National Guideline for Clinical Management of

Dengue Syndrome

4th Edition 2018 (Revised)

National Malaria Elimination &
Aedes Transmitted Diseases Control Program
Disease Control Unit
Directorate General of Health Services
Mohakhali, Dhaka

World Health Organization
Bangladesh

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Foreword

Dengue was fairly unfamiliar disease in Bangladesh when first outbreak occurred in 2000. The enormous morbidity and unacceptable mortality during early years were taken care with great emphasis and importance by early response team. The Disease Control Division of Directorate General of Health Services felt the necessity of developing national guideline in 2000 for the clinical management of dengue by customizing the SEARO/ WHO guidelines in accordance with the prevailing local situation for providing appropriate management for dengue patients to mitigate the morbidity, prevent regrettable mortality and raise awareness for appropriate prevention and control in community.

The third Edition of the 'National Guidelines for Clinical Management of Dengue Syndrome 'was updated in 2013 by the participation of physicians, pediatricians, national control program personnel and researchers as a tool to provide a uniform, scientific, affordable and appropriate clinical management as well as to eradicate prevailing confusions and ambiguity.

Later, based on the newer version of WHO/SEARO guideline this group had exercised and provided their scholastic input for updating the guideline to be compiled as 'National Guideline for Clinical Management of Dengue Syndrome 4th Edition 2018'.

In 2019, the magnitude of the disease was comparatively higher than that of previous years, as it spread throughout the whole country. The presentation of the disease with different serotypes was non-identical to previous years as well. So, we felt the necessity of publishing a revised and expanded edition of the existing guideline with some updates and modifications.

I would like to thank everyone, who contributed to this guideline. It will surely serve to the need of the physicians at all levels in clinical management of Dengue. Together, we will march forward to create a healthy Bangladesh.

Prof. Dr. Abul Kalam Azad
Director General
Directorate General of Health Services

Preface

Dengue is an important tropical infection caused by an Arbo-virus named 'Dengue'. As a mosquito borne disease it is widely spread in many tropical endemic countries. Millions of world populations are affected by this viral infection. Each year, thousands of dengue infections are reported and there are several outbreaks of dengue in many countries including Bangladesh.

Fighting with dengue outbreak is important in public health. Usually, patients of dengue outbreak usually present the classical symptoms, acute febrile illness with or without hemorrhagic complication. However, in recent days some outbreaks presented atypical clinical presentations made the diagnosis and management procedures complicated.

The severity of infection as well as the mortality vary in different outbreaks. The medical facilities and skill of local practitioners are important determinants in the outcomes of dengue case management. All these highlight the needs of the updated knowledge on clinical management of dengue illness. I hope this updated version of the guideline will be very helpful to effective management of dengue.

I extend my gratitude to the expert group for their valuable contribution in updating this guideline. I am also thankful to those who contributed at different sectors of the finalization of this document including the Development partners. Constructive advice from the users and multiple stakeholders will help to update the guideline in future.

I wish the best utilization of this guideline.

Prof. Dr. Shahnila Ferdousi
Director, Diseases Control &
Line Director, Communicable Disease Control
Directorate General of Health Services

From the Desk of Editor in Chief

Dengue fever is closely known to us for about 2 decades. The impact of the illness due to Dengue on our health care system has made it very familiar in our society. The disease is very much related to our environment, economy and national policy. The need for publishing this 4th edition is very rational in the context of national and global demand. Updating the knowledge on clinical management of dengue illness is very essential. The first edition published in 2000, 2nd edition in 2009, 3rd edition in 2013.

Disease Control Division of DGHS, Ministry of Health and Family welfare in collaboration with World Health Organization local office conducted series of meetings, group discussion and draft presentation by a group of Physicians, Pediatricians, Microbiologist, Gynecologists and Entomologists for updating this edition of national guideline. I express my heartfelt thanks and gratitude to the authorities that they entrusted on us. I am also thankful to the specialists who have contributed a lot for making the 4th edition a successful one.

This guideline is intended to reach all level of the health care services which could lead to reduce in morbidity and mortality due to dengue illness. The 4th edition 2018 (revised) contains new conception regarding pediatric management as well as management of Dengue in pregnancy, which will help with the aim of early diagnosis and effective management of Dengue. Due to the change in disease pattern of Dengue in 2019, some modifications were needed to be included to this existing edition.

I extend my gratitude to each and every one who contributed towards the development of this guideline.

Professor Quazi Tarikul Islam
Professor and Head
Department of Medicine
Popular Medical College

Acknowledgement

Bangladesh has become a role model for other developing countries in achieving the targets of the health-related millennium development Goals. The 4th sector-wide program named 'Health, Population and Nutrition Sector Program (HPNSP)' is being implemented to achieve the targets of the health-related Sustainable Development Goals (SDGs) within 2030.

National Malaria Elimination & Aedes Transmitted Diseases Control Program (NME & ATDCP) under the leadership of Disease Control Division, DGHS is playing strategic stewardship and governance roles in combating the deadly diseases like dengue and malaria in Bangladesh. National program deemed it as utmost priority to update the existing National Guideline for Management of Dengue Syndrome (4th edition 2018) and included paediatric management as well as management of Dengue in pregnancy in the updated version.

Here I gratefully acknowledge the contributions of Physicians, Paediatricians and Epidemiologists working in various reputed institutes of Bangladesh, WHO Bangladesh and program personnel for finalizing this document through various consultative meetings and workshops. I extend my heartiest congratulations to all of them for their hard work in bringing out this updated guideline to light. I am grateful to the Ministry of Health and Family Welfare and DGHS for continuous guidance in preparation and finalization of thisdocument.

Dr. Afsana Alamgir Khan
Deputy Programme Manager
National Malaria Elimination & Aedes Transmitted Disease
Control Programme, Programme Manager, BAN-MAL & Dengue
Communicable Disease Control
Directorate General of Health Services

Abbreviation & Acronym

ACEI	Angiotensin Converting Enzyme Inhibitors
ADE	Antibody Dependent Enhancement
AFRIMS	Armed Forces Research Institute of Medical Sciences
AHA	Anti Hypertensive Agent
ALT	Alanine Amino Transferase
ARB	Angiotensin Receptor Blocker
AST	Aspartate Aminotransferase
BCC	Behavioral Change Communication
BHE	Bureau of Health Education
CBC	Complete Blood Count
CCB	Calcium Channel Blockers
CFR	Case Fatality Rate
CLD	Chronic Liver Disease
CMCH	Chittagong Medical College Hospital
CMOSGH	Chittagong Ma O Sishu General Hospital
CNS	Central Nervous System
CRF	Chronic Renal Failure
CRT	Capillary Refill Time
DEN	Dengue
DF	Dengue Fever
DGHS	Directorate General of Health Services
DHF	Dengue Hemorrhagic Fever
DIC	Disseminated Intravascular Coagulation
DS	Dengue Syndrome
DSS	Dengue Shock Syndrome
ELISA	Enzyme Linked Immunosorbent Assay
G	Gauze i.e. Part of an Inch
GBS	Guillain–Barré syndrome
GI	Gastro Intestinal
HcT	Hematocrit
HELLP	Hemolytic Anemia Elevated Liver Enzymes Low Platelet Count
HI	Hemagglutination Inhibition
ICOVED	Integrated Control of Vector Borne Diseases
IEDCR	Institute of Epidemiology Diseases Control & Research
LFT	Liver Function Test
M&PDC	Malaria & Parasitic Diseases Control
MHD	Maintenance Hemodialysis
MP	Malarial Parasite
NGO	Non-Government Organization

Abbreviation & Acronym

NIPSOM	National Institute of Preventive & Social Medicine
ORT	Oral Rehydration Therapy
PCR	Polymerase Chain Reaction
PEARL	Personal Experience & Resource Listing
PM	Programme Manager
PSO	Principal Scientific Officer
PV	Per Vaginal
SEARO	Regional office for South East Asian
TBV	Total Blood Volume
TLC	Total Leucocyte Count
TPC	Total Platelet Count
ULV	Ultra Light Volume
WHO	World Health Organization
Yr	Year

Aim of this Guideline

- Understanding Dengue syndromes in a comprehensive way and offers best clinical advice.
- Diagnosis and management at all tiers of care, community to hospital through a triage system.
- Uniform use of available tools in a systematic manner customized to local situation

To whom this Guideline is intended

- Clinicians and nurses who are in direct care of Dengue Syndromes patients Programme personnel who are involved for prevention and control of Dengue Syndromes
- Health Care Managers and Policy Makers and Hospital Managers responsible for the planning and implementing various plans, operations, programs and activities.
- Medical Students and Residents for customizing the working knowledge.

Chapter 1

Introduction & Epidemiology of Dengue

1. Introduction & Epidemiology of Dengue

1.1 Introduction

Dengue is a disease caused by an arbovirus, which has four serotypes and that is transmitted by Aedes mosquito. It is regarded as the most important arthropod transmitted human viral disease, and constitutes an important global health problem. Dengue ranks as the most important, rapidly emerged disease in recent years and is endemic in all continents. It has shown an increase due to various reasons-construction activities, lifestyle changes, deficient water management, improper water storage, stagnation of rain water in containers lying outside houses and practices leading to proliferation of vector breeding sites in urban, semi-urban and rural areas. With the huge outbreak of dengue in Bangladesh in 2000, it has established itself as an important health problem of Bangladesh. In the year 2019 there was significant increase in number of cases of dengue occurring throughout the country and even from the rural areas though the case fatality rate (CFR) was not very high.

Dengue virus infections may be asymptomatic or may lead to undifferentiated fever, dengue fever, or dengue haemorrhage fever (DHF) with plasma leakage that may lead to hypovolaemic shock Dengue Shock Syndrome (DSS). This range of manifestations of dengue virus infection may be defined as Dengue Syndrome.

1.2 Epidemiology

The epidemiology of dengue exhibits a complex relationship among host (man and mosquito), agent (virus) and the environment. These relationships determine the level of endemicity in an area. The transmission of dengue remains low due to extremes of temperature with low relative humidity. Temperatures in the range of 25oC ± 5oC, relative humidity around 80% and innumerable small water collections result high transmission.

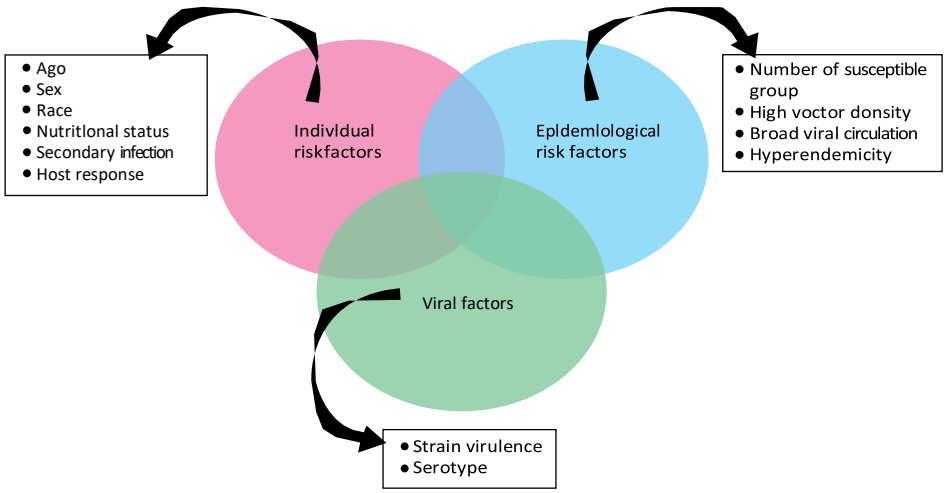


Figure 1 Dengue Epidemiological Triad

Dengue Virus

The dengue virus forms a distinct complex under the genus flaviviruses based on antigenic and biological characteristics. There are four dengue virus serotypes which are designated as DENV-1, DENV-2, DENV-3, and DENV-4. A recent study in 2017 (until February 2018) in Dhaka, described DENV-2 as the dominant type, but also detected some DENV-1 and DENV-3. In the present study, despite a small sample size, DENV-3 accounted for 46% of the samples in September and October 2018, Infection with anyone of these serotypes confers lifelong immunity to that virus serotype. Although all four serotypes are antigenically similar yet they elicit cross protection for only few months. Secondary infection with dengue serotype 2 or multiple infection with different serotypes enhance chances of occurring more severe form of diseases.

Vector

Aedes aegypti is the primary vector and *Aedes albopictus* is secondary vector for dengue in Bangladesh. *Aedes aegypti* is highly domesticated and strongly anthropophilic. It needs more than one bite to complete one blood meal and needs more than one blood meal to complete one gonotropic cycle.

These habits result in the generation of multiple cases and clustering of dengue cases in the cities *Aedes aegypti* breeds almost entirely in domestic man-made water receptacles found in and around households, water storage containers, water reservoirs, overhead tanks, desert coolers, unused tires, coconut shells, disposable cups, unused grinding stones, industrial and domestic junk, construction sites, etc.

Results of Aedes Survey in the year 2019 conducted by Communicable Disease Control (CDC) unit of Directorate General of Health Services (DGHS) shows percentages of positive breeding sources during pre-monsoon, monsoon and post-monsoon showed high positivity rates in drinking water storages (plastic drums, buckets and water tanks) at pre & post monsoon indicating safe water scarcity.

Larval positivity rates reduced may be due to enhanced awareness among the urban inhabitant other breeding source.

A. albopictus is an aggressive feeder and can take the amount of blood they need for each gonotropic cycle in one bite. They usually are distributed in the peripheral areas of urban cities. It prefers natural larval habitats which include tree holes, latex collecting cups in rubber plantations, leaf axils, bamboo stumps, coconut shells, etc.

Transmission Cycle

The female usually becomes infected with the dengue virus when it takes a blood meal from a person during the acute febrile (viremia) phase of dengue illness. After an extrinsic incubation period of 8 to 10 days, the mosquito becomes infected. The virus is transmitted when the infected female mosquito bites and injects its saliva into the wound of the person bitten. The cycle of dengue continues by this process. Dengue begins abruptly after an intrinsic incubation period of 4 to 7 days (range 3–14 days). There is also evidence of vertical transmission of dengue virus from infected female mosquitoes to the next generation.

The Global Burden of Disease

Before 1970, only nine countries had experienced severe dengue epidemics. Today, the disease is endemic in more than 100 countries throughout the globe. The actual numbers of dengue cases are under reported and many cases are misclassified. World Health Organization estimate indicates that 390 million dengue infections occur every year (95% credible interval 284–528 million), of which 96 million (67–136 million) manifest clinically (with any severity of disease). Another (2012) study, of the prevalence of dengue, estimates that 3.9 billion people in 128 countries are at risk of infection with dengue viruses.

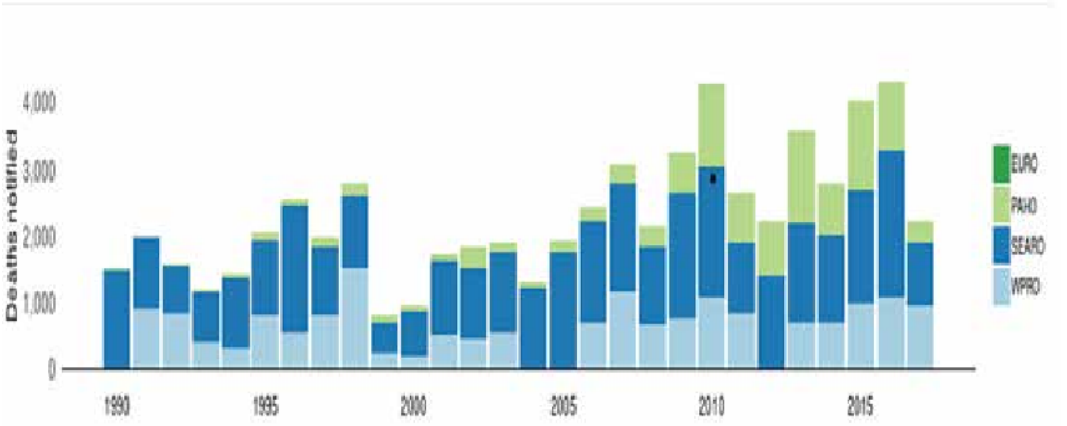


Figure 2 Dengue Cases among WHO Regions

Dengue Case Burden in Bangladesh

The first epidemic of dengue hemorrhagic fever occurred in mid-2000 when 5,551 dengue infections were reported from Dhaka, Chittagong, and Khulna cities, occurring mainly among adults. Among the reported cases- 4,385 (62.4%) cases were Dengue Fever (DF) and 1,186 (37.6%) cases were Dengue Hemorrhagic Fever (DHF). The Case-Fatality Rate (CFR) was 1.7%, with 93 reported deaths. *Aedes aegypti* was identified as the main vector responsible for the epidemic, also *Aedes albopictus* was identified as a potential vector in Chittagong. According to WHO, the worst outbreak occurred in 2002, with 6,232 cases and 58 deaths.

In the year 2019 dengue case burden was the worst with 101354 cases and 179 deaths and proliferation of cases spread were not limited to major cities but to most of the districts of Bangladesh. Since 2000-2004, the average of number of annual cases was 3,626; which is quite high in comparison to the last 5 years (2015-2019) average of 24,614. However, the average number of deaths was same ranges from 41-42.

The prevalent serotypes of dengue virus are DENV-1, DENV-2, DENV-3 and DENV-4 with the highest number of reported cases attributed to DENV-3. A similar situation can be seen in other countries, such as India and Sri Lanka, where DENV3 has been reported most of the time in DF/DHF-related illnesses.

Over the last 10-15 years, dengue fever and dengue hemorrhagic fever have become the leading causes of hospitalization and death among both children and adults in South-East Asian regions. The dengue cases are reported based upon information collected from the Control Room at the DGHS. The source of information is mainly the public sector, private clinics and some selected urban NGOs. Moreover, the information sources at present are based in Dhaka city. Information from other parts of the country is still insufficient. So, it is very difficult to come to a definitive conclusion regarding the program perspective.

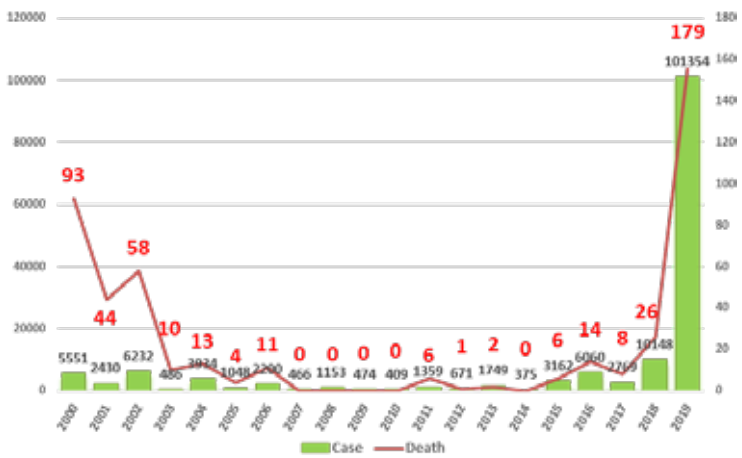


Figure 3 - *Number of Dengue Cases and Death in Bangladesh (2000-2019)*

Figure 4 *- Dengue Prevalence in Bangladesh*

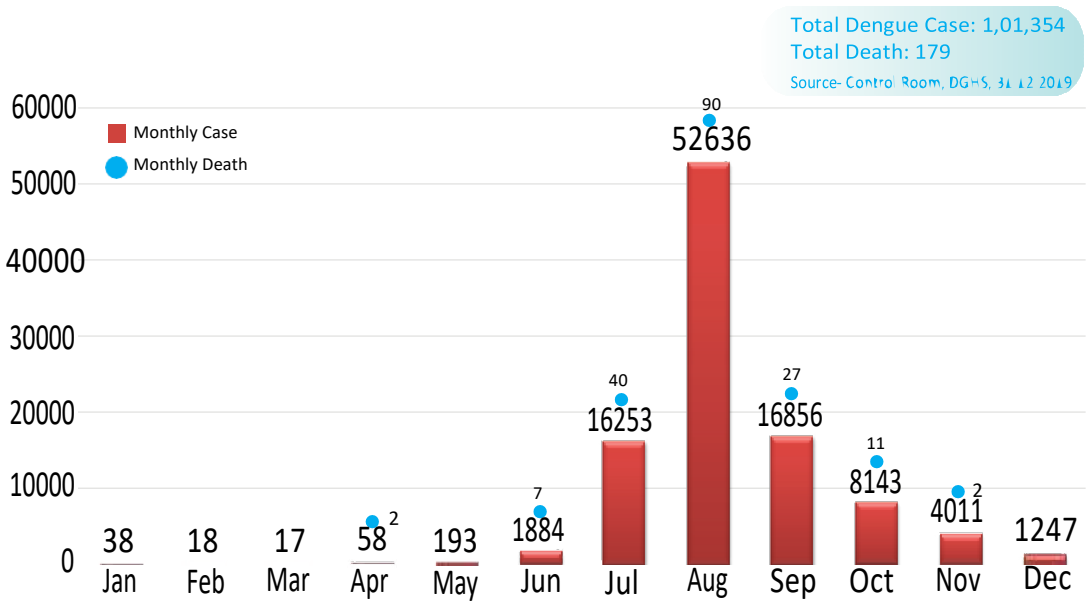


Figure 5 - *Graphical presentation of dengue cases in Bangladesh 2019*

Chapter 2

Pathophysiology and Clinical Manifestation of Dengue Infection

2 Pathophysiology and Clinical Manifestation of Dengue Infection

2.1 Pathophysiology of Dengue Infection

- Dengue virus, which has 4 distinct serotypes, i.e. DENV-1, DENV-2, DENV-3, DENV-4 is transmitted by Aedes aegypti and Aedes albopictus to human.
- Infection with one serotype confers life long immunity to that serotype and cross immunity to other serotypes for 2-3 months only.
- The pathogenesis of dengue involves a complex interaction between virus and host factors, and remains incompletely understood. The immune system plays a key role in disease pathogenesis. Various mechanisms of severe disease have been suggested, including:

  (a) Antibody-dependent enhancement or ADE,
  (b) T-cell mediated immunopathology,
  (c) Complement activation by virus-antibody complexes and
  (d) Cytokine abundance.
- Non-neutralizing cross-reactive antibodies elicited in a primary infection bind virus in a secondary infection and then have a greater ability to infect Fc-receptor bearing cells (Monocytes, macro phages). This is called antibody-dependent enhancement (ADE), and potentially leads to an increased viral biomass, and therefore more chance of developing severe disease. In addition, there is evidence that ADE immunologically modulates infected cells in such a way that the micro environment becomes more supportive of DENV replication.
- The proliferation of activated memory T cells and the production of pro-inflammatory cytokines contribute to the development of plasma leak observe in severe dengue.
- Dengue infected monocytes act as antigen presenting cells (APCs) to induce release of lymphokines and other factors from activated T cells. Tumour Necrosis Factor-α, Interleukin (IL) IL-1b, IL-2, IL-6, IL-8, Interferon gamma (IFNɣ), RANTES etc. are the cytokines that are released from these cells.
- These cytokines along with complement breakdown products (C3a, C5a) activated in DHF/DSS, increases vascular permeability of vascular endothelial cells leading to DSS.
- Antibody dependent enhancement and inappropriate memory T-cell response are central to the pathogenesis of DHF/DSS.

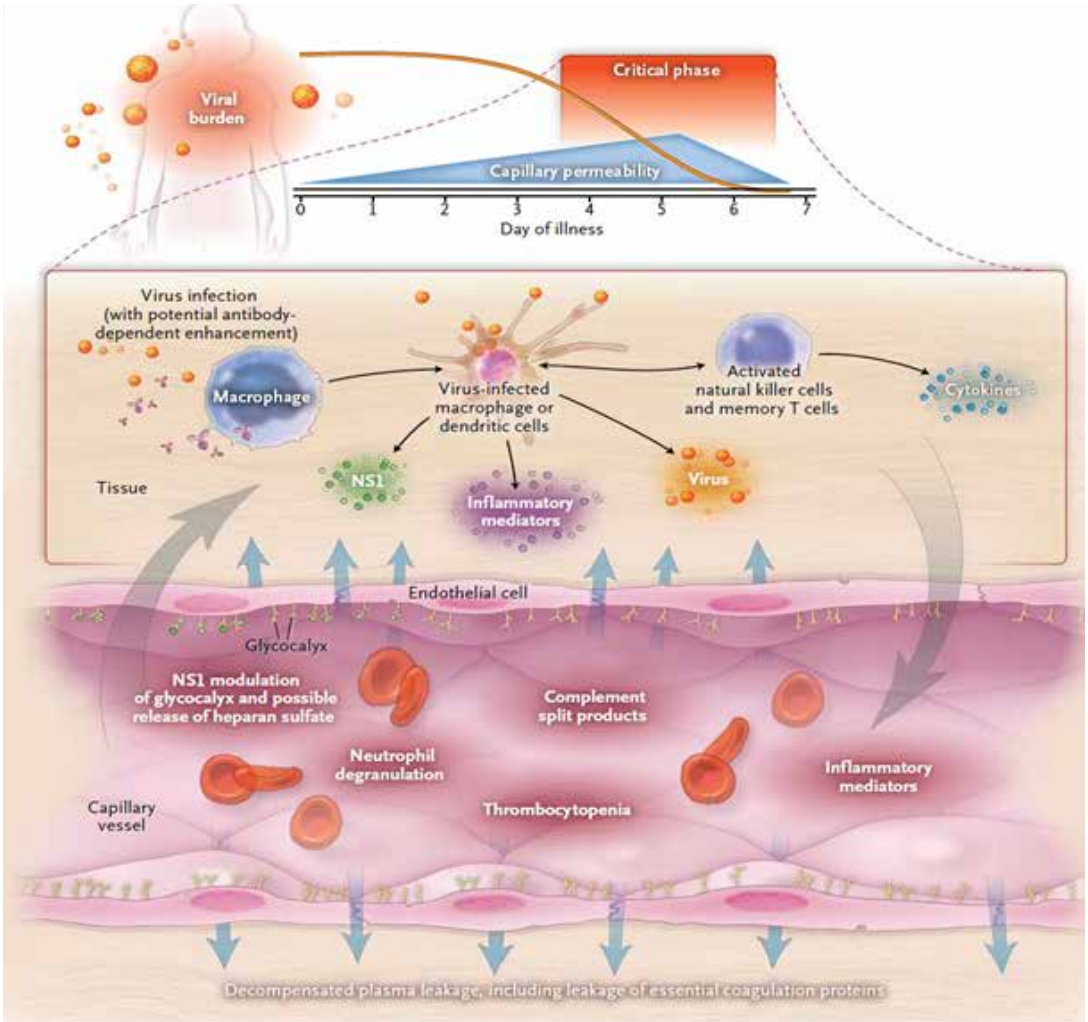


Figure 6 *- Pathophysiology of dengue infection*

Dengue: Review article, Simmons CP, Jeremy J. Farrar JJ, Vinh Chau NV,Wills B, N Engl J Med: April, 2012: 366:pp-1427)

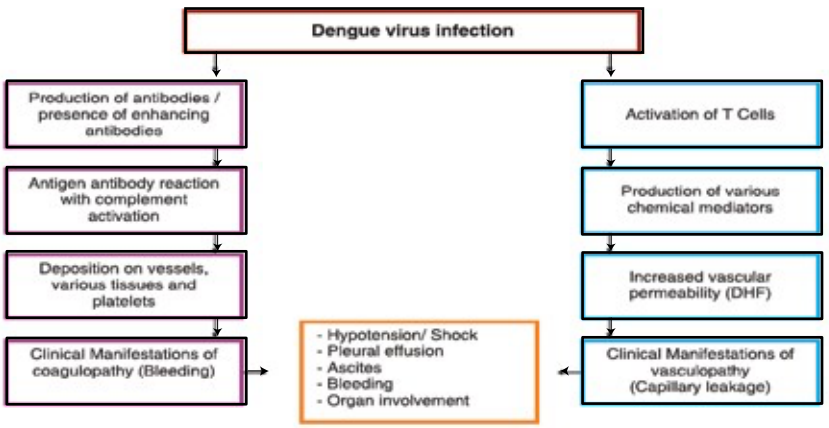


Figure 7 *- Flow Chart of Pathophysiology of dengue infection*

Cause of Bleeding in Dengue Syndrome

- Abnormal Coagulogram
- Thrombocytopenia
- Platelet dysfunction
- Prothrombin complex Deficiency secondary to liver involvement
- Endothelial injury
- DIC and prolonged APTT
- Decreased fibrinogen level
- Increased level of fibrinogen degradation product (FDP)
- Increase level of D-Dimer
- Consumptive coagulopathy (activation of mononuclear phagocytes)
- Sequestration of platelet

Factors Responsible for DHF/DSS

- Antibodies: Presence of enhancing and non-neutralizing antibodies.
- Age: susceptibility to DHF/DSS drops significantly after 12 yrs of age.
- Sex: female more often affected than male.
- Race: Caucasians more often affected than blacks.
- Sequence of Infection: Example, serotype 1 followed by serotype 2 is more dangerous than serotype 4 followed by serotype 2.
- Infecting Serotype: Type 3 is more dangerous than others.
- Infecting Genotype: Asian type 2 causes DHF/DSS while American type is not responsible for the illness.

2.2 Clinical Manifestation of Dengue Infection

Many patients infected with dengue virus remain asymptomatic. Others, after an incubation period of 4-7 (range 3-14) days, develop a febrile illness the manifestations of which are similar and overlapping in nature grouped into 'Dengue Syndromes' which encompass the following:

- Undifferentiated fever
- DF
- DHF
- Expanded Dengue Syndrome (rare)

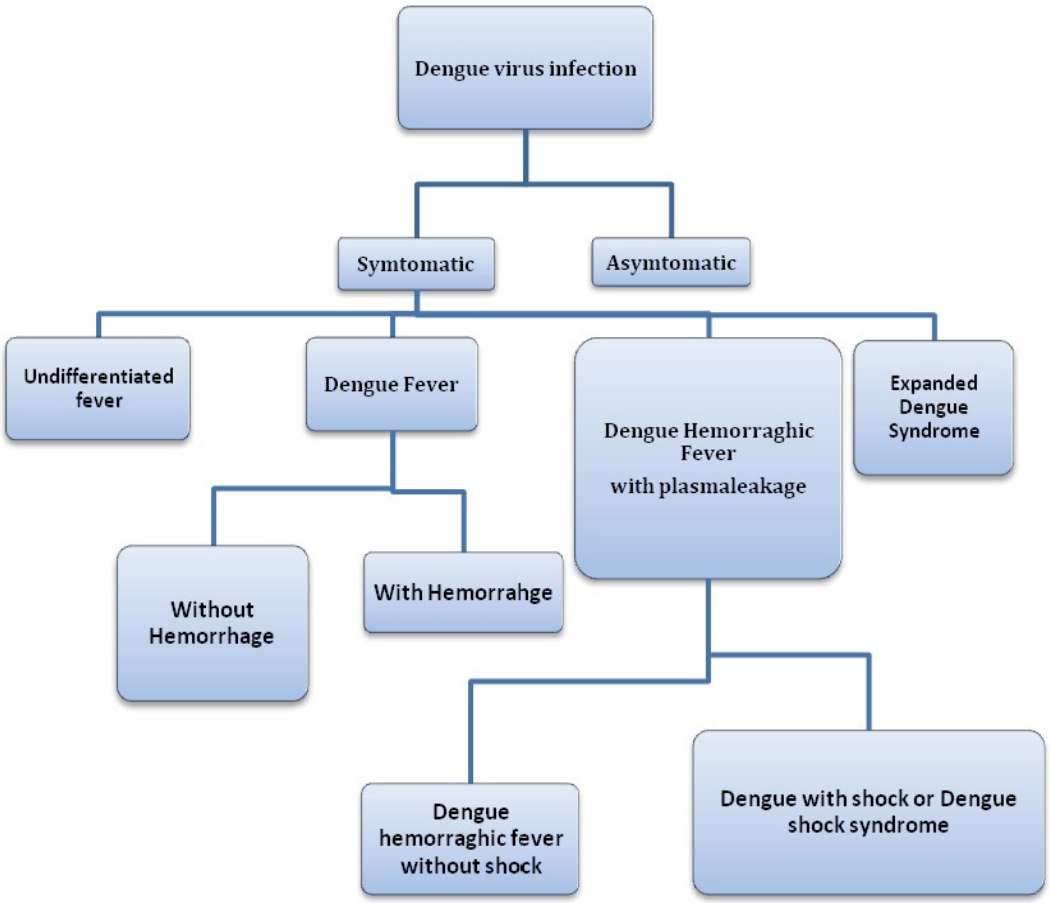


Figure 8 *- Clinical Manifestation of Dengue*

Asymptomatic Infection

Majority of dengue virus infections are asymptomatic. However, age appears to influence the prevalence of symptomatic disease. The majority of infections in children under age 15 years are asymptomatic or minimally symptomatic.

Symptomatic Infection

Undifferentiated fever

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

Dengue fever

Typically, the onset of DF is sudden with a sharp rise in temperature and is frequently associated with a flushed face and headache. Occasionally, chills accompany the sudden rise in temperature. The following features are usually observed:

- Retro-orbital pain on eye movement or pressure on eye
- Photophobia
- Backache and pain in the muscles and joints/bones.
- The other common symptoms include anorexia and altered taste sensation, constipation, colicky pain and abdominal tenderness.

It is noteworthy that these symptoms and signs of DF vary markedly in frequency and severity.

Fever:

The body temperature is usually between 39°C and 40°C (102°F to 104°F) and the fever may be biphasic, lasting 2-7 days in the majority of cases.

Rash:

- First 2 to 3 days-Diffuse flushing or fleeting eruptions may be seen on the face, neck and chest
- Third and fourth day-a conspicuous rash that may be maculopapular or rubelliform
- Afebrile period or defervescence - Petechiae surrounding scattered pale, round areas of normal skin may appear over the dorsum of the feet, on the legs, and on the hands and arms. Skin itching maybe observed.

Hemorrhagic manifestations:

In DF with unusual hemorrhage, Petechiae may be present. Other bleeding such as massive epistaxis, menorrhagia and gastrointestinal bleeding rarely occur in DF, complicated with thrombocytopenia. Tourniquet test will be positive in this case.

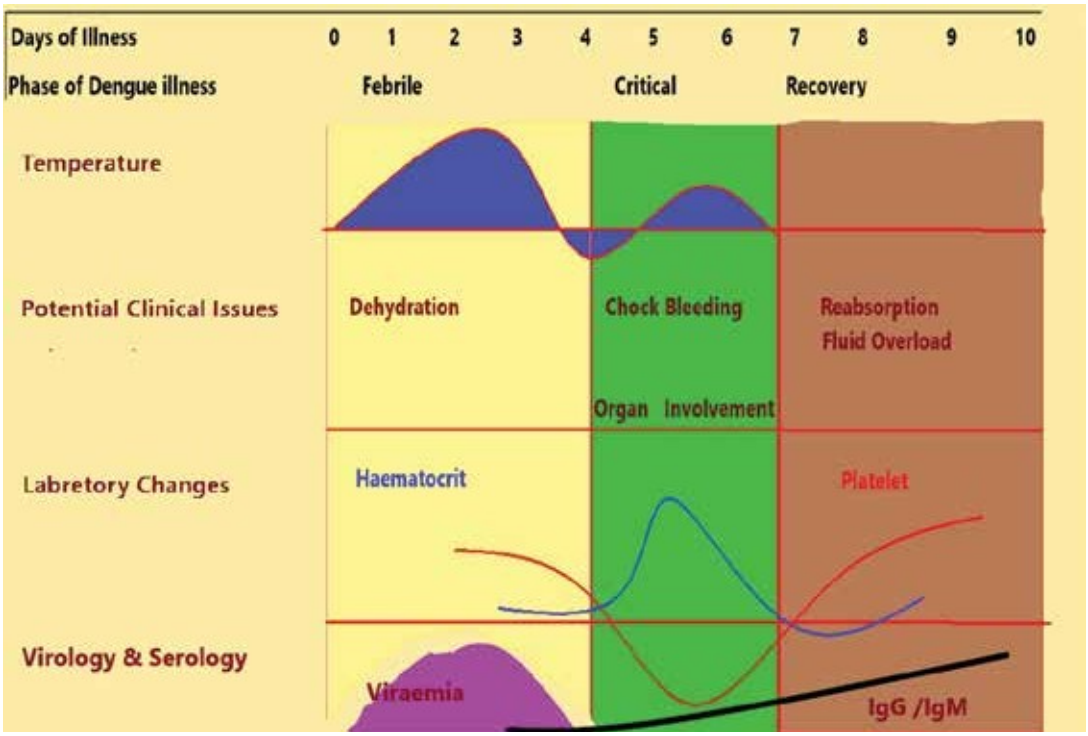


Figure 9 *- Clinical Course of Dengue Fever*

Dengue Hemorrhagic fever

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. Critical phase with plasma leakage is the hallmark of DHF which occurs soon after the end of the febrile phase. There is a tendency to develop hypovolemic shock (dengue shock syndrome) due to plasma leakage.

Hemorrhagic Manifestation:

The clinical course of illness passes through the following three phases:

- Febrile phase
- Critical phase
- Convalescent phase

Febrile Phase

The onset of dengue fever is usually with sudden rise in temperature which may be biphasic, lasting 2-7 days and commonly associated with headache, flushing and rash. There may be pain in retro-orbital area, muscles, joint or bone. Rash may be maculopapular or rubelliform and usually appear after 3 or 4 days of fever and commonly seen in face, neck and other part of the body which generally fades away in the later part of the febrile phase. Localized cluster of petechiae may appear over upper and lower limbs.

Critical Phase

DF/DHF patients usually go to critical phase after 3 to 4 days of onset of fever. During this critical phase plasma leakage and high haemoconcentration are documented and patients may develop hypotension. Abnormal haemostasis and leakage of plasma leads to shock, bleeding, accumulation of fluid in pleural and abdominal cavity. High morbidity and mortality in DHF/DSS are commonly associated with various organ involvements and metabolic derangement. The period of plasma leakage usually persists for 36-48 hrs. Commonly in DHF, platelet count is less than 100000 per/cumm of blood.

Convalescent Phase

During the recovery phase the extracellular fluid which was lost due to capillary leakage returns to the circulatory system and signs and symptoms improve. This phase usually after 6-7 days of fever and last for 2-3 days. Longer convalescence may be expected in some of the patients with severe shock, organ involvement and other complications which may require specific treatment. Patient may develop pulmonary oedema due to fluid overload if the fluid replacement is not optimized carefully.

Photo 1 : *Conjunctival hemorrhage*

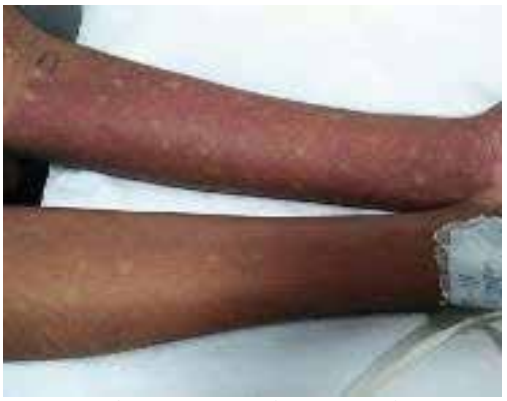


Photo 2 : *Convalescent Rash*

Evidence of Plasma leakage

- Haematocrit (HcT) - With the leakage of plasma there will increase in HcT. A 20% rise of HcT from the baseline is indicative of significant plasma leakage.
- Plasma leakage is due to increased capillary permeability.
- Plasma leakage in DHF is selective and transient and usually lasts for 24-48 hours.
- Ascites and pleural effusion may develop.

Therefore, early detection of critical period (onset of plasma leakage) and appropriate fluid management is of paramount importance. These patients may develop overt or concealed bleeding during the course of illness.

Other evidence of plasma leakage is:

- non-fasting serum cholesterol (<100 mg/dl).
- The degree and the rate of plasma leakage in DHF can vary.
- Severe leakage may develop shock, which may be complicated with organ impairment, metabolic acidosis and disseminated intravascular coagulation (DIC).

Tourniquet Test (TT)

This is a very important clinical test for detecting covert hemorrhage. The tourniquet test is performed by inflating a blood pressure cuff applied usually to the forearm to a point mid-way between the systolic and diastolic pressures for five minutes. After deflating wait for return of normal skin hue and then count the number of petechie. A test is considered positive when 10 or more petechiae per 1 inch² are observed in the exposed part below the cuff. In DHF, the test usually gives a definite positive result when there is ≥ 20 petechiae per 1 inch² with a sensitivity of more than 90%. Sometimes in lieu of petechiae linear steaks of echymosis may be seen in the cuff applied area. The test may be negative or mildly positive only during the phase of profound shock.

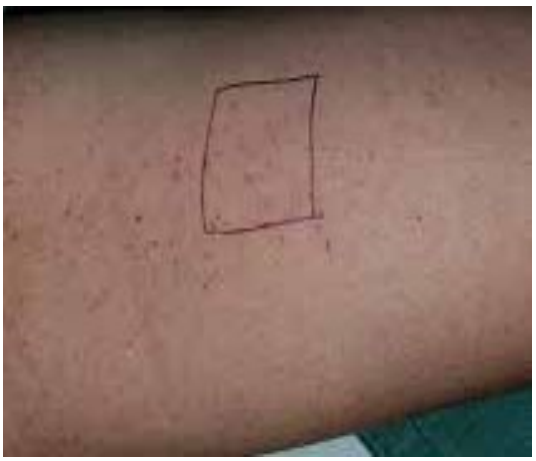


Photo 3: *Tourniquet Test (TT)*

Photo 4 : *Capillary Refill Time*

Capillary Refill Time

This is a clinical examination for volume status of the body. It can be measured by pressing the nail of the thumb of left hand in right handed person or vice versa till blanching then suddenly release the pressure. The time taken for flushing is the capillary refill time and if it is more than 3 sec, there is gross hypovolumia.

Dengue Shock Syndrome

Significant loss of plasma leads to hypovolemic shock. Even in these shock cases, prior to intravenous fluid therapy, pleural effusion and ascites may not be detected clinically. Radiographic and ultrasound evidence of plasma leakage precedes clinical detection. A right lateral decubitus chest radiograph to detect pleural effusion and gall bladder wall oedema is associated with plasma leakage and may precede the clinical detection.

Dengue Shock Syndrome is a prevention of Dengue Syndromes when there are criteria of DHF plus signs of circulatory failure, manifested by:

- Rapid and weak pulse
- Narrow pulse pressure (≤ to 20 mm Hg)
- Hypotension for age
- Cold clammy skin
- Restlessness
- Undetectable pulse and blood pressure

Expanded Dengue Syndrome/Isolated Organopathy (unusual manifestations)

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

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

Table 1 : *Expended Dengue Syndrome*

2.3 Differential Diagnosis

- **Arboviruses:** Chikungunya virus
- **Other viral diseases:** Measles; Rubella and other viral exanthems; Epstein-Barr Virus (EBV); Enteroviruses; Influenza; Hepatitis A; Hantavirus.
- **Bacterial diseases:** Meningococcemia, Leptospirosis, Enteric fever, Melioidosis, Rickettsia diseases, Scarlet fever, Sepsis.
- **Parasitic diseases:** Malaria.

Differentiating points between dengue fever and chikungunya fever

While fever, arthralgia, rash, malaise and leukopenia are common in both Chikungunya and dengue, symmetric arthritis of small joints is pathognomonic of the former. A bleeding tendency and pronounced thrombocytopenia are more frequent in dengue

Clinical & Laboratory Criteria	Dengue	Chikungunya
Fever (>39°C or 102°F)	++	+++
Arthralgia	+/-	+++
Arthritis	-	+
Headache	++	++
Rash	+	++
Myalgia	++	+
Haemorrhage	++	+/-
Shock	+	-
Leukopenia	+++	++
Neutropenia	+++	+
Lymphopenia	++	+++
Elevated Hematocrit	++	-
Thrombocytopenia	+++	+

Table 2 : *Difference between Dengue & Chikungunya*

Chapter 3

Lab Investigation for Dengue Diagnosis and Management

3. Lab Investigation for Dengue Diagnosis and Management

Dengue virus, which has 4 distinct serotypes, i.e. DEN-1, DEN-2, DEN-3 & DEN-4 Early laboratory confirmation of clinical diagnosis may be important because some patients progress within a short period from mild to severe disease and sometimes to death. Early intervention may be life-saving.

3.1 Lab Tests for Diagnosis and Monitoring

The management of DS is based on clinical judgment rather than laboratory evaluations alone. However, few indirect tests may be suggestive of DS from the outset. The following tests may be done-

1. Complete Blood Count (CBC):

Including Total Leucocyte Count, Total Platelet Count and HcT should be done on first consultation of the patient to have the baseline:

Recommendations:

- All febrile patients at the first visit within one week
- All patients with warning signs.

Leucopenia is common in both adults and children with DF and has an important diagnostic implication in early period. The change in total white cell count (≤5000 cells/mm^3) and ratio of neutrophils to lymphocyte (neutrophils <lymphocytes) is useful to predict the critical period of plasma leakage. This finding precedes thrombocytopenia or rising haematocrit. These changes seen in DF and DHF.

Thrombocytopenia is observed in some patients with DF. Mild (100,000 to 150,000 cells/mm^3) is common and about half of all DF patients have platelet count below 100,000 cells/mm^3; A sudden drop in platelet count to below 100,000 occurs before the onset of shock or subsidence of fever. The level of platelet count is correlated with severity of DHF. Severe thrombocytopenia (<100,000/mm^3) usually precedes/accompanies overt plasma leakage.

Haematocrit: A slight increase may be due to high fever, anorexia and vomiting (10%). A sudden rise in haematocrit is observed simultaneously or shortly after the drop in platelet count. Haemoconcentration or rising haematocrit by 20% from the baseline, e.g. from haematocrit of 35% to ≥42% is objective evidence of leakage of plasma. It should be noted that the level of haematocrit may be affected by early volume replacement and by bleeding.

2. Biochemical Tests:

Serum AST (SGOT) and ALT (SGPT):

AST and ALT levels are frequently elevated in both adults and children with DF and DHF; AST and ALT Levels are significantly higher (5 to 15 times the upper limit of normal) in

patients with DHF. Commonly AST is more than ALT in these cases.

In Special Cases:

- Hypoproteinemia/Hypoalbuminaemia (as a consequence of plasma leakage).
- Hyponatremia is frequently observed in DHF and is more severe in shock.
- Hypocalcemia (corrected for hypoalbuminemia) has been observed in DHF.
- Metabolic acidosis is frequently found in cases with prolonged shock.
- Blood urea nitrogen is elevated in prolonged shock.

3. Coagulation Profile:

Assays of coagulation and fibrinolytic factors show reduction in DSS cases. Partial thromboplastin time and prothrombin time are prolonged in about half and one third of DHF cases respectively. Thrombin time is also prolonged in severe cases.

4. Other tests:

- Urine R/M/E: Albuminuria
- Stool test: Occult blood is often found in the stool.
- Chest X-Ray or Ultrasonography: For detection of pleural effusions or ascites.
- Other tests for exclusion: Malaria (MP/ICT), Enteric fever (Blood culture) may be required for patients with compatible clinical syndromes.
- Other test as and when clinically indicated (especially for Dengue expanded syndrome): Serum Albumin, Liver Function Tests, Renal Function test, Serum electrolytes, Imaging, ECG, Echocardiography, CSF etc.

N.B: It should be noted that the use of medications such as analgesics, antipyretics, anti-emetics and antibiotics can interfere with liver function and blood clotting.

3.2 Time and frequency of investigation

Within 3 days - CBC, Haematocrit, NS1 antigen, SGOT, SGPT

These tests should be done during first consultation to get the baseline characteristics like Haematocrit and Complete blood count if the patient presented within 3 days of fever. Follow up testing may be done on 1st afebrile day, but should be done daily once DHF is suspected. A regular haematocrit is more important for management than the thrombocytopenia. Even in severe dengue especially with shock) hourly haematocrit is crucial for management. Once the platelet count begins to rise and reaches ≥ 50,000/mm3, daily lab evaluations may be discontinued.

For clinical purpose, Complete blood count, NS1 antigen and SGOT (AST) and or SGPT (ALT) done within three days will confirm the diagnosis and guides for monitoring and management.

3.3 Dengue Diagnostic Test

Detection of Antigen: NS1 antigen (non-structural protein 1):

- NS1 antigen rapid test- positive within minutes of starting symptoms.
- The ELISA NS1 antigen will be positive on first day of illness.
- This test becomes negative from day 4-5 of illness.
- Commercial kits for the detection of NS1 antigen are now available in ELISA or rapid test format.

Dengue IgM /IgG test (MAC ELISA or Rapid ICT):

- Anti-dengue IgM specific antibodies can be detected after 5 days of the onset of fever and highest level achieved after 7 days.
- It can be detected in low level up to 1-3 months after fever.
- In primary dengue infection- IgM will be more than IgG early period and sed IgG at 9 or 10^{th} day of fever. Level of this IgG may persist at low levels for decades, indicating past dengue infection.
- In secondary dengue infection- higher elevation of anti-dengue specific IgG antibodies and lower levels of IgM. The higher IgG levels remain for 30–40 days.
- Rapid ICT test provides result within 15 to 20 minutes.

Nucleic Acid Detection:

- The reverse transcriptase polymerase chain reaction (RT-PCR)- confirm diagnosis (<5 days of illness).
- The amplified DEN viral RNAs can be detected either by tradition or real time PCR.
- This test is expensive and available only in referral centers.

Dengue Virus Isolation:

- Dengue virus isolation from serum, plasma and leucocytes is the most definitive test for dengue infection, which can be accomplished in majority of cases if the sample is taken in the first few days of illness.
- Isolation of dengue virus from serum, CSF or autopsy samples.
- Detection of dengue virus or antigen in tissue, serum or cerebrospinal fluid by immunohistochemistry, immunofluorescence or enzyme-linked immuno-sorbent assay.
- Detection of dengue virus genomic sequences by reverse transcription-polymerase chain reaction.

Tests for objective evidence of dengue infection are not helpful for guiding the management. NS1 (nonstructural protein) rapid antigen is an excellent test for confirmation of dengue syndrome.

	Clinical Sample	Diagnostic Method	Methodology	Time of Result
Virus Detection and its component	Acute Serum (1-5 days of fever) and necropsy tissue	Viral Isolation	Mosquito or mosquito cell culture inoculation	One Week or more
			RT-PCR & Real Time RT PCR	1 to 2 days
		Nucleic Acid Detection	NS1 Antigen Rapid Test	Minutes
			NS1Ag ELISA	1day
		Antigen Detection	Immunohistochemistry	2-5 days
Serological response	Paired Sera (Acute Serum from 1-5 days and second serum from 15-21 days after)	IgM or IgG sero -conversion	ELISA HA	1-2 days
			Neutralization Test	Minimum 7 days
	Serum after 5 days of fever	IgM Detection (Recent Infection)	ELISA	1 or 2 days
			Rapid Test	Minute
		IgG detection	IgG, ELISA, HIA	1 or 2 days

Table 3 - *Time & Frequency of Investigation*

Available Dengue Diagnostic Tests at Different Level of Health Care Centers:

Primary Health care: For diagnosis and surveillance purpose, at primary-health care level, rapid tests for Dengue specific IgM/ IgG and dengue NS1 antigen should be used.

Secondary Health care: At district health centers, both ELISA and rapid tests for detection of antigen and antibody can be performed.

Tertiary health care: All diagnostic methods should be available at refer centers, including virus isolation, nucleic acid detection and all serological technique.

Method	Diagnostic Tools	Primary Health Care Center	District Health Center	Tertiary Level Health Center/ Reference Center
Virus isolation		-	-	Yes
Genome Detection		-	-	Yes
NS1 Antigen detection	Rapid Test	----	Yes	Yes
	ELISA	----	Yes	Yes
IgM Detection	Rapid Test	----	Yes	Yes
	ELISA	----	Yes	Yes
IgG Detection	ELISA	----		Yes
	IHA	----		Yes
	Neutralization assay	----		Yes

***Table 4** - Dengue Diagnostic Service Delivery Level*

ELISA=enzyme-linked immunosorbent assay; IgG=immunoglobulin G; IgM=immunoglobulin M; IHA = indirect haemagglutination; NS1 Ag = non-structural protein 1

	Method	Interpretation	Sample characteristics
Confirmed Dengue Infection	Viral isolation	Viral isolation	Serum (collected at 1- 5 days of fever) Necropsy tissues
	Genome detection	Positive RT-PCR or positive real-time RT-PCR	
	Antigen Detection	**Positive NS-1 Ag**	
		Positive immunohistochemical	Necropsy tissues
	IgM sero -conversion	**From negative IgM to positive IgM in paired sera**	Acute serum (1–5 days) and convalescent serum (15–21 days) after first serum
	IgG sero -conversion	From negative IgG to positive IgG in paired sera or 4-fold increase IgG levels among paired sera	
Probable Dengue Infection	Positive IgM	**Positive IgM**	Single serum collected after day 5
	High IgG levels	High IgG levels by ELISA or HI (≥ 1280) ELISA	

***Table 5** - Confirmed and probable dengue diagnosis, interpretation of results and sample characteristics*

Chapter 4

Dengue Case Management

4. Dengue Case Management

4.1 Dengue Case Classification by Severity

Changes in the epidemiology of dengue, especially with an increasing number of cases in adults (with and without co-morbidities) and the expansion of dengue into other regions of the world, has led to problems with the use of the existing WHO classification. This clinical guide uses three categories for case management (A, B, C) based on the model of case classification that follows (Figure 10) after a patient has fulfilled the criteria for probable dengue.

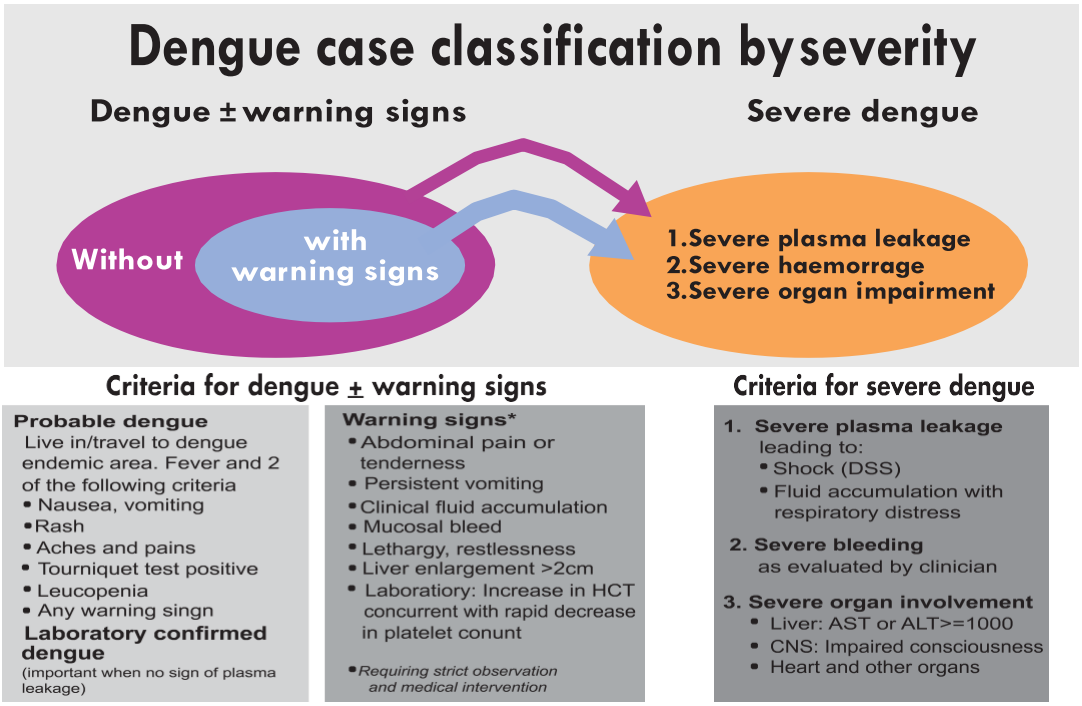


Figure 10 *- Dengue case classifications*

ALT = alanine aminotransferase; AST = aspartate aminotransferase; CNS = central nervous system; DSS = dengue shock syndrome; HCT = haematocrit

Patients Group A: These are patients who are dengue patients without warning sign and they may be sent home. These patients are able to tolerate adequate volumes of oral fluids, pass urine at least once every six hours.

Patients Group B: These include patients with warning signs. These are patients who should be admitted for in-hospital management for close observation as they approach the critical phase. Rapid fluid replacement in patients with warning signs is the key to prevent progression to the shock state.

Warning Sign

- No clinical improvement or worsening of the situation just before or during the transition to afebrile phase or as the disease progresses.
- Persistent vomiting.
- Severe abdominal pain.
- Lethargy and/or restlessness, sudden behavioural changes.
- Bleeding: Epistaxis, black stool, haematemesis, excessive menstrual bleeding, dark colored urine (haemoglobinuria) or haematuria.
- Giddiness.
- Pale, cold and clammy hands and feet.
- Less/no urine output for 4 – 6 hours
- Liver enlargement > 2cm
- Haematocrit >20%

Those with co - existing conditions or risk factors may need careful monitoring and hospitalization even without warning signs:

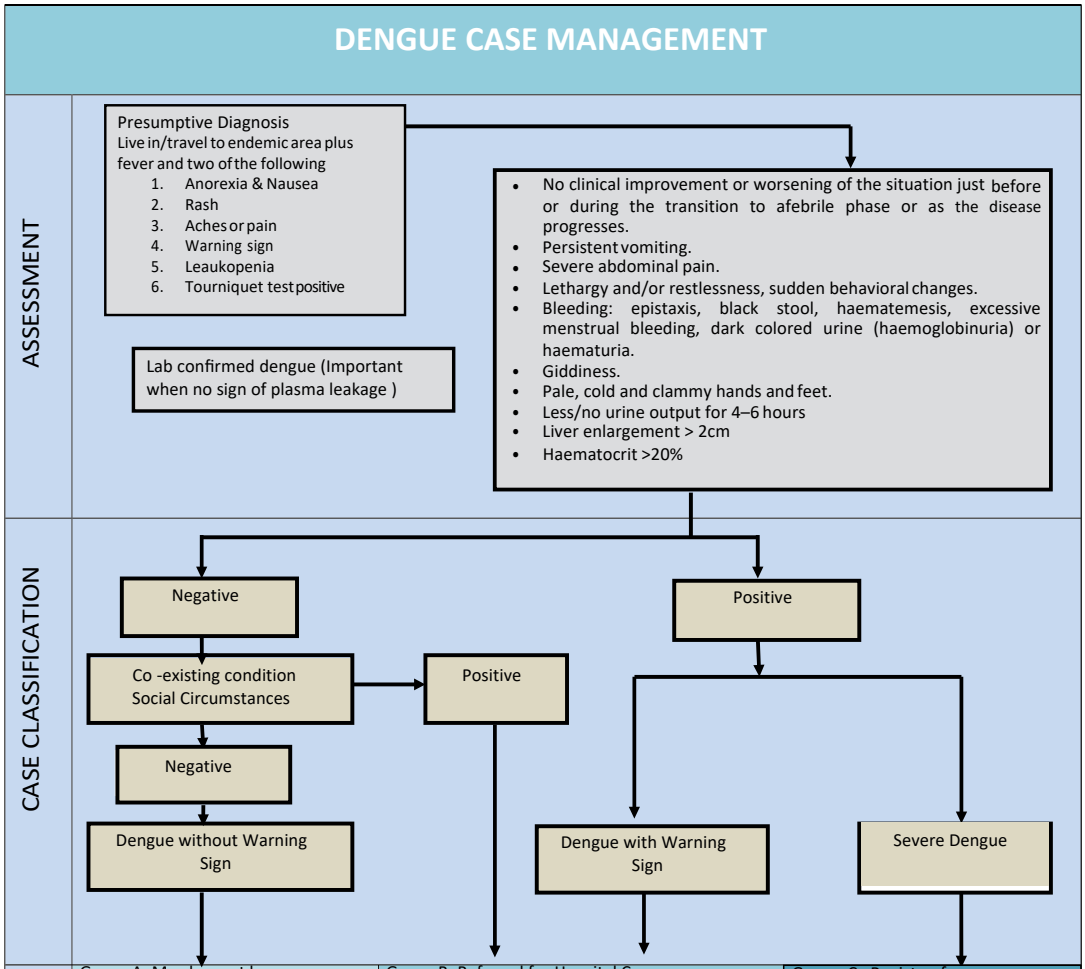
- pregnancy
- infancy
- old age
- obesity
- diabetes mellitus
- hypertension
- heart failure
- renal failure
- chronic hemolytic diseases such as (sickle - cell disease and autoimmune diseases) those with certain social circumstances (such as living alone, or living far from a health facility without reliable means of transport).

Patients Group C: These are patients with severe dengue who require emergency treatment and urgent referral because they are in the critical phase of the disease and have:

- Severe plasma leakage leading to dengue shock and/or fluid accumulation with respiratory distress.
- Severe organ impairment (hepatic damage, renal impairment).
- Myocarditis, cardiomyopathy, encephalopathy or encephalitis.
- Severe metabolic abnormalities (metabolic acidosis, severe hypocalcaemia etc).

Normal Circulation	Compensated Shock	Decompensated/ Hypotensive shock
Clear consciousness	Clear consciousness – shock can be missed if you don't touch the patient	Change of mental state- restless, combative or lethargy
Brisk capillary refill time (<2 sec)	Prolonged capillary refill time (>2 sec)	Mottled skin, very prolonged capillary refill time
Warm & pink extremities	Cool extremities	Cold, clammy extremities
Good volume peripheral pulses	Weak& thread peripheral pulse	Feeble or absent peripheral pulse
Normal heart rate for age	Tachycardia	Severe tachycardia with bradycardia in late shock
Normal blood pressure for age	Normal systolic pressure with raised diastolic pressure Postural hypotension	Hypotension/unrecordable BP
Normal pulse pressure for age	Narrowing pulse pressure	Narrowed pulse pressure (<20mmHg)
Normal respiratory rate for age	Tachypnoea	Metabolic acidosis/ hyperpnoea/ Kussmaul's breathing
Normal urine output	Reduced urine output	Oliguria or anuria

***Table 6** - Clinical symptoms and signs in compensated and decompensated shock*


DENGUE CASE MANAGEMENT
ASSESSMENT
Presumptive Diagnosis
Live in/travel to endemic area plus fever and two of the following
1. Anorexia & Nausea
2. Rash
3. Aches or pain
4. Warning sign
5. Leaukopenia
6. Tourniquet test positive
Lab confirmed dengue (Important when no sign of plasma leakage)
No clinical improvement or worsening of the situation just before or during the transition to afebrile phase or as the disease progresses.
Persistent vomiting.
Severe abdominal pain.
Lethargy and/or restlessness, sudden behavioral changes.
Bleeding: epistaxis, black stool, haematemesis, excessive menstrual bleeding, dark colored urine (haemoglobinuria) or haematuria.
Giddiness.
Pale, cold and clammy hands and feet.
Less/no urine output for 4–6 hours
Liver enlargement > 2cm
Haematocrit >20%
CASE CLASSIFICATION
Negative
Co -existing condition Social Circumstances
Positive
Negative
Dengue without Warning Sign
Positive
Dengue with Warning Sign
Severe Dengue
GROUP
Group A: May be sent home (Mild)
Group B: Referred for Hospital Care (Moderate)
Group C: Register for Emergency Treatment (Severe)
MANAGEMENT
GROUP A
-Who may sent home
Group B
Referred for in-hospital care
Group C
Require emergency treatment
Group criteria
Patient Who do not have warning sign AND Who are able
- to tolerate adequate amount of ORAL Fluids
- to pass urine at least once in every 6 hours
Group criteria
Patients with any of the following features:
• C o- existing conditions such as pregnancy, infancy, old age, diabetes mellitus
•Social circumstance es such as living alone, living far from hospital
OR
Existing warning signs:
• Abdominal pain or tenderness
• Persistent vomiting
• Clinical fluid accumulation
• Mucosal bleeding
• Lethargy/ restlessness
• Liver enlargement >2cm
• Laboratory: increase in Hct
Group criteria
Patients with any of the following features.
• Severe plasma leakage with shock and/or fluid accumulation with respiratory distress
• Severe bleeding
• Severe organ impairment
• Severe Metabolic dysfunction
Laboratory tests
- Full Blood Count (FBC)
- Hematocrit (HCT)
Laboratory tests
• Full blood Count (FBC)
• Haematocrit (Hct)
Laboratory tests
• Full blood Count (FBC)
• Haematocrit (Hct)
• Other organ function tests as indicated

Advice for:	Treatment	Treatment
• Adequate rest • Adequate fluid intake • Paracetamol, 4 gram max. per day in adults and accordingly in children Patients with stable Hct can be sent home	• Encouragement for oral fluids • If not tolerated, start intravenous fluid therapy 0,9% saline or Ringer Lactate at maintenance rate • Obtain reference Hct before fluid therapy • Give isotonic solutions such as 0,9% saline, Ringer lactate, start with 5-7 ml/kg/hr for 1-2 hours, then reduce to 3-5 ml/kg/hr for 2-4 hr, and then reduce to 2-3 ml/kg/hr or less according to clinical response **Reassess clinical status and repeat Hct** • If Hct remains the same or rises only minimally -> continue with 2-3 ml/kg/hr for another 2-4 hours • If worsening of vital signs and rapidly rising Hct -> increase rate to 5-10 ml/kg/hr for 1-2 hours **Reassess clinical status, repeat Hct and review fluid infusion rates accordingly** • Reduce intravenous fluids gradually when the rate of plasma leakage decreases towards the end of the critical phase **This is indicated by:** • Adequate urine output and/or fluid intake • Hct decreases below the baseline value in a stable patient	Treatment of compensated shock: o Start I.V. fluid resuscitation with isotonic crystalloid solutions at 5-10 ml/kg/hr over 1hr o Reassess patient's condition, If patient improves: o I. V. fluids should be reduced gradually to 5-7 ml/kg/hr for 1-2 hr, then to 3- 5 ml/kg/hr for 2-4 hr, then to 2-3 ml/kg/hr for 2-4 hr and then reduced further depending on haemodynamic status o I. V. fluids can be maintained for up to 24 - 48 hours If patient still unstable o Check Hct after first bolus If Hct increases/ still high (>50%), repeat a second bolus of crystalloid solution at 10-20 ml/kg/hr for 1 hr. If improvement after second bolus, reduce rate to 7-10 ml/kg/hr for 1-2 hr, continue to reduce as above. If Hct decreases, this indicates bleeding and need to cross-match and transfuse blood as soon as possible Treatment of hypotensive shock o Initiate I.V. fluid resuscitation with crystalloid or colloid solution at 20 ml/kg as a bolus for 15 min If patient improves o Give a crystalloid / colloid solution of 10 ml/kg/hr for 1 hr, then reduce gradually as above If patient still unstable o Review the Hct taken before the first bolus o If Hct was low (< 45% in adult males) this indicates bleeding, the need to crossmatch and transfuse (see above) o If HcT was high compared to the baseline value, change to I.V. colloids at 10-20 ml/kg as a second bolus over to 1 hour; reassess after second bolus o If improving reduce the rate to 7-10 ml/kg/hr for 1-2 hours, then back to I.V. crystalloids and reduce rates as above o I f condition still unstable, repeat Hct after second bolus o If HcT decreases, this indicates bleeding, see above o If HcT increases/ remains high (> 50%), continue colloid infusion at 10-20 ml/kg as a third bolus over 1 hr, then reduce to 7-10 ml/kg /hr for 1-2 hours, then change back to crystalloid solution and reduce rate as above Treatment of haemorrhagic complications: o Give 5-10 ml/kg of fresh packed red cells or 10-20 ml/kg fresh whole blood
Monitoring • Daily review for disease progression: • Decreasing WBC • Defervescence • Warning signs (until out of critical period) • Advice for immediate return to hospital if development of any warning signs • Written advice of management (e.g. home care card for Dengue)	**Monitoring** • Temperature pattern Volume of fluid intake and losses • Urine output – volume and frequency • Warning signs • Hct, white blood cell and platelet counts • Vital signs and peripheral perfusion (1-4 hourly until patient is out of critical phase • Urine output (4-6 hourly) • Hct (before and after fluid replacement, then 6-12 hourly) • Blood glucose • Other organ functions (renal profile, liver profile, coagulation profile, as indicated	
Discharge Criteria: All of Flowing criteria must be present • No fever for 48 hours • Improvement in clinical picture • Increasing trend of platelet count • No respiratory distress • Stable haematocrit without intravenous fluids		

Table 7 *- Dengue Case Management Algorithm*

4.2 Stepwise Approach of Dengue Case Management

Step 1 - Overall Assessment	
1.1	History, including symptoms, past medical and family history
1.2	Physical examination, including full physical and mental assessment
1.3	Investigation, including routine laboratory tests and dengue-specific laboratory tests
Step 2 - Diagnosis, assessment of disease phase and severity	
Step 3 - Management	
3.1	Disease notification
3.2	Management decisions. Depending on the clinical manifestations and other circumstances, patients may: - be sent home (Group A) - be referred for in-hospital management (Group B) - require emergency treatment and urgent referral (Group C)

Table 8 - *Step Wise Dengue Case Management*

Step 1 – Overall assessment

1.1 The history should include:

- Date of onset of fever/illness;
- Quantity of oral fluid intake;
- Diarrhoea;
- Urine output (frequency, volume and time of last voiding);
- Assessment of warning signs ;
- Change in mental state/seizure/dizziness;
- Other important relevant history, such as family or neighbourhood dengue, travel to dengue-endemic areas, co-existing conditions (e.g. infancy, pregnancy, obesity, diabetes mellitus, hypertension), jungle trekking and swimming in waterfalls (consider leptospirosis, typhus, malaria), recent unprotected sex or drug abuse (consider acute HIV-seroconversion illness).

1.2 The physical examination should include

- Assessment of mental state;
- Assessment of hydration status;
- Assessment of haemodynamic status;
- Checking for quiet tachypnoea/acidotic breathing/pleural effusion;
- Checking for abdominal tenderness/hepatomegaly/ascites;
- Examination for rash and bleeding manifestations;
- Tourniquet test (repeat if previously negative or if there is no bleeding manifestation).

1.3 The investigation

- A full blood count (CBC) should be done at the first visit (it may be normal); Platelet count and haematocrit repeated daily until the critical phase is over.
- The haematocrit in the early febrile phase could be used as the patient's own baseline.
- Decreasing white blood cell and platelet counts make the diagnosis of dengue very likely.
- Leukopenia usually precedes the onset of the critical phase and has been associated with severe disease.
- A rapid decrease in platelet count, concomitant with a rising haematocrit compared to the baseline, is suggestive of progress to the plasma leakage/critical phase of the disease.
- These changes are usually preceded by leukopenia (≤ 5000 cells/mm3). In the absence of the patient's baseline, age-specific population haematocrit levels could be used as a surrogate during the critical phase.
- If facilities for a full blood count are not available or if resources are limited, such as in outbreak settings, a full blood count or microhaematocrit should be done at the

first visit to establish the baseline. This should be repeated after the 3rd day of illness and in those with warning signs and risk factors for severe disease.

- Dengue-specific laboratory tests should be performed to confirm the diagnosis. However, it is not necessary for the acute management of patients, except in cases with unusual manifestations.

Additional tests should be considered in patients with co-morbidities and severe disease as indicated. These may include tests of liver function, glucose, serum electrolytes, urea and albumin.

Step 2 - Diagnosis, Assessment of disease phase and severity

Diagnosis, assessment of disease phase and severity on the basis of evaluations of the history, physical examination and/or full blood count and haematocrit.

Clinicians should determine whether the disease is dengue, which phase it is in (febrile, critical or recovery), whether there are warning signs, the hydration and haemodynamic state of the patient, and whether the patient requires admission. For blood pressure assessment follow age specific blood pressure chart (see annexure).

Step 3 - Management

- Disease notification in dengue-endemic countries:

  Suspected dengue: acute febrile illness with or without non-specific signs and symptoms.

  Probable dengue: an acute febrile illness with serological diagnosis.

  Confirmed dengue: An acute febrile illness with positive dengue NS1 antigen or PCR test.

- For the purpose of the management the definition of the cases will be defined as group A, B & C. During the time of reporting both will be incorporate in the reporting system.
- Laboratory confirmation is not necessary before notification, but it should be obtained.

  In non-endemic countries, usually only confirmed cases will be notified.
- Management decisions: Depending on the clinical manifestations and other circumstances, patients may-
  - either be sent home (Group A);
  - be referred for in-hospital management (Group B); or
  - require emergency treatment and urgent referral (Group C).

4.3 Treatment According to Group A-C

Group A

These patients will be advised to

- adequate bed rest
- adequate fluid intake (> 6 glasses for an average-sized adult, or accordingly in children) - e.g. milk, fruit juice (caution with diabetes patient), oral rehydration solution (ORS) or barley/rice water/coconut water Note: Plain water alone may cause electrolyte imbalance
- take paracetamol (not more than 3 grams per day for adults; 10-15 mg/kg/dose, not more than 3 to 4 times in 24 hours in children)
- Tepid sponging
- look for mosquito breeding places in and around the home and eliminate them

These patients will be advised to avoid

- Acetylsalicylic acid (aspirin), mefenemic acid, ibuprofen or other NSAIDs
- Steroids
- Antibiotics

If any of following is observed, the patient should be immediately taken to the nearest hospital; these are warning signs for danger:

Bleeding:

- red spots or patches on the skin
- bleeding from nose or gums
- vomiting of blood
- black-coloured stools
- heavy menstruation/vaginal bleeding

- Frequent vomiting or not able to drink
- Severe abdominal pain
- Drowsiness, mental confusion or seizures
- Pale, cold or clammy hands and feet
- Difficulty in breathing
- Postural dizziness
- No urine output for 4–6 hours

Group B

Management of Patients in Group B

- Obtain a reference haematocrit before intravenous fluid therapy begins.
- Intravenous fluid therapy in DHF during the critical period.

Indications for IV fluid:

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

he general principles of fluid therapy in DHF include the following:

The following fluids are recommended both crystalloids and colloids

Crystalloids

1. 0.9% NaCl (isotonic normal saline solution) (0.9%NS) (Preferable)
2. 0.45% half strength normal saline solution (0.45%NS) (For children <6 months)
3. 5% dextrose in lactated Ringer's solution (5%DRL)
4. 5% dextrose in acetated Ringer's solution (5%DRA)
5. Hartman solution (Preferable)

Colloids

1. Plasmasol
2. Dextran 40
3. Human Albumin
4. Plasma
5. Hemaceel
6. Blood & Blood Components

- Isotonic crystalloid solutions should be used throughout the critical period except in the very young infants <6 months of age in whom 0.45% sodium chloride may be used. Give only isotonic solutions such as 0.9% saline, Ringer's lactate or Hartmann's or Lactate solution.
- Hyper-oncotic colloid solutions (osmolarity of >300 mOsm/l) such as dextran 40 or starch solutions may be used in patients with massive plasma leakage, and those not responding to the minimum volume of crystalloid. Iso-oncotic colloid solutions such as blood and blood component may not be as effective.
- A volume of about maintenance +5% dehydration should be given to maintain "just adequate" intravascular volume and circulation. The duration of intravenous fluid therapy should not exceed 24 to 48 hours for those with shock. However, for those patients who do not have shock, the duration of intravenous fluid therapy may have to be longer but not more than 60 to 72 hours. This is because the latter group of patients has just entered the plasma leakage period while shock patients have experienced a longer duration of plasma leakage before intravenous therapy is begun.

- In obese patients, the ideal body weight should be used as a guide to calculate the fluid volume
- Fluid Requirement:

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

  5% deficit is calculated as 50 ml/kg up to 50kg.

Calculations for normal maintenance of intravenous fluid Infusion:

Normal maintenance fluid per hour can be calculated on the basis of the following formula* (equivalent to Holliday - Segar formula):

4 ml/kg/hr for first 10 kg body weight
+ 2 ml/kg/hr for next 10 kg body weight
+ 1 ml/kg/hr for subsequent kg body weight

For overweight/obese patients calculate normal maintenance fluid based on ideal body weight (IBW), using the following formula:

Height (cm)	Estimated IBW for adult male(kg)	Estimated IBW for adult female(kg)
150	50	45.5
160	57	52
170	66	61.5
180	75	70

Table 9 - *Estimated ideal body weight for overweight or obese adults*

Ideal wt (kg)	Maintenance (ml)	M+5% deficit (ml)	Ideal body wt (kg)	Maintenance (ml)	M+5% deficit (ml)
5	500	750	35	1800	3550
10	1000	1500	40	1900	3900
15	1250	2000	45	2000	4250
20	1500	2500	50	2100	4600
25	1600	2850	55	2200	4950
30	1700	3200	60	2300	5300

Table 10 - *Requirement of fluid based on ideal body weight*

Note	Children (ml/kg/hr)	Adult(ml/hr)
Half of maintenance (M/2)	1.5	40-50
Maintenance	3	80-100
M+5% deficit	5	100-120
M+7% deficit	7	120-150
M+10% deficit	10	300-500

Table 11 *- Rate of IV fluid in adults and children*

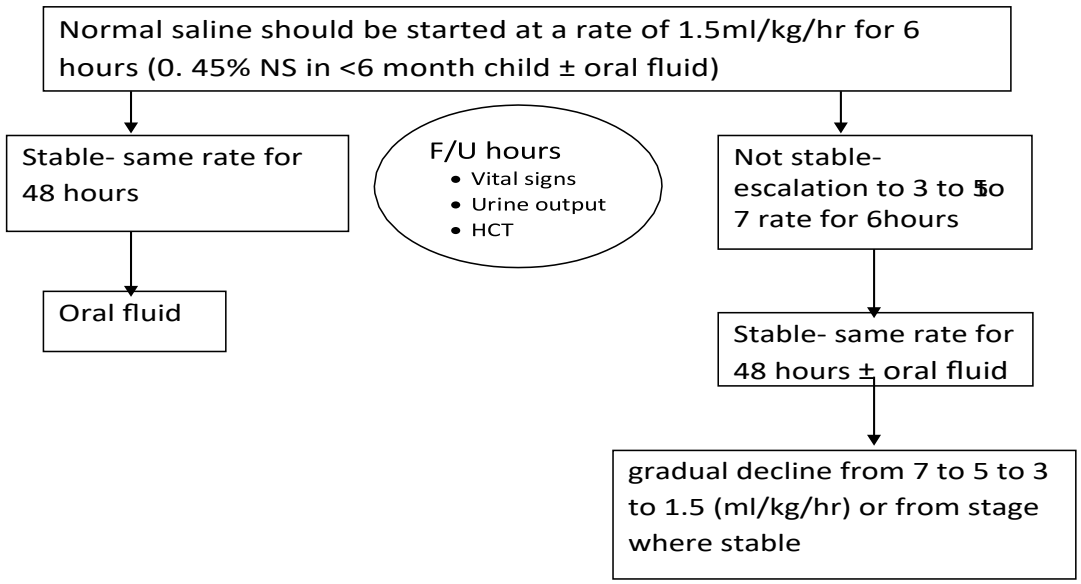
- In general, the fluid allowance (oral + IV) is about maintenance (for one day) + 5% deficit (oral and IV fluid together), to be administered over 48 hours. For example, in a child weighing 20 kg, the deficit of 5% is 50 ml/kg x 20 = 1000 ml. The maintenance is 1500 ml for one day. Hence, the total of M + 5% is 2500 ml. This volume is to be administered over 48 hours in non shock patients. The rate of IV replacement should be adjusted according to the rate of plasma loss, guided by the clinical condition, vital signs, urine output and haematocrit levels.
- The admitted patient (Category B) should be started with recommended fluid at a rate of 1.5ml/kg/hr or 40ml/hr (12 d/min) for adults and should be given for 6 hours. If patient's vital signs are stable, then the escalation of fluid is not needed and the same rate can be maintained for a period of 48 hours.
- If patient started with 1.5ml/kg/hr (adult 40ml/hr) for 6 hours doesn't have stable vital signs and adequate urine output, the fluid should be escalated to 3ml/kg/hr (adult 80ml/hr or 20 drops/min) for another 6 hours. If patient's vital signs are stable, then the escalation of fluid is not needed and the same rate can be maintained for a period of 48 hours. This fluid can be escalated to 5ml/kg/hr (adult 120ml/hr or 30d/min and then upto 7ml/kg/hr or adult 200ml/hr or 50d/min) if every 6 hours doesn't have stable vital sign or urine output.
- Patient should be monitor every 2 hours with special attention to vital signs, urine output, respiratory signs and haematocrit etc. In 6 hours of escalation, if patient become stable regarding clinical parameters, the fluids can be gradually decline from 7 to 5 to 3 to 1.5 (ml/kg /hr) or from stages where he was stable. But the fluids should be maintained always for at least 48 hours.
- Reassess the clinical status, repeat the haematocrit and review fluid infusion rates accordingly.
- Patients with warning signs should be monitored by health-care providers until the period of risk is over. A detailed fluid balance should be maintained. Parameters that should be monitored include :
    - vital signs and peripheral perfusion (1–4 hourly until the patient is out of the critical phase),
    - urine output (4–6 hourly),
    - haematocrit (before and after fluid replacement, then 6–12 hourly),
    - blood glucose

- other organ functions (such as renal profile, liver profile, coagulation profile, as indicated).

Platelet transfusion is not recommended for thrombocytopenia (no prophylaxis platelet transfusion). The indication of which may be as follows:

1. Very severe Thrombocytopania who need urgent surgery
2. Clinical judgement of the treating physician

If platelet concentrate is not available fresh whole blood may be transfused as per guidelines given under DHF management.



Fluid Management- Group B (Children with warning signs)

Example: In a child weighing 10 kg, the starting fluid should be (1.5 x 10) = 15 ml/hr (15 µdrops/min). If needed, escalation should be done @ 3 ml/kg/hr (3x10) = 30 ml/hr (30 µdrops/min), Then 5 ml/kg/hr (5x10) = 50 ml/hr (50 µdrops/min) and subsequently like this.

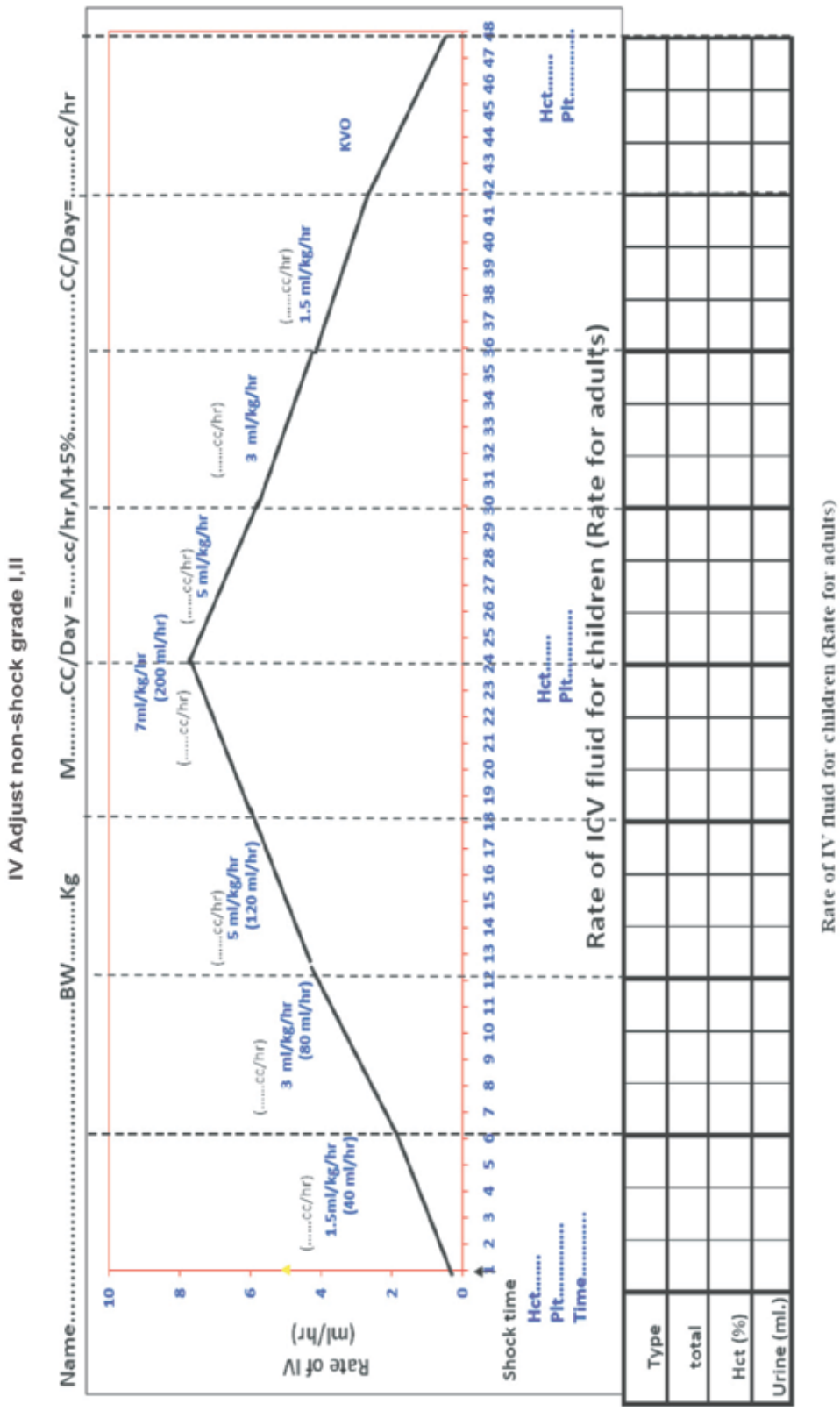


Figure11 *- Fluid Management for Dengue Non Shock*

If the patient has dengue with co-existing conditions but without warning signs, the plan should be as follows:

- Encourage oral fluids.
- If not tolerated, start intravenous fluid therapy of 0.9% saline or Ringer's lactate with or without glucose at the appropriate maintenance rate.
- Use the ideal body weight for calculation of fluid infusion for obese and overweight patients.
- Give the minimum volume required to maintain good perfusion and urine output. Figure 8 should be follow
- Intravenous fluids are usually needed only for 24–48 hours.
- Patients should be monitored by health-care providers for temperature pattern, volume of fluid intake and losses, urine output (volume and hrly), warning signs, haematocrit, white blood cell and platelet counts.
- Depending on the clinical picture and the facilities of the hospital or health center, other laboratory tests (such as liver and renal functions tests) can also be carried out.

Name															
Date of onset of fever															
Date of warning sings onset															
Body weight															
Time*															
HCT															
(%)															
Temp															
WBC															
Platelet															
Temperature (°C)															
Respiratory rate															

Crystalloids ml/ kg/hr Cum Vol																
Colloids ml/ kg/hr Cum vol																
Blood product Type ml/kg/h Cumulative																
Oral quantity Cum oral																
Cum input																
Hourly urine																
Cum urine																
Others																

Table 12 - *Patient monitoring chart*

WBC = white blood cell; Cum vol = cumulative volume i.e. total volume since start of treatment; Cum oral = cumulative oral intake since start of treatment; Cum input = cumulative intravenous and oral fluid input; Cum urine = cumulative urine i.e. total urine volume since start of treatment

*** Laboratory results should be tabulated under the time of blood sampling, not time of results being available**

Group C

The goals of fluid resuscitation include:

- improving central and peripheral circulation – i.e. decreasing tachycardia, improving BP and pulse volume, warm and pink extremities, a capillary refill time<2 seconds
- improving end-organ perfusion – i.e. achieving a stable conscious level (more alert or less restless)
- urine output ≥ 0.5 ml/kg/hour or decreasing metabolic acidosis.

Treatment of shock

Compensated shock :

- DSS is hypovolemic shock caused by plasma leakage and characterized by increased systemic vascular resistance, manifested by narrowed pulse pressure (systolic pressure is maintained with increased diastolic pressure, e.g. 100/90 mmHg).
- When hypotension is present, one should suspect that severe bleeding, and often concealed gastrointestinal bleeding, may have occurred in addition to the plasma leakage.
- Most cases of DSS will respond to 10 ml/kg in children or 300–500 ml in adults over one hour or by bolus if necessary further, fluid administration should follow the graph as in Figure 12.
- However, before reducing the rate of IV replacement, the clinical condition, vital signs, urine output and haematocrit levels should be checked to ensure clinical improvement.
- It is essential that the rate of IV fluid be reduced as peripheral perfusion improves; but it must be continued for a minimum duration of 24 hours and discontinued by 36 to 48 hours.
- Excessive fluids will cause massive effusions due to the increased capillary permeability. The volume replacement flow for patients with DSS is illustrated below.

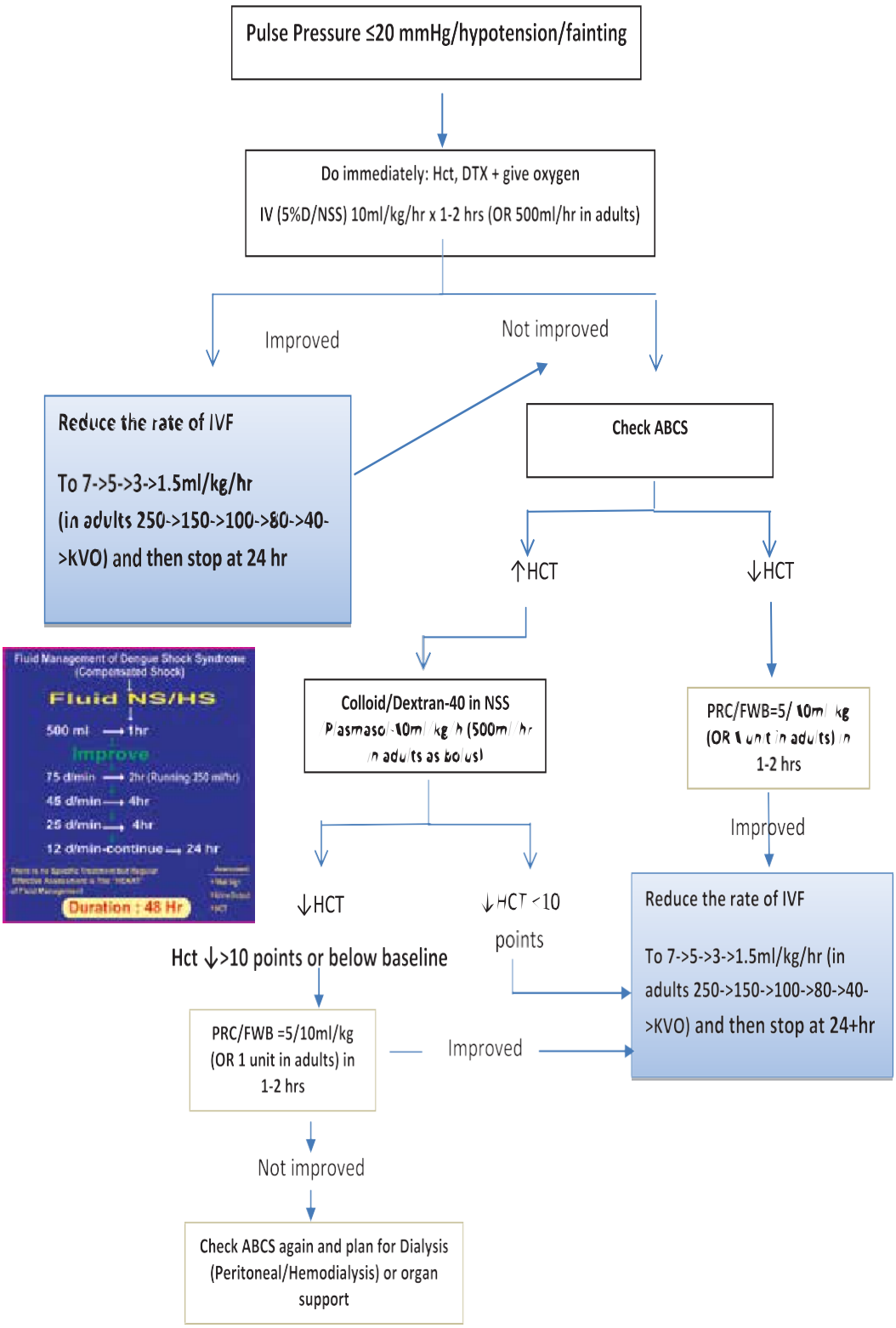


Figure 12 - *IV FLUID THERAY for Compensated Shock*

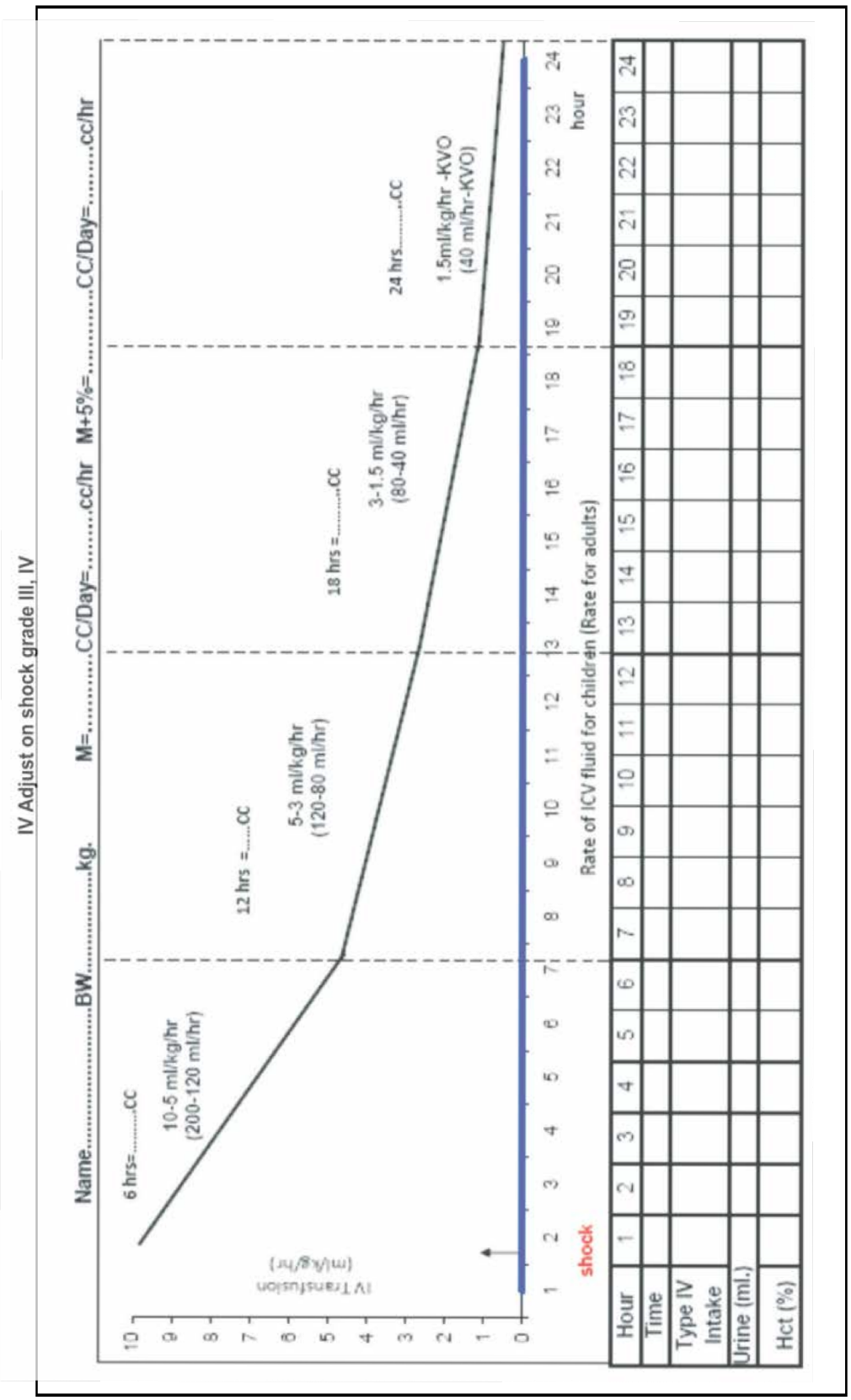


***Figure 13** - Fluid Management for Dengue Shock*

Laboratory investigations (ABCS) should be carried out in both shock and non-shock cases when no improvement is registered in spite of adequate volume replacement

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 - 1 ml/kg, dilute two times, IV push slowly (and may be repeated every 6 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.

Table 13 *- IV Fluid Therapy for Compensated shock*

Decompensated shock (DSS, Profound hypotension)

- Preferably this group of patient need to manage in ICU setting.
- Oxygen should be started immediately.
- The bolus 10-20 ml/kg crystalloids should be given within 15-30 min.
- If the vital signs and HcT improved, the fluid can be reduced from 10 ml/kg/hr to 6ml/kg/hr for 2 hours, then from 6 to 3 ml/kg/hr for 2-4 hrs and then 3 to 1.5 ml/kg/hr for another 2-4 hrs. Fluid should be discontinued after 24-48 hrs.
- If there is no clinical improvement after bolus crystalloids, check HcT. If the HcT is raising (more than 45%, then the fluid should be changed to colloid at (10-20ml/kg/hr) and if there is improvement, then changes the fluid to crystalloids and successfully reduce as stated before. The highest dose of colloid will be 30 ml/kg/24 hour.
- If the initial bolus crystalloids fluid does not have improvement in vitals sign and HcT is reduced, then suspect concealed bleeding and blood transfusion should be started immediately at 10ml/kg whole blood or packed RBC at 5ml/kg.
- In case of refractory hypotension, look for ABCS and IV inotropes with crystalloids as per requirement is to be continued.
- In case of acidosis, hyperosmolar or ringers' lactate should not be used.
- HcT measurement every hour is more important than platelet count during management.

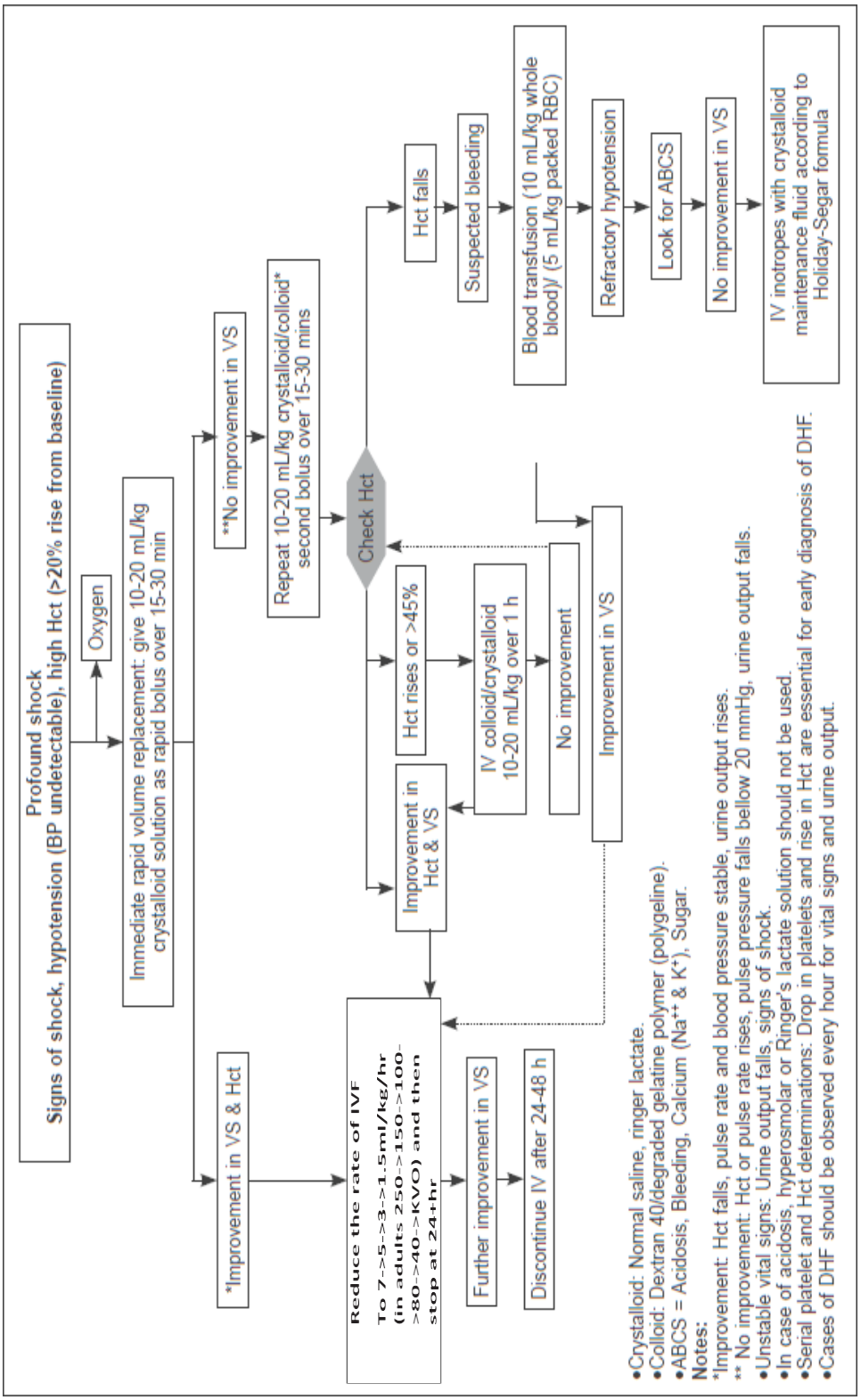
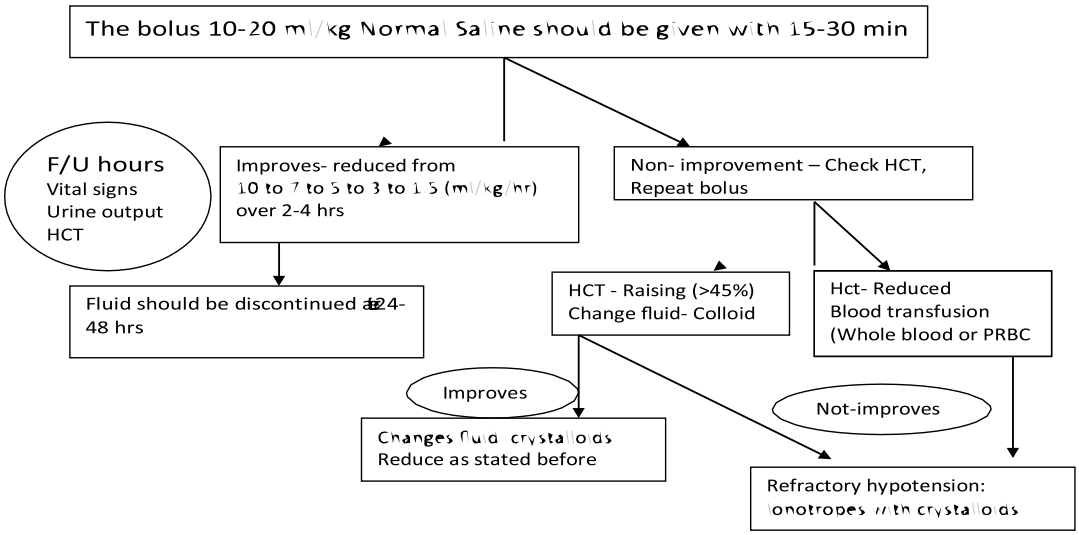


Figure 14 *- Volume Replacement Algorithm for Patient With DSS*

Group C (Decompensate Shock) For Children



Example: In a child weighing 10 kg, the bolus fluid should be (10 x 10) = 100 ml over 30 min (50 drops/min). When patient becomes vitally stable, fluid should be continued @ 10 ml/kg/hr (10x10) = 100ml/ hr (25 drops/min). If improves, reduction should be done @ 7ml/kg/hr (7x10) = 70 ml/hr (18 drops/min), Then 5 ml/kg/hr (5x10) = 50 ml/hr (12 µdrops/min) and subsequently like this.

When to stop intravenous fluid therapy

- Cessation of plasma leakage;
- Stable BP, pulse and peripheral perfusion;
- Hematocrit decreases in the presence of a good pulse volume;
- Apyrexia (without the use of antipyretics) for more than 24–48 hours;
- Resolving bowel/abdominal symptoms;
- Improving urine output.
- Continuing intravenous fluid therapy beyond the 48 hours of the critical phase will put the patient at risk of pulmonary oedema and other complications such as thrombophlebitis

Treatment of hemorrhagic complications

Patients at risk of severe bleeding are those who:

- Have profound/prolonged/refractory shock;
- Have hypotensive shock and multi-organ failure
- Have pre-existing peptic ulcer disease;
- Have any form of trauma, including intramuscular injection.
- Are given non-steroidal anti-inflammatory agents;
- Are on anticoagulant therapy;

Severe bleeding should be recognized in the following situations:

- Persistent and/or severe overt bleeding in the presence of unstable haemodynamic status, regardless of the haematocrit level;
- Decrease in haematocrit after bolus of fluid resuscitation unstable haemodynamic status;
- Refractory shock that fails to respond to consecutive fluid resuscitation of 40–60 ml/kg;
- Hypotensive shock with inappropriately low/normal haematocrit;
- Persistent or worsening metabolic acidosis;
- Well-maintained systolic BP, especially in those with severe tenderness and distension.

The action plan for the treatment of hemorrhagic complications is as follows:

- If possible, attempts should be made to stop bleeding if the source of bleeding is identified e.g. severe epistaxis may be controlled by nasal adrenaline packing.
- Give aliquots of 5–10 ml/kg of fresh -packed red cells or 10–20 ml/kg. Of fresh whole blood (FWB) at an appropriate rate and observe the clinical response.
- It is important that fresh whole blood or fresh red cells are given.
- Oxygen inhalation-2-4 L/min
- Consider repeating the blood transfusion if there is further overt blood loss or no appropriate rise in haematocrit after blood transfusion in an unstable patient.
- There is no evidence that supports the practice of transfusing platelet concentrates and/or fresh-frozen plasma for severe bleeding in dengue.
- Transfusions of platelet concentrates and fresh frozen plasma in dengue were not able to sustain the platelet counts and coagulation profile. Instead, in the case of massive bleeding, they often exacerbate the fluid overload.
- In certain situations, such as obstetrical deliveries or other surgeries, transfusions of platelet concentrate with or without fresh blood should be considered in anticipation of severe bleeding.
- In gastrointestinal bleeding, H-2 antagonist and proton pump inhibitors have been used, but their efficacy have not been studied.
- Great care should be taken when inserting a nasogastric tube or bladder catheters which may cause severe hemorrhage. A lubricated orogastric tube may minimize the trauma during insertion. Insertion of central venous catheters should be done with ultra-sound guidance or by an experienced person.
- It is essential to remember that blood transfusion is only indicated in dengue patients with severe bleeding.

Glucose control

- Hyperglycaemia and hypoglycaemia may occur in the same patient at different times during the critical phase.
- Hyperglycaemia is associated with increased morbidity and mortality in critically ill

adult and paediatric patients.

- Hypoglycaemia may cause seizures, mental confusion and unexplained tachycardia.
- Most cases of hyperglycaemia will resolve with appropriate (isotonic, non-glucose) and adequate fluid resuscitation.
- In infants and children, blood glucose should be monitored frequently during the critical phase and into the recovery phase if the oral intake is still reduced.
- However, if hyperglycemia is persistent, undiagnosed diabetes mellitus or impaired glucose tolerance should be considered and intravenous insulin therapy initiated.
- Hypoglycaemia should be treated as an emergency with 0.1–0.5g/kg of glucose, rather than with a glucose-containing resuscitation fluid.
- Frequent glucose monitoring should be carried out and euglycaemia should then be maintained with a fixed rate of glucose-isotonic solution and external feeding if possible.

Electrolyte and acid-base imbalances

- Hyponatraemia is a common observation in severe dengue
- The use of isotonic solutions for resuscitation will prevent and correct this condition.
- Hyperkalaemia is observed in association with severe metabolic acidosis or acute renal injury.
- Appropriate volume resuscitation will reverse the metabolic acidosis and the associated hyperkalaemia.
- Life-threatening hyperkalaemia, in the setting of acute renal failure should be managed with Resonium A and infusions of calcium gluconate and/or insulin-dextrose.
- Renal support therapy may have to be considered.
- Hypokalaemia is often associated with gastrointestinal fluid losses and the stress-induced hypercortisol state;
- It should be corrected with potassium supplements in the parenteral fluids.
- Serum calcium levels should be monitored and corrected when large quantities of blood have been transfused or if sodium bicarbonate has been used (Table 12)

Metabolic acidosis

- Compensated metabolic acidosis is an early sign of hypovolaemia and shock.
- Lactic acidosis due to tissue hypoxia and hypoperfusion is the most common cause of metabolic acidosis in dengue shock.
- Correction of shock and adequate fluid replacement will correct the metabolic acidosis.
- If metabolic acidosis remains uncorrected by this strategy, one should suspect severe bleeding and check the haematocrit. Transfuse fresh whole blood or fresh packed red cells urgently.
- Sodium bicarbonate for metabolic acidosis caused by tissue hypoxia is not

recommended for pH ≥ 7.10. Bicarbonate therapy is associated with sodium and fluid overload, an increase in lactate and pCO2 and a decrease in serum ionized calcium. A left shift in the oxy– haemoglobin dissociation curve may aggravate the tissue hypoxia.

- Hyperchloraemia, caused by the administration of large volumes of 0.9% sodium chloride solution (chloride concentration of 154 mmol/L), may cause metabolic acidosis with normal lactate levels.
- If serum chloride levels increase, use Hartmann's solution or Ringer's lactate as crystalloid. These do not increase the lactic acidosis

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 hematocrit at baseline level.**
- **Convalescent confluent petechiae rash or itching, especially on the extremities.**

Discharge Criteria:

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

Fluid Overloaded Patient:

Some degree of fluid overload is inevitable in patients with severe plasma leakage. The skill is in giving them just enough intravenous fluid to maintain adequate perfusion and at the same time avoiding excessive fluid overload.

Causes of excessive fluid overload:

- Excessive and/or too rapid intravenous fluids during the critical phase.
- Incorrect use of hypotonic crystalloid solutions e.g. 0.45% sodium chloride solutions.
- Inappropriate use of large volumes of intravenous fluids in patients with unrecognized severe bleeding.
- Inappropriate transfusion of fresh-frozen plasma, platelet concentrates and cryoprecipitates.
- Prolonged intravenous fluid therapy, i.e., continuation of intravenous fluids after plasma leakage has resolved (> 48 hours from the start of plasma leakage)
- Co-morbid conditions such as congenital or ischaemic heart disease, heart failure, chronic lung and renal diseases.

Clinical features of fluid overload:

- Rapid breathing
- Suprasternal in-drawing and intercostal recession (in children)
- Respiratory distress, difficulty in breathing
- Wheeze, crepitations
- Large pleural effusions tense ascites, persistent abdominal discomfort/pain/tenderness (this should not be interpreted as warning signs of shock)
- Increased jugular venous pressure (JVP)
- Pulmonary oedema (cough with pink or frothy sputum, wheezing and crepitations, cyanosis) - this may be mistaken as pulmonary hemorrhage
- Irreversible shock (heart failure, often in combination with ongoing hypovolaemia)
- Puffy Face & leg oedema

Additional investigations needed:

- Blood gas and lactate analysis
- Chest X-ray which shows cardiomegaly, pleural effusion, features of heart failure
- ECG to exclude ischaemic changes and arrhythmia
- Echocardiogram for assessment of left ventricular function
- Cardiac enzymes

Management of fluid overload:

- Review the total intravenous fluid therapy and clinical course & check and correct for ABCS.
- All hypotonic solutions should be stopped.
- Switch from crystalloid to colloid solutions as bolus fluids.
- Dextran 40 is effective as 10 ml/kg bolus infusions, but the dose is restricted to 30 ml/kg/day because of its renal effects.

In the late stage:

- Intravenous Furosemide may be administered if the patient has stable vital signs.
- If the patient is in shock, together with fluid overload 10 ml/kg/hr of colloid (dextran) should be given.
- When the blood pressure is stable, usually within 10 to 30 minutes of administer IV 1 mg/kg/dose of furosemide and continue with infusion, dextran infusion until completion.
- Intravenous fluid should be reduced to as low as 1 ml/kg/hr until when haematocrit decreases to baseline or below (with clinical improvement).

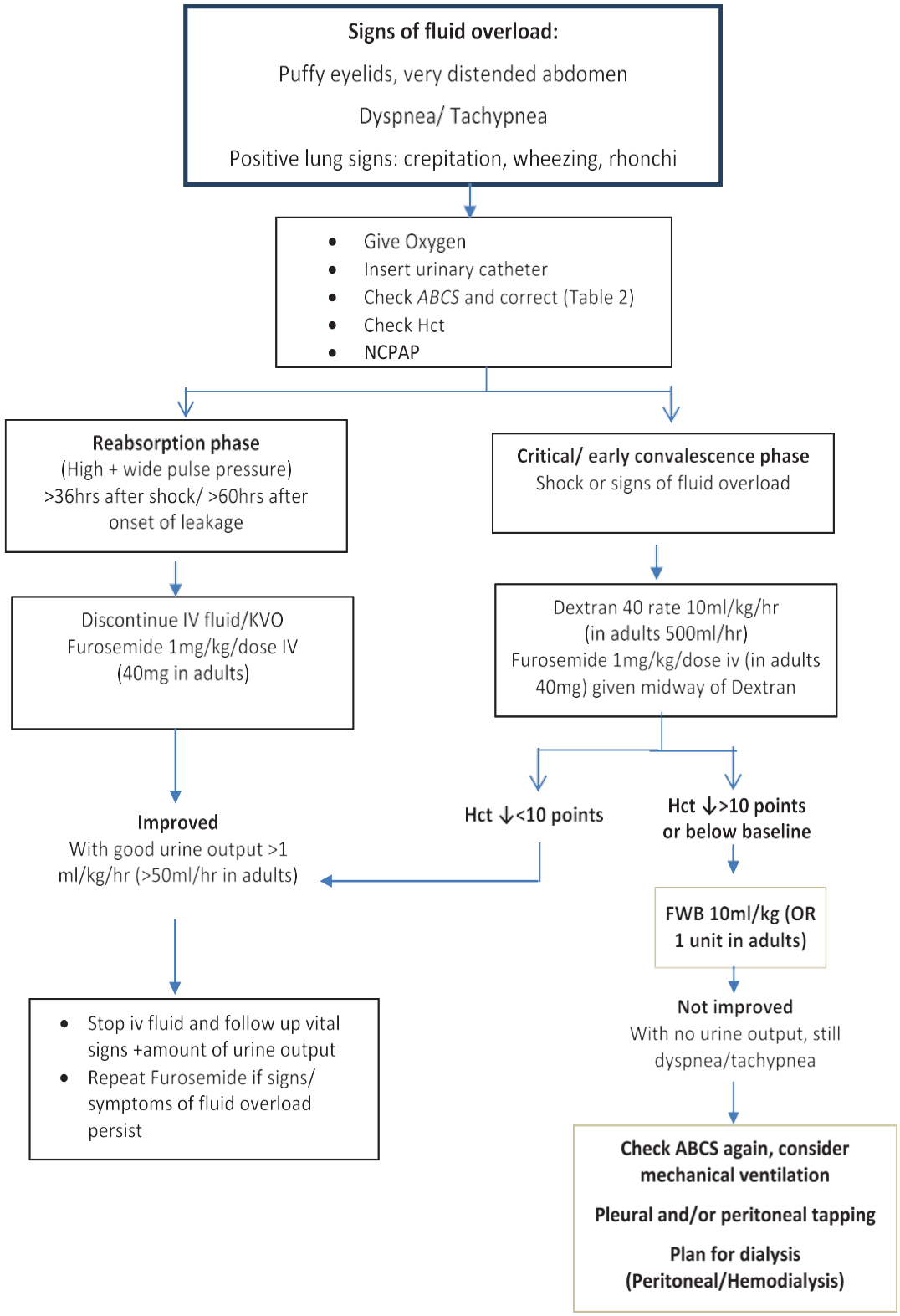


Figure 15 *- Flow diagram for the Management of Fluid Overload*

The following points should be noted:

- These patients should have a urinary bladder catheter to monitor hourly urine output
- Intravenous Furosemide should be administered during dextran infusion because the hyperoncotic nature of dextran will maintain the intra vascular volume while furosemide depletes in the intravascular compartment. After administration of furosemide, the vital signs should be monitored every 15 minutes for one hour to note its effects.
    - If there is no urine output in response to furosemide, check the intravascular volume status (CVP or lactate). If this is adequate, pre-renal failure is excluded, implying that the patient is in an acute kidney injury state. These patients may require ventilator support soon. If the intravascular volume is inadequate or the blood pressure is unstable, check the ABCS and other electrolyte imbalances
    - In cases with no response to furosemide (no urine obtained), repeated doses of furosemide and doubling of the dose are recommended. If oliguric renal failure is established, renal replacement therapy is to be done as soon as possible. These cases have poor prognosis.
    - Pleural and/or abdominal tapping may be indicated and can be life-saving in cases with severe respiratory distress and failure of the above management. This has to be done with extreme caution because traumatic bleeding is the most serious complication and can be detrimental. Discussions and explanations about the complications and the prognosis with families are mandatory before performing this procedure.

Management of encephalopathy:

- Some DF/DHF patients present 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 hemorrhage or occlusion associated with DIC or hyponatremia.
- Most of the patients with encephalopathy are reported to have hepatic encephalopathy. The principal treatment of 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 hemorrhage.

Recommendations for supportive therapy for this condition:

- Maintain adequate airway oxygenation with oxygen therapy.
- ICP by the following measures:
    - Give minimal IV fluid to maintain adequate intravascular volume; ideally the total IV fluid should not be >80% fluid maintenance.
    - Switch to colloidal solution earlier if haematocrit continues to rise and a large volume of IV is needed in cases with severe plasma leakage.
    - Administer a diuretic if indicated in cases with signs and symptoms of fluid overload.

- positioning of the patient must be with the head up by 30 degrees.
- early intubation to avoid hypercarbia and to protect the airway.
- may consider steroid to reduce ICP. Dexamethasone 0.15 mg/kg/dose IV to be administered every 6–8 hours.

- Decrease ammonia production by giving lactulose 5–10 ml every six hours for induction of osmotic diarrhoea. local antibiotic gets rid of bowel flora; it is not necessary if systemic antibiotics are given.
- Maintain blood sugar level at 80–100 mg/dl per cent. Recommend glucose infusion rate is anywhere between 4–6 mg/kg/hour.
- Correct acid-base and electrolyte imbalance, e.g. correct hypo/hypernatremia, hypo/ hyperkalemia, hypocalcemia and acidosis. 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 as platelets and fresh frozen plasma may not be given because the fluid overload may cause increased ICP.
- Empiric antibiotic therapy may be indicated if there are suspected superimposed bacterial infections.
- H2-blockers or proton pump inhibitor may be given to alleviate gastrointestinal bleeding.
- Consider plasmapheresis or haemodialysis or renal replacement therapy in cases with clinical deterioration.

4.4 Types of Fluids Required for Intravenous Therapy

The general principles of fluid therapy in DHF include the following:

The following fluids are recommended both crystalloids and colloids

Crystalloids

1. 0.9% NaCl (isotonic normal saline solution) (0.9% NS) (Preferable)
2. 0.45% half strength normal saline solution (0.45% NS) (For children <6 months)
3. 5% dextrose in lactated Ringer's solution (5% DRL)
4. 5% dextrose in acetated Ringer's solution (5% DRA)
5. Hartman solution (Preferable)

Colloids

1. Plasmasol
2. Dextran 40
3. Human Albumin
4. Plasma
5. Hemaceel
6. Blood & Blood Components

Ringer's lactate is a safe, effective, and inexpensive alternative in initial resuscitation of patients with moderate shock. In patients with shock, dextran and starch perform similarly although repeated dextran 40 is associated with more hypersensitivity reactions.

Precautions

In order to ensure adequate fluid replacement and avoid fluid over infusion, the rate of intravenous fluid should be adjusted throughout the 24 to 48 hours period of plasma leakage by periodic HcT determinations and frequent assessment of vital signs.

The volume of fluid replacement should be just sufficient to maintain effective circulation during the period of plasma leakage.

Excessive fluid replacement and continuation for a longer period after cessation of leakage will cause respiratory distress from massive pleural effusion, ascites, and pulmonary congestion or edema. This may be dangerous.

Remember that 1 ml is equal to 15 drops in standard macro infusion set. In micro system (micro burette infusion set) 60 drops are equal to 1 ml.

- It is advised to procure only a bag of 500 ml initially, and order more as and when required. The decision about the speed of fluid should be reviewed every 1-3 hours. The frequency of monitoring should be determined on the basis of the condition of the patient. The higher the flow rate the more frequent should be the monitoring.
- It is needed to be careful about the adequacy of the fluid flow rate as high fluid flow rate may require appropriate adjustment of the fluid administration set, height of the saline stand and, sometimes positive pressure application by sphygmomanometer cuff around the fluid bag.

4.5 Some Important Notes

Role of steroid

Basis of DHF pathogenesis is hypothesized to be immunologic that is tempting for immunomodulatory drugs for therapy most common of which is steroid. Currently there is no specific recommendation of steroids for patients with dengue syndrome.

But steroid has been used in Dengue Encephalopathy and Hemophagocytic Syndrome empirically with anecdotal benefits.

There has been used of different formulation of steroids in severe dengue with refractory shock case in different regions of globe, but there is lack of sufficient conclusive evidence.

Well-designed Randomized Control Trial for steroids in severe dengue should be completed before strong recommendation can be solicited.

Special Concerns

Older patients, particularly those with congestive heart failure, must not be given excessive amounts of intravenous fluids.

Rare cases of vertical dengue transmission have been reported. Dengue should be suspected in pregnant patients with compatible clinical features. The potential for a neonate to be born with signs and symptoms of dengue fever should be anticipated.

Pitfalls

- Failure to suspect dengue infection in febrile patients with a history of travel to dengue endemic areas within 2 weeks of the onset of illness.
- Failures to suspect, identify, and treat other possible diseases such as meningitis or malaria.
- Failure to admit patients with signs and symptoms of intravascular volume loss for intravenous hydration.
- Failure to administer appropriate fluids to patients with dengue hemorrhagic fever or dengue shock syndrome (moderate and severe) in proper rate.
- Failure to refer or transfer potentially critical or critical patients to better facility in time.
- Failure to notify public health authorities about suspected cases of dengue infection.

Check list

- Cases of DHF should be observed every hour.
- Serial platelet and HcT determinations for drop in platelets and rise in HcT are essential for early diagnosis of DHF
- Timely intravenous therapy with isotonic crystalloid solution may prevent shock and or lessen the severity. Be careful about the temperature of fluid to avoid chills and rigors.

- If patient's condition becomes worse despite giving 10 ml/kg/hour, replace crystalloid solution with colloid solution such as Dextran or plasma. As soon as improvement occurs replace with crystalloid.
- Preferred dose of colloid is 10 ml/kg (maximum dose 30 ml/kg/day).
- If improvement occurs, reduce the speed from 10 ml to 7 ml, then 5 ml, then 3ml and finally to 1.5 ml/kg.
- If HcT falls, give blood transfusion 10 ml/kg and then give crystalloid IV fluids at the rate of 10 ml/kg/hour.
- In case of severe bleeding, give blood transfusion about 10 ml/kg over 1 - 2 hours. Then give crystalloid at 10 ml/kg/hour for a short time (30-60 minutes) and later reduce the speed.
- In case of shock, give oxygen.
- For correction of acidosis, use sodium bicarbonate. Acidosis should be partially corrected if base deficit is more than 6 mmol/L. Half of the calculated based deficit should be administered as 1-2 mmol/kg of Sodibicarbonate IV over 20 minutes. Available Sodibicarbonate solution in Bangladesh is of the strength 7.5% i.e. 1 ml contains 2 mmol/ml. So, 50 - 100 ml of Sodibicarbonate is to be added to make up to one liter of IV fluid of glucose containing crystalloid.
- Check for any concomitant other medical or surgical condition and or any maintenance therapy.

Don't

- Do not give aspirin or NSAID for the treatment of fever.
- Avoid giving blood transfusion or platelet concentrate unless there is hemorrhage and bleeding, fall in HcT or severe bleeding.
- Do not use antibiotics per see for dengue syndromes.
- Do not change the infusion rate of fluid rapidly or abruptly i.e., avoid rapidly increasing or rapidly slowing the infusion rate of fluids.
- Insertion of nasogastric tube to determine concealed bleeding or to stop bleeding (by cold lavage) is not recommended since it is hazardous.
- Avoid IM injections.
- Avoid tooth brushing in presence of gum bleeding.

Good Medical Practice for IV Therapy

- Always collect and check necessary appliances before proceeding to IV puncture.
- Use gloves to protect yourself and mask to protect the patient. Wash hands with antiseptic before handling cannula/needle. Always use disposable items. Be careful about needle stick injury.
- For IV choose a vein at a site having the following criteria: Distal, relatively less mobile and inactive, away from joint with overlying healthy skin and after shaving hairs. If necessary, immobilize the part with sprint. Keep proximal sites reserve for future puncture if necessary.
- Preferably use cannula having wider bore (18G or wider), which may allow high flow rate and blood transfusion if necessity arises for avoiding further puncture. Properly fix the cannula with adhesive tape. Put date and time of infusion/transfusion beginning on bag and on adhesive tape.
- Insert the cannula or needle along the lengths of vein appropriately to avoid extravasation and check the site frequently for it. Avoid multiple punctures.
- Don't keep the cannula/needle in a same site for more than 48 hours to avoid phlebitis.
- If extravasation occurs immediately remove the cannula/needle and keep the part elevated.
- Always check the fluid bag for deposits, puncture, leaking, proper seals in the port, dirt and labels. In such cases discard the bag. Similarly check the infusion/transfusion sets and cannula. Never reuse any disposables and remaining fluid in bag.
- For high flow rate never use cold fluid to avoid chills and discomfort. Warm the fluid near to body temperature by placing on the cover of the sterilizer and not immersing in that.
- Always dispose the disposables and sharps in a bin to be managed properly.
- Hang the fluid bag at appropriate height and check for proper fluid flow.

4.6 Special Clinical Situations

DF and DHF may develop in a patient stop some other clinical situations. Dengue syndromes with the co-morbid diseases/ situations demand special attention. Even in the well equipped specialized center the risk of mortality will be very high. Some common situations are as follows:

- Pregnancy and labour
- Elderly patient
- Infant patient
- Mandatory Surgery
- Chronic Liver Disease
- Chronic Kidney Disease
- Cardiac diseases: Heart Failure, Ischemic Heart Disease, HTN
- Diabetes and Dengue
- Patient on steroid therapy
- Fluid hypersensitivity and anaphylaxis

Effects of Dengue on pregnancy

- Impact on physiology of pregnancy.
- Cardiovascular - tachycardia, lower blood pressure.
- Hematological - lower HcT at 3rd trimester.
- HCO3 (Bicarbonate) level - lower.

The following physiological changes in pregnancy may make the diagnosis and assessment of plasma leakage challenging:

- Elevation of HcT in dengue is marked by hemodilution due to increase in plasma volume especially in the 2nd and 3rd trimester.
- Serial HcT measurement is crucial for disease monitoring in pregnancy.
- The detection of third space fluid accumulation is difficult due to the presence of gravid uterus.
- Baseline blood pressure is often lower and pulse pressure wider.
- Baseline heart rate may be higher.

Impact of dengue on pregnancy and delivery.

- Early Abortion (3%-13%).
- Embryopathy specially neural tube defect.
- Antepartum haemorrhage (APH) due to retro placental hemorrhage or abruptio placenta.
- Preterm birth (3%-33%).
- Low-birth weight (9%-16%).
- IUGR.

- Fetal Distress.
- IUD or Still birth (4.7%-13%.).
- Increased incidence of caesarean deliveries.
- Post-Partum Haemorrhage (PPH).

New born presentation

- Fever
- Hepatomegaly
- Thrombocytopenia
- Circulatory insufficiency

Causes of Maternal death

- Sever Antepartum Hemorrhage (APH)
- Sever Post-partum Hemorrhage (PPH)
- Dengue shock syndrome (DSS)
- Multi organ failure (MOF)

Causes of Fetal death

- Fetal distress
- Fetal circulatory insufficiency
- Fetal coagulopathy

Fetal well-being evaluation

USG of pregnancy profile

- Gestational age
- Fetal Heart Rate (FHR)
- Fetal weight
- Fetal Presentation
- AFI
- Placental position and maturation

Cardiotocography (CTG)

- Baseline fetal heart rate (110-180 b/min)
- Beat to beat variability (5-25 b/min)
- Acceleration (2 or more)
- Deceleration (No deceleration)

→ Reactive

Biophysical profile

Sl. no	Parameters	Minimal normal criteria	Score
1	Non stress test (NST)	Reactive pattern	2
2	Fetal breathing movement	1 episode lasting>30 sec	2
3	Gross body movement	3 discrete body/ limb movements	2
4	Fetal muscle tone	1 episode of extension (limb or trunk) with return of flexion	2
5	Amniotic fluid	1 pocket measuring 2cm in two perpendicular planes	2

BPP Scoring interpretation and management

BPP Score	Interpretation	Management
8-10	No fetal asphyxia	Repeat testing at weekly interval or more
6	Suspect chronic asphyxia	If > 36 weeks deliver; but If L/S < 2.0 repeat test in 4-6 hours
4	Suspect chronic asphyxia	If >/ 36 weeks deliver, if < 32 weeks repeat testing in 4-6 hours
0-2	Strongly suspect asphyxia	Test for 120 minutes → persistent score < 4 → deliver regardless of gestational age

Note - When the patient in critical phase then we will try to delay the delivery to prevent complications.

Admission is required and close follow up with CBC daily is very important

The gestation and the phase of dengue are important factors in determining the management. A multi-disciplinary team consisting of obstetricians, physician, anesthetist and the paediatrician should get involved in the management.

- When a Suspected dengue (febrile patient) is first seen, look for warning signs and admit if anyone is found.
- If admitted to the obstetric ward urgent referral to the physician is essential.
- Explanation to the family members about the course of DHF and the management is important.

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

Complication:

- Premature fetal loss or vertical transmission in Dengue infection may be one of the grave fetal complications in pregnancy.
- The vertical transmission in fetus is evidenced by fever, thrombocytopenia, raised liver enzymes, gastric bleeding, pleural effusion, convalescent rash and Dengue-specific IgM (+).
- The important maternal complications include thrombocytopenia, raised liver enzymes, febrile illness, gum bleeding and bilateral pleural effusions.
- Moreover, uncomplicated pregnancy may be complicated with DHF.
- Delivery should be conducted in a tertiary hospital where all advanced facilities are available.

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

- Pulse, blood pressure (BP), pulse pressure. (Baseline BP is often lower and pulse pressure wider & heart rate may be higher)
- CBC - (Haemoglobin, HCT & platelet count may be lower than in nonpregnant patient)
- SGOT/SGPT
- Clinical detection of pleural effusion and ascites may be difficult due to the presence of gravid uterus. Use of Ultra Sound Scan to detect the following, is advisable
- Pleural effusion
- Ascites (Gallbladder wall oedema may be seen in both DF & DHF)

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

Management of pregnant patients with DF/DHF close to delivery

Risk of bleeding is at its highest during the period of plasma leakage (critical phase). Therefore, unless to save mothers life, avoid Lower uterine segment Caesarean Section (LUCS) or induction of labour during the Critical (plasma leakage) phase. Obstetric procedures (such as amniocentesis or external cephalic version) should be avoided during the illness. If obstetric procedures are to be undertaken,

- Maintain the platelet count above 50,000/mm3 Single donor platelet transfusion is preferred, if available.
- If patient goes into spontaneous labour during critical phase take steps to prevent vaginal tears by performing an episiotomy.
- In a case of fetal compromise priority should be given to the mother's life and decision making should involve the multidisciplinary team.
- Counseling the family on the probable outcome is essential.

Management of patients with DF/DHF during immediate postpartum

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

Dengue in the elderly

Clinical manifestations

- Little is known about dengue in the elderly.
- Clinical manifestations of dengue in the elderly are similar to those of younger adults.
- However, rash, hepatomegaly and mucocutaneous hemorrhage are less frequent but gastrointestinal tract bleeding and microhaematuria are more common.
- The elderly has significantly lower incidences of fever, abdominal pain, bone pain and rashes.
- Higher frequencies of concurrent bacteraemia, gastrointestinal bleeding, acute renal failure, and pleural effusion.
- Higher incidence of prolonged prothrombin time and lower mean haemoglobin levels than younger adult patients.
- A higher incidence of plasma leakage and case fatalities has been reported in the elderly compared to young adult dengue patients

Issues in management

- About 10% of elderly dengue patients may have no complaints of fever
- Higher rate of acute renal failure
- The impact of increased co-morbidities.
- Ageing-related decline in cardiopulmonary function is another important consideration during fluid replacement and/or resuscitation in dengue illness.
- Complications such as congestive heart failure and acute pulmonary oedema may occur.
- Frequent assessments and adjustments of the fluid regime are required to avoid or to minimize such complications.

Dengue in infancy

Symptoms:

fever, runny nose, cough, loose motion, vomiting, seizures, Signs: high fever, sore throat, dehydration, bulged fontanel, neck rigidity, hepatomegaly, splenomegaly.

Investigations:

Leukopenia unlikely, positive NS1 during febrile period, IgM positive during defervescence, hypoglycemia, hyponatremia, hypocalcemia, raised AST.

USG: hepato-splenomegaly, ascites

CXR: pleural effusion

Treatment

- Home care
- Caution on over hydration
- Insecticide-treated mosquito net for the infants who sleep by day Hospital care Fluid restriction (infants have shorter duration of plasma leakage)
- Frequently evaluated for oral fluid intake and urinary output (catheterization needed)
- Fluid therapy during the plasma leakage phase
- Half strength normal saline in 5% dextrose for < 6 months infants; normal saline in 5% dextrose in infants > 6 months
- Colloids (dextran 40) should be considered when high rates of crystalloids are required

Mandatory Surgery

- If surgery is mandatory in a patient with DHF, proper assessment of the patient, hematological and biochemical investigations should be available immediately prior to surgery.
- Fresh blood and or platelet concentrate also has to be made available prior to surgery.
- Platelet count should be raised up to 100000/mm3.
- Fluid replacement should be according to stage the of DHF. Other treatment is to be given as usual tailored to the need.

Chronic Liver Disease (CLD)

- The disease may be decompensated in DHF who was well compensated before Dengue episode.
- As DHF involves in hepatic enzyme elevation so critical patient care and regular LFT should be done.
- Decompensated CLD should be managed as non-infected patient.
- Platelet concentrate & fresh blood maybe required. Patient should be treated in a hospital where facilities are available.

Chronic Kidney Disease (CKD)

- Dengue patients with Chronic Kidney Disease (CKD) have a significantly higher risk of severe dengue and mortality. The outcome correlates with the renal function.
- The warning signs of severe dengue are similar to those of uraemia in CKD.
- Ascites and/or pleural effusion, and signs of plasma leakage in dengue, are not uncommon findings in patients with CKD and fluid retention.
- The ambiguity of these symptoms and signs could delay the recognition of plasma leakage and severe dengue.
- Patients with CKD have a low baseline haematocrit and platelet count
- A low baseline platelet count is not an uncommon finding in dialysis patients.

Challenges in fluid management:

- Narrow window of fluid tolerance: Patients with CKD have limited fluid tolerance. Frequent assessments of the haemodynamic state and frequent fluid regime adjustments are mandatory.
- Urine output: The urine output should not be used as an indicator of the intravascular volume status because patients with CKD can have either low or high urine-output renal failure. Low urine output in CKD contributes to the risk of fluid overload whereas high urine output may aggravate hypovolaemia.
- Limited effect of diuretics: Diuretics have a limited effect in CKD, making patients more susceptible to fluid overload. Dialysis may be required.
- Patient on MHD preferably dialysis session should be deferred.

Acid base balance and electrolyte balance

Patients with CKD are at risk of metabolic acidosis and electrolyte imbalance which will become worse during dengue shock. If these persist after adequate fluid replacement, dialysis may be considered after haemodynamic stability is achieved.

Platelet dysfunction

Platelet dysfunction, well recognized in CKD together with severe thrombocytopenia with or without coagulopathy, predispose the dengue patient to severe bleeding that may be difficult to control.

Chronic heart disease with or without heart failure:

- Congenital or acquired cardiac lesions such as valvular heart disease or ischaemic heart disease, especially the later, are common co-morbidities in adults or the elderly.
- In dengue with high fever, tachycardia and increased metabolic demands may precipitate decompensation of cardiac functions.
- Such patients have limited ability to compensate for hypovolaemia or hypervolaemia.
- Fluid therapy should be guided by frequent clinical assessments, haematocrit and blood gas determinations.
- Patients with cyanotic heart diseases have polycythemia and a high baseline haematocrit.
- Non-invasive positive pressure ventilation should be considered to support patients with cardiac decomposition. Failing this, mechanical ventilation should be instituted.
- Loop diuretics should be used cautiously and in a timely way: after achieving haemodynamic stability when intravenous fluid therapy has been discontinued or reduced and in patients with fluid overload.

Ischemic Heart Disease

- Aspirin/clopidogrel should be avoided for certain days, until the patient recovers from DHF.
- Patients with IHD are more prone to cardiac dysrhythmia, cardiac failure and thrombo-embolism.

Hypertension

Interpretation of BP:

- Hypotension is a late sign of shock. However, in patients with uncontrolled hypertension a BP reading that is considered normal for age may, in reality, be low for patients with uncontrolled hypertension.
- What is considered as "mild" hypotension may in fact be profound.
- Patients with chronic hypertension should be considered to be hypotensive when the mean arterial pressure (MAP) declines by 40 mmHg from the baseline, even if it still exceeds 60 mmHg. (For example, if the baseline MAP is 110 mmHg, a MAP reading of 65 mmHg should be considered as significant hypotension).
- Look for other manifestations of shock.

Management Issue:

- ß-blockers, a common antihypertensive medication, cause bradycardia and may block the tachycardic response in shock. The heart rate should not be used as an assessment of perfusion in patients on ß-blockers.
- Antihypertensive agents such as calcium channel blockers may cause tachycardia. Tachycardia in these patients may not indicate hypovolemia.
- Knowing the baseline heart rate before the dengue illness is helpful in the haemodynamic assessment.

The Impact on Hypotension:

- The continuation of antihypertensive agents during the acute dengue illness should be evaluated carefully during the plasma leaking phase.
- The BP lowering effects of these agents and diuretic therapy may exacerbate the hypotension and hypoperfusion of intravascular volume depletion.

Diabetes Mellitus and Dengue:

- Hyperglycaemia results in osmotic diuresis and worsens intravascular hypovolaemia.
- Not correcting the hyperglycaemic state exacerbates the shock state
- Hyperglycaemia also puts patients at risk of bacterial infection.

Diabetic ketoacidosis and hyperosmolar hyperglycaemia:

- Clinical manifestations of diabetic ketoacidosis and hyperosmolar hyperglycaemia (nausea, vomiting and abdominal pain) are similar to the warning signs of severe dengue.
- It is not uncommon for dengue shock to be misdiagnosed as diabetic ketoacidosis.

Hypoglycaemia:

- Hypoglycaemia may occur in those patients taking oral hypoglycaemic gents (e.g. long-acting sulphonylurea), but who had poor oral intake.
- Hypoglycaemia could be aggravated by severe hepatitis from dengue.
- Oral hypoglycaemic agents: Gastrointestinal absorption of oral hypoglycaemic agents is unreliable because of vomiting and diarrhoea during the dengue illness.
- Some hypoglycaemic agents such as metformin may aggravate lactic acidosis, particularly in dengue shock. These agents should be avoided or discontinued during dengue shock and also in those with severe hepatitis.

Management

- Dengue patients with known diabetes mellitus should be admitted for closer monitoring of the diabetic as well as dengue states.
- If the patient has gastrointestinal disturbances, blood glucose should be controlled with intravenous short-acting insulin during the dengue illness.
- A validated protocol for insulin dose adjustments to a target glucose level of < 150 mg/dl (8.3 mmol/L) should be used.
- A source of glucose may be maintained once the target is achieved while receiving intravenous insulin.
- Blood glucose should be monitored every 1–2hours until glucose values and insulin rates are stable and then every 4 hours thereafter.

Patient on Steroid Therapy for Other Condition

In this situation steroid should not be abruptly stopped. But if necessary, equivalent dosage may be given per IV route during the DS period.

Fluid Hypersensitivity and Anaphylaxis

High flow rate of fluid of room temperature may cause shivering, that needs fluid to be warmed up to near body temperature to avoid that which may create discomfort and terrorize the patient or attendant and jeopardize the management as well. In some instances, hypersensitivity or anaphylaxis may occur for which immediate standard treatment of hypersensitivity and anaphylaxis should be

instituted.

Dengue and Global Crisis

In any global clinical crisis (i.e. pandemic, epidemic) some diseases can represent symptoms like DF. 'Dengue' has been pandemic in many countries around the world. Dengue widely affected in countryside areas, urban poor regions, and suburbs areas.

During such situation patient's history is more important. Signs & symptoms and laboratory investigations should be done accordingly. Physicians should take necessary steps according to his/her clinical suspicion.

As example; Dengue fever and COVID-19 are difficult to distinguish because they share some same clinical and laboratory features. Some authors described cases who were wrongly diagnosed as dengue but later confirmed to be COVID-19. Besides, co-infections

with arboviruses and SARS-CoV-2 have not been well studied. There may scarcity of intensive care units to accommodate hospitalized patients with COVID-19, specific diagnostic tests, especially the RT-PCR, would also make it challenging to perform early detection of virus importation and prevent onward transmission. Another concern lies in the costs of hospitalization due to dengue fever. COVID-19 alone has a great potential to overwhelm the health system. If it is accompanied by dengue fever, this burden would have been even greater.

General Rules

In these special situations or other upcoming similar unforeseen conditions not experienced before the following general rule may be adopted:

- Assessment and management by risk versus gain approach
- Frequent consultations with peers of relevant specialties
- If necessary multidisciplinary team management
- Patient should be hospitalized under close monitoring
- Searching for references and evidence of similar conditions
- Keep document and arrange for dissemination, publication or communication

PEARLs

Some PEARLs may help for taking some spot decision, these are:

- Leukocyte count has a very important prognostic guide in early phase of dengue infection. Leucopenia < 5000 cells/mm3 indicates that within the next 24 hours the patient will have no fever and he will be entering the critical phase.
- What should not be done is as important as what should be done and what should be done should not be overdone.
- Hemorrhage during febrile phase signifies DF with unusual hemorrhage and possibly not DHF. But hemorrhage without fever should be critically assessed for DHF.
- Multiplying Hb level by 3 is usually found to be around the HcT level.
- Sudden pallor signifies internal bleeding.
- When HcT cannot be done or is not available the following clinical tips may help to speculate in DHF setting:
    - If the patient has/ had deep/massive bleeding from gut or other sites the possibility is that the patient may have lower HcT because of blood loss.
    - If the patient has/had surface/mild bleeding the possibility is that the patient may have higher HcT.
    - Sudden unexplained deterioration of hemodynamic status and or refractory to adequate fluid therapy the possibility is more of blood loss and hence low HcT level.
- In any complicated situation frequent consultations with other colleagues and multi-disciplinary team approach are useful.

Chapter 5

Dengue Prevention and Control

5. Dengue Prevention and Control

We know that, Dengue is an arthropod borne viral disease. Dengue viruses are transmitted to humans through the bites of infective female Aedes mosquitoes. Aedes aegypti is a confirmed vector and Aedes albopictus is a secondary vector of this disease in Bangladesh. Dengue is predominantly an urban disease occurring mostly in the rainy season. Mosquitoes generally acquire the virus while feeding on the blood of a dengue infective person. After an incubation period of 8 to 10 days, an infective mosquito is capable of transmitting the virus throughout its life time.

This mosquito is a small insect with black and white stripes on its legs and back. For the control, the distribution and seasonal density of the vector should be known for the area. Other important information includes the biology, bionomics and breeding habitats. Such information can be collected through vector surveillance.

Integrated vector management (IVM)

Following approaches are to be taken for IVM:

- Larval source reduction is the main tool for vector control. Effective control requires a concerted effort among the government agencies, NGOs and communities.
- Community understanding and involvement remains the key for implementation of preventive and control activities. The control measures should be implemented at personal, community and institutional levels.

Household level actions

- Wearing protective clothing such as full sleeved shirts and full pants during day time.
- Use of mosquito coils, aerosols, mats etc.
- Use of mosquito net (preferably insecticide-treated) even during day time.
- Use of repellents and creams during the day.
- Placing screens/wire mesh/net on windows.
- Water in containers (earthen jars, cement tanks, plastic drums etc.) should not be allowed to be stored for more than three days uncovered.

Community level actions

- Raising awareness regarding community involvement and participation about prevention and control of dengue.
- Involving community in source reduction for prevention and control of dengue.
- Cleaning and covering water storage, keeping surroundings clean, improving basic sanitation measures
- Promoting use of insecticide treated nets and curtains.

Institutional level action

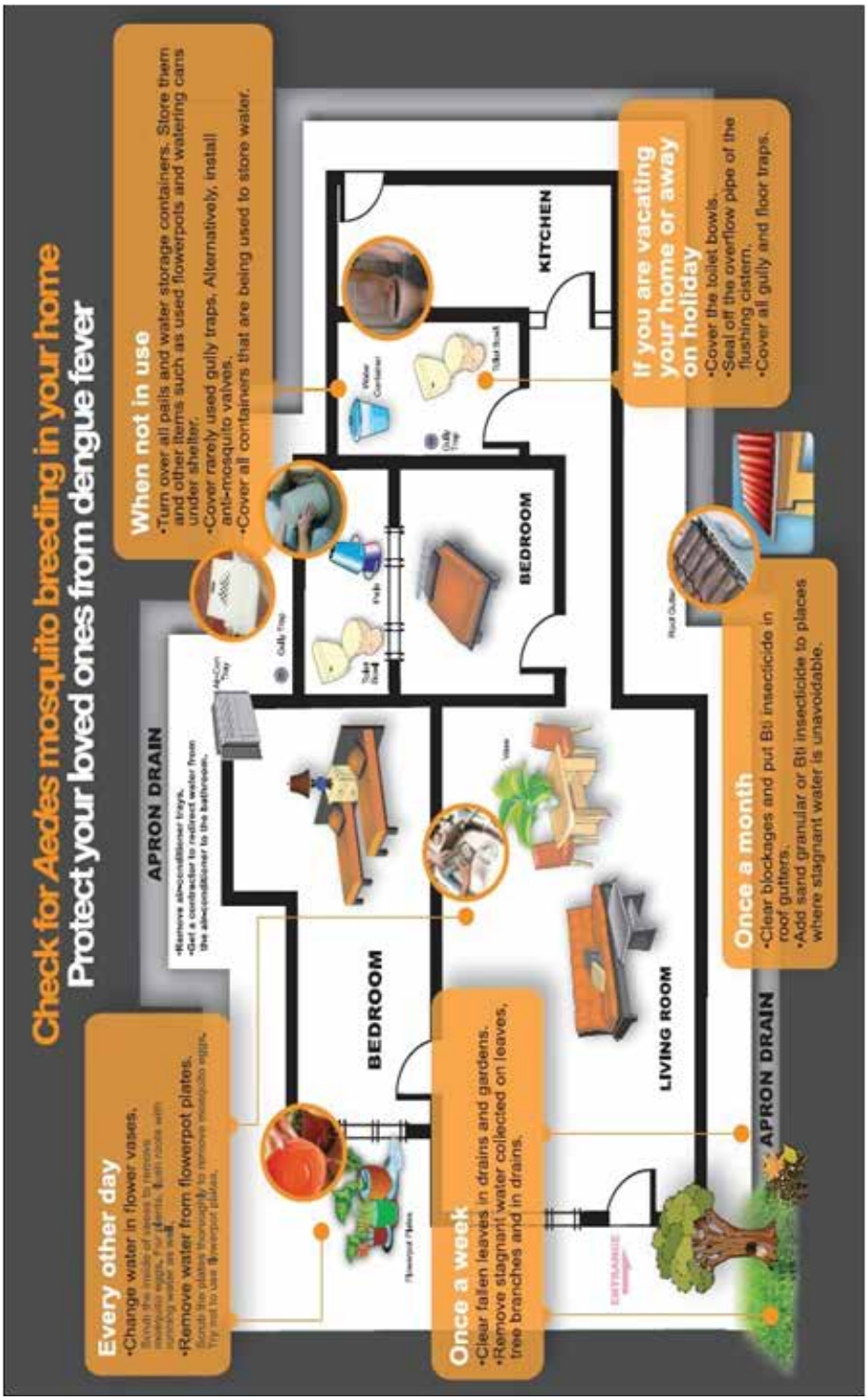
- Keeping Hospitalized patients under mosquito net during febrile phase even during day time
- Cleaning of larval habitats like overhead tanks, ground water storage tanks, air coolers, planters, flower vases etc. every five days
- Carrying out indoor and outdoor space spraying (fogging, ULV etc.)
- Promoting personal protection measures
- Reporting of fever cases to health authorities

Outbreak Response for Dengue/DHF

For Dengue/DHF prevention and control *Aedes aegypti* mosquito control through multisectoral involvement is the mainstay. Dengue epidemics and outbreaks occur in the monsoon and the control program should start preparedness and containment measures well ahead of the rainy season. The major activities for prevention and containment of outbreaks are:

- Rapid assessment of the existence of outbreak; magnitude of the problem and ensuring containment measures
- Community awareness through mass media campaign (including print and electronic media)
- Community drive for Aedes aegypti control (eliminating breeding sources; appropriate vector control measures; personal protection; and micro-environmental management)
- Strengthening of the public health infrastructure, intersectoral collaboration and community participation
- Establishing a responsive health care system for appropriate care of the patients in hospitals (including trained doctors, paramedics and nurses; and provision of logistic)
- National Dengue/DHF Control Program should have appropriate policy to undertake suitable and effective control activities during the inter-epidemic period
- Dengue outbreaks receive considerable adverse publicity and coverage in the media (both in the case of real epidemics or rumors) which impacts negatively on tourism and other sectors that inflicts heavy economic losses to the country affected by the disease. Measures should be taken to address this issue.

Care provider's role in educating the patients and attendants during clinical management has an important value for increasing awareness for Dengue/DHF control.


Check for Aedes mosquito breeding in your home
Protect your loved ones from dengue fever
Every other day
•Change water in flower vases.
•Remove water from flowerpot plates.
Once a week
•Clear fallen leaves in drains and gardens.
•Remove stagnant water collected on leaves, tree branches and in drains.
When not in use
•Turn over all pails and water storage containers. Store them and other items such as used flowerpots and watering cans under shelter.
•Cover rarely used gully traps. Alternatively, install anti-mosquito valves.
•Cover all containers that are being used to store water.
Once a month
•Clear blockages and put Bti insecticide in roof gutters.
•Add sand granular or Bti insecticide to places where stagnant water is unavoidable.
If you are vacating your home or away on holiday
•Cover the toilet bowls.
•Seal off the overflow pipe of the flushing cistern.
•Cover all gully and floor traps.
APRON DRAIN
BEDROOM
BEDROOM
KITCHEN
LIVING ROOM
APRON DRAIN
ENTRANCE

Annexure

ANNEXURE

ANNEX 1: LABORATORY INVESTIGATION FORM FOR DENGUE INFECTION

Hospital / Clinic / Practice:_____ Registration no:_____

Name of the patient:_____ Age: _____ Sex:_____

Date of admission/consultation:_____ Date of onset:_____

Suspected diagnosis:_____

Clinical findings:

1. Fever: _____ºC Duration:_____ Days
2. Petechiae _____ Epistaxis _____ Melena _____

   Other bleeding :_____
3. Tourniquet test:_____
4. Shock:_____

Specimen	**Date of Collection**	**Result of serology**
Critical Phase	_____	_____
Convalescent phase	_____	_____

LaboratoryDiagnosis:

Signature: _____

Date: _____

ANNEX 2: HANDOUT FOR PATIENT WITH DENGUE FEVER

(Important information to be given to the patients or family members of outpatients with suspected dengue fever ***It's better and appropriate to translate in local dialect these instructions for good understanding by the people in a given community or area.***)

Your child or family member probably has dengue fever. Since this disease can rapidly become very serious and may lead to medical emergency, it is important for you to carefully watch your child or relative for the next few days. The complications associated with dengue fever usually appear between the third and fifth days of illness. You should therefore watch the patient for two days after the fever disappears.

"WHAT SHOULD YOU DO?"

Keep body temperature below 39ºC. Give the patient paracetamol (not more than four times in 24 hours) as per the dose prescribed below:

Age up to 12 Years	**Per Dose (Syrup 1 TSF=120 mg)**	**Dose: 15 mg/kg/dose 6 hourly after food**
< 1 Year	1-1.5 TSF	
1 - 4 Years	1.5- 2 TSF	
≥ 5 Years	2-2.5 TSF	

"Don't give Aspirin or any analgesic and antipyretics other than paracetamol"

Give large amount of fluids (water, soups, milk and juices) along with patient's normal diet. The patient should rest. Immediately consult your physician if any of the following manifestations appear: Red spots or points on skin; bleeding from nose or gums; frequent vomiting; vomiting with blood; black stools; sleepiness; constant crying; abdominal pain; excessive thirst; pale, cold or clammy skin; or difficulty in breathing.

If you encounter such a situation

ANNEX 3: HANDOUT FOR PATIENT WITH DENGUE FEVER (BENGALI)

সংযুক্তি

(ডেঙ্গু জ্বর সন্দেহ হলে রোগীকে অথবা রোগীর পরিবারের সদস্যদেরকে কিছু প্রয়োজনীয় তথ্য প্রদান করতে হবে)

ডেঙ্গু রোগীর জন্য প্রয়োজনীয় তথ্যঃ

আপনার রোগী খুব সম্ভবত ডেঙ্গু জ্বরে আক্রান্ত্ম। আপনার রোগীকে সতর্কতার সাথে লড়্যা রাখা প্রয়োজন কারণ পরবর্তী কয়েকদিনের মধ্যে ডেঙ্গু রোগ দ্রুন্নত জটিল আকার ধারন করতে পারে। এই রোগের জটিলতা সাধারনত তিন থেকে পাঁচ দিনের মধ্যে দেখা দেয়। কাজেই আপনার রোগীকে জ্বর সেরে যাওয়ার পর পরবর্তী দুই দিন খুব ভালভাবে লড়্যা রাখতে হবে।

ডেঙ্গু জ্বর হলে অথ্যাবশ্যকীয় কর্তব্যঃ

১। শরীরের তাপমাত্রা অবশ্যই ৩৯° সেন্টিগ্রেড বা ১০২° ফাররেনহাইট এর নীচে রাখতে হবে। এ জন্য শুধুমাত্র ট্যাবলেট/সিরাপ প্যারাসিটামল খাওয়াতে হবে (দিনে ৪ বারের বেশী নয়)

প্যারাসিটামল খাওয়ার হিসাব নিম্নে দেওয়া হলো ঃ

১২ বৎসরের নীচে শিশু	প্রতি ডোজ/মাত্রা/সিরাপ (১চামচ-১২০ মিঃ)	পূর্ণ বয়স্কদের জন্য
১ বৎসরে	১-১½ চা চামচ	মাত্রাঃ ১৫ মিঃ গ্রাম/কেজি/মাত্রা ৬ ঘন্টা পর পর খাওয়ার পর
১-৪ বৎসরে	১-½ ২ চা চামচ	
৫ বৎসরে	২-২½ চা চামচ	

২। কোন অবস্থাতেই প্যারাসিটামল ব্যতিত এসপিরিন বা ব্যাথানাশক এবং জ্বরনাশক বড়ি বা সিরাপ খাওয়া যাবে না।

৩। রোগীকে স্বাভাবিক খাবারের সাথে প্রচুর পরিমাণে তরল খাবার (পানি, সুপ, দুধ বা ফলের রস ইত্যাদি) খাওয়াতে হবে।

৪। রোগীকে পূর্ণ বিশ্রামে রাখতে হবে।

৫। নিম্নোক্ত কোন সমস্যা দেখা দিলে অতিদ্রন্নত চিকিৎসকের কাছে যেতে হবে ঃ
চামড়ায় লাল দানা, নাক বা দাঁতের মাড়ি দিয়ে রক্তপড়া, বারে বারে বমি, রক্ত বমি, কালো পায়খানা, ঘুম ঘুম ভাব, অনবরত কান্না, পেটে ব্যাথা, অত্যাধিক পানি পিপাসা, ফ্যাকাসে ভাব ও ঠান্ডা ত্বক বা শ্বাস কষ্ট।

৬। যদি এই সব সমস্য দেখা যায় তবে সাথে সাথে নিকটস্থ চিকিৎসক এর পরামর্শ নিন। তা না হলে রোগীর মারাত্তক জটিলতা দেখা দিতে পারে।

ANNEX 4

Normal Blood Pressure by Age (mm Hg)			
Age	Systolic Pressure	Diastolic Pressure	Systolic Hypotension
Birth (12, <1000g)	39-59	16-36	<40-50
Birth (12 h, 3 kg)	60-76	31-45	<50
Neonate (96 h)	67-84	35-53	<60
Infant (1-12 mon)	72-104	37-56	<70
Toddler (1-2 y)	86-106	42-63	<70+ (age in year x 2)
Preschool (3-5 y)	89-112	46-72	<70+ (age in year x 2)
School-Age (6-11 y)	97-115	57-76	<70+ (age in year x 2)
Preadolescent (10-11 y)	102-120	61-80	<90
Adolescent (12-15 y)	110-131	64-83	<90

Table - 3: Normal Blood Pressure in Children

Recommended Size of BP cuffs are also different in children:

Using a wrong sized Blood Pressure Cuff can affect accuracy up to 30 mmHg.

Adults (by arm circumference)

22 to 26 cm 12 × 22 cm (small adult)

27 to 34 cm 16 × 30 cm (adult)

35 to 44 cm 16 × 36 cm (large adult)

45 to 52 cm 16 × 42 cm (adult thigh)

Children (by age)

Newborns and premature infants 4 × 8 cm

Infants 6 × 12 cm

Older children 9 × 18 cm

Pulse Pressure

- It is the difference between systolic and diastolic blood pressure
- A pulse pressure is considered abnormally low if it is less than 25% of the systolic value or less than 20 mmHg

ANNEX 5: CALCULATION OF IDEAL BODY WEIGHT

Calculation of Ideal Body Weight

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

Weight for height using a growth chart (50th centile) -

<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

Annex 6: Indication & preparing patient or family members for possible requirement

Indications for whole blood

1. Hemoglobin level ≤ 5 gm %
2. Significant bleeding > 10% of total blood volume (TBV). TBV of body is 80 ml/kg.
3. Concealed bleeding manifested by HcT drop and unstable vital signs in spite of adequate volume replacement.

Dose of whole fresh blood: 10 ml/kg/dose at a time.

Indication for platelet concentrate

It has been observed that there is very limited role of platelet transfusion. In most of the situation fresh whole blood transfusion is sufficient. However, it may be required in some special situation. The indication of which may be as follows:

1. Very severe Thrombocytopania who need urgent surgery
2. Clinical judgement of the treating physician

If platelet concentrate is not available fresh whole blood may be transfused as per guidelines given under DHF management.

Preparing patient or Family members for Blood Transfusion

- **Alert:** Tell the patient or family member that a possible transfusion may require when you find that platelet count is < 100,000 /mm^3 or there are bleedings.
- **Attention:** Tell the patient or family members to contact blood donors to remain in attention that at any moment onward blood may be required at short notice when you find that platelet count is < 10000 /mm^3 or there are progressive unstable vital signs.
- **Collection:** Tell the patient or family members to collect blood, which may in all possibility, will be required at any moment when you found that platelet count is ≤ 5,000 /mm^3 or there is dropping of HcT and unstable vital signs despite adequate volume replacement.

ANNEX 7: DF/DHF HOSPITAL FLOW SHEETS

DF/DHF HOSPITAL FLOW SHEETS

Hospital: _____ Ward:_____ Bed:_____

Unit: _____ Date of Admission:|___|___|___|___|___|___|

Name:_____ Age:_____ Sex: □ Male □ Female

BASE LINE PARAMETER

Body Weight: _____ Hct:_____ Hb:____ Platelet:_____ WBC:_____	Maintenance Fluid: ---------- M = _____ M+5%D=_____	Date Fever: __|__|__ Day of illness:_____ T Test:_____ Bleeding:_____	Diagnosis: □ Patient Group A □ Patient Group B □ Patient Group C

VITAL SIGNS MONITORING FLOW SHEET

Date	Time	Pulse	BP	Temp	Res	Hct	Treatment	Symptoms	Remarks

Pulse: F = Full / M = Moderate / R = Rapid / N = Not palpable

I V Infusion / Transfusion Log

Date	Type of Fluid	Start Time	Rate Q/Min	End Time	Total	Note

Fluid Balance Chart

Date	Time	Intake			Output				Balance
		Oral	SC/ IM/IV	Total 24 Hours	Urine	Vomit/ Suction	Invisible	Total 24 Hours	

Doctor:_____ Nurse: _____

ANNEX 8 DENGUE REPORTING FORM FOR PRACTITIONER

DENGUE REPORTING FORM FOR PRACTITIONER

(Photocopy & Use)

From:

Dr _____

_____

_____

_____

To

Civil Surgeon

_____

_____

POSTAGE

Staple after folding

Staple after folding

◄ ►

PATIENT

Name:|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_| Age:|_|_| Sex:□ Male □ Female

[Put √ in appropriate box]

Guardian: |_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|

Address : |_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|

|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|

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|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|

DIAGNOSIS

□ Patient Group A

□ Patient Group B

□ Patient Group C

OUTCOME

□ Recovered □ Referred □ Death □ Not known [Put √ in appropriate box]

Second fold here up

Date of first Attendance / Admission: |_|_|_|_|_|_|

[dd/mm/yy]

Date of outcome: |_|_|_|_|_|_| [If known]

[dd/mm/yy]

Signature: _____

Full name: |_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|

Position: |_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|

Date: |_|_|_|_|_|_|

[dd/mm/yy]

ANNEX 9: DENGUE REPORTING FORM FOR HOSPITAL /CLINIC

DENGUE REPORTING FORM FOR HOSPITAL/CLINIC

(Photocopy & Use)

From:
Dr _____
_____
_____
_____

To

Civil
Surgeon_____
_____

_____

POSTAGE

Staple after

First fold here down *Second fold at next arrow marks up*

Report serial no:|_|_|_| Date: |_|_|_|_|_|_| [dd/mm/yy]

Name of Hospital/Clinic:_____

Address:_____

Date of Report:|__|__|__|__|__|__| [dd/mm/yy]

Date of Report Beginning: |__|__|__|__|__|__| [dd/mm/yy]

Patient Category	Cases in last 24 hours		Deaths in last 24 hours	Cumulative from beginning of reporting		At present admitted	Total Outcome		
	OPD	IPD		Total Cases	Total Deaths		Recovered & Discharged	Deaths	DORB / Referred/ Not known
Group A									
Group B									
Group C									
Grand Total									

Signature _____

Full name: |_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|

Position: |_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|

Date: |_|_|_|_|_| [dd/mm/yy]

ANNEX 10: BLOOD PRESSURE TABLES FOR BOYS AND GIRLS BY AGE AND HEIGHT PERCENTILE

TABLE 3. BP Levels for Boys by Age and Height Percentile

Age, y	BP Percentile	SBP, mm Hg							DBP, mm Hg						
		Percentile of Height							Percentile of Height						
		5th	10th	25th	50th	75th	90th	95th	5th	10th	25th	50th	75th	90th	95th
1	50th	80	81	83	85	87	88	89	34	35	36	37	38	39	39
	90th	94	95	97	99	100	102	103	49	50	51	52	53	53	54
	95th	98	99	101	103	104	106	106	54	54	55	56	57	58	58
	99th	105	106	108	110	112	113	114	61	62	63	64	65	66	66
2	50th	84	85	87	88	90	92	92	39	40	41	42	43	44	44
	90th	97	99	100	102	104	105	106	54	55	56	57	58	58	59
	95th	101	102	104	106	108	109	110	59	59	60	61	62	63	63
	99th	109	110	111	113	115	117	117	66	67	68	69	70	71	71
3	50th	86	87	89	91	93	94	95	44	44	45	46	47	48	48
	90th	100	101	103	105	107	108	109	59	59	60	61	62	63	63
	95th	104	105	107	109	110	112	113	63	63	64	65	66	67	67
	99th	111	112	114	116	118	119	120	71	71	72	73	74	75	75
4	50th	88	89	91	93	95	96	97	47	48	49	50	51	51	52
	90th	102	103	105	107	109	110	111	62	63	64	65	66	66	67
	95th	106	107	109	111	112	114	115	66	67	68	69	70	71	71
	99th	113	114	116	118	120	121	122	74	75	76	77	78	78	79
5	50th	90	91	93	95	96	98	98	50	51	52	53	54	55	55
	90th	104	105	106	108	110	111	112	65	66	67	68	69	69	70
	95th	108	109	110	112	114	115	116	69	70	71	72	73	74	74
	99th	115	116	118	120	121	123	123	77	78	79	80	81	81	82
6	50th	91	92	94	96	98	99	100	53	53	54	55	56	57	57
	90th	105	106	108	110	111	113	113	68	68	69	70	71	72	72
	95th	109	110	112	114	115	117	117	72	72	73	74	75	76	76
	99th	116	117	119	121	123	124	125	80	80	81	82	83	84	84
7	50th	92	94	95	97	99	100	101	55	55	56	57	58	59	59
	90th	106	107	109	111	113	114	115	70	70	71	72	73	74	74
	95th	110	111	113	115	117	118	119	74	74	75	76	77	78	78
	99th	117	118	120	122	124	125	126	82	82	83	84	85	86	86
8	50th	94	95	97	99	100	102	102	56	57	58	59	60	60	61
	90th	107	109	110	112	114	115	116	71	72	72	73	74	75	76
	95th	111	112	114	116	118	119	120	75	76	77	78	79	79	80
	99th	119	120	122	123	125	127	127	83	84	85	86	87	87	88
9	50th	95	96	98	100	102	103	104	57	58	59	60	61	61	62
	90th	109	110	112	114	115	117	118	72	73	74	75	76	76	77
	95th	113	114	116	118	119	121	121	76	77	78	79	80	81	81
	99th	120	121	123	125	127	128	129	84	85	86	87	88	88	89
10	50th	97	98	100	102	103	105	106	58	59	60	61	61	62	63
	90th	111	112	114	115	117	119	119	73	73	74	75	76	77	78
	95th	115	116	117	119	121	122	123	77	78	79	80	81	81	82
	99th	122	123	125	127	128	130	130	85	86	86	88	88	89	90
11	50th	99	100	102	104	105	107	107	59	59	60	61	62	63	63
	90th	113	114	115	117	119	120	121	74	74	75	76	77	78	78
	95th	117	118	119	121	123	124	125	78	78	79	80	81	82	82
	99th	124	125	127	129	130	132	132	86	86	87	88	89	90	90
12	50th	101	102	104	106	108	109	110	59	60	61	62	63	63	64
	90th	115	116	118	120	121	123	123	74	75	75	76	77	78	79
	95th	119	120	122	123	125	127	127	78	79	80	81	82	82	83
	99th	126	127	129	131	133	134	135	86	87	88	89	90	90	91
13	50th	104	105	106	108	110	111	112	60	60	61	62	63	64	64
	90th	117	118	120	122	124	125	126	75	75	76	77	78	79	79
	95th	121	122	124	126	128	129	130	79	79	80	81	82	83	83
	99th	128	130	131	133	135	136	137	87	87	88	89	90	91	91
14	50th	106	107	109	111	113	114	115	60	61	62	63	64	65	65
	90th	120	121	123	125	126	128	128	75	76	77	78	79	79	80
	95th	124	125	127	128	130	132	132	80	80	81	82	83	84	84
	99th	131	132	134	136	138	139	140	87	88	89	90	91	92	92
15	50th	109	110	112	113	115	117	117	61	62	63	64	65	66	66
	90th	122	124	125	127	129	130	131	76	77	78	79	80	80	81
	95th	126	127	129	131	133	134	135	81	81	82	83	84	85	85
	99th	134	135	136	138	140	142	142	88	89	90	91	92	93	93
16	50th	111	112	114	116	118	119	120	63	63	64	65	66	67	67
	90th	125	126	128	130	131	133	134	78	78	79	80	81	82	82
	95th	129	130	132	134	135	137	137	82	83	83	84	85	86	87
	99th	136	137	139	141	143	144	145	90	90	91	92	93	94	94
17	50th	114	115	116	118	120	121	122	65	66	66	67	68	69	70
	90th	127	128	130	132	134	135	136	80	80	81	82	83	84	84
	95th	131	132	134	136	138	139	140	84	85	86	87	87	88	89
	99th	139	140	141	143	145	146	147	92	93	93	94	95	96	97

The 90th percentile is 1.28 SD, the 95th percentile is 1.645 SD, and the 99th percentile is 2.326 SD over the mean.
For research purposes, the SDs in Table B1 allow one to compute BP Z scores and percentiles for boys with height percentiles given in Table 3 (ie, the 5th, 10th, 25th, 50th, 75th, 90th, and 95th percentiles). These height percentiles must be converted to height Z scores given by: 5% = −1.645; 10% = −1.28; 25% = −0.68; 50% = 0; 75% = 0.68; 90% = 1.28; and 95% = 1.645, and then computed according to the methodology in steps 2 through 4 described in Appendix B. For children with height percentiles other than these, follow steps 1 through 4 as described in Appendix B.

TABLE 4. BP Levels for Girls by Age and Height Percentile

Age, y	BP Percentile	SBP, mm Hg							DBP, mm Hg						
		Percentile of Height							Percentile of Height						
		5th	10th	25th	50th	75th	90th	95th	5th	10th	25th	50th	75th	90th	95th
1	50th	83	84	85	86	88	89	90	38	39	39	40	41	41	42
	90th	97	97	98	100	101	102	103	52	53	53	54	55	55	56
	95th	100	101	102	104	105	106	107	56	57	57	58	59	59	60
	99th	108	108	109	111	112	113	114	64	64	65	65	66	67	67
2	50th	85	85	87	88	89	91	91	43	44	44	45	46	46	47
	90th	98	99	100	101	103	104	105	57	58	58	59	60	61	61
	95th	102	103	104	105	107	108	109	61	62	62	63	64	65	65
	99th	109	110	111	112	114	115	116	69	69	70	70	71	72	72
3	50th	86	87	88	89	91	92	93	47	48	48	49	50	50	51
	90th	100	100	102	103	104	106	106	61	62	62	63	64	64	65
	95th	104	104	105	107	108	109	110	65	66	66	67	68	68	69
	99th	111	111	113	114	115	116	117	73	73	74	74	75	76	76
4	50th	88	88	90	91	92	94	94	50	50	51	52	52	53	54
	90th	101	102	103	104	106	107	108	64	64	65	66	67	67	68
	95th	105	106	107	108	110	111	112	68	68	69	70	71	71	72
	99th	112	113	114	115	117	118	119	76	76	76	77	78	79	79
5	50th	89	90	91	93	94	95	96	52	53	53	54	55	55	56
	90th	103	103	105	106	107	109	109	66	67	67	68	69	69	70
	95th	107	107	108	110	111	112	113	70	71	71	72	73	73	74
	99th	114	114	116	117	118	120	120	78	78	79	79	80	81	81
6	50th	91	92	93	94	96	97	98	54	54	55	56	56	57	58
	90th	104	105	106	108	109	110	111	68	68	69	70	70	71	72
	95th	108	109	110	111	113	114	115	72	72	73	74	74	75	76
	99th	115	116	117	119	120	121	122	80	80	80	81	82	83	83
7	50th	93	93	95	96	97	99	99	55	56	56	57	58	58	59
	90th	106	107	108	109	111	112	113	69	70	70	71	72	72	73
	95th	110	111	112	113	115	116	116	73	74	74	75	76	76	77
	99th	117	118	119	120	122	123	124	81	81	82	82	83	84	84
8	50th	95	95	96	98	99	100	101	57	57	57	58	59	60	60
	90th	108	109	110	111	113	114	114	71	71	71	72	73	74	74
	95th	112	112	114	115	116	118	118	75	75	75	76	77	78	78
	99th	119	120	121	122	123	125	125	82	82	83	83	84	85	86
9	50th	96	97	98	100	101	102	103	58	58	58	59	60	61	61
	90th	110	110	112	113	114	116	116	72	72	72	73	74	75	75
	95th	114	114	115	117	118	119	120	76	76	76	77	78	79	79
	99th	121	121	123	124	125	127	127	83	83	84	84	85	86	87
10	50th	98	99	100	102	103	104	105	59	59	59	60	61	62	62
	90th	112	112	114	115	116	118	118	73	73	73	74	75	76	76
	95th	116	116	117	119	120	121	122	77	77	77	78	79	80	80
	99th	123	123	125	126	127	129	129	84	84	85	86	86	87	88
11	50th	100	101	102	103	105	106	107	60	60	60	61	62	63	63
	90th	114	114	116	117	118	119	120	74	74	74	75	76	77	77
	95th	118	118	119	121	122	123	124	78	78	78	79	80	81	81
	99th	125	125	126	128	129	130	131	85	85	86	87	87	88	89
12	50th	102	103	104	105	107	108	109	61	61	61	62	63	64	64
	90th	116	116	117	119	120	121	122	75	75	75	76	77	78	78
	95th	119	120	121	123	124	125	126	79	79	79	80	81	82	82
	99th	127	127	128	130	131	132	133	86	86	87	88	88	89	90
13	50th	104	105	106	107	109	110	110	62	62	62	63	64	65	65
	90th	117	118	119	121	122	123	124	76	76	76	77	78	79	79
	95th	121	122	123	124	126	127	128	80	80	80	81	82	83	83
	99th	128	129	130	132	133	134	135	87	87	88	89	89	90	91
14	50th	106	106	107	109	110	111	112	63	63	63	64	65	66	66
	90th	119	120	121	122	124	125	125	77	77	77	78	79	80	80
	95th	123	123	125	126	127	129	129	81	81	81	82	83	84	84
	99th	130	131	132	133	135	136	136	88	88	89	90	90	91	92
15	50th	107	108	109	110	111	113	113	64	64	64	65	66	67	67
	90th	120	121	122	123	125	126	127	78	78	78	79	80	81	81
	95th	124	125	126	127	129	130	131	82	82	82	83	84	85	85
	99th	131	132	133	134	136	137	138	89	89	90	91	91	92	93
16	50th	108	108	110	111	112	114	114	64	64	65	66	66	67	68
	90th	121	122	123	124	126	127	128	78	78	79	80	81	81	82
	95th	125	126	127	128	130	131	132	82	82	83	84	85	85	86
	99th	132	133	134	135	137	138	139	90	90	90	91	92	93	93
17	50th	108	109	110	111	113	114	115	64	65	65	66	67	67	68
	90th	122	122	123	125	126	127	128	78	79	79	80	81	81	82
	95th	125	126	127	129	130	131	132	82	83	83	84	85	85	86
	99th	133	133	134	136	137	138	139	90	90	91	91	92	93	93

* The 90th percentile is 1.28 SD, the 95th percentile is 1.645 SD, and the 99th percentile is 2.326 SD over the mean.
For research purposes, the SDs in Table B1 allow one to compute BP Z scores and percentiles for girls with height percentiles given in Table 4 (ie, the 5th, 10th, 25th, 50th, 75th, 90th, and 95th percentiles). These height percentiles must be converted to height Z scores given by: 5% = −1.645; 10% = −1.28; 25% = −0.68; 50% = 0; 75% = 0.68; 90% = 1.28; and 95% = 1.645 and then computed according to the methodology in steps 2 through 4 described in Appendix B. For children with height percentiles other than these, follow steps 1 through 4 as described in Appendix B.

Annex 11: Further Reading & Reference

Further Reading & Reference

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