased and dehydration should be corrected.

It should be emphasized that over-hydration during this phase will not prevent patients developing shock in the Critical phase. In fact it may cause fluid overload during the Critical phase.

6.5.2 When the platelet count drops below 100,000/mm³

18 G (green) cannula should be inserted and an intravenous infusion of normal saline or Hartmann's solution should be started. Fluid intake per hour should be about 100ml (IV and oral) for an average adult of 50kg or more. If the body weight is less than 50kg maintenance fluid should be given (2ml/kg/hour).

Total (both oral and I.V) amount of fluid intake should be about 2500ml per day for an average adult unless the patient has vomiting / diarrhoea.

6.5.3 When the patient is in the critical phase (leakage phase)

The fluid requirement, **both oral and intravenous, in critical phase (48 hours)** is calculated as **M+5% (maintenance + 5% deficit)**. Maintenance (M) is calculated as follows:

- For the 1st 10 kg -100 ml/kg
- For the 2nd 10 kg - 50 ml/kg
- From 20 kg and above up to 50 kg - 20 ml/kg
- 5% deficit is calculated as 50 ml/kg up to 50kg

Example of fluid calculation for a 65 kg person (maximum body weight for fluid calculation is 50 kg)

- For the 1st 10 kg - 100 ml/kg = 1000 ml
- For the 2nd 10 kg - 50 ml/kg = 500 ml
- From 20 kg and above up to 50 kg -20 ml/kg = 600 ml
- 5% deficit is calculated as 50 ml/kg up to 50 kg = 2500 ml

Therefore the **maximum fluid** requirement for an **average adult** for the entire phase of critical 48 hours is **4600 ml**.

If the body weight is less than 50 kg, calculation should be done according to the ideal body weight or actual body weight whichever is less.

Fluid quota is aimed at giving just adequate amount of fluid to maintain perfusion to vital organs without causing fluid overload. Once the fluid quota is exceeded chances of fluid overload is high. All patients will not need the full fluid quota of M+ 5% and some may need less than this.

The recommended intravenous fluid is **normal saline or Hartmann's solution**. Oral fluids should consist of electrolyte solutions such as king coconut water, other fruit juices, oral rehydration fluid and kanji. **Drinking plain water should be minimized.**

How this volume should be infused during the critical period depends on the haemo-dynamic status of the patient.

If the patient is haemo-dynamically stable (non-shock), but in the Critical (leaking) phase this volume (M+5%) could be spread over 48 hours. However this volume should not be given at a uniform rate. The volume given should be just sufficient to maintain an effective circulation during the period of plasma leakage as too much fluid could lead to fluid overload.

In keeping with the dynamic nature of the leakage, fluid should be started at a slower rate. The rate of fluid should be increased in a step wise pattern, guided by HCT and other parameters. Since plasma leakage does not persist at a higher rate for more than a few hours, it is necessary to reduce the rate of fluid intake in a step wise pattern again. Urine output should be maintained at 0.5-1 ml/kg/hour (Calculate the urine output in ml/kg/hr, using the same weight used for fluid calculation) and pulse pressure around 30mmHg during the entire critical period.

It should be emphasized that the HCT is a guide for fluid management. Trying to normalize the HCT will generally result in fluid overload.

Given above is the general pattern of fluid leakage during the critical phase. It is important to note that there are individual variations of leakage. In rapid leakers peak of the leakage will be reached much earlier (before 24 hours). In slow leakers peak of the leakage will be reached much later (after 24 hours).

If the patient has signs of Pre-shock (refer 6.3) rate of fluid should be increased to maintain the vital parameters stable. However a rate as high as 7ml/kg/hr is only very rarely needed and even rates as high as 5ml/kg/hr if needed will only be needed for a short period (usually less than a couple of hours) in a very large majority of patients.

6.5.4 If a patient presents with shock/goes into shock while in ward

In any patient presenting with shock Dengue Shock Syndrome should be considered as a differential diagnosis in the present context of hyper-endemicity. Fluid therapy in an in-ward DHF patient is aimed at giving just sufficient volume to maintain an effective circulation during the leaking period thereby preventing patient from going into shock.

If the volume given is inadequate or if the leak is very rapid, the patient may go into shock. Close monitoring and appropriate fluid therapy is aimed at preventing this from happening.

In a patient with shock a blood sample should be collected for measurement of HCT as soon as possible.

- IV fluid should be started as a bolus. Usually with this the blood pressure and the peripheral circulation improves. Since the fluid leakage continues at a high rate during this period it should be matched by a high infusion rate of intravenous fluids. Therefore, the fluid bolus should be followed by high initial rate of I.V. fluid, which should be reduced gradually in a step wise manner.
- If the initial HCT is low or normal the shock is due to significant concealed haemorrhage with or without plasma leakage. Therefore such patients need urgent blood transfusion.

The initial rate of fluid replacement depends on whether the patient is in shock with narrow pulse pressure (compensated shock) or in hypotensive / profound shock (Refer flow algorithms).

The rate of I.V. fluid given should be adjusted according to the clinical status, pulse pressure (and other vital signs), urine output and serial HCT.

The amount of fluid given during and after shock depends on how much the patient has received prior to onset of shock in the critical phase. If the patient has been managed in the hospital and the onset of the Critical phase has been identified the volume of fluid already given would be known.

In a patient who arrives from home or transferred from another institution and found to be in shock on admission, every effort should be taken to find out how much fluid was given during the preceding 12-24 hours. This is because the critical phase would have started 12-24 hours prior to the detection of shock in such a patient. This fluid amount should be subtracted from M+5% and only the balance amount of fluid should be given for the next 24-36 hours.

Hence, it is important for all transferred patients from smaller hospitals to have this information clearly mentioned in the Transfer Forms

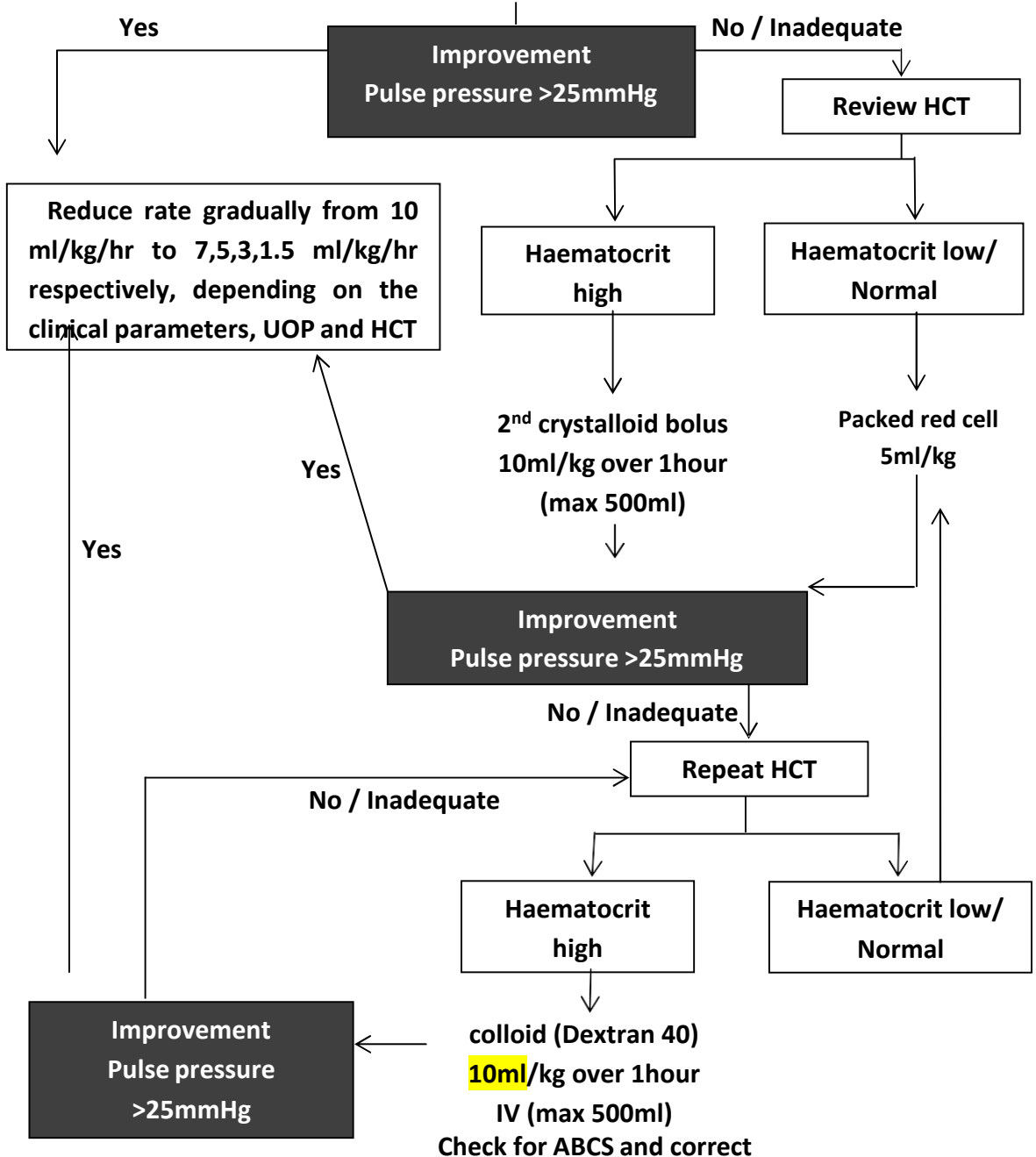
SHOCK WITH NARROW PULSE PRESSURE (COMPENSATED SHOCK)

Oxygen via face mask or nasal catheter

Take blood for HCT

Immediate volume replacement: Initiate IV therapy

10ml/kg/hr isotonic crystalloid solution for 1 hour



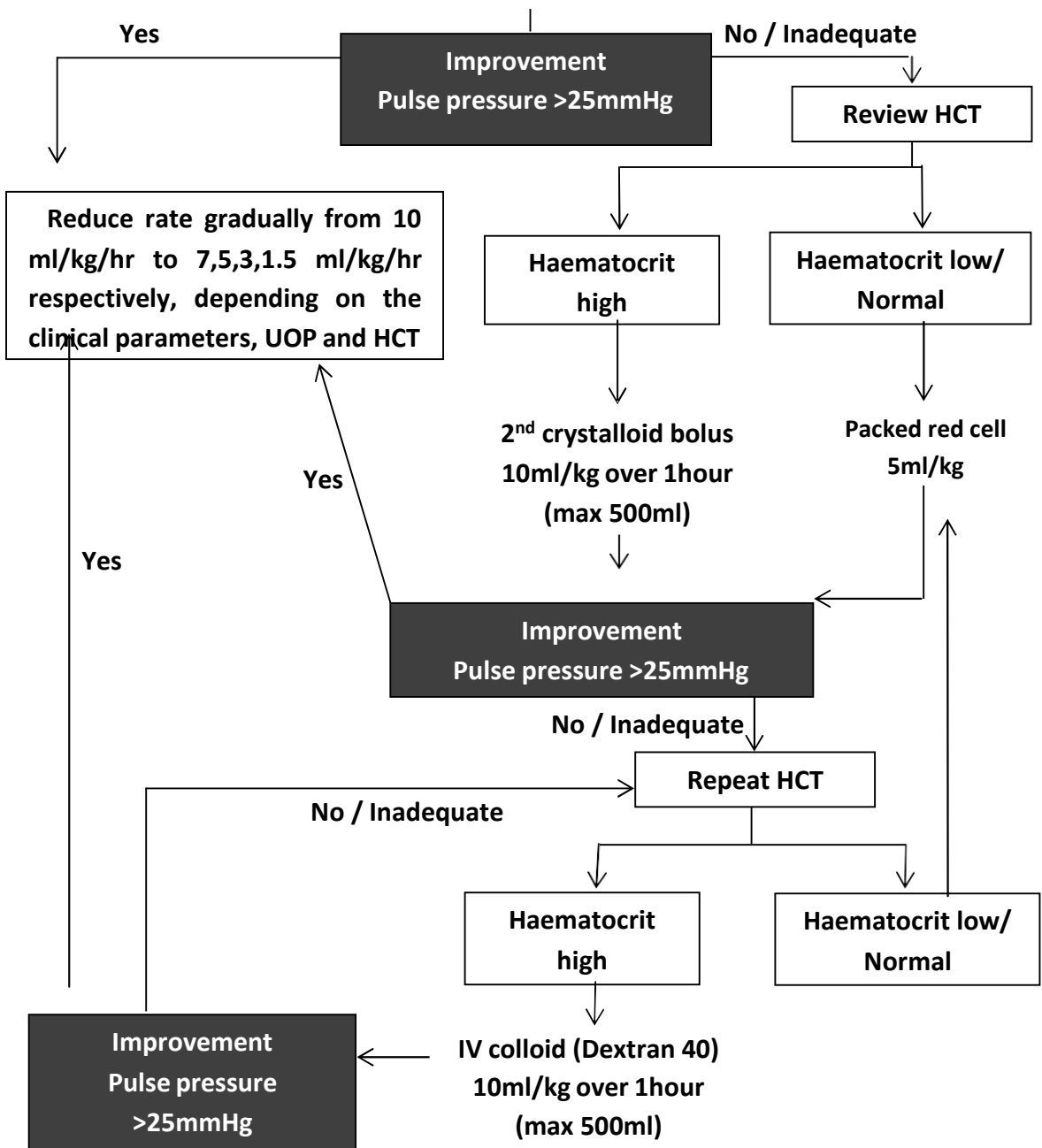
ABCS A- Acidosis B- Bleeding C- Calcium S- Sugar (refer 6.7)

Calculate the urine output in ml/kg/hr, using the same weight used for fluid calculation.

DECOMPENSATED OR PROFOUND SHOCK

Rapid bolus of 10ml/kg crystalloid

(Free flow until pulse palpable and BP recordable)



ABCS A- Acidosis B- Bleeding C- Calcium S- Sugar (refer 6.7)

Calculate the urine output in ml/kg/hr, using the same weight used for fluid calculation.

In all patients with shock –

Call for help; ensure adequate oxygenation, Keep flat/head low

6.5.5 *Fluid over-loaded patient*

A patient may become over-loaded with fluid while in the ward or may be transferred from another unit in an over-loaded state due to over-enthusiastic treatment with IV fluid (too much oral fluid also can contribute to this). Hypotension and moderately high HCT due to dehydration (in the febrile phase) may lead to the misdiagnosis of shock in the Critical phase and fluid resuscitation in such a situation also may lead to over-hydration.

Features of fluid overload

- Early signs and symptoms include puffy eyelids, distended abdomen (ascites), tachypnoea, mild dyspnoea.
- Late signs and symptoms include all of the above, along with moderate to severe respiratory distress, shortness of breath, wheezing, crepitations and low oxygen saturation which are also early signs of interstitial pulmonary oedema. Restlessness/agitation and confusion are signs of hypoxia and impending respiratory failure.

Fluid over-loading should be treated according to the haemo-dynamic status and the HCT of the patient.

- If the patient is in shock or has features of fluid overload (**haemo-dynamically unstable**) and has high HCT, a bolus of colloid (dextran 40 or Tetrastarch) should be given as 10 ml/ kg (500 ml for an average adult) over an hour. In the midway of the bolus, frusemide 10-20mg should be given. Frusemide can be repeated if necessary
- If the patient is in shock (**haemo-dynamically unstable**) and has a normal or low HCT, immediate blood transfusion is necessary. Until blood is available, a bolus of colloid (500 ml of Dextran 40 or Tetrastarch) could be administered.
- If the patient is **haemo-dynamically stable** and has a normal or low HCT, fluid should be restricted and the patient should be monitored carefully, as the patient is likely to improve within hours. The most probable reason for low haematocrit is haemo-dilution. However consider the possibility of concealed bleeding and reserve blood to transfuse if the patient becomes unstable. If the patient develops features of pulmonary oedema, frusemide 10-20mg should be given intravenously. This dose can be repeated after half an hour.

- If the patient is **haemo-dynamically stable** and has high HCT, fluid should be restricted and patient should be monitored carefully. It is likely that the patient will go into polyuric phase and the HCT will settle within several hours.
- In a patient with evidence of fluid overload and poor peripheral circulation consider therapeutic aspiration if there is gross ascites or massive pleural effusion.

Rarely, severe ascites can cause abdominal compartment syndrome. (This should be suspected if the abdomen is very tense even without distension). Drainage of ascitic fluid, in addition to transfusion of colloids, may be indicated if this causes impairment of venous return or interference with renal function.

6.6 Options of Fluid for Resuscitation

6.6.1 *Crystalloids:*

Normal saline or Hartmann's solution, should be used for initial fluid resuscitation

6.6.2 *Colloids:*

Only hyper-oncotic colloids are effective. They are used only as boluses of 10 ml/kg/hour. It is recommended to use Dextran 40. If Dextran 40 is not available or maximum quota of Dextran 40 is used Tetrastarch (6% starch solution) can be used.

These can be used:

- In patients who present in shock and fluid overload
- In patients whose shock does not respond to two boluses of crystalloids with rising HCT or still high HCT
- In patients who are being treated for shock, and has high HCT and whose fluid quota (M+5%) is nearing completion

As dextran can sometimes interfere with cross matching, blood should be drawn for grouping and cross matching before starting on dextran (However this may defer when using newer technique for cross-matching). The maximum amount of dextran for 24 hours is 3 boluses of 500 ml/hour (10 ml/kg/hour). The maximum of Tetrastarch is 5 boluses of 500 ml/hour (10 ml/kg/hour) in 24 hours.

Note: colloids should not be used in a dehydrated patient who presents with shock and high HCT, until the hydration is corrected with crystalloid

Refer algorithms in page 17 and 18 also

6.7 ABCS

If the patient is not responding to two boluses of crystalloid, contributory causes for shock other than plasma leakage should be considered. These are,

Acidosis *check venous blood gas (if present, check liver and renal profiles)*

Bleeding *check HCT*

Calcium and other electrolytes (sodium and potassium) - *check serum*

Sugar *check random capillary blood sugar*

It is important to correct these conditions as quickly as possible. If the patient is clinically acidotic one dose of 50 ml of 8.4% sodium bicarbonate may be given empirically if blood gas cannot be assessed.

Empirical treatment with 10% calcium gluconate 10 ml over 10 minutes is justifiable if a patient is in shock and is not responding to adequate fluid replacement, this may be continued six hourly. IV calcium gluconate may be used in patients who show evidence of myocardial involvement as well, as hypocalcaemia is common in DHF patients and calcium may improve the myocardial contractility in such patients.

If the blood glucose level is less than 70 mg/dl correct it by giving 15 – 20g glucose orally or intravenously. At the time of shock, use 30–40 ml of 50% Dextrose (15-20g) intravenously. Re-check capillary blood sugar in 15 minutes and if it is less than 70 mg/dl repeat 30- 40ml of 50% Dextrose intravenously.

6.8 Indications for Blood Transfusion

Bleeding, if occurring during the early phase of DHF, is usually due to drugs, such as NSAIDs. Bleeding during the critical phase is usually due to DIC and liver failure which occurs as a consequence of prolonged shock causing multi-organ dysfunction.

Even without these causes bleeding can occur during the critical period and can be the main reason for shock or contribute to development of shock.

If there is significant overt bleeding (e.g. haematemesis, malena, bleeding per vagina etc.) of more than 6-8 ml/kg body weight, blood transfusion is necessary.

However, bleeding could be concealed. Suspect significant concealed bleeding in the following situations and transfuse blood early:

- Haematocrit not as high as expected for the degree of shock to be explained by plasma leakage alone. (Hypotensive shock with low or normal HCT)
- A drop in HCT without clinical improvement despite adequate fluid replacement (40-60 ml/kg).
- Hypotension (refer page 10) not responding to fluid therapy
- Severe metabolic acidosis and end-organ dysfunction despite adequate fluid replacement.

Note:

- Blood grouping and DT are essential in patients with above features.
- Concealed bleeding should be suspected if there is unexplained tachycardia.
- The haemoglobin level may remain normal initially despite significant blood loss.
- 5 ml/kg of packed red cells can be given at a time. HCT is expected to rise by 5 points (e.g. from 30 to 35) with this amount of blood.

6.9 Indications for Haemodynamic Support

In dengue, hypotension is usually due to plasma leakage or internal bleeding. Fluid resuscitation is crucial and should be initiated first. However, vasopressors (e.g. dopamine and noradrenaline) may be considered when the mean arterial pressure is persistently <60 mmHg despite adequate fluid resuscitation (40-60 ml/kg). Intra-arterial blood pressure monitoring or at least central venous pressure monitoring, if possible, would be very useful in this situation.

Caution: While vasopressors increase the blood pressure, tissue hypoxia may be further compromised by the vasoconstriction.

End of critical phase is indicated by stable vital signs, returning of HCT to normal along with clinical improvement and diuresis.

7. Management of Hepatic Encephalopathy in DHF

Mild to moderate rise of liver enzymes (SGOT, SGPT) is a common finding in DF and in DHF. This does not warrant any specific treatment. Higher rise of liver enzymes is usually due to ischemic hepatitis caused by prolonged shock. If there are no features of hepatic encephalopathy, no specific treatment is indicated in these patients. If there are features of encephalopathy (with or without features of coagulopathy) such patients should be treated as for liver failure with the following:

- Maintain adequate airway and oxygenation
 - Infuse minimal intravenous fluids sufficient to maintain intravascular volume (80% of maintenance)
 - Use hyper-oncotic colloid solution early if HCT is increased
 - Infuse Mannitol to reduce intracranial pressure if renal functions are normal
 - Take measures to maintain serum sodium in-between 145-155 meq/L. (3% hypertonic saline may be of use if Mannitol cannot be used, and if serum sodium is very low)
 - Maintain blood sugar above 60 mg/dl
 - Give a single dose of Vitamin K 10 mg IV
 - Give Lactulose to maintain 3-4 bowel motions per day. However, lactulose commonly causes gaseous abdominal distension and this may interfere with respiration in these patients and may even cause aspiration
 - Treat with broad spectrum antibiotics, which are not excreted through liver, if secondary bacterial infection is suspected (Cefotaxime is preferred)
 - Oral Metronidazole may be used (supportive evidence is limited)
 - Ventilate (IPPV) early, if the features of encephalopathy are getting worse
- *Fresh Frozen Plasma (FFP) should not be used routinely, but may be used if there is active bleeding or prior to invasive procedures. (However, be aware of possible fluid overload with FFP)*
- *Bowel washes and enemas should be avoided*

There is no evidence to support the use of L- Arginine L-Ornithine (LOLA) or N-Acetyl Cysteine (NAC) in these patients and therefore, use of which is not recommended.

8. Dengue in Pregnancy

Admission on the second day of fever and close follow up with FBC daily is very important

The gestation and the phase of dengue are important factors in determining the management. A multi-disciplinary team consisting of obstetricians, physician, anaesthetist and the paediatrician should get involved in the management. When a febrile patient is first seen, look for symptoms and signs of dengue fever and admit if suspected. All patients with fever more than 24 hours without a definite cause should be advised to get admitted to hospital. If admitted to the obstetric ward urgent referral to the physician is essential. Explanation to the family members about the course of DHF and the management is important.

The signs, symptoms and lab investigations may be confused with other complications of pregnancy such as toxemia and HELLP syndrome (Haemolysis, Elevated Liver Enzymes and Low Platelets). It is essential to consider the possibility of dengue in a patient with features of HELLP (Page 6). Increased incidence of abruptio placentae, death in-utero and prematurity are reported.

The normal physiological changes in pregnancy make the diagnosis and assessment of plasma leakage difficult. Therefore, the following baseline parameters should be noted as early as possible on the first day of illness. Subsequent management will be based on the changes of baseline levels.

- Pulse, blood pressure (BP), pulse pressure. (Baseline BP is often lower and pulse pressure wider & heart rate may be higher)
- FBC - (Haemoglobin, HCT & platelet count may be lower than in non-pregnant patient)
- SGOT/SGPT

Clinical detection of pleural effusion and ascites may be difficult due to the presence of gravid uterus.

Use of Ultra Sound Scan to detect the following, is advisable

- Pleural effusion
- Ascites

(Note: Gallbladder wall oedema may be seen in both DF and DHF)

There are very few studies addressing the management of dengue in pregnancy. Generally the presentation and clinical course of dengue in pregnant women is similar to that in non-pregnant individuals. The fluid volume for the critical period (M+5%) for a pregnant mother should be calculated (Page 13) based on the weight prior to pregnancy.

8.1 Management of pregnant patients with DF/DHF close to delivery

Risk of bleeding is at its highest during the period of plasma leakage (critical phase). Therefore,

- Unless to save mothers life, avoid Lower Segment Caesarean Section (LSCS) or induction of labour during the Critical (plasma leakage) phase.
- Obstetric procedures (such as amniocentesis or external cephalic version) should be avoided during the illness.
- If obstetric procedures are to be undertaken,
 - Maintain the platelet count above 50,000/mm³
 - Single donor platelet transfusion is preferred, if available, if platelet transfusion is necessary
- If patient goes into spontaneous labour during critical phase take steps to prevent vaginal tears by performing an episiotomy.
- In a case of fetal compromise priority should be given to the mother's life and decision making should involve the multi-disciplinary team.
- Counseling the family on the probable outcome is essential.

8.2 Management of patients with DF/DHF during immediate postpartum

Dengue fever should be suspected in patients having fever in the immediate post-partum period since this may be overlooked. Early referral to a physician is recommended.

9. Myocardial Involvement in Dengue

Global dysfunction of myocardial contractility may be seen in DHF patients who are in prolonged shock and the most likely reason is metabolic acidosis. However hypocalcaemia (which is a common finding in DHF patients with moderate to large pleural effusion / ascites) should be considered as well.

Hence, if there is evidence of cardiac dysfunction, acidosis and hypocalcaemia should be corrected quickly

Empirical treatment with calcium is justifiable if clinically indicated. Myocarditis is an uncommon finding in Dengue and is very unlikely to cause death in a patient with DHF. However, such a patient could easily develop pulmonary oedema with fluid overload.

Therefore, if myocardial Involvement is suspected fluid should be given very carefully

Treatment of myocardial Involvement is symptomatic.

10. Place of Adjunctive Therapy in the Management of DHF

10.1 Platelet transfusion

Prophylactic transfusion with platelets does not produce sustained changes in the coagulation status and platelet count in patients with DHF. It does not change or reduce the bleeding outcome in DHF either. On the other hand, platelet transfusions can lead to fluid overload resulting in pulmonary oedema causing respiratory embarrassment and allergic reactions including anaphylaxis.

Therefore, prophylactic transfusion of platelets is not recommended

However, platelet transfusions may be required in a patient with thrombocytopenia who is to undergo an urgent surgery, has active bleeding which continues in spite of repeated blood transfusions, DIC or in patients with intracranial haemorrhage.

10.2 Fresh frozen plasma transfusion

Like platelet transfusions, prophylactic FFP transfusions do not produce sustained changes in the coagulation status, and therefore, does not change or reduce the bleeding outcome in patients with DHF/DSS. Like platelet transfusions, FFP transfusions can also lead to fluid overload.

In addition, transfusion of blood products can produce anaphylactic reactions and transmission of blood borne diseases like HIV, Hep B etc.

Therefore, prophylactic transfusion of FFP is not recommended.

However FFP may be useful in a Dengue patient with hepatic encephalopathy and has active bleeding.

10.3 Steroids and I.V. immunoglobulin

There is no evidence to support the use of intravenous immunoglobulin or steroids in the management of dengue patients.

Therefore, use of steroids (hydrocortisone, dexamethasone and methylprednisolone) and / or immunoglobulin is not recommended.

10.4 Recombinant Factor VII

There is no evidence to support the use of recombinant factor VII in DHF patients with bleeding due to prolonged shock, DIC or multi-organ failure. Therefore, use of this as the treatment of bleeding in DHF due to such conditions is not recommended. Recombinant factor VII is useful only in patients who have massive bleeding due to a specific cause such as bleeding peptic ulcer or bleeding from a specific place in the nose prior to surgical intervention. This helps to buy time for the specific surgical treatment like banding, cauterization etc. It should be used only if definite plans are there for surgical intervention as the arrest of bleeding with recombinant factor VII is only temporary.

10.5 Antibiotics

There is no evidence to support prophylactic use of antibiotics in DF or DHF patients with low white blood cell count (WBC). It is also known that the low WBC is a very transient phenomenon. By the time the WBC is at its lowest, the marrow is already hyperplastic.

Therefore, there is no place for the use of prophylactic antibiotics during the first 4-5 days of fever if Dengue is suspected, even in the presence of pleural effusion or ascites.

10.6 Frusemide

Intravenous frusemide (10-20mg) could be used in the following circumstances:

- In fluid overloaded patients who are haemodynamically stable
- In fluid overloaded patients who are haemodynamically unstable in the midway of a colloid infusion or a blood transfusion during the critical phase

10.7 Tranexamic acid

Bleeding per vagina, either menstrual, intermenstrual or premenopausal can be excessive in DHF. Hence those who have such bleeding may be started on tranexamic acid 500mg - 1 gram eight hourly.

Tranexamic acid can also be used together with proton pump inhibitors in Gastric bleeding in DHF.

10.8 Calcium gluconate

Empirical treatment with 10% calcium gluconate 10 ml over 10 minutes may be considered in patients with DHF as hypocalcaemia is a common finding.

11. Dengue in Co-morbid Conditions

Dengue infections in patients with underlying diseases or co-morbid conditions can be severe and may lead to more complications or even death if not managed properly during the early Febrile Phase. Making an early diagnosis of dengue illness in such patients will be challenging. Therefore, early suspicion and close follow-up is important.

Given below are specific issues associated with the management of co-morbidities:

11.1 Liver Disease:

Baseline liver function tests (LFT) including prothrombin time (PT) is of value when dengue is suspected in patients with chronic liver disease. If AST/ALT is very high the patient is likely to develop neurological involvement (Hepatic Encephalopathy) especially in those with gastrointestinal (GI) bleeding. In such patients liver failure regime should be used early (refer page 23). If baseline albumin level is low these patients may have more plasma leakage. Managing these patients with the minimum amount of IV fluids to maintain intravascular volume in order to prevent respiratory distress (acute pulmonary oedema) and/or heart failure is crucial. Prolonged PT or INR (>1.3) indicates that these patients have a tendency for more bleeding and therefore Vitamin K1 IV is recommended. In addition, assessment of the degree of bleeding and transfusing adequate amount of blood and blood components are important considerations.

11.2 Heart Disease:

The key consideration in patients with heart diseases would be to identify the underlying heart disease and the current medication. These patients should be observed carefully with close and continuous monitoring preferably echocardiography especially during the critical phase. Careful adjustment of IV fluid is the key to success and to prevent complications. Those who are on anti-platelet or anti-coagulation therapy are recommended to stop the medication for a few days especially during the critical phase.

11.3 Renal Disease:

The baseline renal function tests (Blood Urea, Creatinine), electrolytes, acid-base balance, GFR, urine output per day and urine analysis should be performed during the early febrile phase and regularly tested during the course of the illness. Close monitoring of fluid intake and urine output is very important. Fluid overload during convalescent phase is the most important cause of death among these patients. Early consultation with a Nephrologist and early planning of any renal replacement therapy in those patients who are oliguric with signs and symptoms of fluid overload is important.

11.4 Diabetes Mellitus:

Frequent monitoring of blood sugar is important from the time the patients are admitted to hospital. All anti-diabetic drugs have to be switched to insulin in order to keep blood sugar level preferably below 150-200mg/dl. Closely monitor the patient and look for the possible development of Diabetic Ketoacidosis where patient will need more IV fluid, IV insulin as an infusion and monitoring of central venous pressure if possible. Manage the commonly associated conditions with DM, e.g. hypertension.

12. Transferring a patient to another Institute

Facilities in some peripheral hospitals may not be adequate to manage a patient in DHF who has entered the critical phase. Furthermore, a patient in prolonged shock needs to be managed in an intensive care unit. Hence, such patients may be transferred to an institution with adequate facilities.

If the patient has signs of shock (ie Tachycardia, low blood pressure (pulse pressure 20 and cold extremities etc.) normal saline bolus of 10ml/kg over one hour (for an average adult – 500ml) is recommended before referral. Check capillary blood sugar (CBS) for hypoglycaemia and correct with oral or IV Dextrose before referral. IV fluids and oxygen inhalation should be continued during the transfer.

Every such transfer should be done after obtaining advice from the Consultant Physician who will be receiving the patient and after resuscitating in accordance with the advice.

Proper resuscitation before transferring is especially important if the journey is going to take long. Adequate information regarding the patient should be provided in the transfer form and this should include daily fluid balance, investigation results and treatment given. Also, it is important to send copies of the temperature and monitoring charts.

13. Discharge

The following criteria should be fulfilled before discharge from hospital.

- No fever for at least 24 hours without the usage of antipyretic drugs
- At least two days have lapsed after recovery from shock
- Good general condition with improving appetite
- Normal HCT at baseline value or around 38 - 40 % when baseline value is not known
- No distress from pleural effusions
- No ascites
- Platelet count has risen above 50,000 /mm³
- No other complications

14. Laboratory Diagnosis

Laboratory diagnosis of dengue is achieved by isolation of the virus, detection of antigen or genome or by detection of antibodies. Dengue virus can be isolated from blood sample collected during the first 4 -5 days of illness or from necropsy tissue samples. Virus isolation and typing is mainly used in research and surveillance.

Detection of genome by PCR from blood or from tissue specimens can be performed during the acute phase of the illness and used in routine diagnosis as well as in research and surveillance. However the cost of the assay and the availability of facilities limit the wide use of it in clinical practice. Dengue serotypes can be identified in both virus isolation and detection of genome.

Detection of NS-1 antigen from blood is another test which can be performed during the first 4 - 5 days of fever. ELISA format and Rapid Immune-chromatographic format is available commercially. ELISA format has a better sensitivity and specificity but rapid test has the advantage of an individual assay. Sensitivity of these tests varies depending on the antigen and other constituents used and ranges from 60-90%. Therefore a negative test result will not exclude dengue illness and treating the patient on clinical grounds is important.

Detection of Dengue IgM, IgG or both is performed on blood samples collected after the 5th day of illness. Range of assays both ELISA format and Rapid Immune-chromatographic format with varying sensitivity and specificity are available. They can be either in-house assays or commercial assays. ELISA assays, Immune-chromatographic assay and Haemagglutination inhibition assay are widely used in routine diagnosis, in research and surveillance. Use of rapid immune-chromatographic assays either as single or as combo assays is becoming popular as point of care assays / bedside assays.

Isolation of the virus, detection of antigen or detection of genome or detection of four fold increase in antibodies (seroconversion) confirms the diagnosis of dengue. Detection of IgM antibody or high titre IgG antibody is highly suggestive of dengue infection.

15. Outbreak Response Plan for Hospitals

There have been an increasing number of dengue outbreaks in many parts of the country. Therefore, having a hospital emergency response plan for dengue outbreaks is vital in early diagnosis and appropriate clinical management of cases to minimize complications and deaths.

Such a plan should include the following key elements:

- Outpatient care (with triage and resuscitation areas)
- Assess bed occupancy in each unit (with a view to identifying additional beds during outbreaks)
- High-dependency care beds
- Staffing and surge capacity needs
- Stock management of essential medicines and supplies
- Laboratory facilities

As the first step, with the available resources, hospitals should develop and strengthen their capacity to screen and triage suspected dengue patients at the outpatient departments.

Hospital staff including doctors, nurses and other categories should be trained and assigned appropriate duties in case of an outbreak. It is essential to conduct regular training for medical staff based on the current guidelines on clinical management of dengue fever and dengue haemorrhagic fever.

Following essential medicines, supplies, equipment and services should be available in the hospitals providing in-ward care for patients with dengue haemorrhagic fever:

Medicines:

- Paracetamol tablets
- Oral Rehydration Solution
- I.V. Fluids –
Crystalloids: 0.9% saline
Colloids: hyper-oncotic (plasma expanders) - 10% Dextran 40 & 6% starch
- 25% or 50% Dextrose
- Parenteral Vitamin K
- IV Calcium Gluconate (10% solution)
- IV KCl (20 or 40 mmol concentrated solution)
- IV Sodium bicarbonate (8.4% solution)

Supplies and equipment:

- Thermometers
- Sphygmomanometers
- I.V. access sets
- Oxygen delivery systems
- Micro centrifuge (for bedside haematocrit assessment)
- Microscopes (for platelet count estimation)
- Glucometers (for blood sugar estimation)
- Observation charts

Laboratory support:

Laboratories should be equipped round the clock for basic tests such as FBC, count.

More complicated patients will need blood sugar, liver function tests, renal function tests, serum electrolytes (including serum calcium), blood gases, coagulation assays, chest x-rays & ultrasonography. haematocrit, platelet count, white blood count (WBC), and differential

Blood Bank:

Packed red cells and other blood products should be available on demand.

Annexure I
In Dengue suspected patients from the time of admission
Intake and Output Chart

Name of the Patient:..... BHT No:..... Age: Ward:.....

[illegible]

Note - Calculate the fluid balance every 6 hours and document

Annexure II

Observation chart for management of Dengue in Adult patients without evidence of fluid leakage

Monitoring should be started at platelet count of $\leq 130,000/\text{mm}^3$

Instructions - Do FBC daily/bd and PCV 6 hrly. Monitor other parameters 3 hrly.

Indications to call for immediate advice

1. Pulse rate > 120/min with fever or >100/min without fever.
2. Pulse Pressure 25-20 mmHg or less (in supine position)
3. Postural drop of SBP >20mmHg.
4. Significant bleeding (Haemetemesis, Malena, Bleeding PV etc.)
5. UOP <0.5ml /Kg/hr
6. CRFT > 2 sec

Name of patient: Age:..... BHT No:..... Ward:.....

Date & Time of admission:..... Weight:.....

Duration of fever:..... Baseline PCV %

[illegible]

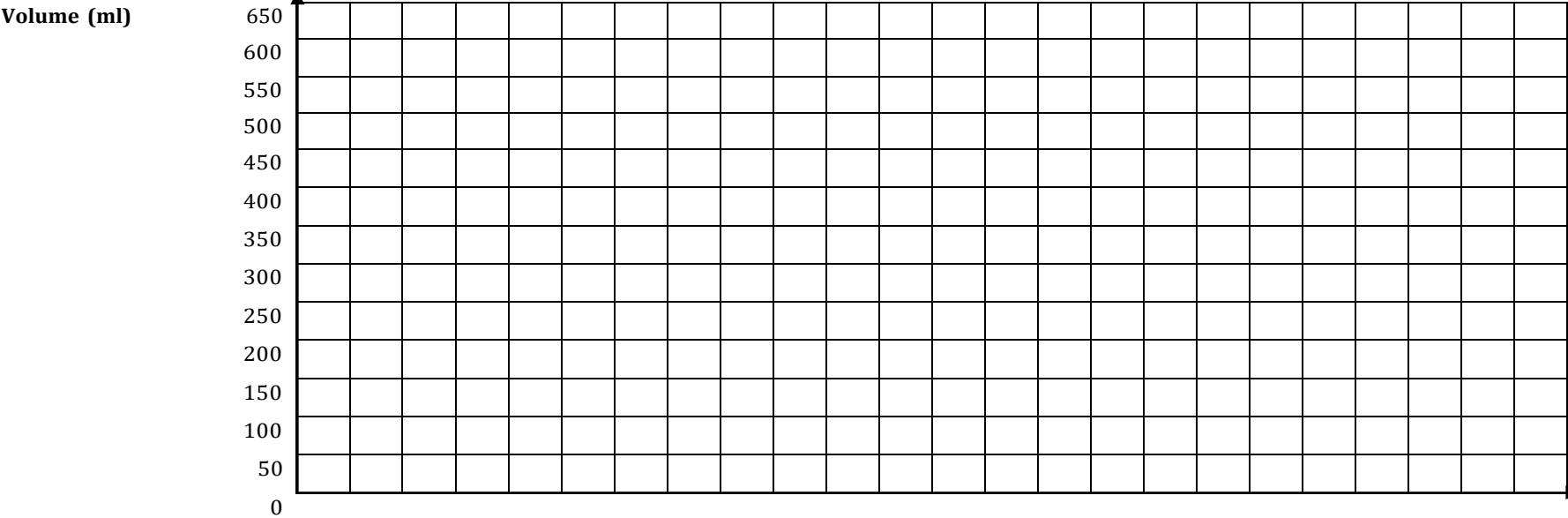
Annexure III
Observation Chart for Management of Dengue in Adult Patients with Fluid Leakage
Monitor hourly and if in shock monitor more frequently until the patient is stable
Do HCT 3 hourly or more frequently

- Oral
- N.Saline
- 40%Dextran
- Tetrastarch
- Blood
- Other

Name of the patient:..... BHT:..... Age:..... Ward:..... Weight:..... M+5%:.....

Commencement of Critical Phase (Date and Time):

Cumulative Volume (ml)																						
------------------------	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--



Time (Hrs)

HCT (%)																						
CRFT (s)																						
PR (/min)																						
BP Supine (mmHg)																						
Pulse Pressure (mmHg)																						
RR (/min)																						
Plt (/mm ³)																						
WBC																						
UOP (ml/kg/hr)																						
Kind of Oral Fluid																						
Remarks																						

105
104
103
102
101
100
99
98
97
Temperature °C

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