Guidelines on Management of Dengue Fever & Dengue Haemorrhagic Fever In Children and Adolescents

Ministry of Health - Sri Lanka

National Guidelines

In Collaboration with the
Sri Lanka College of Paediatricians

December 2010

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This document includes the new concepts on fluid management of Dengue Haemorrhagic Fever patients and replaces the existing national 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. 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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Special thanks are due to all Consultant Paediatricians and others for their comments and contribution in the preparation of these guidelines at different stages.

Contents

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 regularly seen at both out-patient departments as well as in the wards in most hospitals in the country . 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 strengthening of clinical management could further reduce the mortality 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 Sri Lanka College of Paediatricians will be a vital tool to all clinical practitioners in order to further strengthen clinical management.

Dr. Ravindra Ruberu
Secretary Health

Preface I

I wish to extend my appreciation to the team of paediatricians who were trained in WHO Collaborating Centre for Case Management of Dengue/DHF/DSS, Queen Sirikit National Institute of Child Health, Bangkok, Thailand in 2010 for preparing these valuable guidelines.

I wish to thank Consultant Epidemiologist Dr. Hasitha Tissera for his untiring efforts in collaborating with clinicians in producing these guidelines and also disseminating new knowledge.

Appreciation is extended to the WHO for their assistance in providing funds training clinicians and printing this publication

This guide on fluid management could be used by all categories of health care personnel providing care for children and adolescents with Dengue/Dengue Haemorrhagic Fever. Every effort should be made to minimize the case fatality rates in Sri Lanka .

Dr.Deepthi Samarage
President
Sri Lanka College of Paediatricians

Preface II

Dengue infection has become the most important communicable disease in Sri Lanka today with a significant social, economical 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 keeping with new knowledge and all other new developments related to the management of Dengue, the Ministry of Health invited a group of specialists endorsed by the Sri Lanka College of Paediatricians to develop a document with an update on clinical management of Dengue Haemorrhagic Fever, with a view to using it as an authoritative source of reference to be available to all levels of health professionals. This fresh 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 among children and adolescents.

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

Identifying the beginning and predicting the end of the critical phase (leaking phase),
meticulous monitoring,
accurate fluid management in the critical phase,
vigilance, early detection and treatment of concealed bleeding and other complications
are the most crucial factors in reducing case fatality in patients with
Dengue Haemorrhagic Fever

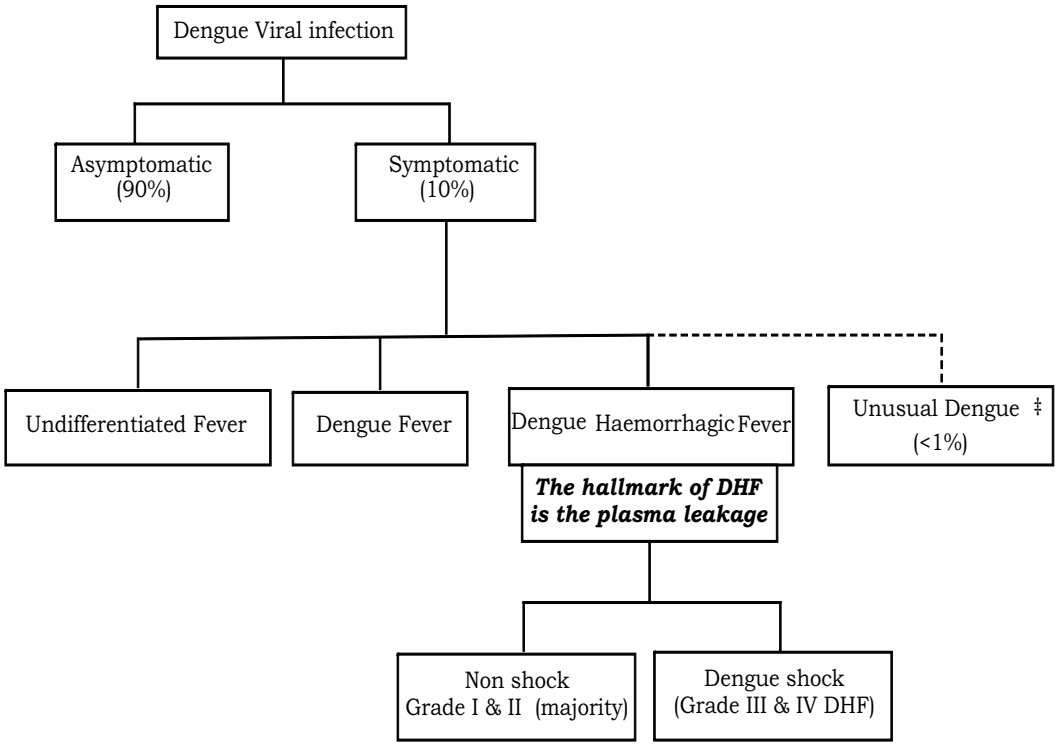
1. Introduction

Many patients infected with dengue virus remain asymptomatic. Others after an incubation period of approximately 6 (3-14) days develop a febrile illness which could turn out to be one of the following:-

1. Undifferentiated febrile illness
2. Dengue Fever (DF)
3. Dengue Haemorrhagic Fever (DHF)
4. Unusual Dengue‡

Inward patients include patients with DF and DHF. Differentiation between the two is difficult during the initial few days.

Figure: Classification of Dengue Viral Infection



‡Unusual Dengue(Expanded Dengue Syndrome)-please see page 34

Case Definitions of DF and DHF

Dengue Fever (DF)

Clinical criteria that define DF include a 2-7 day illness with high fever headache, retro-orbital pain, myalgia, arthralgia/ bone pain, rash and haemorrhagic manifestations E.g. positive tourniquet test, or petechiae, with no evidence of plasma leakage.

Dengue Haemorrhagic Fever (DHF)

First few days of DHF patients will have sign and symptoms similar to that of DF. However in DHF, they will later on develop features of plasma leakage. (usually beyond day 3)

The following criteria are necessary for the case definition of DHF

1. High fever or recent history of acute fever
2. Haemorrhagic manifestations †* (including a positive tourniquet test)
3. Thrombocytopenia of ≤100,000 cell/mm^3
4. Objective evidence of leaky capillaries (described below on page 11)

†* *In patients who have definite evidence of plasma leakage, presence of haemorrhagic manifestations are not essential for the diagnosis of DHF.*

2. Natural course of the illness

A good understanding of the disease process will help in proper management that will lower the degree of morbidity and mortality. Dengue Haemorrhagic Fever is a dynamic disease. Its clinical course changes as the disease progresses and consists of three main phases;

1. Febrile phase
2. Critical phase
3. Convalescent phase

Febrile phase (Occurs in both DF & DHF)

- High fever 2-7 days.
- Facial flushing, skin erythema, headache, retro-orbital pain, myalgia, arthralgia, nausea and vomiting.
- Haemorrhagic manifestations include petechiae, purpura, gum or nasal bleeding, gastrointestinal bleeding, haematuria, menorrhagia and positive tourniquet test.
- Total white cell count could be high or normal initially and drop towards the latter part to levels below 5000/mm^3.
- Platelet count is normal initially and will come down to ≤100,000/mm^3 in about 50% of DF and almost 100% of DHF patients.

- ▲ Tender hepatomegaly favours a diagnosis of DHF
- ▲ Erythematous or maculo-papular rash is seen more in DF than in DHF

DF vs. DHF in febrile phase

Dengue Fever and Dengue Haemorrhagic Fever are two different clinical conditions from the beginning. They look very similar in the first few days. When a patient presents with dengue or dengue like illness the differentiation between DHF and DF will be a key factor in guiding management.

- Thrombocytopenia and Leucopenia (WBC <5,000/mm^3) are seen in the febrile phase of both DF and DHF.

- Presence of haemorrhagic manifestations in febrile phase does not indicate that the patient has DHF because haemorrhagic manifestations can be found in both DF and DHF.

It is often difficult to differentiate DF from DHF in the febrile phase of the illness. Therefore, suspected DF and DHF patients should be closely followed up in order to identify the DHF patients going into the fluid leakage phase to ensure correct fluid management during the critical phase.

3. Diagnosis & Management at OPD level and by primary care physician

3.1 When to suspect DF/DHF in a child with acute onset of fever

Presence of any 2 or more of the following features:

- Headache & retro-orbital pain
- Nausea or vomiting
- Rash- diffuse, erythematous, macular
- Arthralgia & myalgia
- Leucopenia (WBC <5000/mm^3)
- Positive tourniquet test[†*] (negative test does not exclude the possibility of dengue)
- Platelet count ≤ 150,000/mm^3
- Rising HCT 5-10%

[†*] *tourniquet test is done by measuring the blood pressure using a cuff of appropriate size for each patient (the width is to cover 2/3 of the upper arm). Raise the pressure to mid way between systolic and diastolic blood pressure for 5 minutes. Release the pressure and wait for one minute before reading the result. Positive test is considered when there is ≥ 10 petechiae per square inch.*

3.2 Management of those who do not need admission at first contact level

1. Ensure adequate oral fluid intake.
   Approximate guide for fluid intake during this stage is age appropriate maintenance fluid requirement. 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.
2. Adequate physical rest
3. Paracetamol 10-15mg/kg/dose for fever
   (do not exceed 60mg/kg/24hrs) with tepid sponging as needed

4. **Avoid all NSAIDS and steroids**

5. Review daily. A full blood count **must** be done on the third day of illness or earlier if the clinical situation warrants (If the first count is normal may have to repeat the count depending on the clinical situation).

6. Advise immediate return for review if any of the following occur

- **Clinical deterioration with settling of fever**
- Inability to tolerate oral fluid
- refuse to eat or drink
- feeling extremely thirsty
- Severe abdominal pain/ vomiting
- Cold and clammy extremities
- Bleeding manifestations
- Not passing urine for more than 6 hours
- behaviour changes E.g: confusion/ restlessness
  lethargy/ irritability

3.3 Criteria for admission

Medical officers are expected to use clinical judgment regarding admission. However, it is essential to admit the following patients.

- All patients with a platelet count of $\leqslant 100,000/mm^3$

  (Platelet count above $100,000/mm^3$ but below $150,000/mm^3$ and dropping rapidly may be admitted depending on the circumstances)

- All patients with the following **warning signs.**

Following warning signs in suspected DF/ DHF warrant admission for intense and close monitoring:

- Abdominal pain or tenderness
- Persistent vomiting
- Cold extremities and features of shock
- Clinical fluid accumulation-pleural effusion, ascites
- Mucosal bleeding
- Lethargy, restlessness and drowsiness
- Liver enlargement >2cm
- Laboratory:
    - Increase in HCT >10%
    - Decrease in platelet count $\leqslant 100{,}000/mm^3$
    - Elevated SGOT well above SGPT

- The following categories of patients with probable dengue also should be admitted:
    - Infants
    - Obese patients
    - Patients with major co-morbidities / medical problems (diabetes, nephrotic syndrome, CRF, haemolytic diseases, poorly controlled asthma)
    - Adverse social circumstances- living alone, living far from health care facility without reliable means of transport, unreliable parents

4. Inward Management of DF / DHF

4.1 Febrile phase

4.1.1. Management of patients still in febrile phase

1. Ensure adequate oral fluid intake.

   If the patient is vomiting or dehydrated and not taking adequate oral fluid may need IV fluids. Total fluid requirement (oral + IV) will depend on the degree of dehydration (May even go up to Maintenance + 5% over a 24 hr period). The rate of infusion has to be reduced as soon as possible after correction of dehydration. From the 3rd day onwards, one needs to be cautious of the volume of fluid administered as the patients with DHF will be entering the critical phase.

   When IV fluids are needed in the **febrile phase** (when the patient has not entered the critical phase), use 5% dextrose in N/2 for infants below 6 months and N**.** saline for others.
2. Adequate physical rest
3. Paracetamol 10-15mg/kg/dose for fever (do not exceed 60mg/kg/24hrs) with tepid sponging as needed
4. **Avoid all NSAIDS and steroids**
5. Monitoring : Use monitoring chart I (Febrile phase) - Annexure I

4.1.2. Monitoring during febrile phase

- Temperature four hourly
- Vital parameters - pulse, blood pressure (both systolic and diastolic), respiratory rate, and capillary refill time - four hourly (may need more frequent monitoring depending on the clinical situation)
- Intake and output
- FBC daily (or even twice daily when platelet count is dropping below 150,000/mm^3)
- HCT once/twice daily

4.2 Critical phase: (seen only in DHF)

4.2.1. Key Points

- The critical phase is heralded by onset of plasma leakage
- Platelet count dropping below 100,000/mm^3 is the best and the earliest indicator that the patient is probably entering the critical phase (leaking phase).
- **During critical phase plasma leakage is the main cause for shock, subsequent bleeding, organ failure and death.**
- The critical phase occurs towards the late febrile phase (often after the 3rd day, usually occurs between the 4th to 5th day but may sometimes go up to the 7th day). It is extremely rare within the first 2 days of fever.
- Rapid drop in temperature may occur as the patient enters the critical phase (In DF and other viral infections as fever subsides the patient's general condition improves, but in DHF it may get worse). During the early phase of plasma leakage many patients may still have fever, but the intensity will be lower.
- **Critical phase will last only for 24 to 48 hours.**
- DHF is a very dynamic disease where haemodynamic state can change very rapidly to profound shock and death.
- The rate of leaking is highly variable from patient to patient. Generally, during the critical 48 hours fluid starts leaking and gradually the leaking increases in most of the patients reaching a peak around 24 hours. After that the leaking starts slowing down gradually and will stop after a further 24 hours making the total period of leaking (= critical phase) 48 hours.

- If the patient had been in hospital from febrile phase it is important to identify the exact timing of the onset of leakage. **Identifying the beginning of the critical phase and predicting the end is a key factor in guiding fluid therapy in DHF.**

- It is important to monitor patients frequently specially towards the peak of leaking with readiness to resuscitate with fluids immediately. (Predict the peak and look for intense leak around the peak with monitoring.)

- Duration of critical period for a patient detected at the entry into the critical phase is usually 24- 48 hrs. If the patient presented in shock probably he would have been in critical phase for a significant period of time, probably up to 24 hrs. Therefore, in such patients, one can assume that the remaining period of critical phase is another 24 hours only.

Remember: until the very last stage of shock a patient can appear conscious and very alert and if pulse, BP (pulse pressure) are not measured early shock could be missed.

4.2.2. Early detection of the critical phase (plasma leakage)

1. Platelet count dropping below 100,000/mm^3 should alert the clinician that the patient may be in or entering the critical phase of DHF. Remember: The patient with a platelet count below 100,000/mm^3 may be in one of the following three categories:
   - DF (about half of DF patients will have a platelet count below 100,000/mm^3)
   - DHF febrile phase (leaking not started yet)
   - DHF critical phase

2. When the platelet count drops below 100,000/mm^3 any of the following parameters indicates that the patient has entered the critical phase:

   (i) **Rising haematocrit ≥20%**

   The 20% is calculated by taking into consideration the baseline haematocrit (Hct). For example, if the initial Hct is 35% an increase of Hct up to 42% indicates a 20% increase. When the baseline Hct is not known, it is safe to assume that the baseline Hct in an average child is around 33 - 35%.

   (ii) A **progressively rising haematocrit** towards 20% also suggests that the patient may have entered the critical phase.

   Remember: Patients who have received IV fluids (sometimes even with excessive oral fluids) or bleeding may not show a rise in HCT especially as much as 20%**.**

   (iii) **Objective evidence of fluid leak** out of the vascular compartment in **early** critical phase **detected radiologically**
   - Pleural effusion (CXR R/lateral decubitus or USS Chest)
   - Ascites (USS abdomen)

   (iv) When in doubt following **biochemical parameters** suggest that the patient is in the critical phase:
   - Serum albumin* of < 3.5g/dl or if albumin has dropped by ≥0.5g/dl
   - Serum cholesterol* of <100mg/dl or if cholesterol has dropped by 20mg/dl

   (not routinely recommended due to the costs involved, but useful when there is doubt. Since the baseline values may vary a significant drop during the illness is suggestive of plasma leak)*

4.2.3. Monitoring During Critical Phase

Since the critical phase is very dynamic and the rate and total duration of leaking is highly variable from patient to patient **it is of paramount importance to monitor frequently and very carefully** during this phase.

Hence, it is important to maintain monitoring charts. Please refer to annexures II and III

- Annexure II - Monitoring chart II for patients during critical phase
- Annexure III - Monitoring chart III for patients during the peak of leakage and during shock

Monitoring should include total fluid administered (oral+ IV) and the following clinical parameters:

- Pulse
- BP
- Pulse pressure (the aim is to maintain a pulse pressure just above 20mmHg during the critical phase)
- Capillary refill time (CRFT)
- Warmth / coldness of peripheries
- Respiratory rate
- Urine output. ml/kg/hr
  (aim is to maintain UOP between 0.5 - 1.0ml/kg/hr)
- Evidence of overt bleeding

Clinical signs should be monitored hourly when the patient is stable and every 15 minutes when the patient is leaking rapidly or while in shock.

- Regular Hct measurements 4-6 hourly in non-shock patients (Grade I & II DHF) and more regularly in patients with shock (Grade III & IV DHF)

Golden triad of Inward management of Critical phase of DHF

- Early detection and prediction of the end of plasma leakage
- Meticulous monitoring, accurate and fine titration of fluids depending on the rate of leak **(Rate of infusion should match rate of leak)**
- Vigilance, early detection and treatment of concealed bleeding and other complications

4.2.4. Fluid Management in the Critical Phase

▶ ***Calculation of fluid quota for the critical period***

- Fluid quota **is only a guide** for management of dengue patients during the critical period of DHF.
- Patients managed using fluid within this safe quota are less likely to develop fluid overload.
- When fluid requirement is calculated (both oral and IV), calculate it for the Ideal Body Weight (IBW).

The total amount of fluid recommended during the
Entire critical phase
(irrespective of its length)
should be
M + 5% = Maintenance + 5% of body weight

▶ *Calculation of Ideal Body Weight*

- Weight for height using a growth chart (50th centile) -Best Method
- Weight for age using a growth chart(50th centile)
- In an emergency situation use these formulae

<1 year	$\frac{\text{Age (in Months)}+ 9}{2}$
1-7 years	(Age x 2)+ 8
>7 years	Age x 3
APLS	(Age + 4) x 2

Note: Actual body weight is taken for calculation of fluid requirement if it is lower than the IBW

▶ *Calculation of total fluid quota for the critical period*

M (Maintenance) = 100ml/kg for first 10 kg
+50 ml/kg for next 10 kg
+20 ml/kg for balance weight

5% of body weight = 50ml x body weight (kg)

E.g. Body weight 22 kg (This is the ideal or actual body weight, whichever is smaller)

M = 100 x 10 + 50 x 10 + 20 x 2 = 1540 ml

5% = 50 x 22 = 1100 ml

M + 5% = 1540 + 1100 = 2640 ml

This is the total fluid quota for the "critical period" (48hr in patients coming without shock and 24 hr in patients coming in shock)

Note: The maximum weight for which fluid is calculated in any patient **should not exceed 50 kg.** Accordingly M+5% **should not exceed 4600 ml** in any patient.

▶ *Rate of administration of IV fluids*

Guide to rate of administration in a patient without SHOCK

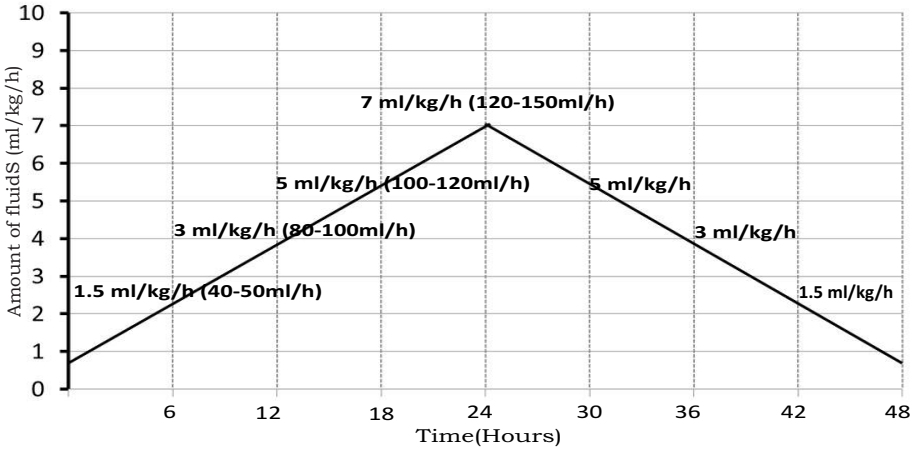
- All patients entering the critical phase to start on IV **normal saline** or Hartmann's solution through IV cannula (largest possible size for the age) in addition to oral fluid. Initial fluid requirement (oral + IV) is 1.5 ml/kg/hr. Those who can drink well may be given IV fluids as 0.5ml/kg/hr to 'keep vein open' and the balance as oral. (Use N/2 + 5% dextrose in < 6 months infants; For those above >6 months when the patient is not taking orally for prolonged periods it is useful to give N saline in 5% dextrose [†*])
- Calculate the total fluid quota for the patient (M+ 5%) at the beginning of critical phase. If the patient has been in the critical phase for some time, need to calculate the remaining volume of fluid which could be administered, considering the duration of critical phase elapsed and the amount of fluid already given during this period of time.
- Subsequent rate of infusion will depend on the rate of leak (which will highly vary from patient to patient and even in the same patient from time to time) judged by pulse, BP, pulse pressure, CRFT, HCT and UOP.
- Patients who are in shock due to plasma leakage usually have narrowing of pulse pressure ⩽ 20mmHg and patients with bleeding usually present with hypotension.
- Calculate the UOP ml/kg/hr at each void. In a patient who is stable **hourly urine output is the best guide to decide the rate of infusion**. Urine output of **only 0.5 -1 ml/ kg/hour** is sufficient to maintain renal functions during the critical period. **If the UOP is above 1 ml it suggests that infusion rates are too high. If the UOP is <0.5ml/kg/hr it may suggest inadequate fluids. In such situations catheterization may be required.**

[†*] *when "dextrose saline" is not available, such a solution could be made by adding 50ml of 50% dextrose to 450ml of normal saline.*

- Patient who had been in the critical phase for a significant period but not gone into shock, the amount of fluid needed for maintenance could go up to 7ml/kg/hr or more, but would be unlikely to require the same amount for a long period as leaking will start slowing down. When pulse, BP are stable it is important to bring down the rate of infusion to avoid fluid overload while repeatedly assessing the UOP, pulse and BP.
- If a higher rate of maintenance fluid is unable to maintain the pulse pressure, fluid boluses (N. saline or colloids 10ml/kg/hr) should be used.
- Individual patient's rate of fluid requirement will depend on his/her rate of leakage. The rate of IV fluid administration has to be adjusted **frequently** depending on vital signs especially pulse rate, BP, pulse pressure, Hct, CRFT, urine output.

Use **Chart I** below as a guide in non-shock patients while remembering that there is wide variation in the rate of leak from patient to patient

Chart II : Guide to rate of fluid intake in Critical Phase - without shock



Courtesy of WHO Collaborating Centre for Case Management of Dengue/DHF/DSS, Queen Sirikit National Institute of Child Health, Bangkok, Thailand

Fluids for adolescents are mentioned with-in brackets.

Remember

The chart on the rate of fluid administration is only a guide.

Individual patient's rate of fluid requirement will depend on the rate of leak in that patient.

The rate of IV fluid administration has to be adjusted all the time depending on vital signs.

Many patients can be managed with very much lower rates than shown and less than the calculated quota of M + 5%

M +5% VOLUME AND THE RATES SHOWN IN THE FIGURE ARE ONLY A GUIDE WHICH ONE SHOULD NOT TRY TO EXCEED

It is worth remembering that though it is possible to manage some patients with less than M+5% volume of fluid it should always be done by maintaining a UOP >0.5ml/kg/hr and adequate BP and pulse THROUGHOUT the critical phase with frequent monitoring. REMEMBER- fluid restriction without such monitoring could lead to prolonged shock!

Guide to Rate of Fluid Intake in a patient with SHOCK

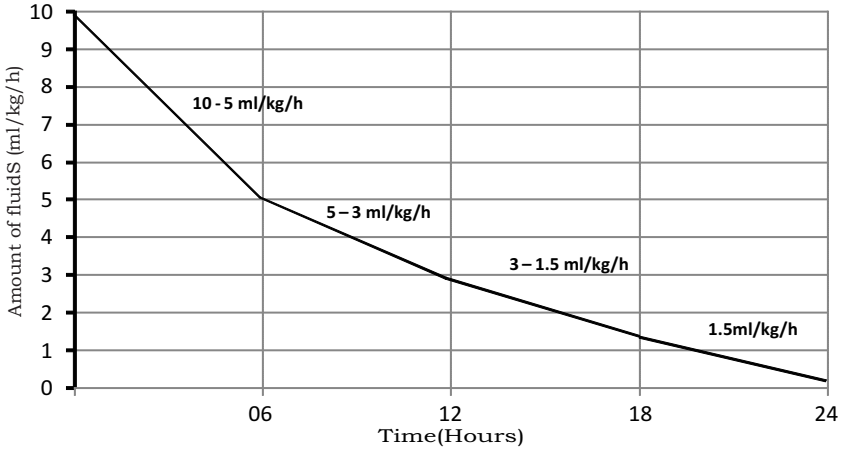
Early detection of shock

Symptoms	**Signs**
• Sweating	• Cold extremities
• Abdominal pain	• Prolonged capillary refill time >2 sec
• Restlessness	• Unexplained tachycardia
• Altered conscious level	• Increasing diastolic pressure
	• Narrowing of pulse pressure ⩽20mmHg

- As the peak of leaking occurs around 24 hours, a patient who has gone into significant shock will be in a stage of leaking that has passed about 24 hours and will only have about a further 24 hours before the leaking stops. Hence, if a patient presents with shock (cold clammy skin, pulse, BP unrecordable) one would assume that the patient had continued to leak before coming to hospital.
- Individual patient's fluid rates administered will depend on his/her rate of leak. The rate of IV fluid administration has to be adjusted all the time depending on vital signs specially pulse rate, BP, pulse pressure, Hct, CRFT, urine output.
- Total fluid quota M+5% should include the fluid given during resuscitation.

(You may use Chart II below as a guide for patients with shock while remembering that there is wide variation in rate of leak from patient to patient)

Chart II : Guide for the rate of IV fluids in profound shock after initial resucsitation



Courtesy of WHO Collaborating Centre for Case Management of Dengue/DHF/DSS, Queen Sirikit National Institute of Child Health, Bangkok, Thailand

Remember

The chart on the rate of fluid administration is only a guide.
Individual patient's fluid rates will depend on the rate of leak in that patient.
The rate of IV fluid administration has to be adjusted frequently depending on vital signs.
Many patients can be managed with very much lower rates than shown and less than the quota of M + 5%.

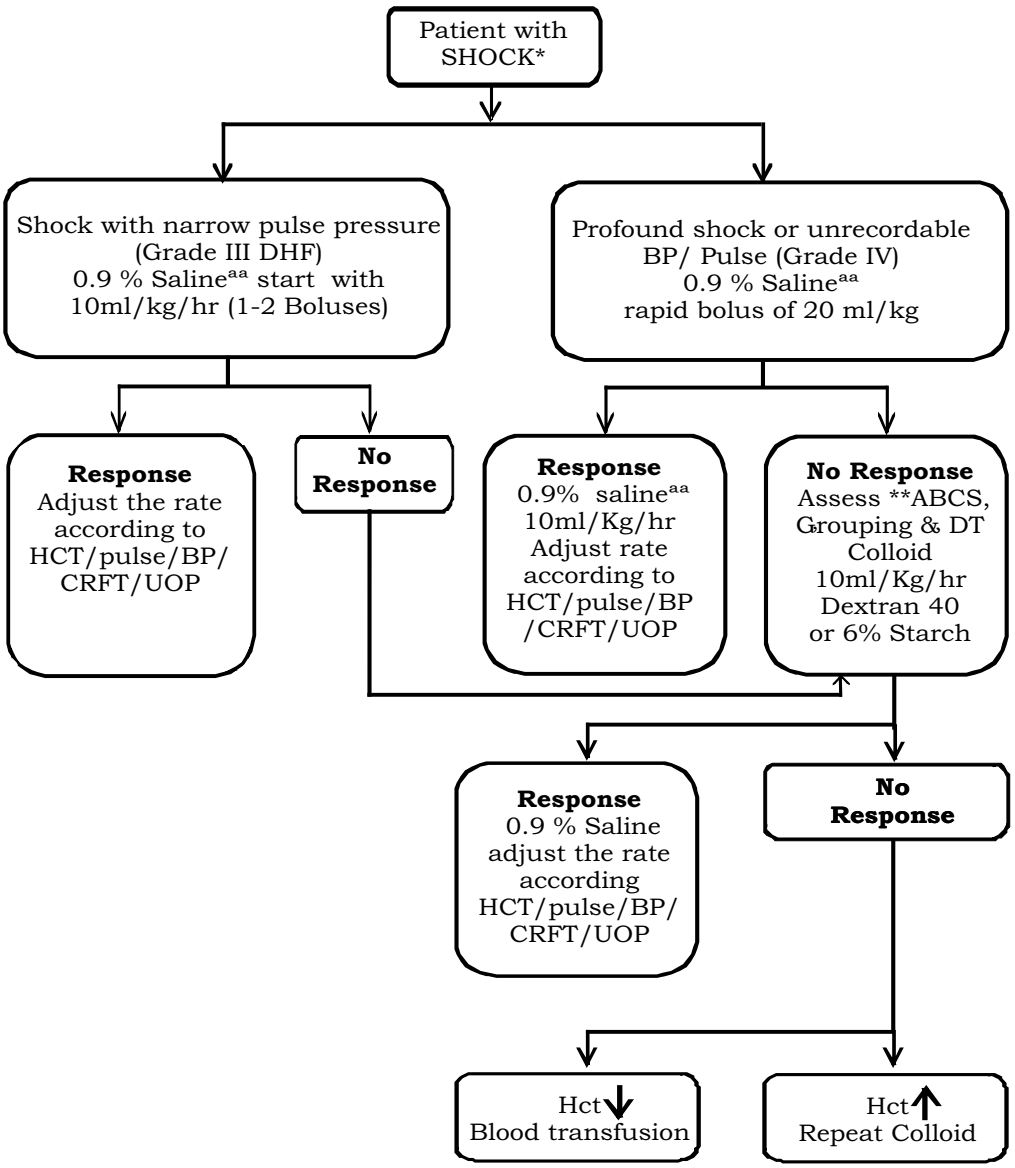
M +5% VOLUME AND THE RATES SHOWN IN THE FIGURE ARE ONLY A GUIDE WHICH ONE SHOULD TRY NOT TO EXCEED

If the rate of IV fluids cannot be reduced gradually as shown in the graph ABCS** should be checked and corrected.
It is also worth noting that though it is possible to manage some patients with less than M+5% volume of fluid it should always be done only by maintaining a UOP >0.5ml/kg/hr and adequate BP and pulse **THROUGHOUT** the critical phase with frequent monitoring.

REMEMBER- fluid restriction without such monitoring would otherwise lead to prolonged shock!

**ABCS A- Acidosis B- Bleeding C- Calcium S- Sugar

Figure: Algorithm on management of Shock in DHF



*All patients in shock – Call for help, Ensure adequate oxygenation, Keep flat/head low

**ABCS A- Acidosis B- Bleeding C- Calcium S- Sugar

[aa] 5% dextrose in N Saline is a useful alternative to N Saline when available especially in patients who are likely be without any food intake for prolonged periods. In such patients assess blood sugar intermittently.

▶ *Indications for Colloids (Dextran 40 and 6% Starch)*

1. In the management of shock after 2 crystalloid boluses if the pulse /BP has not picked up.
2. Development of shock when already having a fluid overload or the amount of fluid received over a period of time appears to be in the direction of exceeding M + 5% deficit

Key points – Colloid administration

- Both dextran 40 and 6% Starch (Hydroxy Ethyl Starch) are recommended only during the critical phase (24 to 48h) of DHF.
- They should only be used as boluses over a maximum period of one hour (10ml/kg/h) at a time and not as infusions unlike saline. (a half bolus could be 5ml/kg given over 30 minutes)
- Dextran may sometimes interfere with grouping and cross matching of blood. It is advisable to preserve a sample of blood for grouping and cross matching before initiating Dextran.
- One could use up to 3 doses of Dextran 40 (each as 10ml/kg/hour) during a 24 hour period(6 doses within 48 hours). 6% Starch (HES) could be given up to 5 doses (each as 10ml/kg/hour) per 24 hours (10 doses within 48 hours).
- When Normal saline is given it remains in circulation only for about 1 to 2 hours or less during rapid leaking. Even fluids like fresh frozen plasma (FFP) will readily leak and will not hold blood pressure for long periods. A colloid (dextran or 6% Starch) will remain longer.

Very Important :
While in the critical phase if the patient deteriorates with no haemoconcentration (or if Hct drops) one has to suspect concealed bleeding

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

Comparable rate of IV fluid in adults and children- (both with Shock and without Shock)

The rates for childern weighing more than 50kg are same as the rate for adults

Note	**Children** Rate (ml/kg/hour)	**Adult** Rate (ml/hour)
Half the maintenance M/2	1.5	40 - 50
Maintenance (M)	3	80 - 100
M + 5% Deficit	5	100 - 120
M + 7% Deficit	7	120 - 150
M + 10% Deficit	10	300 - 500

Source:

Holiday MA, Segar WE. Maintenance need for water in parenteral fluid therapy Pediatrics 1957;19: 823.[79]

4.2.5. Management of complicated DHF

High risk patients for complications:

- Infants
- Obese patients
- `Prolonged shock
- Bleeding
- Encephalopathy
- Underlying diseases
- Pregnancy

Causes of death in DHF patients:

Prolonged shock

- Delayed diagnosis/ delayed resuscitation and late presentations are the usual reasons for prolonged shock
- Untreated prolonged shock > 4 hours will lead to organ failure and prognosis of such a patient is very gloomy;
  - Liver failure - prognosis 50%
  - Liver + Renal failure - prognosis 10%
  - 3 organs failure (+respiratory failure) - prognosis very bleak

Fluid overload

- Use of hypotonic saline, excess fluids or fluid given beyond the time of leakage are the usual causes for fluid overload.

Massive bleeding

Unusual manifestations

- Encephalopathy
- Underlying co-morbidity
- Dual infection

▶ *ABCS*

Consider ABCS when there is no improvement in spite of adequate fluid therapy.

A: Acidosis

B: Bleeding

C: Calcium

S: Sugar

Acidosis

- Acidosis is not uncommon in profound shock and prolonged acidosis makes patients more prone to more advanced DIC which contributes to massive bleeding.
- Acidosis should be corrected early.
- Correction of acidosis when the pH is <7.35 together with HCO_3^- level <15 mmol/l is recomended as early correction of acidosis is known to prevent bleeding and DIC in Dengue. (This is different from the recommendation for correction of acidosis in septic shock.)
- One may use empirical $NaHCO_3$ 1ml/kg slow bolus (max 50ml) diluted in equal volume of normal saline if the patient has no clinical improvement (still in shock with cold clammy skin and cyanosis) after 15-30 minute of initial IV fluid resuscitation for shock. If the amount of $NaHCO_3$ needed in a single dose is above 10ml, a specialist should be consulted.

Hypocalcaemia

- Hypocalcaemia is common in DHF. Almost every patient with complicated DHF has hypocalcaemia.
- When a dengue patient has a convulsion it could be due to hypocalcaemia.
- To detect hypocalcaemia: Measure serum Ca2+ level or Corrected QT interval (not always evident) in ECG

When to give calcium?

- Give empirical calcium **if** the patient is **complicated** and deteriorating or not showing expected improvement to fluid.
- Dose 1ml/kg of 10% Ca Gluconate slow IV bolus over 15-20min diluted in equal volume of N saline (look for bradycardia while pushing slowly) **Max: 10ml**. Can be repeated even 6 hourly if the patient is not improving.

▶ ***Management of Bleeding***

Remember: Bleeding could be **concealed** in DHF.

Indications for Blood Transfusions

1. If there is significant overt bleeding
2. When one suspects concealed bleeding
    - When PCV drops without clinical improvement
    - Severe metabolic acidosis and end-organ dysfunction despite adequate fluid replacement.

Note:

1. Even with bleeding the PCV drop may take time (4-5hrs). When the patient does not show improvement it is important to do repeat PCVs frequently.
2. Haemoglobin level may remain normal despite significant blood loss.

Use Packed Red cells (PRC) or Whole Blood (WB)

- If there is fluid overload use PRC at 5ml/kg once and repeat only if needed
- If there is no fluid overload use 10ml/kg of Whole Blood
- 5ml/kg of PRC or 10ml/kg of WB will increase PCV by 5%
- Even if bleeding is likely and if PCV is >45% do not give blood without bringing down the PCV first by giving a colloid.

Indications for platelet transfusion

- Prophylactic platelet transfusion is **NOT recommended.**
- Each platelet pack is 50-150ml and unnecessary use of platelets will contribute to fluid overload
- Platelet transfusions are needed only on very few occasions, preferably to be decided by the Consultant in the ward.
- Thrombocytopenia is unlikely to produce spontaneous bleeding in DHF/DSS. Even with low platelet counts (close to or <20,000/mm^3) if there is no significant bleeding do not give platelets. Petechiae are not an indication for platelet transfusion. In DHF thrombocytopenia can cause bleeding with trauma or surgery (E.g. Insertion of a CVP line when platelet count is <20,000/mm^3).

▶ *Adjunct Therapy*

Indications for Recombinant factor VII

- Consider **only** in cases with bleeding where the cause of bleeding is due to other reasons

  E.g. Peptic ulcer, trauma etc. as a temporary measure until surgical intervention is done in surgically correctable bleeding. Even when factor VII is used for such exceptional situations it may need to be repeated in 6-10 hours as the action does not last long.
- **No indication for routine use** in cases with generalized bleeding due to DIC,prolonged shock and multiple organ failure**.**

Indications for Inotropic support

- Very limited in DHF
- May do more harm than good by giving a false impression about BP. Sometimes BP could be maintained by inotropes only at the expense of vasoconstriction which further compromises peripheral perfusion.
- May consider using inotropes only if significant persistent hypotension after adequate fluid resuscitation
- If a decision is made to introduce inotropes it is important to ensure that there is adequate volume of fluid in circulation confirmed by adequate CVP (It is best for the patient to have a CVP line in such instances).

Indications for steroids and IV immunoglobulin.

- There is insufficient evidence to support the use of intravenous immunoglobulin and steroids in the management of dengue patients.
- ***Use of steroids (hydrocortisone, dexamethasone and methyl prednisolone) and/or immunoglobulin is NOT recommended.***

Indications for fresh frozen plasma transfusion. (FFP)

- FFP will readily leak and will not hold blood pressure for long periods.
- FFP transfusions lead to fluid overload as even correction of coagulopathy need a large volume (40-50ml/kg).
- FFP transfusions do not produce sustained changes in the coagulation status and do not reduce the bleeding outcome in patients with DHF/DSS.
- Can produce anaphylactic reactions and transmission of blood borne diseases like HIV, Hep B etc.

Prophylactic transfusion of FFP is NOT recommended

I.V. Frusemide

- Useful both in the critical phase and convalescent phase (recovery phase) in many patients.
- Unlike in some other conditions a dose as small as 0.5mg/kg is likely to produce the desired results in most patients with normal renal functions
- Since IV frusemide could produce hypotension and shock it is important to specially monitor patients very frequently (every 10-15minutes) for at least 1-2 hours after each frusemide dose, at all stages.

Indications for IV Frusemide

- During recovery phase when there is suggestion of pulmonary oedema or fluid overload.
- In patients passing less than 0.5ml/kg/hr of urine despite receiving adequate fluids and having stable BP, pulse, Hct to improve the UOP.
- Midway between blood transfusions.
- Midway in the infusion of colloids when colloids are given to patients who are already fluid overloaded or who are likely to be overloaded depending on the fluids already given.

▶*Management of encephalopathy*

Most of the patients with encephalopathy are due to hepatic encephalopathy. The principal treatment of hepatic encephalopathy is to prevent increase in intra cranial pressure.

The following are recommendations for supportive therapy:

- Adequate airway oxygenation with O2 therapy. Intubation may be needed for those with respiratory failure or in semi-coma/coma
- Prevent/ reduction of ICP by;
  - Minimal IV fluid to maintain adequate intra vascular volume, Ideally total IV fluid should not exceed 80% maintenance
  - Switch to colloids earlier if the patient continues to have a rising Hct and a large volume of IV is needed in cases with severe plasma leakage
  - Administer diuretic if indicated in cases with signs and symptoms of fluid leakage
  - Keep head in midline position with a tilt up at 15°-30° degrees
  - Consider steroid to reduce ICP. dexamethasone 0.5 mg /kg/day IV every 6-8 hours
  - Hyperventilation
- Maintain blood sugar level > 60 mg/dl. Recommend glucose infusion rate between 4-6 ml/kg/hr
- Correct acid-base and electrolyte balance e.g. Correct hypernatremia, hypo/ hyperkalaemia, hypocalcaemia and acidosis
- Vitamin K IV administration: 3 mg for < 1yr, 5 mg for 1- 5yrs, 10mg for > 5yrs and adults.
- Anti-convulsants should be given for control of seizures: phenobarbital, phenytoin and diazepam as indicated.
- When high liver enzymes indicate hepatic encephalopathy other evidence for concealed bleeding should be looked for as it is one of the commonest causes of hepatic failure in DHF. Transfuse blood, preferably fresh packed red cells as indicated. Other blood components such as platelets, FFP may not be given because the fluid overload can cause increased ICP.

- Reduce ammonia production – use lactulose, neomycin (may not be necessary if systemic antibiotics are given).

  Empirical antibiotic therapy may be indicated in case of suspected superimposed bacterial infections.
- H2 blockers or Proton pump inhibitors may be given to alleviate GI bleeding.
- Avoid unnecessary drugs because most drugs have to be metabolised by the liver.
- There is no clear indication to use N-Acetyl cysteine in patients who have no paracetamol toxicity. Use of NAC may complicate fluid therapy in DHF patients.

5. 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 convalescent phase:

- Improved general well-being and improved appetite
- Appearance of convalescent rash (typically appears as white patches in a red background)
- Generalized itching
- Hamodynamic stability
- Bradycardia
- Diuresis
- Stabilization of Haematocrit (HCT may even be lower than baseline due to reabsorption)
- Rise of white cell count followed by a rise of platelet count

Complications during Convalescence

- **Fluid Overload** – Management already discussed above
- **Hypokalaemia** – Oral potassium supplements and fresh fruits; rarely may need addtion of potassium chloride to IV fluids.
- **Nosocomial infections**

6. Laboratory Diagnosis

During the first three days of the illness, PCR for dengue virus is usually positive. However, sensitivity and specificity of this test may 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 may not be cost effective.

IgM antibody is likely to become positive after fifth to sixth day of the illness and is considered as the best option for routine diagnosis as a positive result will make a probable case of dengue 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.

7. Transferring a patient to another institution

Facilities in some small hospitals may not be adequate to manage a patient with DHF who has entered the critical phase. Such patients may be transferred to an institution with adequate facilities. Every transfer should be done after obtaining advice from the Consultant Paediatrician who will be receiving the patient. Patient should be transferred after initial resuscitation with a fluid bolus in accordance with the advice given and appropriate intravenous fluid infusion should be given during the transfer. Adequate information regarding the patient should be provided in the transfer form and this should include daily fluid balance, investigation results and treatment given.

Any patient with prolonged shock or multi organ failure is best managed in an intensive care setting if such facilities are available.

8. Unusual Dengue (Expanded Dengue Syndrome)

In different parts of the world there have been some reports of 'Unusual dengue' where the patients developed clinical features which are different to what is usually expected in DF or DHF. These include encephalopathy and neurological manifestations, organ failure such as hepatic renal cardiac and other isolated organ involvement which could be categorized as 'expanded dengue syndrome'. Some of these could be explained as complications of severe profound shock or as associations of underlying host conditions/diseases or co-infections. However if and when they are not associated with plasma leak they will also need different treatment according to the conditions. Currently available evidence on such unusual manifestations has not excluded other factors such as concurrent infections other than dengue through exhaustive methods and such conditions will need to be investigated more. However, it is very important to note that 'unusual dengue' is an extreme minority of the clinical spectrum and patients should not be categorized into this group without very detailed and careful evaluation of the clinical events , treatment given and response to treatment.

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Annexure I

Monitoring Chart I - for Management of Dengue Patients – Febrile Phase (4 – 6 hrly)

Name of the patient

……BHT…….

Date time	HR	BP	Pulse Pressure	CRFT Sec	Extremity Warm /Cold	RR	UOP	UOP mlKg/hr	PCV	Platelet Count	Treatment /Remarks

Monitoring Chart II for Management of DHF Patients during Critical Phase

Annexure II

Patient to be monitored hourly

Name of the patient ……BHT……Date and time of admission ……ward -……

Weight - ……	Height - ……	Ideal body weight - ……	M- ……	M+ 5% = ……ml

Critical Phase Commencing date and time -…….,,,,,,,,,,,,,, End date and time ----------

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UOP ml/Kg/hr																								
Platelet count																								

Monitoring Chart II for Management of DHF Patients During Critical Phase page2

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UOP																								
UOP ml/Kg/hr																								
Platelet count																								

Annexure III

Monitoring Chart III to be used during the Peak of leakage and during the shock

Patient to be monitored every 15 minis

Fluid Boluses Given
Normal Saline: ……
Dextran ----------Maximum 3 per 24h / 6 per 48h
Starch: ----------Maximum 5 per 24h / 10 per 48 h
Other fluid :PRC/WB----------

Fluid ml/Kg/ hr																							
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extremities																							
UOP ml/Kg/hr																							
Platelet count																							

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