Guidelines on Management of Dengue Fever & Dengue Haemorrhagic Fever In Adults

Ministry of Health - Sri Lanka

National Guidelines

In Collaboration with the
Ceylon College of Physicians

December 2010

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The guidelines, published in December 2010, supersede the previous guidelines on Clinical Management of Dengue Fever / Dengue Haemorrhagic Fever published by Epidemiology Unit, Ministry of Health in 2005.

These guidelines were developed based on the best available evidence at the time of writing. It is expected to be used in the clinical management of dengue infection in Sri Lanka. The guidelines will be reviewed periodically when new evidence becomes available.

Please forward your comments and suggestions to the following address by post or e-mail.

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Foreword

Dengue haemorrhagic fever (DHF) has become a major public health problem in Sri Lanka in recent years. A large number of suspected Dengue fever (DF) and DHF patients are seen at both out-patient departments as well as at inward levels in most hospitals in the country regularly. The number of deaths due to dengue show an upward trend despite the case fatality rate remaining under 1% probably due to the high case load used as the denominator. Therefore, a thorough evaluation of the clinical management could reduce the mortality further due to this disease.

I hope that these guidelines on clinical management of dengue fever and dengue haemorrhagic fever prepared by the Epidemiology Unit in collaboration with the Ceylon College of Physicians will be a vital tool for all clinical practitioners in order to further strengthen clinical management.

Dr. Ravindra Ruberu
Secretary
Ministry of Health

Preface I

Dengue Fever (DF) is currently the most important mosquito-borne viral infection of public health significance in Sri Lanka, with thousands of patients acquiring the infection each year. During the Last two to three years we have witnessed hyper-endemicity with more severe manifestations such as Dengue Haemorrhagic Fever (DHF) and Dengue Shock Syndrome (DSS) leading to considerable morbidity and mortality with a significantly high case fatality rate.

These guidelines on clinical management of dengue fever have been developed by a team of physicians who are experienced in the field, in consultation with the Ceylon College of Physicians. This document is intended to provide guidance for physicians and all categories of doctors to carry out appropriate treatment for patients with Dengue Fever/Dengue Haemorrhagic Fever and would help to bring down complications and the case fatality rate to a minimum in the future.

Dr. Kamani Wanigasuriya
President
Ceylon College of Physicians

Preface II

Dengue infection has become the most important communicable disease in Sri Lanka today with a significant social, economic and political impact. Recent dengue epidemics were reportedly more severe. Nevertheless, it is observed that the knowledge on clinical management of dengue has improved tremendously over the past few years.

In fact, the World Health Organization (WHO-SEAR) is in the process of developing new "Comprehensive Guidelines for Prevention and Control of Dengue & DHF - 2nd Edition, 2010". In keeping with the new developments, the Ministry of Health invited a group of specialists to develop fresh guidelines on clinical management of Dengue Fever & Dengue Haemorrhagic Fever with a view to using it as an authoritative source of reference by all levels of health professionals. This document is intended to expeditiously disseminate and establish new knowledge at all levels of the healthcare services and thereby contribute significantly to reduce morbidity and prevent mortality associated with this disease.

I would like to acknowledge the efforts of all those who contributed to this document and wish to thank each and every one of them.

Appreciation is extended to the WHO for their assistance in providing funds for this publication.

Dr. Sudath Peiris
Acting Chief Epidemiologist

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We greatly appreciate the sharing of experience and the guidance of Professor Siripen Kalyanroogh and her team at the WHO Collaborating Centre for Case Management of Dengue/DHF/DSS, QSNICH, Bangkok, Thailand.

Special thanks are due to the following individuals for their contributions and comments in the preparation of these guidelines at different stages – Dr. Lak Kumar Fernado, Consultant Paediatrician, General Hospital Gampaha, Dr. Sunethra Gunasena, Consultant Virologist - MRI, Dr. Rasnayaka Mudiyanse, Senior Lecturer in Paediatrics, Faculty of Medicine, Peradeniya, Dr. Kapila Gunawardane, Senior Lecturer in Obstetrics & Gynaecology, Faculty of Medicine Peradeniya, Dr. N. M. M. Navaratne, Consultant Gastroenterologist - NHSL, Dr. Udaya Karunarathne, Consultant Anaesthetist, General Hospital Matara, Dr. J. S. D. K. Weeraman, Consultant Paediatrician, Dr. Paba Palihawadana, Chief Epidemiologist and Dr. Nihal Abeysinghe, former Chief Epidemiologist, Ministry of Health.

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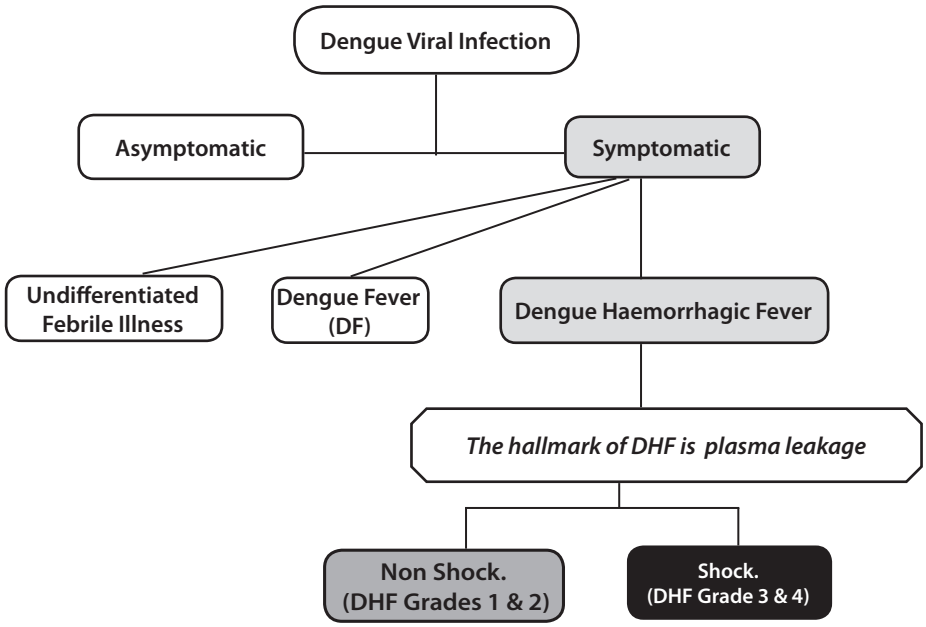
1. Introduction

The 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 early detection of plasma leakage and prevention of shock, early detection of shock, treatment of shock, management of special situations and the place for adjunctive treatment in patients with Dengue.

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 following.

- Undifferentiated febrile illness
- Dengue fever (DF)
- Dengue Haemorrhagic Fever (DHF)



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.

Therefore suspected DF and DHF patients should be closely monitored to identify patients with DHF. It is the patients with DHF who develop plasma leakage and resultant complications.

Patients with dengue fever can sometimes develop unusual manifestations such as massive bleeding, hepatitis and encephalitis without evidence of fluid leakage and therefore do not fall into the category of DHF. These conditions are very rare and management of these conditions is symptomatic.

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

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

2.1 Febrile phase

Febrile phase is characterized by continuing high fever lasting 2-7 days. Other features seen in the febrile phase include facial flushing, skin erythema, 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 mm^3) and mild thrombocytopenia (< 150,000 /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. Platelet count less than 100,000/mm^3 usually suggests the end of the febrile phase, and may indicate the entry to the critical phase.

2.2 Critical phase (leakage phase)

- **The critical phase is heralded by 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 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 in 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 haemoconcentration 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 I.V. fluids or in patients with bleeding.

In the absence of a baseline value consider HCT values of 40 and 36 in males and females respectively as baseline values.

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

The degree 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 after 48 hours).

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.

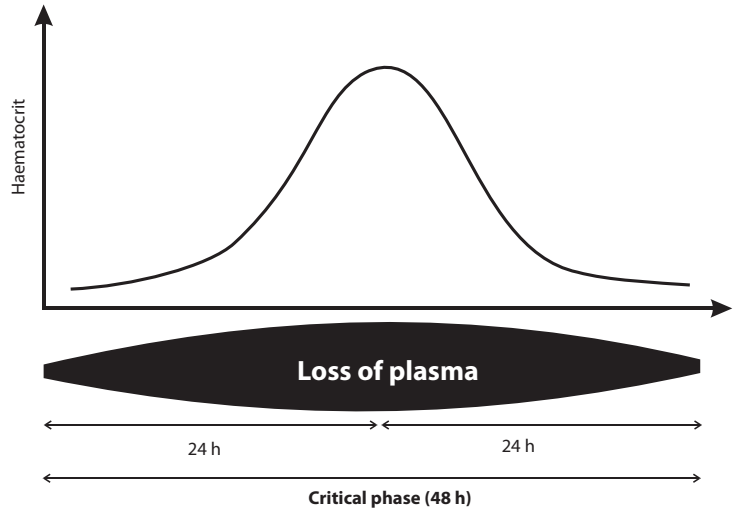


Figure : Fluid leakage in the critical phase

2.3 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.

Indicators that the patient has reached the convalescent phase

- Improved general well being 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 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.

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

In the present hyper-endemic setting in Sri Lanka, dengue fever should be considered in the differential diagnosis of patients presenting with acute onset of fever **with two or more of the following**:

- Headache, especially retro-orbital pain
- Myalgia /Arthralgia
- Rash (diffuse, erythematous, macular)
- Haemorrhagic manifestation (petechiae, positive tourniquet test etc.)
- Leukopenia (< 5000 /mm^3)
- Rising haematocrit of 5 - 10 %
- Platelet count ≤ 150,000 /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 platelet count less than 100,000/mm^3**
- **With the following warning signs :**
  - **Abdominal pain or tenderness**
  - **Persistent vomiting**
  - **Clinical signs of plasma leakage: pleural effusion, ascites**
  - **Mucosal bleeding**
  - **Lethargy, restlessness**
  - **Liver enlargement >2 cm**
  - **Increase in haematocrit (HCT) concurrent with rapid decrease in platelet count in a Full Blood Count (FBC)**

Other patients who may need admission even without 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

Ensure adequate oral fluid intake of around 2500 ml 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.

Following treatment measures are recommended :

- 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, but not to take excess.
- Anti emetics and H_2 receptor blockers if necessary
- **Avoid all NSAIDS and steroids**
- Withhold Aspirin, Clopidogrel & Dipyridamole in patients who take these on long term basis
- Review daily. A full blood count should be done at least on the third day of illness. (A full blood count should be done on the first day of fever in pregnant patients and in patients with chronic renal failure)
- Advise **immediate return** for review if any of the following occur:

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

6. Inward Patients

6.1 Introduction

Inward patients include patients with DF and patients with DHF. Differentiation between these two is difficult during 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 inward care is

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

6.2 Detection of critical phase (onset of plasma leakage)

A white cell count of 5000/mm^3 or less with predominance of lymphocytes and a platelet count less than 100,000/mm^3 may indicate that the patient is in danger of going into critical phase within the next 24 to 48 hours.

A progressively rising haematocrit, 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** indicate that the patient is already in the critical phase. Pleural effusion detected clinically may not be obvious in a CXR-PA, but may be seen only in a CXR right lateral decubitus film. If appropriate interventions are not adopted early the patient may develop shock.

6.3 Early detection of shock

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 annexures for the charts.

Symptoms of Shock

- **Sweating**
- **Abdominal pain**
- **Persistent vomiting**
- **Restlessness / altered conscious level**
- **Postural dizziness**
- **Decreased urine output (<0.5 ml/kg/hour)**

Signs of Shock

- **Cold extremities**
- **Prolonged capillary refill time >2 seconds**
- **Unexplained tachycardia**
- **Tender hepatomegaly >2 cm**
- **Increasing diastolic pressure**
- **Narrowing of pulse pressure ≤ 20 mmHg**
- **Postural drop ≥ 20 mmHg of systolic blood pressure**
- **Hypotension (from patient's baseline)**

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
- Watch for evidence of bleeding specially malena or bleeding per vagina
- Assess vital signs
- Do a full blood count on admission and then daily

6.4.2 *When platelet count drops below 100,000/mm^3*

Start monitoring using the monitoring chart 1.

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

Monitor,

- Temperature four hourly
- Vital parameters- pulse, blood pressure (both systolic and diastolic), respiratory rate, and capillary refill time-four hourly
- Detailed fluid balance with:
    - ♦ Intake with type and route of fluid – assess six hourly
    - ♦ Output urine/vomitus - assess six hourly
    - ♦ FBC daily
    - ♦ HCT twice daily

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

Start monitoring using the monitoring chart 2.

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

Entry into 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
- HCT- six hourly

in addition to monitoring other parameters mentioned in 6.4.2

6.4.4 *If there is evidence of shock (compensated or uncompensated shock)*

Vital parameters should be checked every 15 minutes till the patient is haemodynamically stable. During intense fluid resuscitation HCT should be checked immediately before and after each fluid bolus and then at least two to four 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 BW/ 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*

Watch for symptoms and signs of fluid overload such as cough, wheeze and tachypnoea, rise of both systolic and diastolic blood pressures, basal crepitations and rhonchi. Urine output is usually high during this phase. Some patients may develop bradycardia which is usually asymptomatic and transient.

6.5 Management of inward patients

6.5.1 *Febrile phase with platelet count more than 100,000/mm^3*

Management of this phase is essentially similar to outpatient management except for the addition of intravenous fluids. Intravenous fluids (I.V.) may be indicated in patients who are unable to take orally, 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 up-to a maximum of 50 Kg of weight).

However, if there is vomiting or diarrhoea this amount should be increased accordingly.

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

6.5.2 *When the platelet count drops below 100,000/mm^3*

Insert a 18 G (green) cannula and start a slow intravenous infusion of Hartmann's solution or normal saline to keep vein open (1000 ml may be given over 24 hours).

▶ **However the total (both oral and I.V.) amount of fluid intake should not exceed 2500 ml for an average adult unless the patient has vomiting or diarrhoea.**

6.5.3 *When the patient is in the critical phase*

Total 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 50 kg

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 total 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.

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 of plain water should be actively discouraged**.

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

If the patient is haemodynamically stable (non-shock), but in 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, for example 50-75 ml/hour (1-1.5 ml/kg body weight/hour).

The rate of fluid should be increased in a step wise pattern, according to the rise

of HCT and/or reduction of urine output below 0.5 ml/kg/hour, for example to a rate of 150 ml/hour (3 ml/kg/hour). Since the 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.

6.5.4 *If the patient goes into shock while in the ward or if a patient presents 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 in addition to 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 and/or hypotension or in profound shock with unrecordable blood pressure (Refer flow algorithms).

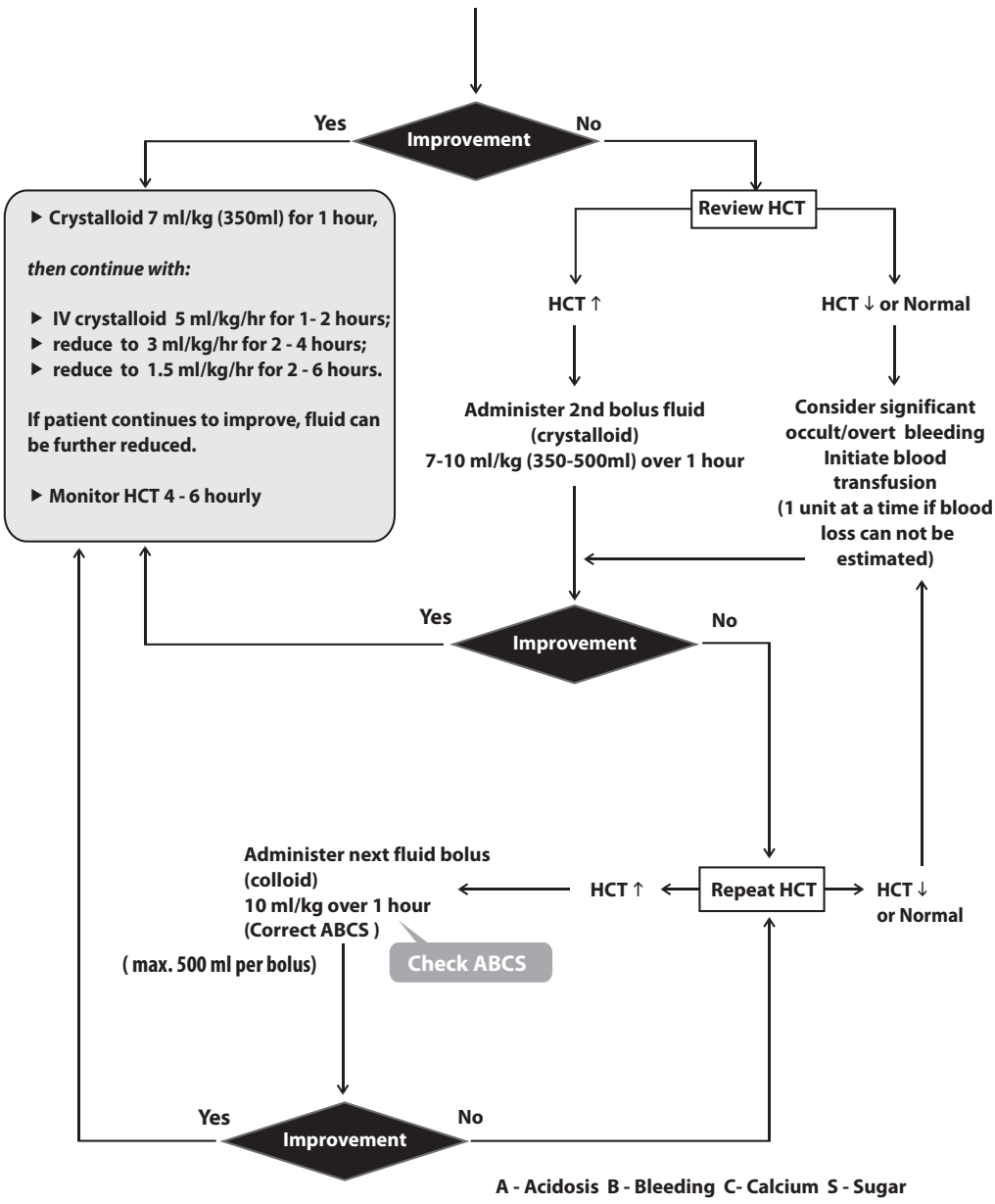
- **The rate of I.V. fluid given should be adjusted according to the pulse pressure, capillary refill time, urine output and HCT.**

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 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 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 & HYPOTENSION



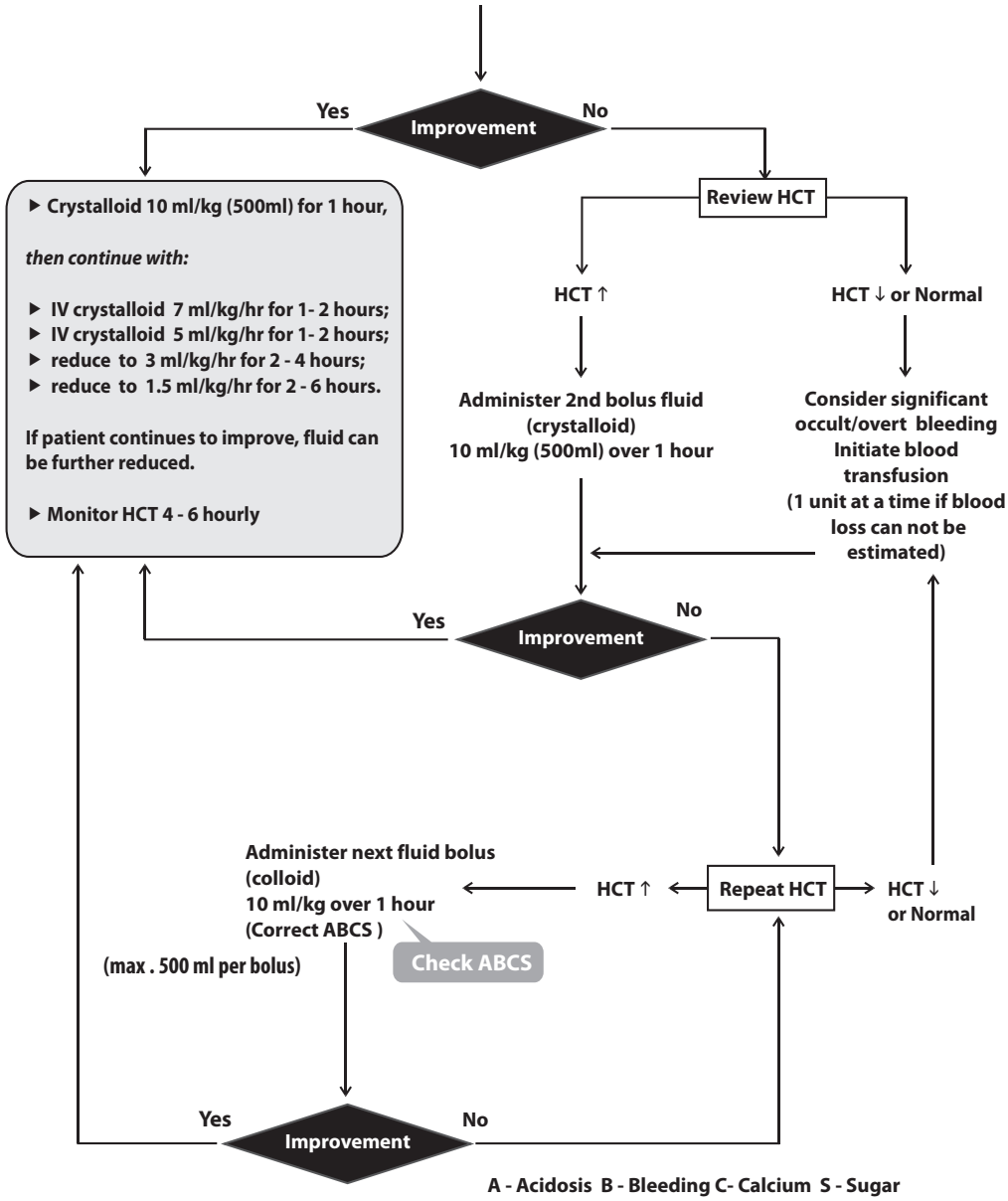
*** In the elderly and in patients with heart disease & renal disease consider using lower infusion rates.**

Algorithm 1

PROFOUND SHOCK (UN-RECORDABLE BLOOD PRESSURE)

Fluid resuscitation with 10 ml/kg (500ml) isotonic crystalloid over 15 minutes

(Try to obtain a haematocrit before fluid resuscitation)



Algorithm 2

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 I.V. 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 critical phase and fluid resuscitation of such situation also may lead to over-hydration.

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

- **If the patient is in shock or has features of pulmonary oedema 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 1 mg/kg should be given.**

- **If the patient is in shock and has a normal or low HCT, immediate blood transfusion is necessary. In the midway of the transfusion, frusemide 1 mg/kg should be given. Until blood is available, a bolus of colloid (300-400 ml of Dextran 40 or Tetrastarch) could be administered.**

- **If the patient is haemodynamically 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.**

- **If the patient is haemodynamically stable and has a normal or low HCT, fluid should be restricted and patient should be monitored carefully, as the patient is likely to improve within hours. The most probable reason for low haematocrit is haemodilution. If the patient develops features of pulmonary oedema, frusemide 0.5 mg/kg should be given intravenously. This dose can be repeated after half an hour.**

Fluid over-load will worsen the fluid extravasation. This may result in large pleural effusions and severe ascites. Usually these settle with colloid boluses. However, the pleural effusion may rarely be big enough to interfere with ventilation and may need to be drained out in addition to giving colloids.

Rarely, severe ascites can cause abdominal compartment syndrome. (If the abdo-

men is very tense even without distension, suspect this). 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. Dextran 40 or Tetrastarch (6% starch solution) 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%) in nearing completion

As dextran can sometimes interfere with cross matching, blood should be drawn for grouping and cross matching before starting on dextran. 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**

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. Therefore empiri-

cal treatment with 10% calcium gluconate 10 ml over 10 minutes is justifiable if a patient in shock is not responding to adequate fluid replacement, and this may be continued six hourly.

I.V. calcium gluconate may be used in patients who show evidence of myocarditis as well, as hypocalcaemia is common in DHF grade I.V. patients and calcium may improve the myocardial contractility in such patients.

- If the patient is clinically acidotic one dose of 8.4% sodium bicarbonate 50 ml may be given empirically if blood gas cannot be assessed.
- Correct the blood glucose if it is less than 60 mg/dl

6.8 Indications for Blood Transfusion

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

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 occult bleeding in the following situations and transfuse blood:

- **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).**
- **Severe metabolic acidosis and end-organ dysfunction despite adequate fluid replacement.**

(Note: that the haemoglobin level may remain normal initially despite significant blood loss.)

5 ml/kg of packed red cells (preferred in over-hydrated patients and in patients with heart disease) or 10 ml/kg of whole blood 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.**

7. Management of Hepatitis and 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 (70 ml/hour)
- 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 I.V.
- Give Lactulose to maintain 1 -2 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

▶ **Early admission and close follow up with FBC daily is very important**

The gestation and the phase of dengue are important factors in determining the management. Discussion with the team of obstetricians, physician and the paediatrician about the management is mandatory. Consultation and explanation with the family members about the course of DHF and the management are also important for decision making.

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 based on the weight **prior** to pregnancy.

However, the signs and symptoms may be confused with other complications of pregnancy such as toxaemia, Haemolysis, Elevated Liver Enzymes, Low Platelets (HELLP) syndrome There are some reports of an increased incidence of prematurity, in-utero death and abruptio placentae in these women

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

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

The detection of ascites and pleural effusions is difficult due to the presence of gravid uterus.

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,

▶ **If possible, avoid Lower Segment Caesarean Section (LSCS) or induction of labour during critical (plasma leakage) phase.**

▶ **Procedures/manoeuvres that may provoke or augment labour should be avoided during the critical phase**

9. Myocardial Involvement in Dengue

Global dysfunction of myocardial contractility may be seen in DHF patients who are in prolonged shock. The most likely reason for this is metabolic acidosis. Hypocalcaemia, which is a common finding in DHF grade III and IV, is another probable cause.

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

Empirical treatment 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 myocarditis is suspected fluid should be given very carefully**

Treatment of myocarditis 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 and respiratory embarrassment.

▶ **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, Hepatitis 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 and 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 (1 mg/kg body weight) 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

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 1 gram eight hourly.

11. Transferring a patient to another Institute

Facilities in some small 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.

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.

12. 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 or ascites
- When platelet count has risen above 50,000 /mm^3
- No other complications

13. Laboratory Diagnosis

During the first three days of the illness, PCR for dengue virus is usually positive. However, sensitivity and specificity of this test vary from laboratory to laboratory. NS-1 antigen is another test which can be done during the first 5 days of fever. Sensitivity of this test varies and ranges from 60-90%. Though this is a simple and a rapid test it is not cost effective.

IgM antibody is likely to become positive after fifth to sixth day of the illness and considered as the best option for routine diagnosis as a positive result will make a probable case of dengue to a highly suggestive case. IgM will persist in the blood for about three months (in Primary Dengue) after the acute illness and IgM response may not be detectable in 5-10% of Secondary Dengue. The best way to confirm the diagnosis would be to detect a rising titre of IgG/HI antibody or seroconversion of IgM or IgG in paired sera.

▶ **Laboratory confirmation of Dengue Infection is generally not required for clinical management of patients.**

14. Outbreak Response Plan for Hospitals

There have been 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 out-patient 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 inward 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
- Calcium Gluconate (10% solution)
- KCl (20 or 40 mmol concentrated solution)
- 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 – full-blood count (FBC), haematocrit, platelet count, white blood count (WBC), and differential 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.

Blood Bank:

Fresh whole blood, packed red cells and other blood products should be available on demand.

Observation Chart for Management of Dengue in Adult Patients (Plt <100,000/mm^3)

Annexure I

Chart 1: **To Be Filled 4 hourly**

Name of the patient: ..... BHT: .....

Date and time of admission: ..... ward: .....

Duration of Fever: ..... WBC on admission: T: ..... /mm^3; N: .....% L: .....% Platelets: ...../mm^3 Hct: .....%

Liver: .....cm BP: ..... /.....mmHg HR: ..... /min RR: ...../min CRFT: .....seconds

Dehydration	+	-

Hess +/-	D1	D2	D3	D4

Indications to call for immediate advice

i. Pulse Rate > 120/min with fever or > 100/min without fever
ii. Pulse Pressure ≤ 20mmHg
iii. Postural Drop of SBP >20mmHg
iv. Significant Bleeding (haematemesis, melena, bleeding PV, etc...)
v. UOP < 100ml/ 4hrs (< 0.5ml/kg/hr)
vi. CRFT > 3 sec

Date time	**Pulse Rate** /min	**BP** SBP/DB mmHg	**Pulse pressure**	**CRFT** seconds	**RR** bpm	**PCV** %	**Plt** /mm^3	**Intake**		**Output**	**Observations** (Dry mouth, Tender hepatomegaly, Ascites, pl. effusion)	**Treatment**	**Sig**
								PO	IV	UOP ml/hr			

Monitoring chart during pre-critical phase

Observation Chart for Management of Dengue in Adult Patients with Fluid Leakage

Annexure II

Chart 2: **To Be Filled hourly**

Name of the patient: …… BHT: ……

Date and time of admission: …… ward: ……

Duration of Fever: ……. WBC on admission: T: …… /mm^3; N: …..% L: …..% Platelets: ……/mm^3 Hct: ……%

Liver: ……cm BP: …… /……mmHg HR: …… /min RR: ……/min CRFT: ……seconds

Indications to call for immediate advice

i. Pulse Rate > 120/min with fever or > 100/min without fever
ii. Pulse Pressure ≤ 20mmHg
iii. Postural Drop of SBP >20mmHg
iv. Significant Bleeding (haematemesis, melena, bleeding PV, etc…)
v. UOP < 100ml/ 4hrs (< 0.5ml/kg/hr)
vi. CRFT > 3 sec

Dehydration	+	-

Hess +/-	D1	D2	D3	D4

Date/ time	**Pulse Rate** /min	**BP** SBP/DB mmHg	**Pulse Pressure**	**CRFT** seconds	**RR** /min	**PCV** %	**PLT** /mm^3	**Intake**		**Output**	**Observations** (Dry mouth, Tender hepatomegaly, Ascites, pl. effusion)	**Treatment**	**Sig**
								PO	IV	UOP ml/hr			

Both Oral and IV Fluid given:

100ml				500					1000					1500					2000					2500					3000					3500					4000					4600

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