Guideline for the Management of Dengue Fever in Children

Dr. Ahmed Faisal

Consultant in Paediatrics

Ministry of Health
Male' Republic of Maldicves
2022

Author: Dr. Ahmed Faisal, Consultant in Pediatrics

Indhira Gandhi Memorial Hospital

Dr. Ahmed Saeed, Consultant in Pediatrics IGMH

Dr. Sanjaya Shreshtha, Senior Consultant in Pediatrics ADK Hospital

Dr. Amit Bishwakarma, Consultant in Pediatrics Tree Top Hospital

Dr. Mohamed Abdel Wahab Areed, Consultant in Pediatrics IGMH

Published by: Quality Assurance and Regulations Division

Document number: MOH-QA/G/22/117-0

Ministry of Health

Male' Republic of maldives

Contents

1. INTRODUCTION

Dengue fever is very common in Maldives. The largest epidemics noted in Maldives was in 2011 followed by 2015 and 2016. There were 8 deaths in 2015 and 4 deaths in 2016. A neonate with congenital dengue expired in 2017. W.H.O approves the first dengue vaccine, Dengvaxia (CYD-TDV) from Sanofi Pasteur for individuals 9-45 years. The efficacy of this vaccine depends on serostatus. A 3-dose series with a schedule of 0-6-12 month is approved. There is no antiviral drug for against dengue.

1.1 Dengue virus

Dengue viruses are single stranded Ribonucleic Acid (RNA) viruses from Flavivirus group. There are 4 major types of dengue viruses with sub types. These are designated as DENV-1, DENV2, DENV-3 and DENV-4. After infection with each serotype it produces lifelong immunity to the specific serotype and short term immunity to other serotypes. Therefore, a person may acquire dengue infection 4 times in his/her life time.

Dengue infection increases after rainy season. Removal of breeding sites remain the most effective way to prevent dengue infection.

1.2 Dengue vector

Female Aedes aegypti and Aedes albopictus are the most important vectors of dengue. Both are found in Maldives. It is a very domestic insect. They usually bite at sunrise and early evening. Human blood is used for development of its reproductive process. Aedes aegypti takes blood from multiple humans in one feed. Vector movements are limited to 100m. These mosquitoes rest in damp dark areas such as under tables, sink, shoes and dark clothes.

Mosquitoes lay eggs in clean water. The eggs can survive up to 1 year in dry condition. Once the condition become appropriate, they can hatch in 7 days. Female Aedes aegypti mosquitoes suck

blood from lots of people to complete one single meal. Feeding habits increase the incidence of infection rapidly. Mosquitoes fly up to 200m. People with viremia carry the virus to distant places.

2. NATURAL HISTORY AND GRADING OF SEVERITY OF DENGUE ILLNESS

Dengue viral infection may be asymptomatic, with danger signs or severe in grading. After the incubation period, the disease has 3 clinical phases. Febrile phase, critical phase, and recovery phase.

2.1 Natural history of illness

It is critically important to understand natural history of dengue fever. Appropriate management of dengue fever requires identifying the phase of illness and managing fluids accordingly. Patients become sick in critical phase. Delay or failure to detect patients entering this phase leads to complications and mortality. Most patients are stable in critical phase and recover if fluids are managed well.

Dengue is a dynamic disease. It has 3 phases;

1. Febrile phase
2. Critical phase
3. Recovery phase

Febrile phase

Febrile phase usually lasts 2-7 days. Fever may be biphasic. There might be associated myalgia, retro orbital pain, headache, arthralgia, maculopapular rash, erythema and sometimes unusual bleeding manifestations such as epistaxis. There may be pharyngitis and neurological impairment and febrile seizures. A positive Tourniquet test increases the possibility of dengue. White blood cell count falls prior to decrease in platelet count. Early significant drop in platelet has been associated with severe disease.

Critical phase

Critical phase is the most important period that needs to be identified. Failure to detect and treat this phase may lead the patient to severe dengue causing death. Critical phase begins when the fever starts decreasing or when patient becomes afebrile. It lasts for 24- 48 hours. During this period plasma leakage occurs resulting in periorbital edema, pleural effusion, ascites and shock. These effusions are difficult to detect clinically until shock appears. It may need Xray or USG studies.

An increase or rising trend of hematocrit more than 20%, pleural effusion and ascites indicates significant plasma leakage. Right lateral decubitus Chest X- ray film is more sensitive in detecting mild pleural effusion than supine films.

In Dengue Shock Syndrome, it is very peculiar to find Narrow **pulse pressure** in early stage of shock while patient looks well and alert. Here the systolic pressure remains normal while diastolic pressure increases. Pulse pressure of less than 20mmHg is an early sign of compensated shock and requires immediate management with adequate fluids. Frequent monitoring of the patient is critical in this period. It should include pulse rate, blood pressure, capillary refill time and urine output (Refer Chart 3). In infants' signs of shock are not readily apparent. Re-shock is not uncommon during the 24-48 Hrs of critical period. Patients who have been given bolus for initial shock should be carefully monitored.

The cause of shock can be either severe plasma leakage or bleeding. If patient bleeds hematocrit falls. A decrease of HCT by more than 20% signifies severe bleeding. It is important to remember that patients bleeds when shock is prolonged. Patient also might have severe organ involvement such as hepatitis, renal impairment, myocarditis and encephalitis.

Recovery phase

Recovery face lasts for 2-3 days after the critical phase. During the recovery phase edema starts resolving and fluid returns to intravascular space. Patient's general wellbeing and appetite improves. There could be severe itching specially on palms and soles. Diuresis sets in, hematocrit falls to baseline and platelet start increasing.

If the patient were given excess intravenous fluids, they can develop marked pleural effusion and ascites that may result in respiratory distress and cardiac failure. Cardiac failure is common in patients with existing cardiomyopathy such as Thalassemia with iron overload.

2.2 Grading the severity of Dengue fever

Severity of dengue fever can be divided into

1. Dengue fever without danger signs
2. Dengue fever with danger signs
3. Severe dengue
4.

Dengue fever without danger signs

Initial symptoms of dengue fever resemble undifferentiated viral fever. Symptoms include high grade fever, severe headache, retro-orbital pain, myalgia, arthralgia, nausea, vomiting and rash.

Fever is usually between 39^{o}Cto 40^{o}C and may be biphasic and last for 3-7 days. Diffuse erythema and fleeting eruptions may be observed in the initial days of fever. In convalescent period normal skin surrounded by erythema (white islands in a red sea) may be observed. Skin itching specially over soles and feet is found when in recovery.

Clinical course of dengue fever varies between individuals. But the febrile phase lasts for an average of 5 days. Fever persisting more than 6 days should be investigated for other causes. Bradycardia may be found during convalescence.

In dengue endemic areas like Maldives, positive tourniquet test has a higher positive predictive value for dengue infection. **Tourniquet** test is done by maintaining an inflated blood pressure cuff between systolic and diastolic pressure for 5 minutes. The test is considered positive if 10 or more petechial rash is present per inch square around the skin where cuff was applied. This test may be negative in obese patients and in profound shock.

Dengue fever with danger signs

Danger signs in dengue fever include persistent vomiting, abdominal pain and tenderness, unable to take orally, bleeding from any site (gum, epistaxis, melena or hematemesis), severe lethargy, unable to walk, restlessness, ascites, pleural effusion, narrow pulse pressure, hypotension and tender hepatomegaly. There is also increasing hematocrit and rapidly falling platelet count. Skin hemorrhages may be present as petechia or after tourniquet test. Mild epistaxis and mild hematemesis should be observed closely.

As the patient becomes afebrile, there might be some plasma leakage. Circulatory disturbances might be observed in the first 24-48 hours from the time of fever lysis. It may be associated with sweating and circulatory disturbances. These should be differentiated from Severe Dengue.

Severe Dengue

Severe Dengue present with either or all of the following;

1. Severe plasma leakage
2. Severe bleeding
3. Severe organ involvement

Severe plasma leakage

Severe plasma leakage results in circulatory disturbances and shock. Hematocrit may increase more than 20%. There may also be a progressive increase in hematocrit from baseline. In the early phase it will be compensated shock and if failed to treat, results in decompensated shock. In compensated shock tachycardia with or without narrow pulse pressure of less than 20 mmHg is present (Pulse pressure is difference between systolic and diastolic pressure). In decompensated shock, systolic pressure drops more than 20 percent of normal systolic pressure or less than 90mmHg and mean of less than 60 mmHg in adults and bigger children.

Shock can manifest as severe acute abdominal pain, irritability, restlessness and unable to sleep specially in children. Patients in dengue shock can be conscious and some even walk into hospital in shock. Significant fluid accumulation in the extravascular space leads to pleural effusion and ascites. The patient may have disorientation, sweating, tachypnea, cyanosis, cold peripheries, low pulse volume, increased capillary refill time, hypotension and narrow pulse pressure.

Severe bleeding

Bleeding is considered severe if there is associated shock or fall in HCT more than 20%. Bleeding may be either internal or external such as hematemesis, severe epistaxis, hypermenorrhea and malena. Internal bleeding should be ruled out when hematocrit falls with signs of shock. Hematocrit may be normal at the early stages of bleeding.

Bleeding is usually manifested when shock is prolonged. It can also occur spontaneously when nonsteroidal anti-inflammatory drugs and steroids are used.

Severe organ involvement

Severe organ involvement could be marked rise in liver enzymes (ALT and AST more than 1000), impaired consciousness, seizures, disorientation, renal and other major organ involvements.

2.3 Differential diagnosis of dengue fever

Differential diagnosis of dengue fever includes measles, rubella, scrub typhus, chikungunya, influenza, adenovirus infection, SARS, typhoid, hepatitis and leptospirosis. Malaria is not found in Maldives but can be positive if a person come from a malaria endemic country.

In Maldives Chikungunya is common in adults and could be mistaken for dengue fever. Typhoid, Scrub typhus and Meningococcemia also can have high grade fever with rash. Vaccine preventable disease such as measles and rubella are less likely to be found. Maldives is certified as measles free in 2017 by W.H.O. All the cases of fever with rash need to be notified (refer form

1 of Annex) immediately to HPA. Serum and throat sample should be collected and transported to IGMH laboratory for measles and rubella.

2.4 High risk patients

The following groups are at higher risk for severe dengue.

1. Infants and elderly
2. Pregnancy
3. Expatriate workers
4. G6PD deficiency
5. Obesity
6. Beta thalassemia major
7. Patients on NSAIDS and steroids
8. Congenital heart disease
9. Chronic diseases like hypertension and diabetes mellitus

3. DIAGNOSING DENGUE FEVER

3.1 Diagnosis

Clinically dengue fever presents as a high-grade fever lasting 2-7 days with or without myalgia, headache, retro orbital pain, diffuse erythematous macular rash, leukopenia or thrombocytopenia. If undifferentiated fever persists for more than 3 days, a full blood count should be done to rule out dengue fever. A positive Tourniquet test is suggestive of dengue fever and is especially useful when laboratory services may not available in some islands. Platelet counts has a decreasing trend and, in most patients, falls for 2 days after been afebrile. However, a normal or high total leucocyte count or platelet count in the initial days of fever does not rule out dengue fever. Workup must include total white blood cell count, thrombocyte count and hematocrit. Persistent fever must be further evaluated with repeated investigations.

In Maldives other common infective causes of high-grade fever include scrub typhus and typhoid fever. Since dengue fever is very common, dengue serology is not mandatory to diagnose it. In fact, it can result in confusion since false negative results are common in the initial days of illness. However, in case of atypical presentations with suspicion of other conditions antigen and serology tests plays an important role.

3.2 Laboratory findings

Total leucocyte and platelet count are usually normal in the first day of fever. Leucopenia is the first to appear followed by thrombocytopenia. Platelet shows a daily drop and tends to fall further in afebrile phase. There could be a rise in hematocrit if dehydration is present. If there is marked plasma leakage, it increases more than 20% and if there is significant bleeding, it falls more than 20% of baseline. Liver enzymes (ALT, AST) may be elevated. In severe dengue it can be more than 1000 IU/L.

A lateral decubitus Chest X-ray is more sensitive in detecting pleural effusion. Usually, it is present only in right side of chest. USG abdomen may show edema of gall bladder with ascites. Albumin may be low and a decrease of more than 0.5mg/dl from baseline shows plasma leakage. Occult blood is sometimes found in stool. Reduction in vitamin K dependent factors (II, VII, IX and X) are seen. Partial thromboplastin time and prothrombin time are also increased in many cases. Hypocalcemia and hyponatremia are observed in some cases. Metabolic acidosis and impaired renal function set in severe dengue. Erythrocyte sedimentation rate is usually normal in dengue fever and is less than 10mm in the 1st Hour in severe dengue.

When evaluating results of NS1, IgM and IgG antibodies, we need to consider the day of illness and whether it is primary or secondary infection. In primary infection, NS1 may be positive in the first 72 hours of febrile phase but may be removed in a shorter time in secondary infection. In primary infection Dengue IgM antibodies is usually positive by for 4 to 6 days and lasts for 10 weeks, but in secondary infection, 20% patients may not produce IgM antibodies. IgG appears 2

weeks after primary infection and lasts for life, but in secondary infection IgG level rises markedly after 1-2 days.

Cross reactivity for both IgM and IgG occurs in other flavivirus infections. We should not rely solely on antigen and antibody tests to diagnose and manage dengue fever.

4. MANAGEMENT OF DENGUE FEVER

Even though dengue is a multi-systemic and complex disease correct and timely management saves lives. It is critically important to identify phase and severity of illness and treat accordingly.

4.1 Advice to patients regarding management at home

When patient is suspected of having dengue fever and there are no danger signs, they can be sent home with written advice (refer page 25).

1. Patient should take adequate rest.
2. The only recommended medication for fever is Paracetamol. Do not use nonsteroidal anti-inflammatory drugs and steroids. Maximum dose of Paracetamol is 4g/day in adults and 10-15mg/kg/dose with a maximum 5 doses in 24 hours in children. Paracetamol and other medications **should NOT be given intramuscular (IM)**.
3. Fluids should be taken adequately. Oral rehydration solution (ORS) is the best fluid for rehydration. Other advisable fluids include coconut water, milk and fruit juices which are better than plain water. In case of vomiting, it is better to avoid red and dark fluids that may mimic blood in vomitus. ORS should be diluted according to the direction in cover without additional solutes.
4. Tepid sponging may be done if fever recurs within 4 hours of Paracetamol dose.
5. Come back to hospital as soon as possible if you find any of the danger signs mentioned below
    1. General condition worsens specially when the patient becomes afebrile
    2. Persistent vomiting
    3. Severe abdominal pain

4. Unable to take orally
5. Bleeding from any site such as nose, blood in vomitus or stool (red or black stool), intermittent bleeding between periods and menorrhagia.
6. Severe lethargy or unable to walk
7. Restlessness or disorientation, unusual behavior such as inappropriate language
8. Cold clammy hands and feet
9. No urine output for more than 6 hours

6. Even if there is no danger signs as mentioned above, if fever persists more than 3 days, patient is required to review with doctor. Fever more than 3 days requires blood investigations.
7. Patients who are on antithrombotic agents such as Aspirin, Clopidogrel, and Dipyridamole etc. should be discussed with physician regarding withholding the drugs in thrombocytopenia.

4.2 Principle of fluid therapy in dengue fever with danger signs

1. Fluids should be isotonic crystalloid solutions except infants below 6 months where 0.45% dextrose saline (1/2DNS) may be used.
2. Hypertonic solutions such as Dextran 40 can be used if a third fluid bolus is required. That is when the initial 2 crystalloid boluses are not effective.
3. Blood transfusion can be done with whole blood, or packed red cells with a volume of 10ml/kg
4. Initial rate of intravenous fluid infusion is half of the maintenance for patients with no dehydration but poor oral intake. In children initial intravenous fluid can be started at 1.5ml/kg/Hr. Normally hydrated adults should not receive more than 2500ml of total fluids including intravenous and oral fluids per day. Fluids should be as minimum as possible to keep an effective circulation and over hydration should be avoided.

5. Duration of intravenous fluid therapy after patient become afebrile should not exceed more than 48 hours for patients with shock and not more than 72 hours for patients without shock.
6. Ideal body weight is used in obese patients.
7. Rate of intravenous fluid differs for children and adults
8. Routine platelet transfusion is not recommended.

4.3 Management of dengue patients with danger signs

All patients with warning signs need close monitoring in hospital. The critical period starts as the patient becomes afebrile and lasts for 24-48 hours.

Timely detection of critical phase and judicial management of fluids to prevent shock and fluid overload is the key in management of dengue patients.

The following parameters should be monitored in the ward. Use chart 3 in Annex for vitals monitoring.

1. General condition and other symptoms such as vomiting, bleeding and melena.
2. Capillary refill time and peripheries for coldness.
3. Vitals that including pulse rate, respiratory rate, blood pressure should be checked every 4-6 hours, and if abnormal it should be checked every 1-2 hours.
4. Initial investigations should include total white cell count, platelet count, hematocrit, ALT, AST, calcium, and albumin. Hematocrit should be measured at least 12 hourly in stable patients and more frequently in unstable patients. It should be repeated when signs of bleeding are present, before and after every fluid bolus. Platelets are done once daily. In severe dengue coagulation studies, glucose, calcium and blood gas should be done.
5. Input and output measurements are mandatory. It should be assessed every 8-12 hours in stable patients and hourly in shock patients.

6. If patient shows sign of bleeding or platelet count is below 50000, whole blood or packed cell should be made available.

Drugs

Indications for intravenous fluids

1. When the patient is unable to drink adequate amount of fluids either due to vomiting or refusal
2. Impending shock or shock
3. When hematocrit rises more than 10%- 20% despite oral fluids

4.4 Management of severe dengue

In leakage phase, intravenous fluids might be required to increase from 1.5 to 7ml/kg/Hr. In patients who are receiving fluids more than maintenance, fluids should be reduced as soon as possible.

4.5 Management of shock in severe dengue

Shock is caused by severe plasma leakage, bleeding or both. If HCT is increased, it indicates plasma leakage and low HCT indicates bleeding. Plasma leakage cause increase in peripheral resistance. It results in narrowing of pulse pressure. In compensated shock systolic pressure remains normal. In most of the cases of bleeding, it is usually concealed in the gut.

Maintenance of blood pressure is vital for survival of severe dengue patients. If intravenous access fails oral route is used in conscious patients. Intra osseous route should be tried if venous access fails for more than 5 minutes.

Unlike many other types of shock, most patients in dengue shock respond to initial 10ml/kg of normal saline. Even mild hypotension should be treated immediately when there are other signs of shock such as tachycardia and poor perfusion.

In **compensated shock** 5-10 ml/kg of normal saline should be given over one hour (refer Algorithm 1 and 2). If the clinical condition (vitals, capillary refill time, peripheries and urine output) improves, fluid should be reduced by 2ml/kg/Hour every 2 hours (7, 5, 3 to 1.5 ml/kg/Hour). Any change in fluid should be done after clinical assessment.

In **decompensated (hypotensive) shock** give Normal saline 10-20ml/kg as a bolus over 15 minutes. If the blood pressure is not restored give another 10ml/kg normal saline bolus over 30 minutes.

HCT should be done before and after each bolus. If a third bolus is required, 40% Dextran (10ml/kg) should be given over an hour. Dextran should not be repeated more than 3 times in 24 hours due to its adverse effects on kidneys. Inotropes can be tried in fluid refractory shock. If the clinical condition (vitals, capillary refill time, and peripheries) and urine output improves, fluid should be reduced by 2ml/kg/Hr every 2 hours (7, 5, 3 to 1.5 ml/kg/Hour). After each fluid bolus patient should be assessed for fluid overload such as eye puffiness and pleural effusion and tachypnea. Fluid rates should be cut down as soon as possible after clinical reassessment.

A patient not responding to fluid bolus should be evaluated for bleeding. If hematocrit falls with blood pressure, blood transfusion is indicated. Packed red blood cells or fresh whole blood at 10ml/kg should be transfused. In thalassaemia major patients it is better to give blood after initial fluid bolus.

Strict input and output chart in mandatory. Fluids given to the patient in the previous 12-24 hour should be calculated and clearly mentioned in referral documents. If the fluids were given more than maintenance, this amount should be subtracted from the fluids to be given in the next 24-36 hours.

In shock, hematocrit should be monitored 15 minutes after each fluid bolus. Until the clinical conditions are stable HCT should be repeated every 30-60 minutes. Blood gas, AST, ALT, BUN, creatinine, calcium and blood sugar should be monitored.

Calcium should be supplemented in hypocalcemia and shock. The dose is 0.5-1 ml/kg diluted with same volume of normal saline given as slow bolus preferably with cardiac monitoring. Maximum dose is 10 ml of calcium gluconate. It can be repeated every 6 hours.

Intravenous vitamin K1 should be given in case of profound shock with bleeding or impaired prothrombin time. It can be given to patients with such clinical conditions without doing coagulation studies even if laboratory facilities are not available.

4.6 Management of hemorrhage in severe dengue

Blood transfusion is lifesaving in severe hemorrhage. Bleeding site should be identified and bleeding should be quantified. Epistaxis can be stopped by applying ice packs and nasal packing. Whole blood of 10 ml/kg or packed red blood cells 5-10ml/kg can be given and response re-evaluated. Blood transfusion may need to be repeated.

There is no evidence to show any advantage of transfusing platelet or fresh frozen plasma to stop bleeding. They also cause fluid overload. However, these components are frequently used when bleeding continues with refractory shock in spite of initial management. Anti-acids such as H-2 receptor antagonists and proton pump inhibitors may be given.

4.7 Management of organ involvement

1. ***Encephalopathy***
    a. Patient may develop coma or seizures. This is mostly due to encephalopathy rather than encephalitis. Encephalopathy may be due to intracranial hemorrhage or liver impairment. CT scan of brain is done to rule out intracranial hemorrhage. Main objective of treatment is to normalize intracranial pressure.
    b. Airway and breathing should be carefully managed
    c. Minimal IV fluids. Ideally IV fluid should be less than 80% of maintenance.
    d. Avoid using multiple boluses of crystalloids. Use colloids earlier to prevent fluid overload.
    e. Diuretics are used to facilitate diuresis

f. Elevate head end up to 30 degrees.
g. Early intubation to prevent hypercarbia.
h. Consider Dexamethasone 0.15mg/kg/dose 6-8 hourly to reduce ICP.
i. If ammonia is increased, give lactulose 5-10ml every 6 hours to induce osmotic diarrhea
j. Intraluminal antibiotic (Neomycin) to get rid of ammonia producing gut flora. It is not necessary if systemic antibiotics are used.
k. Maintain blood sugar level at 80-100mg/dl.
l. Correct the impaired acid base balance, sodium, calcium and potassium.
m. Administer vitamin K (3 mg for infants, 5 mg for 1-5years and 10mg above 5 years).
n. Anticonvulsants for seizures. Diazepam, phenobarbitone and phenytoin can be used.
o. Transfuse fresh whole blood or packed red cells.
p. Antibiotics if suspicious of secondary infection.
q. H2 blockers or proton pump inhibitors to prevent GI bleeding.
r. Consider plasmapheresis or hemodialysis.

5. MANAGEMENT OF COMPLICATIONS

5.1 Fluid over load

All the patients on intravenous fluids should be observed for early signs of fluid overload. These include puffy eyelids, ascites and dyspnea. Later patient develops respiratory distress, crepitations, wheezing hypoxia and restlessness.

In fluid overload patients with shock, colloids (Dextran 40) are preferred over crystalloid as fluid bolus. Once blood pressure is maintained intravenous frusemide 0.5-1mg/kg can be given. Vitals signs should be observed every 15 minutes after frusemide for an hour. Strict input/output chart should be maintained. If urine output is not improved, exclude post renal causes. Bladder catheterization should be done cautiously as it can cause bleeding. If renal failure occurs renal

replacement therapy must be started. Pleural with or without abdominal tapping may be required. These procedures are usually complicated and should be explained to parents.

5.2 Management of high-risk patients

In **obese** patients' fluid should be calculated for the ideal body weight. Once stabilized intravenous frusemide can be given.

Infants develop fluid retention and liver impairment more rapidly. They should be evaluated frequently for these complications.

Diabetic patients may worsen their glucose control. Diabetic ketoacidosis (DKA) and hyperosmolar hyperglycemia can occur. Insulin is frequently required to control sugar even in type-II DM. Sugar free crystalloids (normal saline) should be used in these patients. Hyperglycemia causes osmotic diuresis and results in dehydration. Hyperglycemia also predisposes to bacterial infection. Symptoms of DKA such as nausea, vomiting and abdominal pain are similar to early signs of dengue shock. It is not uncommon to miss the diagnosis of either early shock or DKA. Hypoglycemia may occur in those with oral hypoglycemic drugs (OHD) such as sulphonylurea with poor intake and those with sever dengue results in hypoglycemia. OHDs may not be well absorbed in diarrhea and vomiting. Metformin may cause lacticacidosis. It should be avoided in dengue shock. Insulin can be used instead to control sugar.

Thalassemia major patients and other hemolytic disease patients on regular blood transfusions may need early blood transfusion. Due to their chronic anemia, HCT may not rise even in severe leakage. Interpretation of HCT should take care of anemia and other clinical features. Reticulocytosis may be absent since bone marrow suppression may be present in dengue fever. Heart failure should be taken care of in case of secondary hemosiderosis. Intravascular and extravascular hemolysis will present with pallor and jaundice. Hemoglobinuria (dark urine) represents massive hemolysis. Hemoglobinuria cause acute renal failure. Appropriate hydration is mandatory. Diuretics are not advised in shock.

Congenital and ischemic heart disease with or without heart failure; These patients may have less reserve of heart function and may be worsen by increased fluids. Fluids must be given cautiously. For patients on steroid therapy, it may have to be stopped or changed to intravenous formulation. Cyanotic heart disease patients usually have high HCT.

Chronic Kidney disease patients have significant high risk for mortality. Uremia and dengue warning signs are similar. They have a low baseline HCT, platelet and urine output. They also have metabolic acidosis. Fluid tolerance levels are very low. Diuretics may not work in these patients. Frequent assessment for fluid status in mandatory.

5.3 Management of convalescence

Improvement of general wellbeing and appetite usually occurs after 24-48 hours when the patient is afebrile. If the patient is stable, intravenous fluid should not be given more than 48hours after patient become afebrile. Diuretics are used if pulmonary edema persists. Severe itching is found especially in palms and soles. Antihistamines and calamine lotion can be used. An ECG should be taken to look for heart blocks if bradycardia persists. Hypokalemia is corrected with supplements. Potassium rich fruits should be advised.

5.4 Criteria for discharge

- ✓ Afebrile for at least 24 hours without antipyretics
- ✓ Clinical improvement in general condition including return of appetite
- ✓ Good urine output
- ✓ No respiratory distress and significant ascites
- ✓ At least 2-3 days after recovery from shock
- ✓ Platelet count of more than 50,000cells/m3

5.5 Common misconceptions in management of dengue fever

1. **Doing Dengue serology in all cases of suspected dengue fever;** Diagnosis of dengue fever can be made without serology tests. If a patient comes with signs and symptoms of dengue fever and leukopenia with or without thrombocytopenia can be treated as

dengue fever. Serology is often false negative depending on the clinical phase where sample was drawn for investigation.

2. **Directly correlating Thrombocyte count for severity of illness;** Significant bleeding in dengue fever (usually in gut) is only found after prolonged shock. Platelet count do not directly correlate with risk for bleeding. Platelet transfusions have not shown to be effective in management of dengue fever. Fresh whole blood or packed cells are used if there is significant bleeding. Platelet count should not be used as the only indication for referral to high centres. Platelet count should not be repeated more than once daily in stable patients and twice a day in critical patients

3. **Hematocrit is not given importance;** Hematocrit is very important in management of dengue fever especially during the critical phase. It will differentiate between bleeding or plasma leakage. This is critical to decide whether to transfuse or use fluid boluses. It can also show if there is any improvement after initial fluid resuscitation.
4. **Trying to correct hematocrit when there is no clinical sign;** investigations should always be correlated with clinical condition. If results does not match with clinical assessment the lab investigations should be repeated.
5. **Failure to detect early signs of severity;** Critical phase of dengue fever starts when fever starts decreasing. This should be looked for if the patient's general condition does not improve despite been afebrile. These symptoms include any danger sign mentioned above such as irritability, unable to sleep, weakness, unable to walk. Often the pulse pressure narrows (less than 20mmHg), where systolic pressure may remain normal with raised diastolic pressure. Early bleeding can come as petechial.
6. **Using NSAIDS for fever;** NSAIDS cause bleeding in dengue fever. It results in deaths. The only antipyretic that must be used is paracetamol. Dose of paracetamol should not exceed the maximum daily dose. NSAIDs are commonly shared among expatriate workers without consulting medical personnel. This need to be brought to attention of those who hire them.

7. **Using too much fluid when patient does not require it;** it is critical to give right amount of fluid at right time. If a patient was started with a higher fluid rate than maintenance, patient should be monitored every 1-2 hours to watch for fluid overload.

5.6 Referral to Tertiary hospital for management of severe dengue

Health facilities in Maldives are divided into 4 tiers. Tertiary government referral centre is Indira Gandhi Memorial Hospital (IGMH). It is located in Male which is the capital city of Maldives. In IGMH on call pediatricians and physicians are available 24 hours. Any doubts and queries regarding management of dengue patients can be asked from them at any time. Patient can be referred to higher center after discussion with receiving end. Patients can be transferred by air or sea. Patients can also be referred to ADK Hospital. As it is a private hospital, additional cost may be applied to patient.

Government Health Insurance covers for transport from peripheries to IGMH. In difficult situations transport can be arranged through sea ambulance of MNDF or by helicopter as well.

The patient should receive adequate initial resuscitation, stabilization and continuous care before and during transport in order to make sure that patient arrives in a stable condition. Safe and timely transport needs good communication between referral and receiving centres.

Special consideration should be given to maintain intravenous lines patent and secured. Patient should be monitored clinically as well as with pulse-oximeter. An experienced nurse or a doctor should accompany any sick dengue patient during transport.

It is very important to make sure that during transport intravenous fluid are running, oxygen is enough, and monitors are charged enough to continue throughout the travel. All documentations including X-rays should be sent. The notes must include input and output chart where type and rate of fluids given to patient and urine output are noted.

Severe dengue patients should be referred to tertiary hospital. Dengue fever and dengue fever with warning signs can be managed at peripheral centers. Every effort should be done to manage

these mild cases of dengue at peripheral health centers and hospitals to avoid unnecessary referrals.

When severe dengue patients are transferred to higher centers the following should be followed.

1. Discussion with referral hospital to inform doctors and nurses who will be receiving the patient.
2. Discuss with family members and explain the risk and probable outcomes.
3. Stabilize the patient before transfer.
4. Detailed referral letter. This should include current conditions, monitoring parameters (vital signs, input output chart, HCT, laboratory findings).
5. At least a nurse should accompany the patient.
6. Intravenous fluid must be continued at correct rate.
7. Review of the patient by specialist at receiving end.

5.7 Preparedness in managing dengue

Each health center must have medical personnel trained in dengue management using this protocol.

Following medicines should be available in each centre.

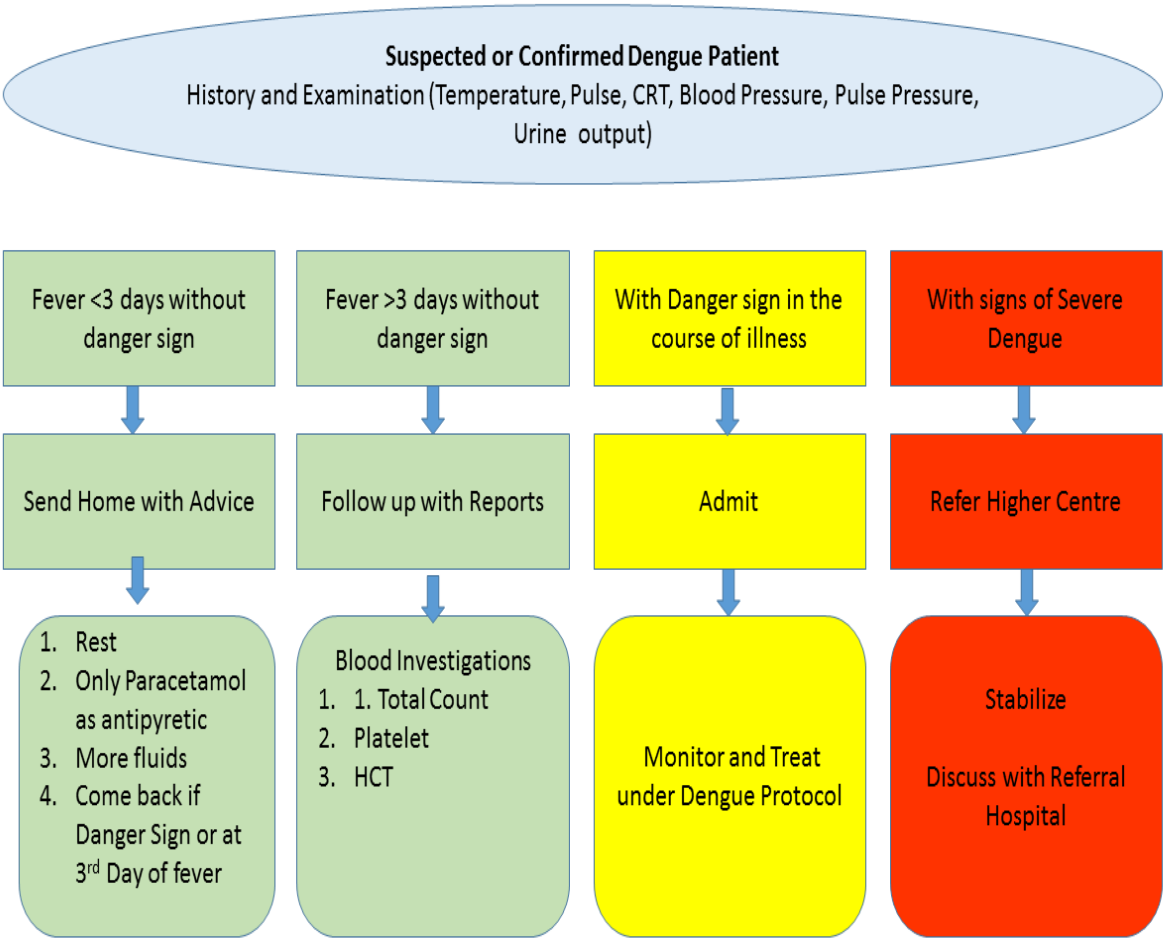
1. Paracetamol
2. ORS
3. IV fluids
4. Crystalloid: DNS (0.9%Normal Saline with 5% Dextrose water, Normal saline)
5. Colloids: Dextran 40
6. Vitamin K1

Indications for Referral to tertiary centre

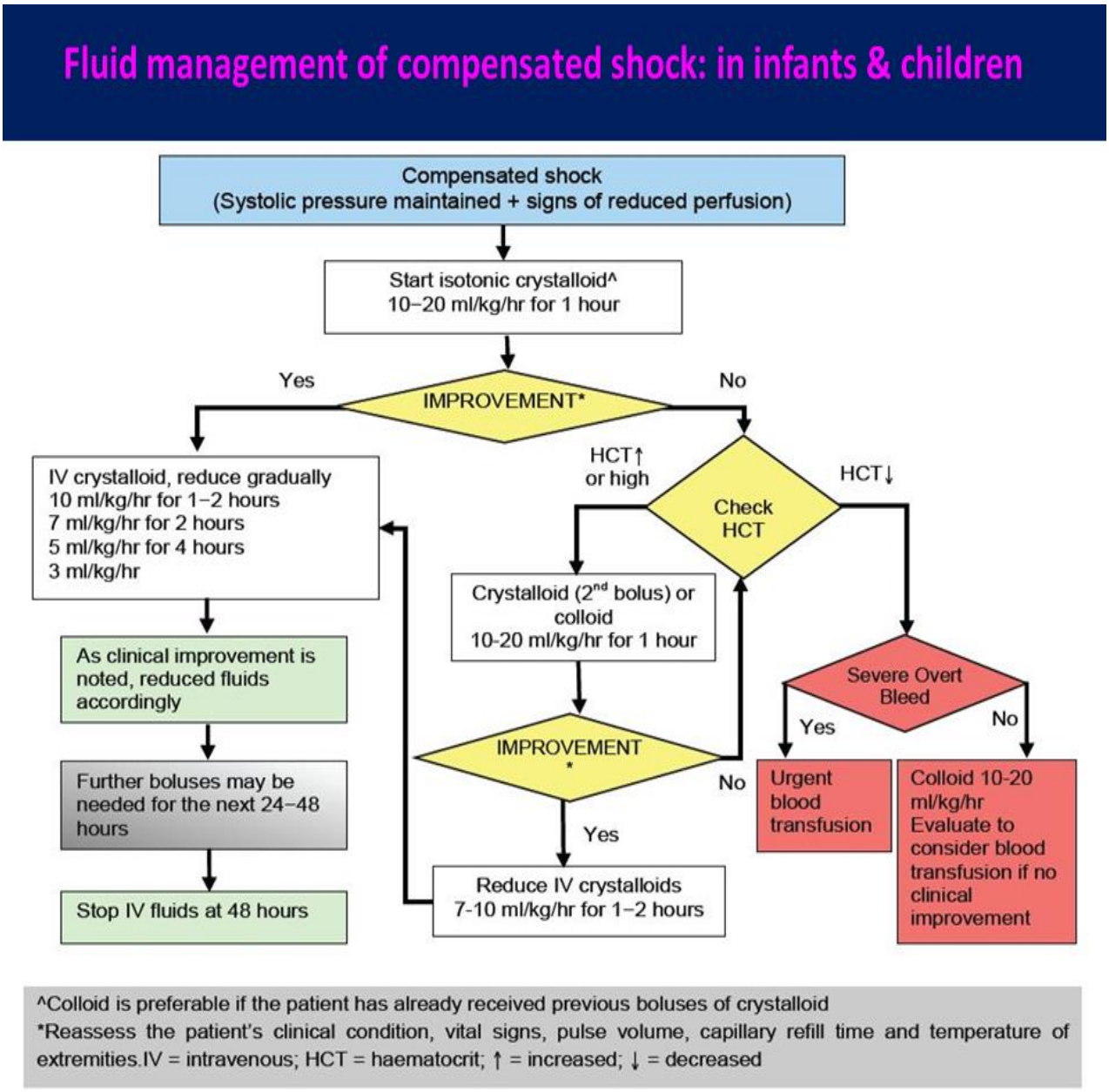
1. SEVERE DENGUE
2. PATIENTS WITH RISK FACTORS THAT NEED SPEICAL CARE

7. Calcium gluconate
8. Potassium chloride
9. Sodium bicarbonate
10. Accessories for the following:
    a. IV access
    b. Oxygen supplementation
    c. Vitals monitoring: BP cuff, pulse-oximeter
11. Lab facilities to monitor HCT, CBC, platelet, sugar, AST, ALT, Urea, Creatinine

Flow chart to manage patients with suspected or confirmed Dengue Fever



Algorithm 1: Fluid management of compensated shock: in infants and children (WHO Guideline)



^Colloid is preferable if the patient has already received previous boluses of crystalloid
*Reassess the patient's clinical condition, vital signs, pulse volume, capillary refill time and temperature of extremities.IV = intravenous; HCT = haematocrit; ↑ = increased; ↓ = decreased

Algorithm 3: fluid management in decompensated shock in all ages (WHO guideline)

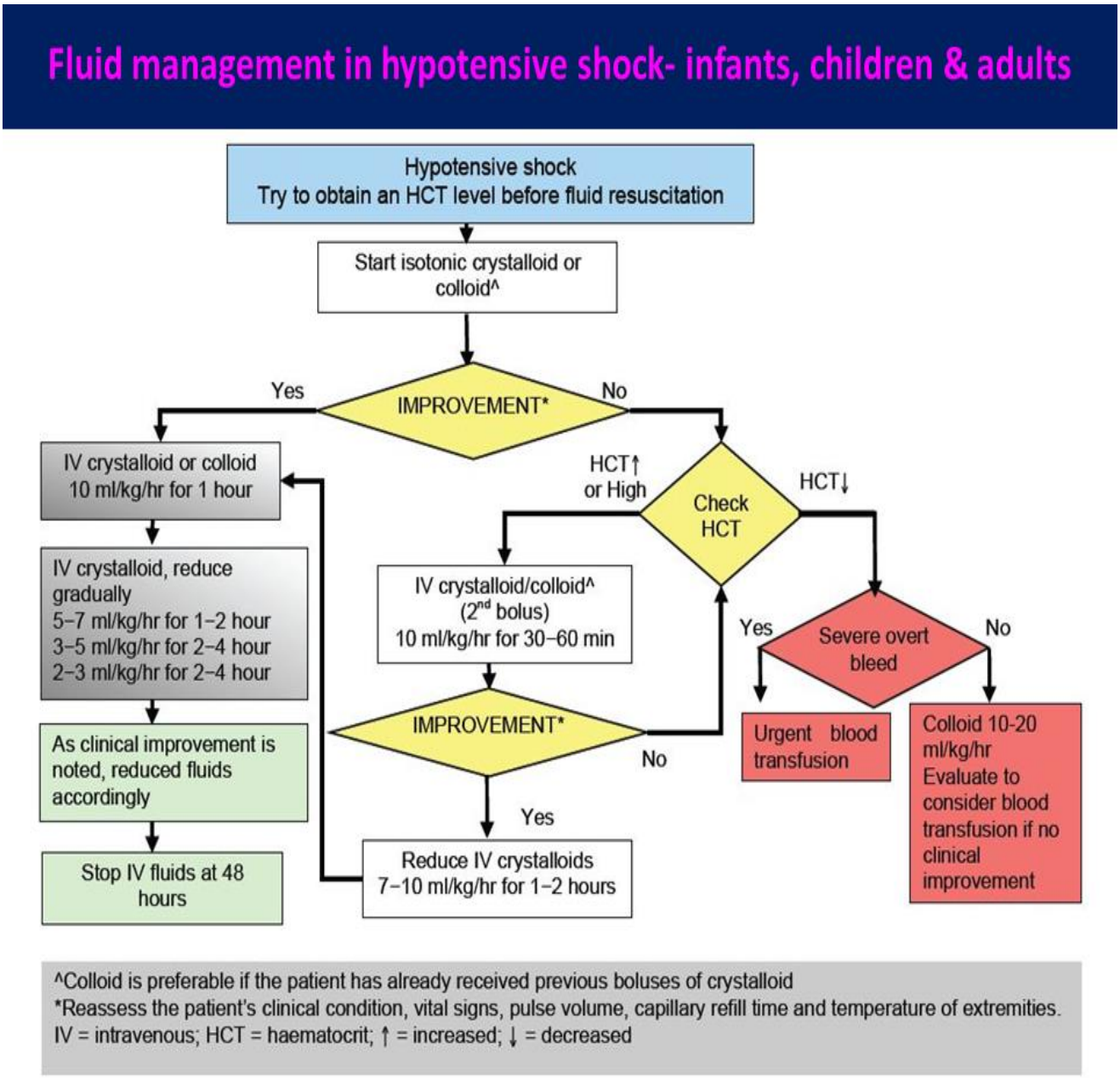


Chart 1; Intake / Output chart for dengue patients

Name		**Age**		**Hospital No**		**Ward**		**Bed**
Time	**Intake**			**Output**				
	Type of IV fluids	Amount (ml)	Oral intake (ml)	Urine	Stool	Emesis	Others	Comment
7 am-1pm								
1pm-6pm								
6pm-12am								
12am-7am								
Total 24 Hrs	IV		Oral					
	Total Intake			Total Output				

Chart 2; Input / Output chart to be used by patient or parent

ތަކުރާރު ކުރަން ޖެހޭނެ ތާރީޚާއި ގަޑި				
ތިމާގައިވޭ ވަގުތު	ދޫކުރި ބޭނުންވާ ދިން (ލީޓަރ)	ކައުންޓް	ލިޔެވުނު ދިން (ލީޓަރ)	ތިމާގައިވާ ވަގުތު

Chart 3; Vitals monitoring chart for dengue patients

Monitoring chart for Dengue patients									
Name		Age		Hospital No		Ward		Bed	
Date	Time	Pulse	RR	BP	Pulse Pressure	CRT (sec)	Peripheries Cold/warm	Symptom	Treatment

Pulse Pressure is Systolic – Diastolic Blood Pressure,

Urgent intervention is required if Pulse Pressure is less than 20mmHg, CRT more than 3 second, Tachycardia and Tachypnea

Trends of change is more important than a specific value

Form1: Communicable disease Notification form

Communicable Disease Notifying Form
Health Protection Agency
Male', Republic of Maldives

FORM 001
HPA/2015

Reporting Facility	☐ *Re-notification (required for changes in diagnosis (e.g. Dengue Fever to DHF), case confirmation or outcome (e.g. death).

Notifiable Diseases (place ✓appropriately)

Immediately notifiable via form and Telephone (❜)+960 3014496)	Notifiable within 24 hrs to HPA
☐ Acute Flaccid Paralysis (use Polio investigation form) ☐ Cholera ☐ Diphtheria ☐ Encephalitis (specify organism if known)_____ ☐ Food Poisoning (use investigation form) ☐ Measles (complete measles investigation form) ☐ Meningitis (specify organism if known)_____ ☐ Mumps ☐ Rabies ☐ Rubella / ☐ Congenital rubella syndrome ☐ Tetanus / ☐ Neonatal tetanus ☐ Tuberculosis (use TB investigation form) ☐ Whooping Cough ☐ Yellow Fever	☐ Chikungunya ☐ DF/☐DHF/☐DSS ☐ Filariasis ☐ Hepatitis A / B/ C/ D/E (circle appropriately) ☐ Leprosy ☐ Leptospirosis ☐ Malaria ☐ Plague ☐ Scrub Typhus ☐ SARI (Severe Acute Respiratory Infection = ARI requiring hospital admission) ☐ Typhoid/ ☐Paratyphoid (complete case investigation form) ☐ Toxoplasmosis/ ☐ Congenital toxoplasmosis ☐ Other emerging disease (specify)_____

Case Details (Mandatory fields are marked with (*) and underlined. Please make sure to complete them.

1-*Case classification: Suspect ☐ Probable ☐ Confirmed ☐ (as per surveillance case definition)

2-*Patient Nation ID No: A_____ For foreigners include passport number	3-*Patient Name:	4-*Age: YY / MM	5-*Sex: ☐M ☐F If pregnant ☐

6- *Patient's residential Address (pls confirm with patient.)	7-*Atoll/Island	8-Contact number❜)	9-Foreigners country of origin

10-*Date of onset of illness: DD / MM / YYYY	11-Date of consultation: DD/ MM /YYYY
12-*Patient category ☐Out-patient ☐In-patient: ☐ Ward _____ Bed _____ ☐ICU _____ Bed _____	13-*Case outcome: ☐ Death ☐ On treatment ☐ Referred to higher center ☐ Recovered with disability ☐ Recovered fully
14- Recent **travel history** if relevant (include countries visited)	15- **Date of arrival** in Maldives: DD/ MM/ YYYY
16-**Clinical details** (include risk factors, mode of transmission, etc.) 17- **Condition of patient**: ☐ Stable ☐ Sick ☐ Critically ill	18-**Laboratory Confirmation:** ☐ Confirmed: Test specifics_____ ☐ If Requested, Date: DD/ MM /YYYY ☐ Not Requested
Notifier details (eg:Dr, Nurse ,HW or other designated person) Name:_____ Designation: _____ Signature: _____ Date: DD/ MM/ YYYY	**Data entry use** (use by PHUs and entry users) Date received: DD/ MM/ YYYY Date of entry: DD/ MM/ YYYY Checked and entered by: _____

For further information or inquiries, please contact:
Health Protection Agency, Ministry of Health,
Roshanee Building, Sosun Magu, Male'.
Telephone: +960-3014 496, Hotline: +960-3014 333, Fax: +960-3014 484 email: hpa@health.gov.mv
Forms and case definition booklet are available on http://www.hpa.gov.mv , http://www.health.gov.mv

Revised 21st Jan2015

ޑެންގީހުން ޖެހުމުން ސަލާމަތްވާނީ ކަންތައްތައް

1. ގިނައިން އަރާމު ކުރާށެވެ.

2. ގިނައިން ދިޔާއެއްޗެހި ބޯނުންކުރާށެވެ. އެންމެ ރަނގަޅު އެއްބުއިމަކީ ކުރުނބާފެނެވެ. ކުރުނބާފެނުގެ ގިރާސީ އެއްލިބަރު ޖޫސްގައި އެއްބުޅެތޯވެ. ސޯޑާ ތެވުންޝާ ޔޫސްޓީރިކަރަ ޕޮއިންޓަރުގެ ރަހަކުރަމާ ގަނޑުކަހާދުވެއްޔާ ދޫސް ބޭނުން ނުކުރާށެވެ. ހުސްފެނަށްވުރެ ކުރިއަށް ދޫއާއި ފަތުރާ ބިކާއި މަރަނގަޅޯވެ. ކޮފީއާއި ސައި ރަނގަޅޯއްނުވޭނެވެ.

3. ހުން މަޑުކުރުމަށް ބޭނުންކުރަންވާނީ ޕެރަސިޓަމޯލް އެކަނިޔެވެ. އެސްޕިރިނާ ސްޓީރޮއިޑް ފަދަ އެހެނިހެން ބޭސްތައް ކެއުމުން ދުރުހެލިވާށެވެ.

4. ތިރީގައިވާ ފަދަ ނުރައްކާތެރި ނިޝާނެއް ފެނިއްޖެނަމަ އަވަހަށް ޑޮކްޓަރަކަށް ދައްކަންވާނެއެވެ. އެފަދަ ނިޝާނެއް ނުފެނުނަސް ތިންދުވަހުންވެސް ފަހަރެއް ހުމަށްފަހުގެ ޑޮކްޓަރުގެ ލަފާ ހޯދަންވާނެއެވެ.

   i. ހުން މަޑުވާއިރުވެސް ބަލިމީހާގެ ޙާލަތު ހަލުވި ދެރަވުން، ވަރުބަލިވެ ނިދިނިދުން، ކަރުކަށިން މާބޮޑަށް ރިއްސުން

   ii. ގިނައިން ހޮޑުލުވި އެއްވެސް އެއްޗެއް ނުބޮވުން

   iii. 6 ގަޑިއިރުވާއިރުވެސް ކުޑަކަމުނުދުވުން

   iv. އަތްފައި ފިނިވުން، މާބޮޑަށް ބަނޑުގައި ރިއްސުން، ވަރުވާނުދުވުން

   v. އެއްވެސް ތަނަކުން ލޭއައުން. ބޮޑުކަމުދާއިރު ކަޅުކުލަ ނުވަތަ ރަތްކުލަގައި ހުރުން، ހަމުގައި ރަތް ލަބަތަކެއްޖެހުން

References:

1. Dengue Guideline for patient care in the region of America; 2nd edition; Pan American Health Organization and World Health Organization
2. Dengue: Guidelines for diagnosis, treatment, prevention and control, 2009: World Health Organization
3. Infectious disease surveillance, Health Protection Agency, Maldives
4. Information by World Health Organization on dengue vaccine research http://www.who.int/immunization/research/development/dengue_vaccines/en/
5. Denuge; Lancet 2019; 393: 350–63 London School of Hygiene & Tropical Medicine, London, UK