CHAPTER 2. CLINICAL MANAGEMENT AND DELIVERY OF CLINICAL SERVICES

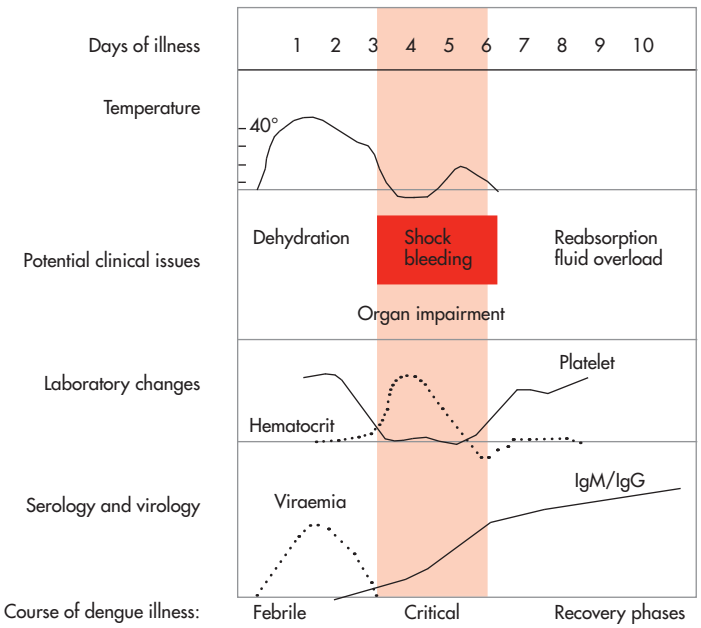
2.1 OVERVIEW

Dengue infection is a systemic and dynamic disease. It has a wide clinical spectrum that includes both severe and non-severe clinical manifestations (*1*). After the incubation period, the illness begins abruptly and is followed by the three phases – febrile, critical and recovery (Figure 2.1).

For a disease that is complex in its manifestations, management is relatively simple, inexpensive and very effective in saving lives so long as correct and timely interventions are instituted. The key is early recognition and understanding of the clinical problems during the different phases of the disease, leading to a rational approach to case management and a good clinical outcome. An overview of good and bad clinical practices is given in Textbox A.

Activities (triage and management decisions) at the primary and secondary care levels (where patients are first seen and evaluated) are critical in determining the clinical outcome of dengue. A well-managed front-line response not only reduces the number of unnecessary hospital admissions but also saves the lives of dengue patients. Early notification of dengue cases seen in primary and secondary care is crucial for identifying outbreaks and initiating an early response (Chapter 5). Differential diagnosis needs to be considered (Textbox B).

Figure 2.1 The course of dengue illness*



* Source: adapted from Yip (2) by chapter authors.

2.1.1 Febrile phase

Patients typically develop high-grade fever suddenly. This acute febrile phase usually lasts 2–7 days and is often accompanied by facial flushing, skin erythema, generalized body ache, myalgia, arthralgia and headache (1). Some patients may have sore throat, injected pharynx and conjunctival injection. Anorexia, nausea and vomiting are common. It can be difficult to distinguish dengue clinically from non-dengue febrile diseases in the early febrile phase. A positive tourniquet test in this phase increases the probability of dengue (3,4). In addition, these clinical features are indistinguishable between severe and non-severe dengue cases. Therefore monitoring for warning signs and other clinical parameters (Textbox C) is crucial to recognizing progression to the critical phase.

Mild haemorrhagic manifestations like petechiae and mucosal membrane bleeding (e.g. nose and gums) may be seen (3,5). Massive vaginal bleeding (in women of childbearing age) and gastrointestinal bleeding may occur during this phase but is not common (5). The liver is often enlarged and tender after a few days of fever (3). The earliest abnormality in the full blood count is a progressive decrease in total white cell count, which should alert the physician to a high probability of dengue.

2.1.2 Critical phase

Around the time of defervescence, when the temperature drops to 37.5–38°C or less and remains below this level, usually on days 3–7 of illness, an increase in capillary permeability in parallel with increasing haematocrit levels may occur (6,7). This marks the beginning of the critical phase. The period of clinically significant plasma leakage usually lasts 24–48 hours.

Progressive leukopenia (3) followed by a rapid decrease in platelet count usually precedes plasma leakage. At this point patients without an increase in capillary permeability will improve, while those with increased capillary permeability may become worse as a result of lost plasma volume. The degree of plasma leakage varies. Pleural effusion and ascites may be clinically detectable depending on the degree of plasma leakage and the volume of fluid therapy. Hence chest x-ray and abdominal ultrasound can be useful tools for diagnosis. The degree of increase above the baseline haematocrit often reflects the severity of plasma leakage.

Shock occurs when a critical volume of plasma is lost through leakage. It is often preceded by warning signs. The body temperature may be subnormal when shock occurs. With prolonged shock, the consequent organ hypoperfusion results in progressive organ impairment, metabolic acidosis and disseminated intravascular coagulation. This in turn leads to severe haemorrhage causing the haematocrit to decrease in severe shock. Instead of the leukopenia usually seen during this phase of dengue, the total white cell count may increase in patients with severe bleeding. In addition, severe organ impairment such as severe hepatitis, encephalitis or myocarditis and/or severe bleeding may also develop without obvious plasma leakage or shock (8).

Those who improve after defervescence are said to have non-severe dengue. Some patients progress to the critical phase of plasma leakage without defervescence and, in

these patients, changes in the full blood count should be used to guide the onset of the critical phase and plasma leakage.

Those who deteriorate will manifest with warning signs. This is called dengue with warning signs (Textbox C). Cases of dengue with warning signs will probably recover with early intravenous rehydration. Some cases will deteriorate to severe dengue (see below).

2.1.3 Recovery phase

If the patient survives the 24–48 hour critical phase, a gradual reabsorption of extravascular compartment fluid takes place in the following 48–72 hours. General well-being improves, appetite returns, gastrointestinal symptoms abate, haemodynamic status stabilizes and diuresis ensues. Some patients may have a rash of "isles of white in the sea of red" (9). Some may experience generalized pruritus. Bradycardia and electrocardiographic changes are common during this stage.

The haematocrit stabilizes or may be lower due to the dilutional effect of reabsorbed fluid. White blood cell count usually starts to rise soon after defervescence but the recovery of platelet count is typically later than that of white blood cell count.

Respiratory distress from massive pleural effusion and ascites will occur at any time if excessive intravenous fluids have been administered. During the critical and/or recovery phases, excessive fluid therapy is associated with pulmonary oedema or congestive heart failure.

The various clinical problems during the different phases of dengue can be summarized as in Table 2.1.

Table 2.1 Febrile, critical and recovery phases in dengue

1	Febrile phase	Dehydration; high fever may cause neurological disturbances and febrile seizures in young children
2	Critical phase	Shock from plasma leakage; severe haemorrhage; organ impairment
3	Recovery phase	Hypervolaemia (only if intravenous fluid therapy has been excessive and/or has extended into this period)

2.1.4 Severe dengue

Severe dengue is defined by one or more of the following: (i) plasma leakage that may lead to shock (dengue shock) and/or fluid accumulation, with or without respiratory distress, and/or (ii) severe bleeding, and/or (iii) severe organ impairment.

As dengue vascular permeability progresses, hypovolaemia worsens and results in shock. It usually takes place around defervescence, usually on day 4 or 5 (range days 3–7) of illness, preceded by the warning signs. During the initial stage of shock, the compensatory mechanism which maintains a normal systolic blood pressure also produces tachycardia and peripheral vasoconstriction with reduced skin perfusion,

resulting in cold extremities and delayed capillary refill time. Uniquely, the diastolic pressure rises towards the systolic pressure and the pulse pressure narrows as the peripheral vascular resistance increases. Patients in dengue shock often remain conscious and lucid. The inexperienced physician may measure a normal systolic pressure and misjudge the critical state of the patient. Finally, there is decompensation and both pressures disappear abruptly. Prolonged hypotensive shock and hypoxia may lead to multi-organ failure and an extremely difficult clinical course (Textbox D).

The patient is considered to have shock if the pulse pressure (i.e. the difference between the systolic and diastolic pressures) is ≤ 20 mm Hg in children or he/she has signs of poor capillary perfusion (cold extremities, delayed capillary refill, or rapid pulse rate). In adults, the pulse pressure of ≤ 20 mm Hg may indicate a more severe shock. Hypotension is usually associated with prolonged shock which is often complicated by major bleeding.

Patients with severe dengue may have coagulation abnormalities, but these are usually not sufficient to cause major bleeding. When major bleeding does occur, it is almost always associated with profound shock since this, in combination with thrombocytopaenia, hypoxia and acidosis, can lead to multiple organ failure and advanced disseminated intravascular coagulation. Massive bleeding may occur without prolonged shock in instances when acetylsalicylic acid (aspirin), ibuprofen or corticosteroids have been taken.

Unusual manifestations, including acute liver failure and encephalopathy, may be present, even in the absence of severe plasma leakage or shock. Cardiomyopathy and encephalitis are also reported in a few dengue cases. However, most deaths from dengue occur in patients with profound shock, particularly if the situation is complicated by fluid overload.

Severe dengue should be considered if the patient is from an area of dengue risk presenting with fever of 2–7 days plus any of the following features:

- There is evidence of plasma leakage, such as:
  - high or progressively rising haematocrit;
  - pleural effusions or ascites;
  - circulatory compromise or shock (tachycardia, cold and clammy extremities, capillary refill time greater than three seconds, weak or undetectable pulse, narrow pulse pressure or, in late shock, unrecordable blood pressure).
- There is significant bleeding.
- There is an altered level of consciousness (lethargy or restlessness, coma, convulsions).
- There is severe gastrointestinal involvement (persistent vomiting, increasing or intense abdominal pain, jaundice).
- There is severe organ impairment (acute liver failure, acute renal failure, encephalopathy or encephalitis, or other unusual manifestations, cardiomyopathy) or other unusual manifestations.

2.2 DELIVERY OF CLINICAL SERVICES AND CASE MANAGEMENT

2.2.1 Introduction

Reducing dengue mortality requires an organized process that guarantees early recognition of the disease, and its management and referral when necessary. The key component of the process is the delivery of good clinical services at all levels of health care, from primary to tertiary levels. Most dengue patients recover without requiring hospital admission while some may progress to severe disease. Simple but effective triage principles and management decisions applied at the primary and secondary care levels, where patients are first seen and evaluated, can help in identifying those at risk of developing severe disease and needing hospital care. This should be complemented by prompt and appropriate management of severe dengue in referral centres.

Activities at the first level of care should focus on:

- recognizing that the febrile patient could have dengue;
- notifying early to the public health authorities that the patient is a suspected case of dengue;
- managing patients in the early febrile phase of dengue;
- recognizing the early stage of plasma leakage or critical phase and initiating fluid therapy;
- recognizing patients with warning signs who need to be referred for admission and/or intravenous fluid therapy to a secondary health care facility;
- recognizing and managing severe plasma leakage and shock, severe bleeding and severe organ impairment promptly and adequately.

2.2.2. Primary and secondary health care centres

At primary and secondary levels, health care facilities are responsible for emergency/ambulatory triage assessment and treatment.

Triage is the process of rapidly screening patients soon after their arrival in the hospital or health facility in order to identify those with severe dengue (who require immediate emergency treatment to avert death), those with warning signs (who should be given priority while waiting in the queue so that they can be assessed and treated without delay), and non-urgent cases (who have neither severe dengue nor warning signs).

During the early febrile phase, it is often not possible to predict clinically whether a patient with dengue will progress to severe disease. Various forms of severe manifestations may unfold only as the disease progresses through the critical phase, but the warning signs are good indicators of a higher risk of developing severe dengue. Therefore, the patient should have daily outpatient health care assessments for disease progression with careful checking for manifestations of severe dengue and warning signs.

Health care workers at the first levels of care should apply a stepwise approach, as suggested in Table 2.2.

Table 2.2 A stepwise approach to the management of dengue

Step I. Overall assessment
I.1 History, including information on symptoms, past medical and family history
I.2 Physical examination, including full physical and mental assessment
I.3 Investigation, including routine laboratory and dengue-specific laboratory
Step II. Diagnosis, assessment of disease phase and severity
Step III. Management
III.1 Disease notification
III.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).

Section 2.3 gives treatment recommendations for the groups A–C.

2.2.3 Referral centres

Referral centres receiving severely ill dengue patients must be able to give prompt attention to referred cases. Beds should be made available to those patients who meet the admission criteria, even if elective cases have to be deferred. If possible, there should be a designated area to cohort dengue patients, and a high-dependency unit for closer monitoring of those with shock. These units should be staffed by doctors and nurses who are trained to recognize high-risk patients and to institute appropriate treatment and monitoring.

A number of criteria may be used to decide when to transfer a patient to a high-dependency unit. These include:

- early presentation with shock (on days 2 or 3 of illness);
- severe plasma leakage and/or shock;
- undetectable pulse and blood pressure;
- severe bleeding;
- fluid overload;
- organ impairment (such as hepatic damage, cardiomyopathy, encephalopathy, encephalitis and other unusual complications).

2.2.4 Resources needed

In the detection and management of dengue, a range of resources is needed to deliver good clinical services at all levels. Resources include (*10*):

- *Human resources*: The most important resource is trained doctors and nurses. Adequate health personnel should be allocated to the first level of care to help in triage and emergency management. If possible, dengue units staffed by

experienced personnel could be set up at referral centres to receive referred cases, particularly during dengue outbreaks, when the number of personnel main need to be increased.

- *Special area*: A well equipped and well staffed area should be designated for giving immediate and transitory medical care to patients who require intravenous fluid therapy until they can be transferred to a ward or referral health facility.
- *Laboratory resources*: The most important laboratory investigation is that of serial haematocrit levels and full blood counts. These investigations should be easily accessible from the health centre. Results should be available within two hours in severe cases of dengue. If no proper laboratory services are available, the minimum standard is the point-of-care testing of haematocrit by capillary (finger prick) blood sample with the use of a microcentrifuge.
- *Consumables*: Intravenous fluids such as crystalloids, colloids and intravenous giving sets should be available.
- *Drugs*: There should be adequate stocks of antipyretics and oral rehydration salts. In severe cases, additional drugs are necessary (vitamin K1, Ca gluconate, $NaHCO_3$, glucose, furosemide, KCl solution, vasopressor, and inotropes).
- *Communication*: Facilities should be provided for easy communication, especially between secondary and tertiary levels of care and laboratories, including consultation by telephone.
- *Blood bank*: Blood and blood products will be required by only a small percentage of patients but should be made readily available to those who need them.

2.2.5 Education and training

To ensure the presence of adequate staffing at all levels, the education and training of doctors, nurses, auxiliary health care workers and laboratory staff are priorities. Educational programmes that are customized for different levels of health care and that reflect local capacity should be supported and implemented widely. The educational programmes should develop capacities for effective triage and should improve recognition, clinical management and laboratory diagnosis of dengue.

National committees should monitor and evaluate clinical management and outcomes. Review committees at different levels (e.g. national, state, district, hospital) should review all dengue deaths, and, if possible, all cases of severe dengue, evaluate the health care delivery system, and provide feedback to doctors on how to improve care.

In dengue-endemic countries, the knowledge of dengue, the vectors and transmission of disease should be incorporated into the school curriculum. The population should also be educated about dengue in order to empower patients and their families in their own care – so that they are prepared to seek medical care at the right time, avoid self-medication, identify skin bleedings, consider the day of defervescence (and during 48 hours) as the time when complications usually occur, and look for warning signs such as intense and continuous abdominal pain and frequent vomiting.

The mass media can give an important contribution if they are correctly briefed. Workshops and other meetings with journalists, editors, artists and executives can

contribute to drawing up the best strategy for health education and communication without alarming the public.

During dengue epidemics, nursing and medical students together with community activists can visit homes with the double purpose of providing health education and actively tracing dengue cases. This has been shown to be feasible, inexpensive and effective (*11*) and must be coordinated with the primary health care units. It is useful to have printed information about dengue illness and the warning signs for distribution to members of the community. Medical care providers must include health education activities such as disease prevention in their daily work.

2.3 RECOMMENDATIONS FOR TREATMENT

2.3.1 A stepwise approach to the management of dengue (see Table 2.2)

2.3.1.1 Step I—Overall assessment

History
The history should include:

- date of onset of fever/illness;
- quantity of oral intake;
- assessment for warning signs (Textbox C);
- diarrhoea;
- change in mental state/seizure/dizziness;
- urine output (frequency, volume and time of last voiding);
- other important relevant histories, 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 waterfall (consider leptospirosis, typhus, malaria), recent unprotected sex or drug abuse (consider acute HIV seroconversion illness).

Physical examination
The physical examination should include:

- assessment of mental state;
- assessment of hydration status;
- assessment of haemodynamic status (Textbox D);
- checking for 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).

Investigation
A full blood count should be done at the first visit. A haematocrit test in the early febrile phase establishes the patient's own baseline haematocrit. A decreasing white blood cell count makes dengue very likely. A rapid decrease in platelet count in parallel with a rising haematocrit compared to the baseline is suggestive of progress to the plasma

leakage/critical phase of the disease. In the absence of the patient's baseline, age-specific population haematocrit levels could be used as a surrogate during the critical phase.

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 (Chapter 4).

Additional tests should be considered as indicated (and if available). These should include tests of liver function, glucose, serum electrolytes, urea and creatinine, bicarbonate or lactate, cardiac enzymes, ECG and urine specific gravity.

2.3.1.2 Step II—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 be able to determine whether the disease is dengue, which phase it is in (febrile, critical or recovery), whether there are warning signs, the hydration and haemodynamic status of the patient, and whether the patient requires admission (Textboxes E and F).

2.3.1.3 Step III—Management

Disease notification
In dengue-endemic countries, cases of suspected, probable and confirmed dengue should be notified as soon as possible so that appropriate public health measures can be initiated (Chapter 5). Laboratory confirmation is not necessary before notification, but should be obtained. In non-endemic countries, usually only confirmed cases will be notified.

Suggested criteria for early notification of suspected cases are that the patient lives in or has travelled to a dengue-endemic area, has fever for three days or more, has low or decreasing white cell counts, and/or has thrombocytopaenia ± positive tourniquet test.

In dengue-endemic countries, the later the notification, the more difficult it is to prevent dengue transmission.

Management decisions
Depending on the clinical manifestations and other circumstances, patients may (*12*) be sent home (Group A), be referred for in-hospital management (Group B), or require emergency treatment and urgent referral (Group C).

2.3.2 Treatment according to groups A–C

2.3.2.1 Group A – patients who may be sent home (see the home care card for dengue in Textbox G)

These are patients who are able to tolerate adequate volumes of oral fluids and pass urine at least once every six hours, and do not have any of the warning signs, particularly when fever subsides.

Ambulatory patients should be reviewed daily for disease progression (decreasing white blood cell count, defervescence and warning signs) until they are out of the critical period. Those with stable haematocrit can be sent home after being advised to return to the hospital immediately if they develop any of the warning signs and to adhere to the following action plan:

- Encourage oral intake of oral rehydration solution (ORS), fruit juice and other fluids containing electrolytes and sugar to replace losses from fever and vomiting. Adequate oral fluid intake may be able to reduce the number of hospitalizations (*13*). [Caution: fluids containing sugar/glucose may exacerbate hyperglycaemia of physiological stress from dengue and diabetes mellitus.]
- Give paracetamol for high fever if the patient is uncomfortable. The interval of paracetamol dosing should not be less than six hours. Tepid sponge if the patient still has high fever. Do not give acetylsalicylic acid (aspirin), ibuprofen or other non-steroidal anti-inflammatory agents (NSAIDs) as these drugs may aggravate gastritis or bleeding. Acetylsalicylic acid (aspirin) may be associated with Reye's Syndrome.
- Instruct the care-givers that the patient should be brought to hospital immediately if any of the following occur: no clinical improvement, deterioration around the time of defervescence, severe abdominal pain, persistent vomiting, cold and clammy extremities, lethargy or irritability/restlessness, bleeding (e.g. black stools or coffee-ground vomiting), not passing urine for more than 4–6 hours.

Patients who are sent home should be monitored daily by health care providers for temperature pattern, volume of fluid intake and losses, urine output (volume and frequency), warning signs, signs of plasma leakage and bleeding, haematocrit, and white blood cell and platelet counts (see group B).

2.3.2.2 Group B – patients who should be referred for in-hospital management

Patients may need to be admitted to a secondary health care centre for close observation, particularly as they approach the critical phase. These include patients with warning signs, those with co-existing conditions that may make dengue or its management more complicated (such as pregnancy, infancy, old age, obesity, diabetes mellitus, renal failure, chronic haemolytic diseases), and those with certain social circumstances (such as living alone, or living far from a health facility without reliable means of transport).

If the patient has dengue with warning signs, the action plan should be as follows:

- Obtain a reference haematocrit before fluid therapy. Give only isotonic solutions such as 0.9% saline, Ringer's lactate, or Hartmann's solution. Start with 5–7 ml/kg/hour for 1–2 hours, then reduce to 3–5 ml/kg/hr for 2–4 hours, and then reduce to 2–3 ml/kg/hr or less according to the clinical response (Textboxes H, J and K).
- Reassess the clinical status and repeat the haematocrit. If the haematocrit remains the same or rises only minimally, continue with the same rate (2–3 ml/kg/hr) for another 2–4 hours. If the vital signs are worsening and haematocrit is rising rapidly, increase the rate to 5–10 ml/kg/hour for 1–2 hours. Reassess the clinical status, repeat the haematocrit and review fluid infusion rates accordingly.

- Give the minimum intravenous fluid volume required to maintain good perfusion and urine output of about 0.5 ml/kg/hr. Intravenous fluids are usually needed for only 24–48 hours. Reduce intravenous fluids gradually when the rate of plasma leakage decreases towards the end of the critical phase. This is indicated by urine output and/or oral fluid intake that is/are adequate, or haematocrit decreasing below the baseline value in a stable patient.
- 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, and other organ functions (such as renal profile, liver profile, coagulation profile, as indicated).

If the patient has dengue without warning signs, the action 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 dextrose at maintenance rate (Textbox H). For obese and overweight patients, use the ideal body weight for calculation of fluid infusion (Textboxes J and K). Patients may be able to take oral fluids after a few hours of intravenous fluid therapy. Thus, it is necessary to revise the fluid infusion frequently. Give the minimum volume required to maintain good perfusion and urine output. 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 frequency), warning signs, haematocrit, and white blood cell and platelet counts (Textbox L). Other laboratory tests (such as liver and renal functions tests) can be done, depending on the clinical picture and the facilities of the hospital or health centre.

2.3.2.3 Group C – patients who require emergency treatment and urgent referral when they have severe dengue

Patients require emergency treatment and urgent referral when they are in the critical phase of disease, i.e. when they have:

- severe plasma leakage leading to dengue shock and/or fluid accumulation with respiratory distress;
- severe haemorrhages;
- severe organ impairment (hepatic damage, renal impairment, cardiomyopathy, encephalopathy or encephalitis).

All patients with severe dengue should be admitted to a hospital with access to intensive care facilities and blood transfusion. Judicious intravenous fluid resuscitation is the essential and usually sole intervention required. The crystalloid solution should be isotonic and the volume just sufficient to maintain an effective circulation during the period of plasma leakage. Plasma losses should be replaced immediately and rapidly with isotonic crystalloid solution or, in the case of hypotensive shock, colloid solutions (Textbox M). If possible, obtain haematocrit levels before and after fluid resuscitation.

There should be continued replacement of further plasma losses to maintain effective circulation for 24–48 hours. For overweight or obese patients, the ideal body weight should be used for calculating fluid infusion rates (textboxes J and K). A group and cross-match should be done for all shock patients. Blood transfusion should be given only in cases with suspected/severe bleeding.

Fluid resuscitation must be clearly separated from simple fluid administration. This is a strategy in which larger volumes of fluids (e.g. 10–20 ml boluses) are administered for a limited period of time under close monitoring to evaluate the patient's response and to avoid the development of pulmonary oedema. The degree of intravascular volume deficit in dengue shock varies. Input is typically much greater than output, and the input/output ratio is of no utility for judging fluid resuscitation needs during this period.

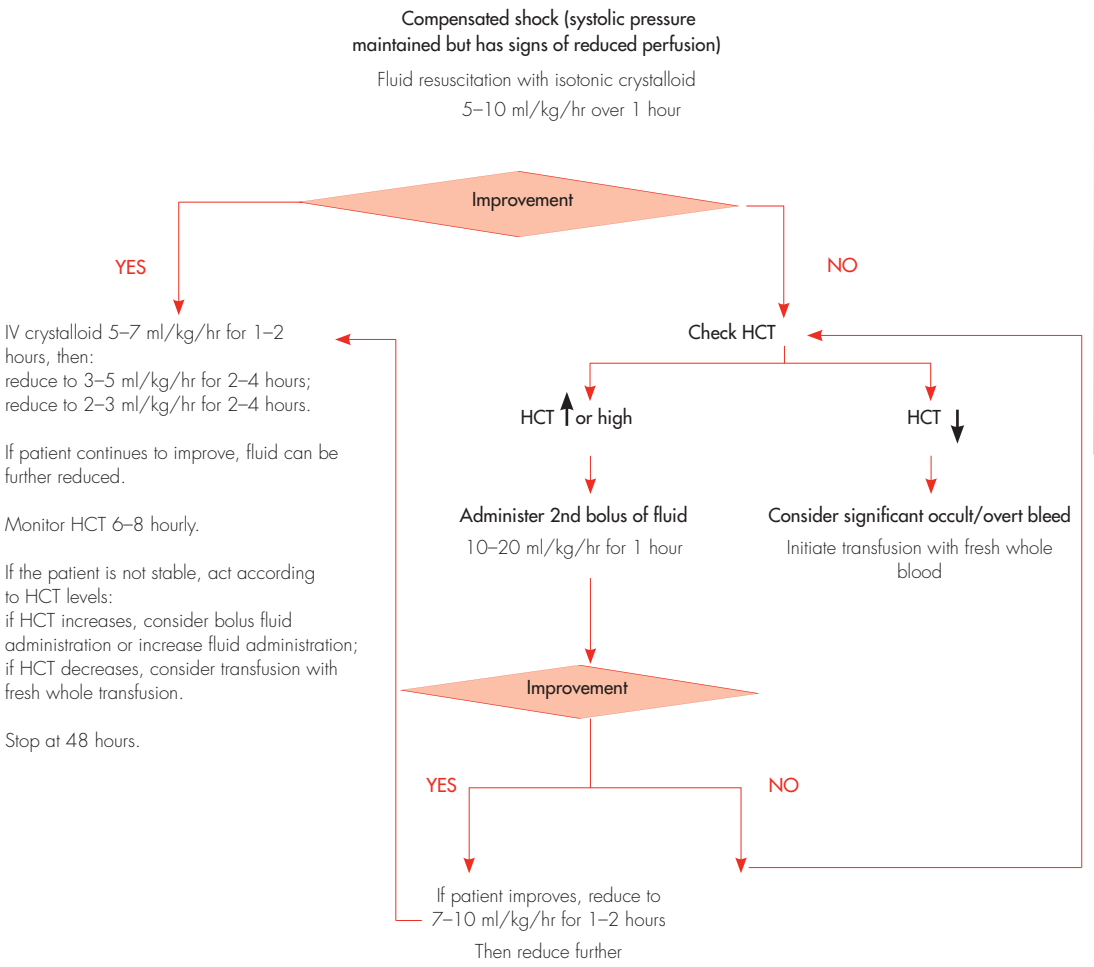
The goals of fluid resuscitation include improving central and peripheral circulation (decreasing tachycardia, improving blood pressure, pulse volume, warm and pink extremities, and capillary refill time <2 seconds) and improving end-organ perfusion – i.e. stable conscious level (more alert or less restless),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

Treatment of shock

The action plan for treating patients with compensated shock is as follows (Textboxes D and N, Figure 2.2):

- Start intravenous fluid resuscitation with isotonic crystalloid solutions at 5–10 ml/kg/hour over one hour. Then reassess the patient's condition (vital signs, capillary refill time, haematocrit, urine output). The next steps depend on the situation.
- If the patient's condition improves, intravenous fluids should be gradually reduced to 5–7 ml/kg/hr for 1–2 hours, then to 3–5 ml/kg/hr for 2–4 hours, then to 2–3 ml/kg/hr, and then further depending on haemodynamic status, which can be maintained for up to 24–48 hours. (See textboxes H and J for a more appropriate estimate of the normal maintenance requirement based on ideal body weight).
- If vital signs are still unstable (i.e. shock persists), check the haematocrit after the first bolus. If the haematocrit increases or is still high (>50%), repeat a second bolus of crystalloid solution at 10–20 ml/kg/hr for one hour. After this second bolus, if there is improvement, reduce the rate to 7–10 ml/kg/hr for 1–2 hours, and then continue to reduce as above. If haematocrit decreases compared to the initial reference haematocrit (<40% in children and adult females, <45% in adult males), this indicates bleeding and the need to cross-match and transfuse blood as soon as possible (see treatment for haemorrhagic complications).
- Further boluses of crystalloid or colloidal solutions may need to be given during the next 24–48 hours.

Figure 2.2 Algorithm for fluid management in compensated shock



HCT = haematocrit

Patients with hypotensive shock should be managed more vigorously. The action plan for treating patients with hypotensive shock is as follows (Textboxes D and N, Figure 2.3):

- Initiate intravenous fluid resuscitation with crystalloid or colloid solution (if available) at 20 ml/kg as a bolus given over 15 minutes to bring the patient out of shock as quickly as possible.
- If the patient's condition improves, give a crystalloid/colloid infusion of 10 ml/kg/hr for one hour. Then continue with crystalloid infusion and gradually reduce to 5–7 ml/kg/hr for 1–2 hours, then to 3–5 ml/kg/hr for 2–4 hours, and then

to 2–3 ml/kg/hr or less, which can be maintained for up to 24–48 hours (textbox H).

- If vital signs are still unstable (i.e. shock persists), review the haematocrit obtained before the first bolus. If the haematocrit was low (<40% in children and adult females, <45% in adult males), this indicates bleeding and the need to cross-match and transfuse blood as soon as possible (see treatment for haemorrhagic complications).
- If the haematocrit was high compared to the baseline value (if not available, use population baseline), change intravenous fluids to colloid solutions at 10–20 ml/kg as a second bolus over 30 minutes to one hour. After the second bolus, reassess the patient. If the condition improves, reduce the rate to 7–10 ml/kg/hr for 1–2 hours, then change back to crystalloid solution and reduce the rate of infusion as mentioned above. If the condition is still unstable, repeat the haematocrit after the second bolus.
- If the haematocrit decreases compared to the previous value (<40% in children and adult females, <45% in adult males), this indicates bleeding and the need to cross-match and transfuse blood as soon as possible (see treatment for haemorrhagic complications). If the haematocrit increases compared to the previous value or remains very high (>50%), continue colloid solutions at 10–20 ml/kg as a third bolus over one hour. After this dose, reduce the rate to 7–10 ml/kg/hr for 1–2 hours, then change back to crystalloid solution and reduce the rate of infusion as mentioned above when the patient's condition improves.
- Further boluses of fluids may need to be given during the next 24 hours. The rate and volume of each bolus infusion should be titrated to the clinical response. Patients with severe dengue should be admitted to the high-dependency or intensive care area.

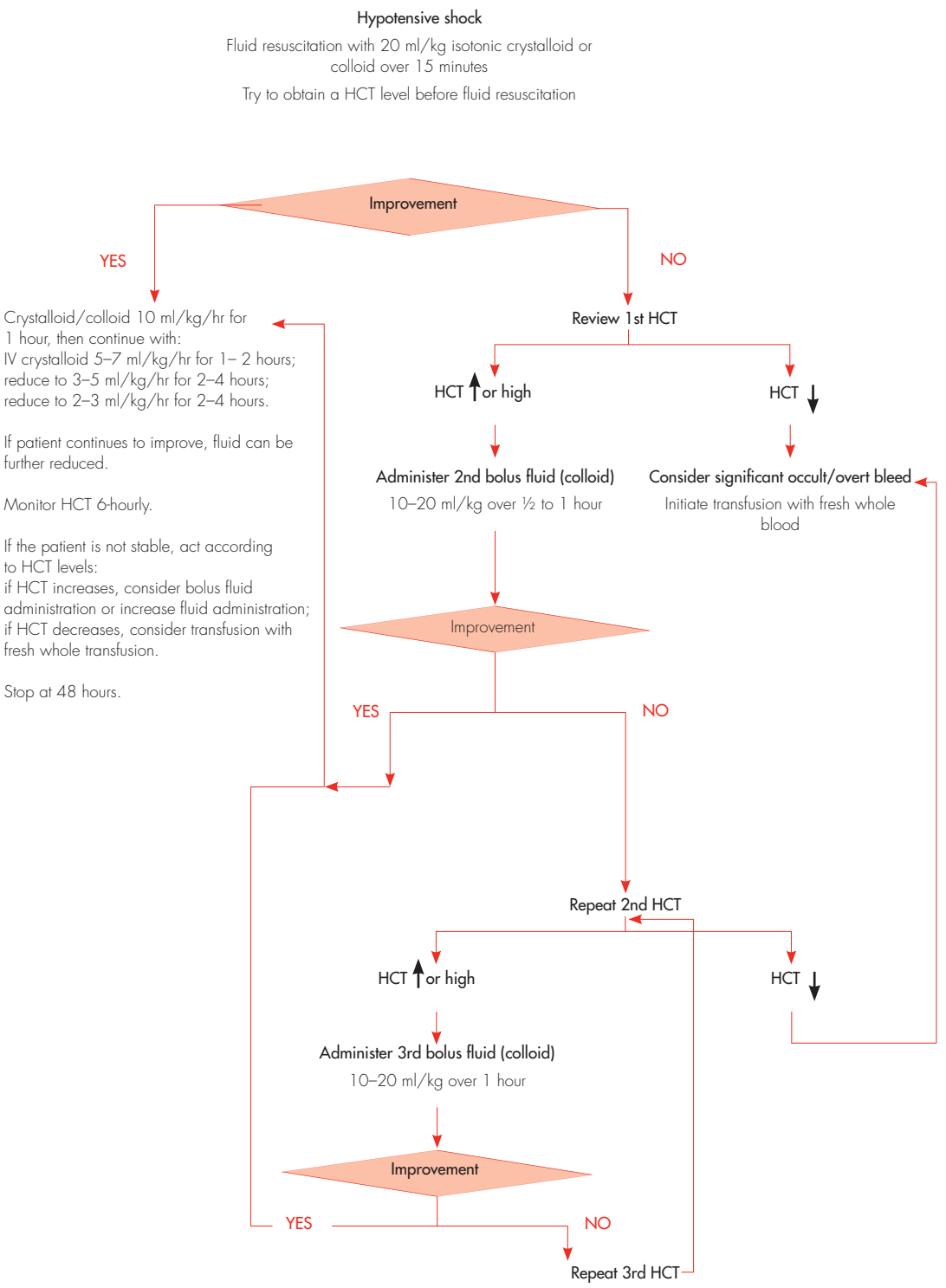
Patients with dengue shock should be frequently monitored until the danger period is over. A detailed fluid balance of all input and output should be maintained.

Parameters that should be monitored include vital signs and peripheral perfusion (every 15–30 minutes until the patient is out of shock, then 1–2 hourly). In general, the higher the fluid infusion rate, the more frequently the patient should be monitored and reviewed in order to avoid fluid overload while ensuring adequate volume replacement.

If resources are available, a patient with severe dengue should have an arterial line placed as soon as practical. The reason for this is that in shock states, estimation of blood pressure using a cuff is commonly inaccurate. The use of an indwelling arterial catheter allows for continuous and reproducible blood pressure measurements and frequent blood sampling on which decisions regarding therapy can be based. Monitoring of ECG and pulse oximetry should be available in the intensive care unit.

Urine output should be checked regularly (hourly till the patient is out of shock, then 1–2 hourly). A continuous bladder catheter enables close monitoring of urine output. An acceptable urine output would be about 0.5 ml/kg/hour. Haematocrit should be monitored (before and after fluid boluses until stable, then 4–6 hourly). In addition, there should be monitoring of arterial or venous blood gases, lactate, total carbon dioxide/bicarbonate (every 30 minutes to one hour until stable, then as indicated), blood glucose (before fluid resuscitation and repeat as indicated), and other organ

Figure 2.3 Algorithm for fluid management in hypotensive shock



functions (such as renal profile, liver profile, coagulation profile, before resuscitation and as indicated).

Changes in the haematocrit are a useful guide to treatment. However, changes must be interpreted in parallel with the haemodynamic status, the clinical response to fluid therapy and the acid-base balance. For instance, a rising or persistently high haematocrit together with unstable vital signs (particularly narrowing of the pulse pressure) indicates active plasma leakage and the need for a further bolus of fluid replacement. However, a rising or persistently high haematocrit together with stable haemodynamic status and adequate urine output does not require extra intravenous fluid. In the latter case, continue to monitor closely and it is likely that the haematocrit will start to fall within the next 24 hours as the plasma leakage stops.

A decrease in haematocrit together with unstable vital signs (particularly narrowing of the pulse pressure, tachycardia, metabolic acidosis, poor urine output) indicates major haemorrhage and the need for urgent blood transfusion. Yet a decrease in haematocrit together with stable haemodynamic status and adequate urine output indicates haemodilution and/or reabsorption of extravasated fluids, so in this case intravenous fluids must be discontinued immediately to avoid pulmonary oedema.

Treatment of haemorrhagic complications

Mucosal bleeding may occur in any patient with dengue but, if the patient remains stable with fluid resuscitation/replacement, it should be considered as minor. The bleeding usually improves rapidly during the recovery phase. In patients with profound thrombocytopaenia, ensure strict bed rest and protect from trauma to reduce the risk of bleeding. Do not give intramuscular injections to avoid haematoma. It should be noted that prophylactic platelet transfusions for severe thrombocytopaenia in otherwise haemodynamically stable patients have not been shown to be effective and are not necessary (*14*).

If major bleeding occurs it is usually from the gastrointestinal tract, and/or vagina in adult females. Internal bleeding may not become apparent for many hours until the first black stool is passed.

Patients at risk of major bleeding are those who:

- have prolonged/refractory shock;
- have hypotensive shock and renal or liver failure and/or severe and persistent metabolic acidosis;
- are given non-steroidal anti-inflammatory agents;
- have pre-existing peptic ulcer disease;
- are on anticoagulant therapy;
- have any form of trauma, including intramuscular injection.

Patients with haemolytic conditions are at risk of acute haemolysis with haemoglobinuria and will require blood transfusion.

Severe bleeding can be recognized by:

- persistent and/or severe overt bleeding in the presence of unstable haemodynamic status, regardless of the haematocrit level;
- a decrease in haematocrit after fluid resuscitation together with unstable haemodynamic status;
- refractory shock that fails to respond to consecutive fluid resuscitation of 40-60 ml/kg;
- hypotensive shock with low/normal haematocrit before fluid resuscitation;
- persistent or worsening metabolic acidosis ± a well-maintained systolic blood pressure, especially in those with severe abdominal tenderness and distension.

Blood transfusion is life-saving and should be given as soon as severe bleeding is suspected or recognized. However, blood transfusion must be given with care because of the risk of fluid overload. Do not wait for the haematocrit to drop too low before deciding on blood transfusion. Note that haematocrit of <30% as a trigger for blood transfusion, as recommended in the Surviving Sepsis Campaign Guideline (*15*), is not applicable to severe dengue. The reason for this is that, in dengue, bleeding usually occurs after a period of prolonged shock that is preceded by plasma leakage. During the plasma leakage the haematocrit increases to relatively high values before the onset of severe bleeding. When bleeding occurs, haematocrit will then drop from this high level. As a result, haematocrit levels may not be as low as in the absence of plasma leakage.

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

- Give 5–10ml/kg of fresh-packed red cells or 10–20 ml/kg of fresh whole blood at an appropriate rate and observe the clinical response. It is important that fresh whole blood or fresh red cells are given. Oxygen delivery at tissue level is optimal with high levels of 2,3 di-phosphoglycerate (2,3 DPG). Stored blood loses 2,3 DPG, low levels of which impede the oxygen-releasing capacity of haemoglobin, resulting in functional tissue hypoxia. A good clinical response includes improving haemodynamic status and acid-base balance.
- Consider repeating the blood transfusion if there is further blood loss or no appropriate rise in haematocrit after blood transfusion. There is little evidence to support the practice of transfusing platelet concentrates and/or fresh-frozen plasma for severe bleeding. It is being practised when massive bleeding can not be managed with just fresh whole blood/fresh-packed cells, but it may exacerbate the fluid overload.
- Great care should be taken when inserting a naso-gastric tube which may cause severe haemorrhage and may block the airway. A lubricated oro-gastric tube may minimize the trauma during insertion. Insertion of central venous catheters should be done with ultra-sound guidance or by a very experienced person.

2.3.3 Treatment of complications and other areas of treatment

2.3.3.1 Fluid overload

Fluid overload with large pleural effusions and ascites is a common cause of acute respiratory distress and failure in severe dengue. Other causes of respiratory distress include acute pulmonary oedema, severe metabolic acidosis from severe shock, and Acute Respiratory Distress Syndrome (ARDS) (refer to standard textbook of clinical care for further guidance on management).

Causes of fluid overload are:

- excessive and/or too rapid intravenous fluids;
- incorrect use of hypotonic rather than isotonic crystalloid 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;
- continuation of intravenous fluids after plasma leakage has resolved (24–48 hours from defervescence);
- co-morbid conditions such as congenital or ischaemic heart disease, chronic lung and renal diseases.

Early clinical features of fluid overload are:

- respiratory distress, difficulty in breathing;
- rapid breathing;
- chest wall in-drawing;
- wheezing (rather than crepitations);
- large pleural effusions;
- tense ascites;
- increased jugular venous pressure (JVP).

Late clinical features are:

- pulmonary oedema (cough with pink or frothy sputum ± crepitations, cyanosis);
- irreversible shock (heart failure, often in combination with ongoing hypovolaemia).

Additional investigations are:

- the chest x-ray which shows cardiomegaly, pleural effusion, upward displacement of the diaphragm by the ascites and varying degrees of "bat's wings" appearance ± Kerley B lines suggestive of fluid overload and pulmonary oedema;
- ECG to exclude ischaemic changes and arrhythmia;
- arterial blood gases;
- echocardiogram for assessment of left ventricular function, dimensions and regional wall dyskinesia that may suggest underlying ischaemic heart disease;
- cardiac enzymes.

The action plan for the treatment of fluid overload is as follows:

- Oxygen therapy should be given immediately.
- Stopping intravenous fluid therapy during the recovery phase will allow fluid in the pleural and peritoneal cavities to return to the intravascular compartment. This results in diuresis and resolution of pleural effusion and ascites. Recognizing when to decrease or stop intravenous fluids is key to preventing fluid overload. When the following signs are present, intravenous fluids should be discontinued or reduced to the minimum rate necessary to maintain euglycaemia:
  - signs of cessation of plasma leakage;
  - stable blood pressure, pulse and peripheral perfusion;
  - haematocrit decreases in the presence of a good pulse volume;
  - afebrile for more than 24–48 days (without the use of antipyretics);
  - resolving bowel/abdominal symptoms;
  - improving urine output.
- The management of fluid overload varies according to the phase of the disease and the patient's haemodynamic status. If the patient has stable haemodynamic status and is out of the critical phase (more than 24–48 hours of defervescence), stop intravenous fluids but continue close monitoring. If necessary, give oral or intravenous furosemide 0.1–0.5 mg/kg/dose once or twice daily, or a continuous infusion of furosemide 0.1 mg/kg/hour. Monitor serum potassium and correct the ensuing hypokalaemia.
- If the patient has stable haemodynamic status but is still within the critical phase, reduce the intravenous fluid accordingly. Avoid diuretics during the plasma leakage phase because they may lead to intravascular volume depletion.
- Patients who remain in shock with low or normal haematocrit levels but show signs of fluid overload may have occult haemorrhage. Further infusion of large volumes of intravenous fluids will lead only to a poor outcome. Careful fresh whole blood transfusion should be initiated as soon as possible. If the patient remains in shock and the haematocrit is elevated, repeated small boluses of a colloid solution may help.

2.3.3.2 Other complications of dengue

Both hyperglycaemia and hypoglycaemia may occur, even in the absence of diabetes mellitus and/or hypoglycaemic agents. Electrolyte and acid-base imbalances are also common observations in severe dengue and are probably related to gastrointestinal losses through vomiting and diarrhoea or to the use of hypotonic solutions for resuscitation and correction of dehydration. Hyponatraemia, hypokalaemia, hyperkalaemia, serum calcium imbalances and metabolic acidosis (sodium bicarbonate for metabolic acidosis is not recommended for $pH \geq 7.15$) can occur. One should also be alert for co-infections and nosocomial infections.

2.3.3.3 Supportive care and adjuvant therapy

Supportive care and adjuvant therapy may be necessary in severe dengue. This may include:

- renal replacement therapy, with a preference to continuous veno-venous haemodialysis (CVVH), since peritoneal dialysis has a risk of bleeding;
- vasopressor and inotropic therapies as temporary measures to prevent life-threatening hypotension in dengue shock and during induction for intubation, while correction of intravascular volume is being vigorously carried out;
- further treatment of organ impairment, such as severe hepatic involvement or encephalopathy or encephalitis;
- further treatment of cardiac abnormalities, such as conduction abnormalities, may occur (the latter usually not requiring interventions).

In this context there is little or no evidence in favour of the use of steroids and intravenous immunoglobulins, or of recombinant Activated Factor VII.

Refer to standard textbooks of clinical care for more detailed information regarding the treatment of complications and other areas of treatment.

ANNEX

Textbox A. Good clinical practice and bad clinical practice

	Good practice	Bad practice
1	Assessment and follow-up of patients with non-severe dengue and careful instruction of warning signs to watch out for	Sending patients with non-severe dengue home with no follow-up and inadequate instructions
2	Administration of paracetamol for high fever if the patient is uncomfortable	Administration of acetylsalicylic acid (aspirin) or ibuprofen
3	Obtaining a haematocrit level before and after fluid boluses	Not knowing when haematocrit levels are taken with respect to fluid therapy
4	Clinical assessment of the haemodynamic status before and after each fluid bolus	No clinical assessment of patient with respect to fluid therapy
5	Interpretation of haematocrit levels in the context of fluid administered and haemodynamic assessment	Interpretation of haematocrit levels independent of clinical status
6	Administration of intravenous fluids for repeated vomiting or a high or rapidly rising haematocrit	Administration of intravenous fluids to any patient with non-severe dengue
7	Use of isotonic intravenous fluids for severe dengue	Use of hypotonic intravenous fluids for severe dengue
8	Giving intravenous fluid volume just sufficient to maintain effective circulation during the period of plasma leakage for severe dengue	Excessive or prolonged intravenous fluid administration for severe dengue
9	Avoiding intramuscular injections in dengue patients	Giving intramuscular injections to dengue patients
10	Intravenous fluid rate and frequency of monitoring and haematocrit measurement adjusted according to the patient's condition	Fixed intravenous fluid rate and unchanged frequency of monitoring and haematocrit measurement during entire hospitalization for severe dengue
11	Close monitoring of blood glucose, i.e. tight glycaemic control	Not monitoring blood glucose, unaware of the hyperglycaemic effect on osmotic diuresis and confounding hypovolaemia
12	Discontinuation or reducing fluid therapy once haemodynamic status stabilizes	Continuation and no review of intravenous fluid therapy once haemodynamic status stabilizes

Textbox B. Differential diagnosis of dengue fever

Conditions that mimic the febrile phase of dengue infection	
Flu-like syndromes	Influenza, measles, Chikungunya, infectious mononucleosis , HIV seroconversion illness
Illnesses with a rash	Rubella, measles, scarlet fever, meningococcal infection, Chikungunya, drug reactions
Diarrhoeal diseases	Rotavirus, other enteric infections
Illnesses with neurological manifestations	Meningo/encephalitis Febrile seizures
Conditions that mimic the critical phase of dengue infection	
Infectious	Acute gastroenteritis, malaria, leptospirosis, typhoid, typhus, viral hepatitis, acute HIV seroconversion illness, bacterial sepsis, septic shock
Malignancies	Acute leukaemia and other malignancies
Other clinical pictures	Acute abdomen – acute appendicitis – acute cholecystitis – perforated viscus Diabetic ketoacidosis Lactic acidosis Leukopenia and thrombocytopaenia ± bleeding Platelet disorders Renal failure Respiratory distress (Kussmaul's breathing) Systemic Lupus Erythematosus

Textbox C. Warning signs

Clinical	Abdominal pain or tenderness Persistent vomiting Clinical fluid accumulation Mucosal bleed Lethargy, restlessness Liver enlargement >2 cm
Laboratory	Increase in HCT concurrent with rapid decrease in platelet count

Textbox D. Haemodynamic assessment: continuum of haemodynamic changes

Parameters	Stable circulation	Compensated shock	Hypotensive shock
Hypotensive shock	Clear and lucid	Clear and lucid (shock can be missed if you do not touch the patient)	Change of mental state (restless, combative)
Capillary refill time	Brisk (<2 sec)	Prolonged (>2 sec)	Very prolonged, mottled skin
Extremities	Warm and pink extremities	Cool peripheries	Cold, clammy extremities
Peripheral pulse volume	Good volume	Weak and thready	Feeble or absent
Heart rate	Normal for age	Tachycardia	Severe tachycardia with bradycardia in late shock
Blood pressure	Normal for age Normal pulse pressure for age	Normal systolic pressure but rising diastolic pressure Narrowing pulse pressure Postural hypotension	Narrowed pulse pressure (<20 mmHg) Hypotension (see definition below) Unrecordable blood pressure
Respiratory rate	Normal for age	Tachypnoea	Metabolic acidosis hyperpnoea/ Kussmaul's breathing

Definition of hypotension:
Systolic blood pressure of <90 mm Hg or mean arterial pressure <70 mm Hg in adults or a systolic blood pressure decrease of >40 mm Hg or <2 SD below normal for age.
In children up to 10 years of age, the 5th centile for systolic blood pressure can be determined by the formula: 70 + (age in years x 2) mm Hg.

Textbox E. Admission criteria

Warning signs	Any of the warning signs (Textbox C)
Signs and symptoms related to hypotension (possible plasma leakage)	Dehydrated patient, unable to tolerate oral fluids Giddiness or postural hypotension Profuse perspiration, fainting, prostration during defervescence Hypotension or cold extremities
Bleeding	Spontaneous bleeding, independent of the platelet count
Organ impairment	Renal, hepatic, neurological or cardiac – enlarged, tender liver, although not yet in shock – chest pain or respiratory distress, cyanosis
Findings through further investigations	Rising haematocrit Pleural effusion, ascites or asymptomatic gall-bladder thickening
Co-existing conditions	Pregnancy Co-morbid conditions, such as diabetes mellitus, hypertension, peptic ulcer, haemolitic anemias and others Overweight or obese (rapid venous access difficult in emergency) Infancy or old age
Social circumstances	Living alone Living far from health facility Without reliable means of transport

Textbox F. Discharge criteria (all of the following conditions must be present)

Clinical	No fever for 48 hours. Improvement in clinical status (general well-being, appetite, haemodynamic status, urine output, no respiratory distress).
Laboratory	Increasing trend of platelet count. Stable haematocrit without intravenous fluids.

Textbox G. Home care card for dengue

Home care card for dengue (please take this card to your health facility for each visit)

What should be done?

- Adequate bed rest
- Adequate fluid intake (>5 glasses for average-sized adults or accordingly in children)
  - Milk, fruit juice (caution with diabetes patient) and isotonic electrolyte solution (ORS) and barley/rice water.
  - Plain water alone may cause electrolyte imbalance.
- Take paracetamol (not more than 4 grams per day for adults and accordingly in children)
- Tepid sponging
- Look for mosquito breeding places in and around the home and eliminate them

What should be avoided?

- Do not take acetylsalicylic acid (aspirin), mefenemic acid (ponstan), ibuprofen or other non-steroidal anti-inflammatory agents (NSAIDs), or steroids. If you are already taking these medications please consult your doctor.
- Antibiotics are not necessary.

If any of following is observed, take the patient immediately to the nearest hospital. These are warning signs for danger:

- Bleeding:
  - red spots or patches on the skin
  - bleeding from nose or gums
  - vomiting blood
  - black-coloured stools
  - heavy menstruation/vaginal bleeding
- Frequent vomiting
- Severe abdominal pain
- Drowsiness, mental confusion or seizures
- Pale, cold or clammy hands and feet
- Difficulty in breathing

Laboratory results monitoring

	1st Visit					
Date						
Haematocrit						
White cell count						
Platelet count						

Textbox H. 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/h for first 10 kg body weight
+ 2 mL/kg/h for next 10 kg body weight
+ 1 mL/kg/h for subsequent kg body weight

*For overweight/obese patients calculate normal maintenance fluid based on ideal body weight (IBW)
(Adapted from reference *16*)

IBW for overweight/obese adults can be estimated on the basis of the following formula

Female: 45.5 kg + 0.91(height -152.4) cm
Male: 50.0 kg + 0.91(height -152.4) cm
(*17*)

Textbox J. Hourly maintenance fluid regime for overweight or obese patients

Estimated ideal body weight, or IBW (kg)	Normal maintenance fluid (ml/hour) based on Holliday-Segar formula	Fluid regime based on 2–3 ml/kg /hour (ml/hour)	Fluid regime based on 1.5 –2 ml/kg/hour (ml/hour)
5	10	10–15	
10	20	20–30	
15	30	30–45	
20	60	40–60	
25	65	50–75	
30	70	60–90	
35	75	70–105	
40	80	80–120	
50	90	100–150	
60	100		90–120
70	110		105–140
80	120		120–150

Notes:
For adults with IBW >50 kg, 1.5–2 ml/kg can be used for quick calculation of hourly maintenance fluid regime.
For adults with IBW≤50 kg, 2–3 ml/kg can be used for quick calculation of hourly maintenance fluid regime.

Textbox K. Estimated ideal body weight for overweight or obese adults

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

Textbox L. Example of a monitoring chart for dengue

Parameters	Time and date					
Body temperature						
Respiratory rate						
Heart rate						
Blood pressure						
Pulse pressure/volume						
Capillary refill time						
Temperature of extremities						
Abdominal pain						
Vomiting						
Bleeding						

Textbox M. Choice of intravenous fluids for resuscitation

Based on the three randomized controlled trials comparing the different types of fluid resuscitation regime in dengue shock in children, there is no clear advantage to the use of colloids over crystalloids in terms of the overall outcome. However, colloids may be the preferred choice if the blood pressure has to be restored urgently, i.e. in those with pulse pressure less than 10 mm Hg. Colloids have been shown to restore the cardiac index and reduce the level of haematocrit faster than crystalloids in patients with intractable shock (*18–20*).

An ideal physiological fluid is one that resembles the extracellular and intracellular fluids compartments closely. However, the available fluids have their own limitations when used in large quantities. Therefore it is advisable to understand the limitations of these solutions to avoid their respective complications.

Crystalloids

0.9% saline ("normal" saline)
Normal plasma chloride ranges from 95 to 105 mmol/L. 0.9% Saline is a suitable option for initial fluid resuscitation, but repeated large volumes of 0.9% saline may lead to hyperchloraemic acidosis. Hyperchloraemic acidosis may aggravate or be confused with lactic acidosis from prolonged shock. Monitoring the chloride and lactate levels will help to identify this problem. When serum chloride level exceeds the normal range, it is advisable to change to other alternatives such as Ringer's Lactate.

Ringer's Lactate

Ringer's Lactate has lower sodium (131 mmol/L) and chloride (115 mmol/L) contents and an osmolality of 273 mOsm/L. It may not be suitable for resuscitation of patients with severe hyponatremia. However, it is a suitable solution after 0.9 Saline has been given and the serum chloride level has exceeded the normal range. Ringer's Lactate should probably be avoided in liver failure and in patients taking metformin where lactate metabolism may be impaired.

Colloids

The types of colloids are gelatin-based, dextran-based and starch-based solutions. One of the biggest concerns regarding their use is their impact on coagulation. Theoretically, dextrans bind to von Willebrand factor/Factor VIII complex and impair coagulation the most. However, this was not observed to have clinical significance in fluid resuscitation in dengue shock. Of all the colloids, gelatine has the least effect on coagulation but the highest risk of allergic reactions. Allergic reactions such as fever, chills and rigors have also been observed in Dextran 70. Dextran 40 can potentially cause an osmotic renal injury in hypovolaemic patients.

DENGUE CASE

ASSESSMENT

PRESUMPTIVE DIAGNOSIS

Live in/travel to dengue endemic area.
Fever and two of the following criteria:
- Anorexia and nausea
- Rash
- Aches and pains
- Warning signs
- Leukopenia
- Tourniquet test positive

Laboratory confirmed dengue
(important when no sign of plasma leakage)

WARNING SIGNS*
- Abdominal pain or tenderness
- Persistent vomiting
- Clinical fluid accumulation
- Mucosal bleed
- Lethargy, restlessness
- Liver enlargment >2 cm
- Laboratory: increase in HCT concurrent with rapid decrease in platelet count

*(requiring strict observation and medical intervention)

CLASSIFICATION

NEGATIVE

Co-existing conditions
Social circumstances

POSITIVE

NEGATIVE

DENGUE WITHOUT WARNING SIGNS

DENGUE WITH WARNING SIGNS

MANAGEMENT

Group A
(May be sent home)

Group criteria
Patients who do not have warning signs
AND
who are able:
- to tolerate adequate volumes of oral fluids
- to pass urine at least once every 6 hours

Laboratory tests
- full blood count (FBC)
- haematocrit (HCT)

Treatment
Advice for:
- adequate bed rest
- adequate fluid intake
- Paracetamol, 4 gram maximum per day in adults and accordingly in children.

Patients with stable HCT can be sent home.

Monitoring
Daily review for disease progression:
- decreasing white blood cell count
- defervescence
- warning signs (until out of critical period).

Advice for immediate return to hospital if development of any warning signs, and
- written advice for management (e.g. home care card for dengue).

Group B
(Referred for in-hospital care)

Group criteria
Patients with any of the following features:
- co-existing conditions such as pregnancy, infancy, old age, diabetes mellitus, renal failure
- social circumstances such as living alone, living far from hospital

Laboratory tests
- full blood count (FBC)
- haematocrit (HCT)

Treatment
- Encouragement for oral fluids. If not tolerated, start intravenous fluid therapy 0,9% saline or Ringer's Lactate at maintenance rate.

Monitoring
Monitor:
- temperature pattern
- volume of fluid intake and losses
- urine output (volume and frequency)
- warning signs
- HCT, white blood cell and platelet counts.

OR: Existing warning signs

Laboratory tests
- full blood count (FBC)
- haematocrit (HCT)

Treatment
Obtain reference HCT before fluid therapy. Give isotonic solutions such as 0.9 % saline, Ringer's 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.

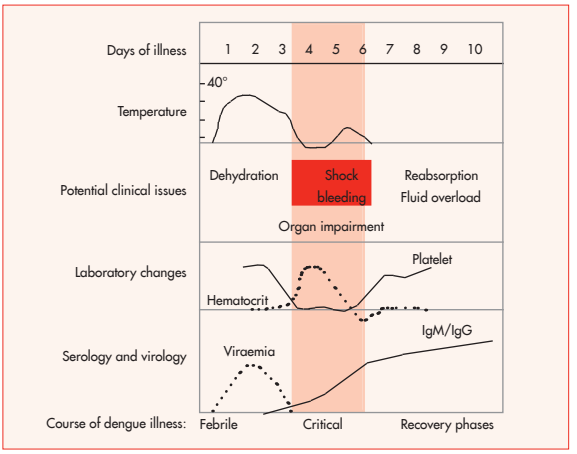
Reassess clinical status and repeat HCT:
- if HCT remains the same or rises only minimally -> continue with 2–3 ml/kg/hr for another 2–4 hours;
- if worsening of vital signs and rapidly rising HCT -> increase rate to 5–10 ml/kg/hr for 1–2 hours.

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 deceases below the baseline value in a stable patient.

Monitoring
Monitor:
- 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).

MANAGEMENT



POSITIVE

SEVERE DENGUE

Group C

(Require emergency treatment)

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

Laboratory tests

- full blood count (FBC)
- haematocrit (HCT)
- other organ function tests as indicated

Treatment of compensated shock

Start IV fluid resuscitation with isotonic crystalloid solutions at 5–10 ml/kg/hr over 1 hour. Reassess patients' condition.

If patient improves:

- IV fluids should be reduced gradually to 5–7 ml/kg/hr for 1–2 hours, then to 3–5 ml/kg/hr for 2–4 hours, then to 2-3 ml/kg/hr for 2–4 hours and then reduced further depending on haemodynamic status;
- IV fluids can be maintained for up to 24–48 hours.

If patient is still unstable:

- 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 hour;
- if there is improvement after second bolus, reduce rate to 7–10 ml/kg/hr for 1–2 hours and 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

Initiate IV fluid resuscitation with crystalloid or colloid solution at 20 ml/kg as a bolus for 15 minutes.

If patient improves:

- give a crystalloid/colloid solution of 10 ml/kg/hr for 1 hour, then reduce gradually as above.

If patient is still unstable:

- review the HCT taken before the first bolus;
- **if HCT was low** (<40% in children and adult females, <45% in adult males) this indicates bleeding, the need to cross-match and transfuse (see above);
- **if HCT was high** compared to baseline value, change to IV colloids at 10–20 ml/kg as a second bolus over 30 minutes to 1 hour; reassess after second bolus.
- **If patient is improving** reduce the rate to 7–10ml/kg/hr for 1–2 hours, then back to IV cystalloids and reduce rates as above;
- **if patient's condition is still unstable**, repeat HCT after second bolus.
- **If HCT decreases**, this indicates bleeding (see above);
- **if HCT increases**/remains high (>50%), continue colloid infusion at 10–20 ml/kg as a third bolus over 1 hour, then reduce to 7–10 ml/kg/h 1–2 hours, then change back to crystalloid solution and reduce rate as above.

Treatment of haemorrhagic complications

Give 5–10 ml/kg of fresh packed red cells or 10–20 ml/kg of fresh whole blood.