PRACTICE GUIDELINES ON THE MANAGEMENT OF DENGUE FEVER AND DENGUE HAEMORRHAGIC FEVER IN CHILDREN

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Prepared by Infectious Diseases Group PPA

Endorsed by Pakistan Paediatric Association

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CONTENTS

Guidelines Development

The working group for the development of these guidelines comprised of Paediatricians having special interest in Paediatric Infectious Diseases, from various tertiary care hospitals of the country. Sources of the guidelines are "Comprehensive Guidelines for Prevention and Control of Dengue and Dengue Hemorrhagic Fever, WHO 2011", "Guidelines on Management of Dengue Fever and Dengue Hemorrhagic Fever in Children and Adolescents, Ministry of Health Sri Lanka, December 2010" and "CDC Case Definitions for Infectious Conditions under public health surveillance."

Aims

The aim of these guidelines is to aid all health care providers in the management of children with dengue infection.

Clinical Questions

The clinical questions for these guidelines are:

i. **What is the clinical spectrum of dengue infection and their pathogenesis?**

ii. **How is dengue fever and dengue haemorrhagic fever diagnosed and classified based on clinical case definition?**

iii. **How can patients with dengue be treated successfully?**

Target Population

These guidelines are developed for children and adolescent with dengue infection.

Target Group

These guidelines are meant for all health care providers particularly Paediatricians.

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LIST OF ABBREVIATIONS

ABCS	Acidosis, bleeding, calcium, sugar
ABW	Actual body weight
BP	Blood pressure
CBC	Complete blood picture
CRFT	Capillary re-fill time
CRF	Chronic renal failure
CSF	Cerebrospinal fluid
CT	Computerized tomography
CVP	Central venous pressure
DF	Dengue fever
DHF	Dengue haemorrhagic fever
DSS	Dengue shock syndrome
ELISA	Enzyme-linked immunosorbent assay

ESR	**Erythrocyte sedimentation rate**
FFP	**Fresh frozen plasma**
G-6-PD	**Glucose-6-phosphatase dehydrogenase**
Hct	**Haematocrit**
HI	**Haemagglutination-inhibition**
Hr	**Hour**
IBW	**Ideal body weight**
ICP	**Intracranial pressure**
IgG	**Immunoglobulin G**
IgM	**Immunoglobulin M**
IV	**Intravenous**
MRI	**Magnetic resonance imaging**
NS1	**Non-structural protein 1**
ORS	**Oral rehydration solution**
RT-PCR	**Reverse transcriptase polymerase chain reaction**
SGOT	**Serum glutamic oxaloacetic transaminase**
SGPT	**Serum glutamic pyruvate transaminase**
UOP	**Urine output**
VPC	**Ventricular premature contraction**
WBC	**White blood cells**

INTRODUCTION OF DENGUE INFECTIONS

Dengue infection has become the most important communicable disease in Pakistan today with a significant social, economical and political impact. Recent dengue epidemics were reportedly more severe.

Dengue infection is caused by one of the four serotypes of Dengue virus. It is spread by the bite of infected female *Aedes* mosquito. Dengue Fever (DF);[Classical, Undifferentiated], and Dengue Haemorrhagic Fever (DHF) / Dengue Shock Syndrome (DSS) are two distinct disease patterns. Which particular individual will have one of these depends upon the age and immune status of the individual due to previous infection. The association between occurrence of DHF/DSS and secondary dengue infections implicates the immune system in the pathogenesis of DHF. Both the innate immunity such as the complement system and NK cells as well as the adaptive immunity including humoral and cell mediated immunity are involved in this process. Enhancement of immune activation, particularly during a secondary infection, leads to exaggerated cytokine response resulting in changes in vascular permeability. In addition, viral products such as NS1 may play a role in regulating complement activation and vascular permeability. Infection with one serotype gives lifelong immunity to that particular serotype, but there is only short term cross-protection for the other serotypes. Secondary infection with heterologous serotype during a critical period, from six month to 5 year after primary infection, would cause more severe form of the disease, i-e-DHF/DSS. Exception is the infants where primary infection may cause DHF/DSS. Majority of the deaths occur in shock syndrome and occasionally with massive haemorrhages.

Features of DF and DHF / DSS may be clinically indistinguishable for the first 2-3 days but they are two distinct entities from the very beginning. DF is self-limiting disease. It has two phases; febrile phase and convalescent phase. DF may have thrombocytopenia and occasional bleeding but is not a fatal illness. However, in DHF

/ DSS, there are 3 phases; febrile phase, critical phase and convalescent phase. The hallmark feature of DHF / DSS is leakage of protein rich plasma to extra- vascular compartment during critical period, leading to hypovolemia and shock in severe cases.

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:-

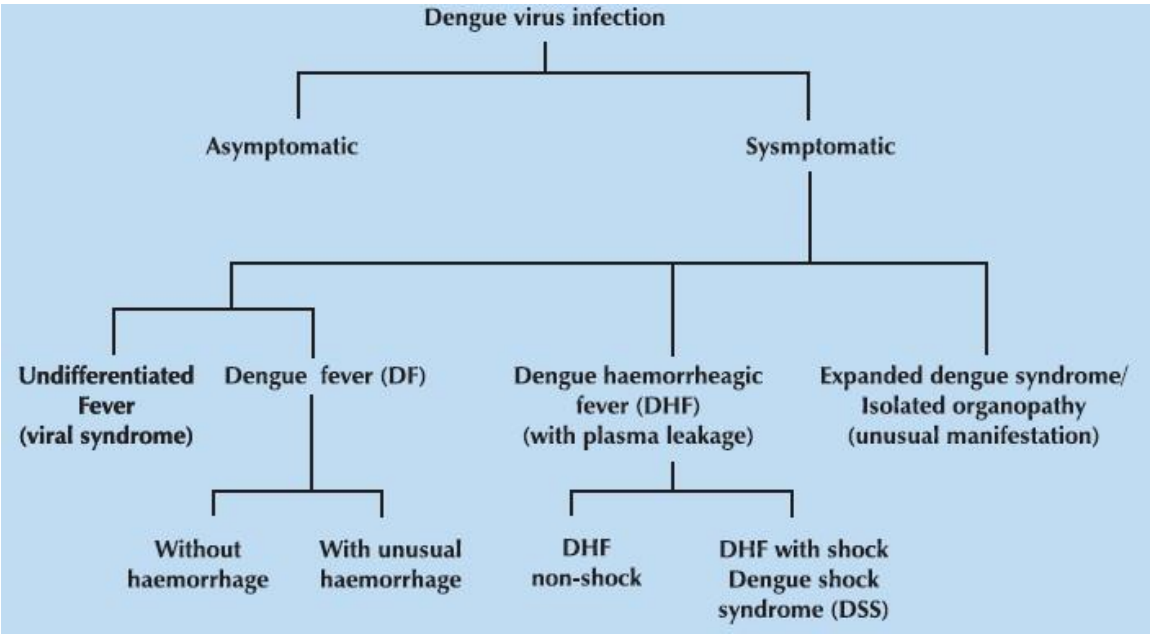
1- Undifferentiated febrile

illness 2- Dengue Fever (DF)

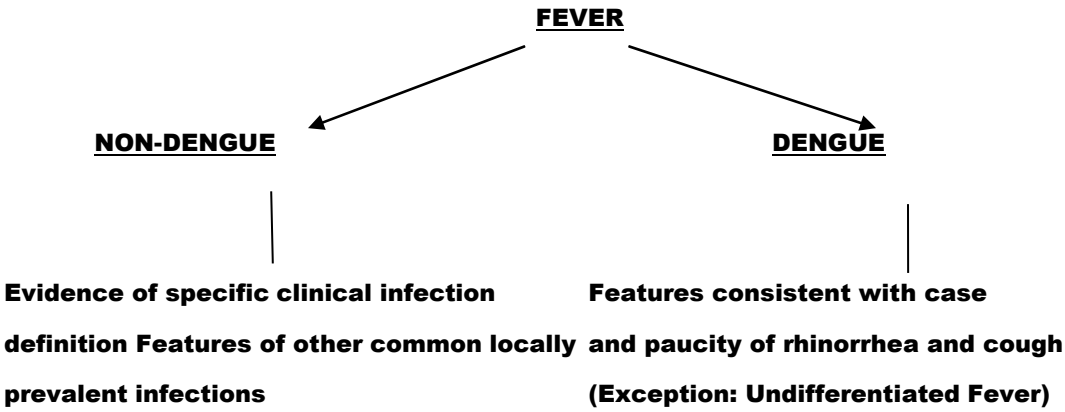
3- Dengue Haemorrhagic Fever (DHF)/Dengue Shock Syndrome (DSS)

4. **Expanded Dengue syndrome**

Figure 1: Manifestations of Dengue Virus infection



- ***Always keep high index of suspicion about dengue infection during peak season of disease.***
- ***Take detail clinical history and examine patient thoroughly to exclude other locally prevalent infections.***
- ***Classify patients on the basis of clinical case definition.***
- ***Do appropriate laboratory workup to gather further evidences***



FEVER WHICH IS NOT DENGUE

Chikungunya Virus Infection: Acute onset of fever >38.5˚C and severe arthralgia/arthritis not explained by other medical conditions. Other common signs and symptoms include muscle pain, headache, nausea, fatigue and rash.

Measles: Any person with fever and maculopapular (i.e. non-vesicular) rash and at least one of the following; cough, coryza (i.e. runny nose), or conjunctivitis (i.e. red eyes)

Rubella: An illness with acute onset of generalized maculopapular rash, temperature >99.0^{0}F (>37.2^{0}C), arthralgia/arthritis, lymphadenopathy (usually suboccipital, postauricular and cervical) or conjunctivitis

Hepatitis: Acute illness including jaundice, dark urine, anorexia, malaise, extreme fatigue, and right upper quadrant abdominal tenderness.

Typhoid Fever: An illness often characterized by insidious onset of sustained fever, headache, malaise, anorexia, in children coated tongue, relative bradycardia, splenomegaly, constipation or diarrhea, nonproductive cough and may have a skin rash (rose spots).

Malaria: A patient residing in malaria endemic area or having a history of visiting a malaria endemic area, presenting with fever or history of fever with chills, rigors and headache. (Non specific symptoms otherwise unexplained, include myalgia, backache and joint pain)

Bacterial Meningitis: Acute onset fever (>38.5^{0}C rectal or >38.0^{0}C axillary), headache and one of the following signs; neck stiffness, altered

consciousness or other meningeal signs (irritability, poor sucking, seizures, bulging fontanells in infants)

Meningococcemia: **Meningococcal disease manifests most commonly as meningitis and/or meningococcemia that may progress rapidly to purpura fulminans, shock, and death.**

Influenza like illness: **Fever ≥100^{0}F, cough and/or sore throat in the absence of known cause other than influenza.**

CLINICAL CASE DEFINITIONS

DENGUE FEVER (DF)

Probable: **An acute febrile illness of 2-7 days duration with 2 or more of the following:**

- **Headache**
- **Retro-orbital pain**
- **Myalgia**
- **Arthralgia/bone pain**
- **Rash ***
- **Leucopenia**
- **Haemorragic manifestations.**

No evidence of Plasma leak

***Rash of DF:** **Diffuse flushing or fleeting eruptions may be observed on the face, neck and chest during the first two to three days, and a conspicuous rash that may be maculopapular or rubelliform appears on approximately the third or fourth day.**

***Convalescent rash:** **This rash is characterized by confluent petechiae surrounding scattered pale, round areas of normal skin. Skin itching may be observed. This rash is recovery rash. The recovery rash may be observed in both DF and DHF but usually is more common in DF.**

Highly Suggestive: **Probable along with one of the following;**

- **Supportive serology on single sample after 5th day; titre 1280 or greater with haemagglutinaion inhibition (HI) test, comparable IgG titre with enzyme- linked immunosorbent assay (ELISA), or testing positive in IgM antibody test**
- **Occurrence at the same location and time as confirmed cases of dengue fever**

Confirmed: **Case confirmed by one of the following;**

- **Isolation of dengue virus from serum, cerebrospinal (CSF) or autopsy samples**
- **Fourfold or greater increase in serum IgG (by HI test or by ELISA) or increase in IgM antibody specific to dengue virus**

- **Detection of dengue virus or antigen (NS-1) in tissue, serum CSF by immunohistochemistry, immunofluorescence or ELISA.**
- **Detection of Dengue virus genomic sequence by RT-PCR**

UNDIFFERENTIATED FEVER

Infants, and children who have been infected with dengue virus, especially for the first time (i.e. primary dengue infection), may develop a fever indistinguishable from other viral infections. Maculopapular rash may accompany the fever or may appear during defervescence. Upper respiratory and gastrointestinal symptoms are common.

- ***Chikungunya is a viral disease that is spread by Ades mosquitoe (same which spreads dengue). The proximity of mosquito breeding sites to human habitation is a significant risk factor for chikungunya.***
- ***The disease shares some clinical feature with dengue. Thrombocytopenia is reported in Chikungunya infection but is less common than Dengue. Chikungunya infection, contrary to Dengue, does not lead to shock syndrome.***
- ***The disease has been found to be endemic in countries where dengue is also endemic. Hence, shall be considered in differential diagnosis.***
- ***Chikungunya is characterized by an abrupt onset of fever frequently accompanied by joint pain. Other common signs and symptoms include muscle pain, headache, nausea, fatigue and rash. The joint pain is often very debilitating, but usually ends within a few days or weeks. Most patients recover fully, but in some cases joint pain may persist for several months, or even years. Occasional cases of eye, neurological and heart complications have been reported, as well as gastrointestinal complaints. Serious complications are not common, but in older***

DENGUE HAEMORRHAGIC FEVER (DHF)

DHF is characterized by the acute onset of high fever and is associated with signs and symptoms similar to DF in the early febrile phase.

The following must all be present:

- **Fever; acute onset, high and continuous, lasting 2-7 days, occasionally biphasic.**
- **Hemorrhagic tendencies, evidenced by at least one of the following: A positive tourniquet test, petechiae, ecchymoses or purpura, bleeding**

from the mucosa, gastrointestinal tract, injection sites or other locations

- **Thrombocytopenia (100,000 cells per mm^3 or less).**

- **Evidence of plasma leakage due to increased vascular permeability, manifested by at least one of the following:**
  - **A rise in the haematocrit ≥20% above average for age, sex and population or baseline value/recovery.**
  - **Pleural effusion, ascites and hypoprotienaemia/hypoalbuminaemia (< 3.5g/dl or if albumin has dropped by ≥ 0.5g/dl), hypocholestrolemia (<100mg/dl or if cholesterol has dropped by 20mg/dl)**

Tourniquet Test

Inflate BP cuff to a point midway between the systolic and diastolic pressures for 5 minutes. Test is positive when ≥10 petechiae/1inch^2 are observed. Test may be negative or only mildly positive in obese patients and during the phase of profound shock. However, it will turn positive after recovery from shock

Evidence of Plasma leakage such as clinical fluid accumulation (Pleural fluid and/or ascites) and increase in Hct ≥20%) will differentiate between bleeding DF with thrombocytopenia and DHF

DENGUE SHOCK SYNDROME (DSS)

All of the above four plus any of following;

- **Tachycardia, cool extremities, delayed capillary refill, weak pulse, lethargy or restlessness**
- **Narrow pulse pressure (<20 mm of Hg) with increased diastolic pressure**
- **Hypotension for age, defined as systolic blood pressure < 80 mmHg for those aged <5 years or 80-90 mmHg for older children and adults**
- **Cold, clammy skin and restlessness.**

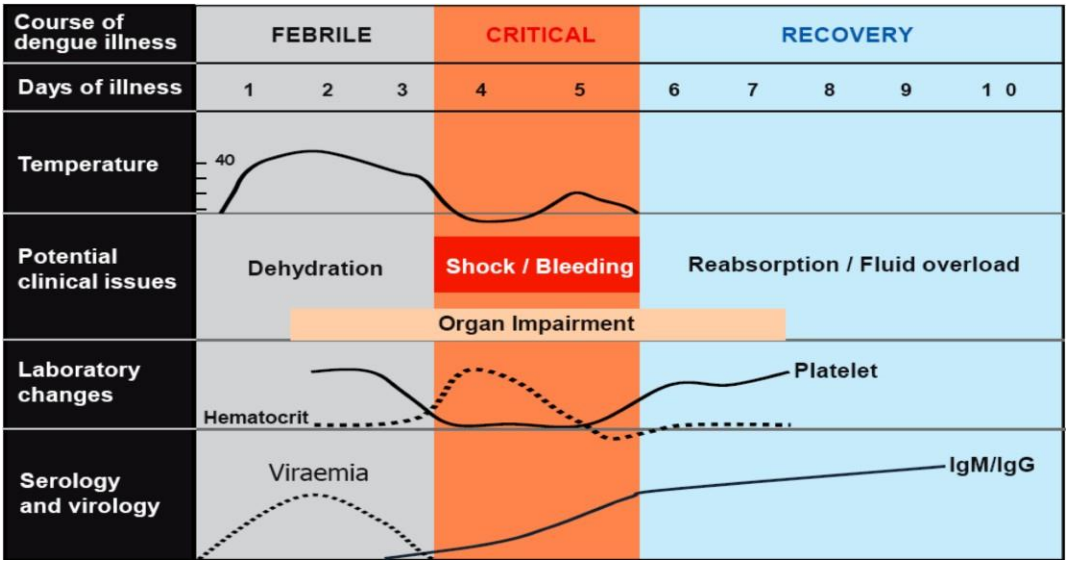
Narrow Pulse Pressure is an early feature of

- ***Elevated levels of SGOT (well above SGPT) is helpful in the diagnosis of DHF in early febrile phase***
- ***Low ESR (<10 mm/1st hour) during shock differentiates DSS from septic shock***

Table 1: WHO classification of Dengue Infections and Grading of severity of DHF

DF/ DHF	Grade	Signs and Symptoms	Laboratory
DF		Fever with two of the following: • Headache. • Retro-orbital pain. • Myalgia. • Arthtralgia/bone pain. • Rash. • Haemorrhagic manifestations. • **No evidence of plasma leakage.**	• Leucopenia (wbc ≤5000 cells/mm³). • Thrombocytopenia (Platelet count <150 000 cells/mm³). • Rising haematocrit (5% – 10%). • No evidence of plasma loss.
DHF	I	Fever and haemorrhagic manifestation (positive tourniquet test) and **evidence of plasma leakage**	Thrombocytopenia <100 000 cells/ mm³; HCT rise ≥20%
DHF	II	As in Grade **I plus** spontaneous bleeding.	Thrombocytopenia <100 000 cells/mm³; HCT rise ≥20%.
DHF#	III	As in Grade **I or II plus** circulatory failure (weak pulse, narrow pulse pressure (≤20 mmHg), hypotension, restlessness).	Thrombocytopenia <100 000 cells/mm³; HCT rise ≥20%.
DHF#	IV	As in Grade **III** plus profound shock with undetectable BP and pulse	Thrombocytopenia < 100 000 cells/mm³; HCT rise ≥20%.

Figure 2: Clinical course of DHF



***Critical phase; the period of plasma leakage, is the hallmark of DHF/DSS. It begins around the transition from febrile to the afebrile phase (usually occurs on day 3 and 4), and lasts for 48 hours only.**

EXPANDED DENGUE SYNDROME

Unusual manifestations of patients with severe organ involvement such as liver, kidneys, brain or heart associated with dengue infection have been increasingly reported in DHF and also in dengue patients who do not have evidence of plasma leakage. These unusual manifestations may be associated with coinfections, comorbidities or complications of prolonged shock.

Table 2: Expanded Dengue Syndrome

System	Unusual or atypical manifestations
Neurological	Febrile seizures in young children. Encephalopathy. Encephalitis/aseptic meningitis. Intracranial haemorrhages/thrombosis. Subdural effusions. Mononeuropathies/polyneuropathies/Guillane-Barre Syndrome. Transverse myelitis.
Gastrointestinal/hepatic	Hepatitis/fulminant hepatic failure. Acalculous cholecystitis. Acute pancreatitis. Hyperplasia of Peyer's patches. Acute parotitis.
Renal	Acute renal failure. Hemolytic uremic syndrome.
Cardiac	Conduction abnormalities. Myocarditis. Pericarditis.
Respiratory	Acute respiratory distress syndrome. Pulmonary haemorrhage.
Musculoskeletal	Myositis with raised creatine phosphokinase (CPK). Rhabdomyolysis.
Lymphoreticular/bone marrow	Infection associated haemophagocytic syndrome. IAHS or Haemophagocytic lymphohistiocytosis (HLH), idiopathic thrombocytopenic purura (ITP). Spontaneous splenic rupture. Lymph node infarction.
Eye	Macular haemorrhage. Impaired visual acuity. Optic neuritis.
Others	Post-infectious fatigue syndrome, depression, hallucinations, psychosis, alopecia.

LABORATORY DIAGNOSIS

The following laboratory tests are available to diagnose dengue fever and DHF:

- **Virus isolation**
  - **serotypic/genotypic characterization**
- **Viral nucleic acid detection by RT-PCR**
- **Viral antigen detection (NS-1)**
- **Immunological response based tests**
  - **IgM and IgG antibody assays**
- **Analysis for haematological parameters**
- **Radiology: CXR and USG-Chest and Abdomen**

Standard haematological parameters such as platelet count and Hct are important and are part of the biological diagnosis of dengue infection. Therefore, they should be closely monitored. Thrombocytopenia, a drop in platelet count below 100,000 per µl, may be observed in DF but is a constant feature of DHF. Thrombocytopenia is usually found between the third and eighth day of illness often before or simultaneously with changes in Hct. Haemoconcentration with an increase in the Hct of 20% or more (for the same patient or for a patient of the same age and sex) is considered to be a definitive evidence of increased vascular permeability and plasma leakage. The white blood cell (WBC) count may be normal or with predominant neutrophils in the early febrile phase. Thereafter, there is a drop in the total number of WBC and neutrophils, reaching a nadir towards the end of the febrile phase. The change in total WBC (≤5000 cells/mm3) and ratio of neutrophils to lymphocyte (neutrophils<lymphocytes) is useful to predict the critical period of plasma leakage. This finding precedes thrombocytopenia or rising Hct. A relative lymphocytosis with increased atypical lymphocytes is commonly observed by the end of the febrile phase and into convalescence. These changes are also seen in DF.

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%. IgM antibody is likely to become positive after 5th to 6th 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 antibody or seroconversion of IgM or IgG in paired sera.

Serum cholesterol, serum protein, albumin, serum sodium, calcium and blood

sugar level, blood gas analysis, coagulation and fibrinolytic factors are indicated according to the individual cases.

MANAGEMENT OF DENGUE INFECTIONS

TRIAGE: On arrival, triage shall be done by a trained person to evaluate the stage of the disease and to decide the further management.

- ***If the patient is critical on arrival, admit in high dependency unit.***
- ***For other patients, take history of duration of fever, and warning signs***
- ***Tourniquet test***
- ***Vital signs; pulse, respiratory rate, temperature, BP and pulse pressure, CRFT***
- ***Immediate medical consultation for patients with shock and***

WARNING SIGNS

- ***No clinical improvement or worsening of situation just before or during the transition to afebrile phase or as the disease progresses.***
- ***Abdominal pain or tenderness***
- ***Persistent vomiting***
- ***Liver enlargement >2cm***
- ***Rapid drop in temperature***
- ***Cold extremities and features of shock***
- ***Bleeding: Epistaxis, black stool, haematemesis, dark coloured urine (haemoglobinuria) or haematuria***
- ***Lethargy, restlessness, drowsiness, sudden behavior change***
- ***Giddiness***
- ***Less or no urine output for 4-6 hours***
- ***Clinical fluid accumulation-pleural effusion, ascites***
- ***Increase in Hct >10%***
- ***Decrease in platelet count ≤100,000/mm^3(OR rapidly falling trend towards <100,000)***

Recommendations for CBC

- ***All febrile patients at the first visit to get the baseline Hct, WBC and Platelets.***
- ***All patients with warning signs.***
- ***All patients with fever >3 days.***

Referral criteria where expertise/facilities are scanty

- **Infants <1 year old.**
- **Obese patients.**
- **Profound/prolonged shock.**
- **Significant bleeding.**
- **Repeated shock 2–3 times during treatment.**
- **Patients who seem not to respond to conventional fluid therapy.**
- **Patients who continue to have rising Hct and no colloidal solution are available.**
- **Patients with known underlying diseases such as Diabetes mellitus, hypertension, heart disease or haemolytic disease etc.**
- **Patients with signs and symptoms of fluid overload.**
- **Patient with isolated/multiple organ involvement.**
- **Patients with neurological manifestations such as change of**

MANAGEMENT OF DF

- **Adequate bed rest.**
- **Adequate intake of fluids (no plain water) such as milk, fruit juice, isotonic electrolyte solution, oral rehydration solution (ORS) and barley/rice water. Avoid red or brown colour juices.**
- ***Beware of overhydration in infants and young children.***
- **Keep body temperature below 39°C. If the temperature goes beyond 39°C, give the patient paracetamol. The recommended dose is 10 mg/kg/dose and should be administered at frequency of not less than six hours.**
- **Avoid using too much paracetamol**
- **Never use aspirin, NSAID and steroids.**
- **Tepid sponging of forehead, armpits and extremities.**
- **Review daily. A complete blood count (CBC) 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).**
- **Monitoring: Advise immediate return for review if any of the warning**

signs appear.

- **The following *high risk categories* of patients with probable dengue fever should be admitted.**

- ***Infants***
- ***Obese patients***
- ***Patients with major co-morbidities / medical problems (diabetes, nephrotic syndrome, CRF, haemolytic diseases such as glucose-6-phosphatase dehydrogenase (G-6PD) deficiency, thalassemia and other haemoglobinopathies, poorly controlled asthma, congenital heart diseases)***
- ***Patients on steroids or NSAIDS treatment***
- ***Adverse social circumstances- living alone, living far from health care facility without reliable means of transport, unreliable parents.***

INDICATIONS OF IV FLUID IN DENGUE INFECTION

- **When the patient cannot have adequate oral fluid intake or is vomiting.**
- **When Hct continues to rise 10%–20% despite oral rehydration.**
- **Impending shock**

MANAGEMENT OF DHF (GRADE I & II; Non-Shock DHF)

The management of DHF during the febrile phase is similar to that of DF. The parents and caretakers must be counseled about the warning signs and return when any one of those is noticed, or after day 3 of febrile illness. It is essential to follow up platelets and Hct levels to detect early plasma leakage that will require IV fluid replacement.

Fluid Calculation

- ***The total amount of fluid recommended (Oral & IV) during the entire critical phase (irrespective of its length) should be***

  M + 5% = Maintenance + 5% of body

  weight 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)

  Example: For 20Kg child, Fluid allowance will be M+5% (1500+1000=2500ml)

- ***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.***

IMPORTANT

- ***Calculate total fluids***
- ***Ideally use Weight for Height charts to calculate ideal body weight (Given in annexure)***
- ***Determine both actual body weight (ABW) and ideal body weight (IBW) and calculate fluids***

Estimate of IBW

<1 year= Age in months+9/2

1-7 years= [Age in years×2]+8

>7 years= Age×3

Choice of Fluids

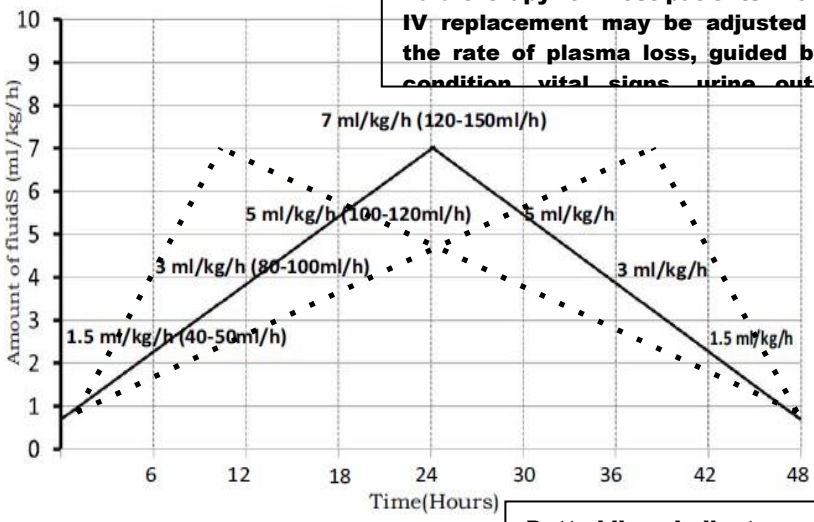
- ***Crystalloids-Isotonic fluids such as N/Saline.***
- ***Colloids-Dextran 40%, Starch 6%***

(Starch 6%: Maximum 5 boluses in 24 hours, Dextran 40: Maximum 3 boluses in 24 hours)

GENERAL PRINCIPLES OF FLUID THERAPY

- **All patients entering the critical phase should be started with 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 at a rate of 0.5ml/kg/hr to 'keep vein open' and the balance as oral. (Use N/2 + 5% dextrose in < 6 months infants; For those >6 months and not taking orally for prolonged periods, it is useful to give N/saline: Use 5% dextrose saline in malnourished children and in children with prolonged starvation to avoid hypoglycemia.**
- **Rate of infusion will depend on the rate of leak judged by pulse, BP, pulse pressure, CRFT, Hct and UOP.**
- **Urine output of 0.5 -1 ml/ kg/hr is sufficient to maintain renal functions during the critical period.**
- **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, BP(Pulse pressure) and Hct.**
- **If a higher rate of maintenance fluid is unable to maintain the pulse pressure, fluid boluses (N. saline) should be used.**

Figure 3: Rate of infusion in Non-Shock Patients



MANAGEMENT OF DSS (DHF GRADE III)

- **Most cases of DHF-III will respond to 10 ml/kg given in children over one hour. Then fluids should be reduced gradually by following the graph below (Figure 5). To avoid over volume replacement, as the rate of plasma leakage is not even, being more rapid during the first 24 hours, the rate and volume of fluid replacement should be adjusted according to the rate of plasma leakage as guided by clinical condition, vital signs, UOP and Hct levels.**

- **As a general guide, the suggested volume of fluid is as follows; gradually reduce IV fluids to 7-5 ml/kg/hr for 1-2 hours, 5-3 ml/kg/hr for 2-4 hours, then 3-2 ml/kg/hr and then further, depending upon haemodynamic status which shall be maintained for upto 24-48 hours.**

- **If vital signs are still unstable after the first bolus, bolus can be repeated with the same dose. In case of no improvement, go to steps of management of uncompensated shock.**

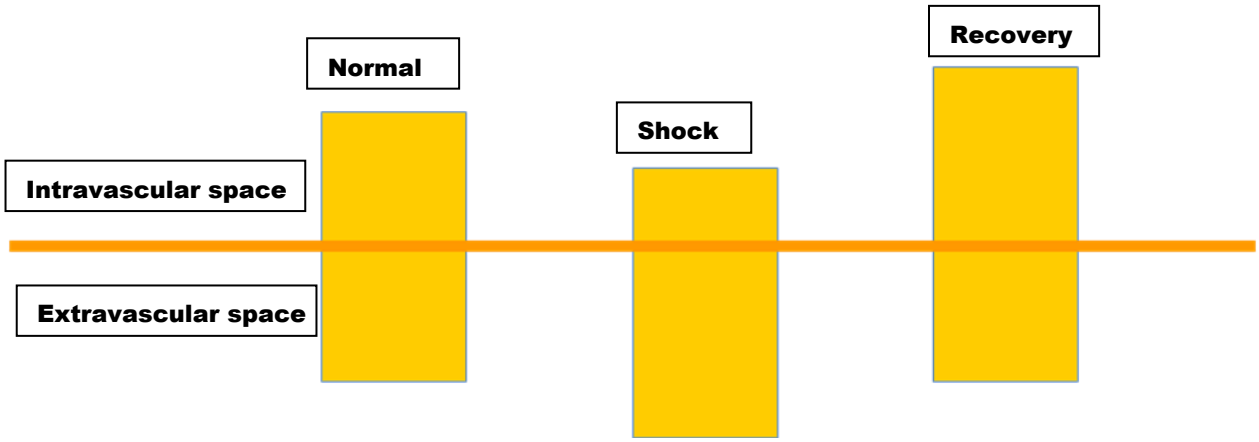
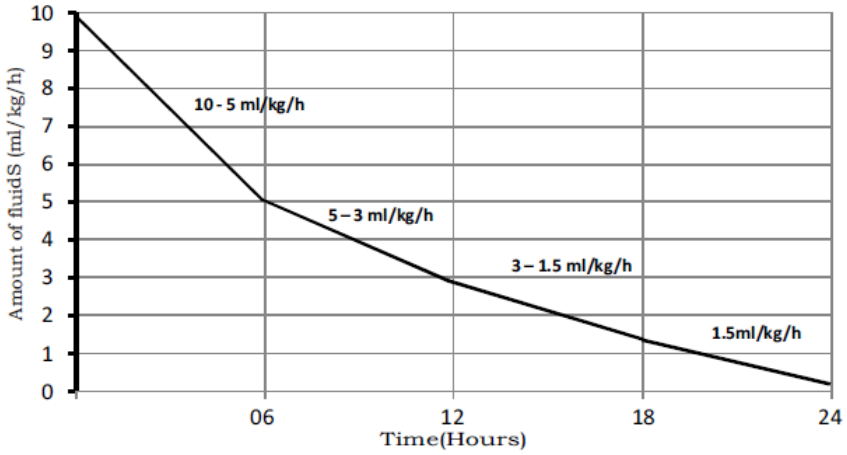


Figure 4: Dynamics of Fluid during dengue shock

***Dengue shock differs from other shock, as during leakage, the fluid from intravascular compartment will leak into the 3rd space causing hypovolemia, and shock in severe cases, without losing any volume from the body. This fluid will return back to the intravascular compartment during recovery phase, which may lead to fluid overload. This fact shall be kept in mind while administering fluid during shock stage.**

Figure 5: Rate of infusion in Shock Patients

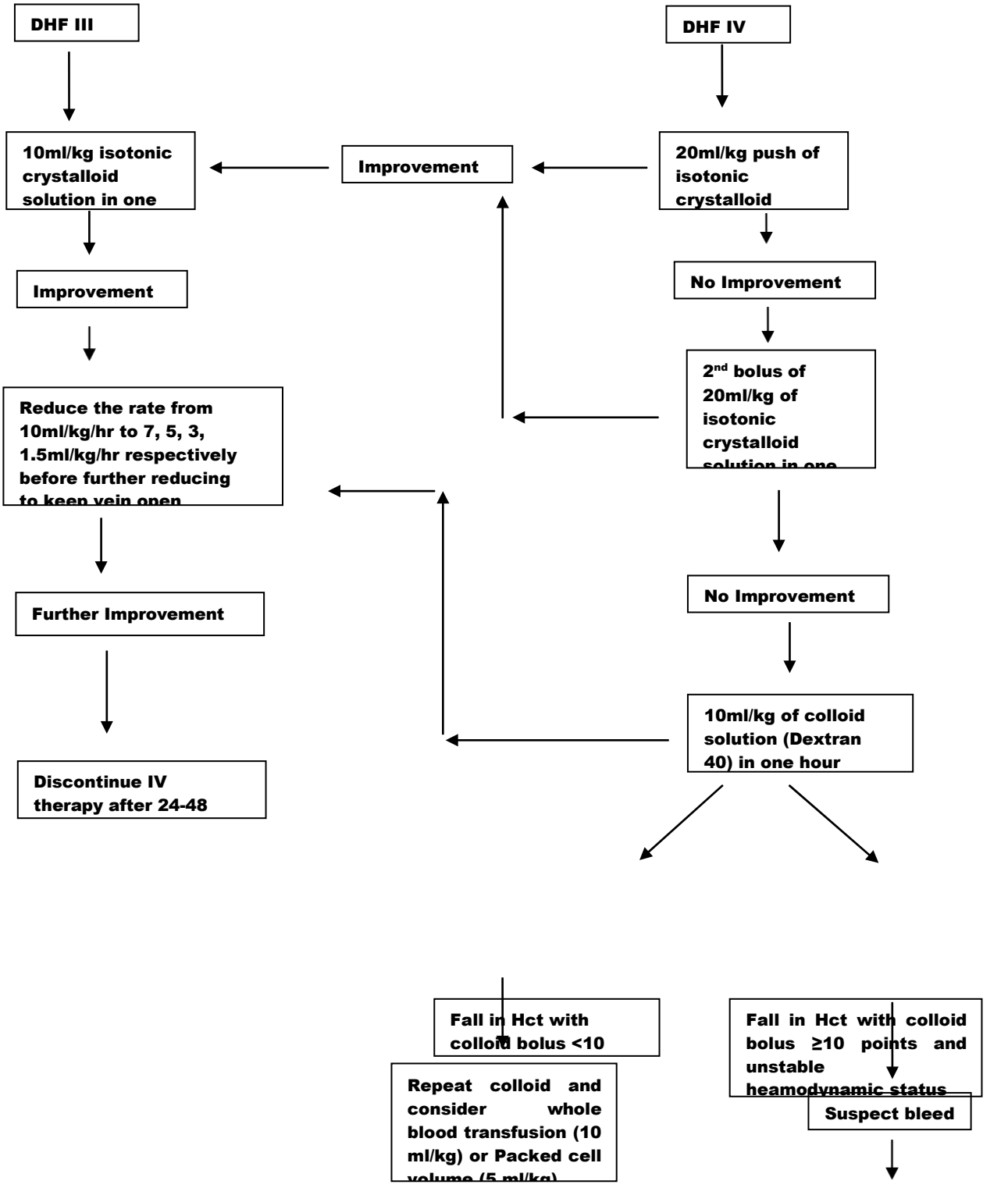


MANAGEMENT OF DSS (DHF GRADE IV)

- **When shock develops, it is a medical emergency.**
- **Initiate intravenous fluid resuscitation with crystalloid at 20 ml/kg as a bolus given over 15 minutes to bring the patient out of shock as quickly as possible.**
- **If the patient's condition improves, continue with crystalloid infusion of 10ml/kg for one hour and gradually reduce to 7-5 ml/kg/hr for 1-2 hours, 5-3 ml/kg/hr for 2-4 hours, then 3-2 ml/kg/hr and then further, depending upon haemodynamic status which shall be maintained for upto 24-48 hours.**
- **If vital signs are still unstable (i.e. shock persists), give 2nd bolus of crystalloid solution, as 20 ml/kg in one hour. In case of improvement, gradually reduce the fluids as mentioned above.**
- **In case of no improvement, give colloids at 10ml/kg in one hour and then reassess.**
- **Correct metabolic and electrolyte disturbances in cases of prolonged shock that do not respond well after initial resuscitation. (ABCS)**
- **Give fresh blood transfusion in cases of significant bleed. A patient with refractory shock, who despite adequate volume replacement, has a drop in Hct, perhaps has significant internal bleed and shall be transfused with fresh whole blood.**

❖ **After 10 minutes of administration of Dextran, Hct can be measured.**
❖ **Expected drop in Hct by Dextran is 10.**

Figure 6: Summary of management of Shock Patients



INDICATIONS FOR COLLOIDS

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

Dextran 40

- ***Dextran is a complex, branched glucan (polysaccharide made of many glucose molecules) composed of chains of varying lengths (from 3 to 2000 kilodaltons).***
- ***Dextran is potent osmotic agent, and is used urgently to treat hypovolemia. The hemodilution caused by volume expansion with dextran use improves blood flow, thus further improving patency of microanastomoses and reducing thrombosis.***
- ***Dextran may interfere with blood group cross matching or biochemical measurements, so these should be carried out before infusion is begun.***
- ***Side effects include anaphylaxis, volume overload, pulmonary edema, cerebral edema, or platelet dysfunction. An uncommon but significant complication of dextran osmotic effect is acute renal failure. Transient increase in bleeding time may occur due to platelet dysfunction.***
- ***Cautions: Cardiac disease, liver disease, renal impairment, urine output should be monitored. Care should be taken to avoid haematocrit concentration from falling below 25-30% and patient should be monitored for hypersensitivity reaction.***

Other Colloids

- ***Haemacel: Plasma expander given as IV infusion***
- ***Gelafusin: IV infusion, 40g (4%) succinylated gelatin, average molecular weight 30000, 154 mmol/L Na, 125 mmol/L Cl.***
- ***Starch 6: Plasma expander given as IV infusion***

MONITORING

- **Total fluid administered (oral+ IV)**
- **Vital parameters - pulse, temperature, respiratory rate, blood pressure (pulse pressure), and capillary refill time (CRFT)- four hourly (may need more frequent monitoring depending on the clinical situation)**
- **Warmth / coldness of peripheries**
- **UOP (ml/kg/hr) for each void**
  - **(aim is to maintain UOP between 0.5 - 1.0ml/kg/hr)**
- **CBC (WBC, Hct, platelets); daily or even twice daily when platelet count is dropping below 150,000/mm^3 and in pre-shock patients while 4-6**

hourly in shock patients.

- **Evidence of overt bleeding**

- **Acidosis, bleeding, calcium, blood sugar (ABCS) in cases of refractory shock Table 3:ABCS**

Correct acidosis at pH <7.35 or HCO_3 at

Abbreviation	Laboratory investigations	Note
A—Acidosis	Blood gas (capillary or venous)	Indicate prolonged shock. Organ involvement should also be looked into; liver function and BUN, creatinine.
B—Bleeding	Haematocrit	If dropped in comparison with the previous value or not rising, cross-match for rapid blood transfusion.
C—Calcium	Electrolyte, Ca++	Hypocalcemia is found in almost all cases of DHF but asymptomatic. Ca supplement in more severe/ complicated cases is indicated. The dosage is 1 ml/kg, dilute two times, IV push slowly (and may be repeated every six hours, if needed), maximum dose 10 ml of Ca gluconate.
S—Blood sugar	Blood sugar (dextrostix)	Most severe DHF cases have poor appetite together with vomiting. Those with impaired liver function may have hypoglycemia. Some cases may have hyperglycemia.

MANAGEMENT OF CONVALESCENCE

- **Convalescence can be recognized by the improvement in clinical parameters, appetite and general well-being.**
- **Haemodynamic state such as good peripheral perfusion and stable vital signs should be observed.**
- **Decrease of Hct to baseline or below and/or any significant change in Hct should be observed.**
- **Intravenous fluid should be discontinued.**
- **In those patients with massive effusion and ascites, hypervolemia may occur and diuretic therapy may be necessary to prevent pulmonary oedema.**
- **Hypokalemia may be present due to stress and diuresis and should be corrected with potassium-rich fruits or supplements.**
- **Bradycardia is commonly found and requires intense monitoring for**

possible rare complications such as heart block or ventricular premature contraction (VPC).

- **Itching and convalescence rash is found in 20%–30% of patients.**

Continuous monitoring during this period is mandatory, as patient may die due to fluid overload

SIGNS OF RECOVERY

- **Stable pulse, blood pressure and breathing rate.**
- **Normal temperature.**
- **No evidence of external or internal bleeding.**
- **Return of appetite.**
- **No vomiting, no abdominal pain.**
- **Good urinary output.**
- **Stable haematocrit at baseline level.**
- **Convalescent confluent petechiae rash or itching, especially on the extremities.**

DISCHARGE CRITERIA

- **Absence of fever for at least 24 hours without the use of anti-pyretic therapy in DF.**
- **Return of appetite.**
- **Visible clinical improvement.**
- **Satisfactory urine output.**
- **A minimum of 2–3 days have elapsed after recovery from shock in DHF/DSS.**
- **No respiratory distress from pleural effusion and no ascites.**
- **Platelet count of more than 50,000/mm3. If not, patients can be recommended to avoid traumatic activities for at least 1–2 weeks till the platelet count return to normal. In most uncomplicated cases, platelet rises to normal range within 3–5 days.**

MANAGEMENT OF COMPLICATIONS

HEMORRAGIC COMPLICATIONS INDICATIONS OF BLOOD & BLOOD PRODUCT TRANSFUSION

Mucosal Bleed

- **Consider as minor, if patient remains stable with fluid replacement.**

Profound thrombocytopenia (< 20,000)

- **Strict bed rest.**
- **Protect from Trauma**
- **Do not give IM injection or NSAIDs**

- **Platelet transfusions for severe thrombocytopenia in otherwise haemodynamically stable patients have not been shown to be effective and are not necessary.**

No Role of Prophylactic Platelet Transfusion; Transfusion may be

Major Bleed

- **These patients are at risk of:**
  - **Prolonged or refractory shock**
  - **Hypotensive shock and renal or liver failure and / or severe and persistent metabolic acidosis.**
- **Give 5-10 ml / Kg packed cell or 10-20 ml / Kg of fresh whole blood with transfusion at appropriate rate.**
- **Consider repeating the whole blood transfusion if there is further blood loss or no appropriate rise in Hct.**

The only indication of transfusion is a major bleed

Suspect Bleed

- **Unable to maintain BP even after colloid bolus and adequate fluid resuscitation**
- **Sudden BIG rise in WBC with neutrophil leukocytosis**
- **Sudden drop in Hct without improvement in patient condition**
- **Sudden rise in SGOT**

FLUID OVERLOAD AND NO SHOCK

- **Oxygen Therapy**
- **Furosemide 1mg/kg/dose-BD**
- **Bed Rest**

FLUID OVERLOAD AND SHOCK

- **Colloids (10 ml/kg of Dextran) should be given.**
- **Consider ionotropes**

- **No diuretics**
- **Aspiration of large serous effusions**
- **Early positive pressure ventilation**

ENCEPHALOPATHY

- **Some DF/DHF patients present with unusual manifestations with signs and symptoms of central nervous system (CNS) involvement, such as convulsion and/or coma. This has generally been shown to be encephalopathy, not encephalitis, which may be a result of intracranial haemorrhage or occlusion associated with DIC or hyponatremia.**
- **Most of the patients with encephalopathy report hepatic encephalopathy. The principal treatment of hepatic encephalopathy is to prevent the increase of intracranial pressure (ICP).**
- **Radiological imaging of the brain (CT scan or MRI) is recommended, if available to rule out intracranial haemorrhage.**
- **Supportive therapy for this condition is recommended**
  - **Maintain adequate airway oxygenation with oxygen therapy.**
  - **Prevent/reduce ICP**
  - **Decrease ammonia production**
  - **Maintain blood sugar level at 80–100 mg/dl. Recommend glucose infusion rate is anywhere between 4–6 mg/kg/hr.**
  - **Correct acid-base and electrolyte imbalance**
  - **Vitamin K1 IV administration; 3 mg for <1-year-old, 5 mg for <5-year-old and 10 mg for>5-year-old and adult patients.**
  - **Anticonvulsants should be given for control of seizures: phenobarbital, dilantin and diazepam IV as indicated.**
  - **Transfuse blood, preferably freshly packed red cells, as indicated. Other blood components such as platelets and fresh frozen plasma, may not be given because fluid overload may cause increased ICP.**
  - **Empirical antibiotic therapy in cases of suspected superimposed bacterial infections.**
  - **H_2-blockers or proton pump inhibitor may be given to alleviate gastrointestinal bleeding.**
  - **Avoid unnecessary drugs because most drugs have to be metabolized by the liver.**
  - **Consider plasmapheresis or haemodialysis or renal replacement therapy in cases with clinical deterioration.**

Tachycardia in the absence of fever in Dengue

- **Shock/Impending Shock**
- **Bleed**
- **Impending respiratory failure**
- **Hypocalcemia**
- **Myocarditis**

ADJUNCT THERAPY

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.**
- **During recovery phase when there is evidence 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 given to patients who are already fluid overloaded or who are likely to be overloaded depending on the fluids already given.**

Inotropic support

- **Very limited role 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 central venous pressure (CVP). (It is best for the patient to have a CVP line in such instances).**

Recombinant factor VII

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

Steroids and IV immunoglobulin

- **There is insufficient evidence to support the use of intravenous immunoglobulin and steroids in the management of dengue patients.**

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.**

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

ANNEXURE

MONITORING

SHEETS

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 ——————————

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24
10																								
9																								
8																								
7																								
6																								
5																								
4																								
3																								
2																								
1.5																								
1																								
used % of fluid quota																								
PCV																								
HR																								
BP																								
Pulse Pressure																								
RR																								
CRFT																								
extremities																								
UOP																								
UOP ml/Kg/hr																								
Platelet count																								

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

10																									
9																									
8																									
7																									
6																									
5																									
4																									
3																									
2																									
1.5																									
1																									
	25..	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	
used % of fluid quota																									
PCV																									
HR																									
BP																									
Pulse Pressure																									
RR																									
CRFT																									
extremities																									
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																								
10																								
9																								
8																								
7																								
6																								
5																								
4																								
3																								
2																								
1																								
time																								
used % of fluid quota																								
PCV																								
HR																								
BP																								
Pulse Pressure																								
RR																								
CRFT																								
extremities																								
UOP ml/Kg/hr																								
Platelet count																								

DENGUE INVESTIGATION SUMMARY

Name:			Age:		Ward:	
MRN # :						
Date:						
Time:						
Full Blood Count						
Hb						
WBC						
N						
L						
PCV/HCT						
Platelet						
Blood Urea						
Se.Creatinine						
Se.Na^+						
Se.K^+						
Se.Ca^{2+}(Ionized)						
SGOT/AST						
SGPT/ALT						
PT/INR						
Se. Albumin						
Se. Cholesterol						
CXR-R. Decubitus/PA						
US Scan Chest: Abdomen:						
Other IX						
Remarks						

Epidemiology Unit, Ministry of Health, Sri Lanka December 2011

Ideal body weight for boys

Ideal weight taken as the weight for height on the 50th centile

Height cm	Ideal Body Weight Kg	Height cm	Ideal Body Weight Kg
100	15.5	138	31.5
101	15.75	139	32.33
102	16	140	33
103	16.33	141	34
104	16.66	142	35
105	17	143	35.5
106	17.33	144	36.33
107	17.66	145	37
108	18	146	38
109	18.5	147	39
110	18.75	148	39.66
111	19	149	40.5
112	19.5	150	41.33
113	20	151	42
114	20.25	152	42.66
115	20.5	153	43.33
116	21	154	44
117	21.33	155	45
118	21.66	156	45.5
119	22	157	46.33
120	22.5	158	47
121	22.75	159	47.75
122	23.33	160	48.5
123	23.5	161	49
124	24	162	49.75
125	24.5	163	50.5
126	25	164	51
127	25.33	165	52
128	25.66	166	53
129	26	167	53.75
130	26.66	168	54.5
131	27.33	169	55.25
132	27.66	170	56.33
133	28.33	171	58
134	28.66	172	58.75
135	29.5	173	60
136	30	174	62
137	30.66	175	64

Ideal body weight for girls

Ideal weight taken as the weight for height on the 50th centile

Height cm	Ideal Body Weight Kg	Height cm	Ideal Body Weight Kg
90	13	127	25.25
91	13.25	128	26
92	13.5	129	26.33
93	13.66	130	27
94	13.75	131	27.66
95	14	132	28.33
96	14.25	133	29
97	14.75	134	29.66
98	15	135	30.5
99	15.25	136	31.5
100	15.5	137	32
101	16	138	32.75
102	16.25	139	33.5
103	16.5	140	34.5
104	17	141	35
105	17.25	142	36
106	17.5	143	36.5
107	17.75	144	37
108	18	145	37.75
109	18.33	146	38.5
110	18.66	147	39
111	19	148	39.75
112	19.5	149	40.5
113	19.75	150	41
114	20	151	41.5
115	20.33	152	42
116	20.66	153	42.5
117	21	154	43.66
118	21.5	155	44
119	21.75	156	45
120	22.25	157	45.66
121	22.5	158	46.75
122	23	159	47.75
123	23.33	160	49
124	23.75	161	50
125	24.25	162	52.5
126	24.66	163	56