Republic of the Philippines
Department of Health
OFFICE OF THE SECRETARY

FEB 13 2018

ADMINISTRATIVE ORDER
No. 2018- 0005

SUBJECT: **Interim Guidelines on Dengue Diagnosis, Referral and Management for Dengvaxia Vaccinated Individuals**

I. RATIONALE

The CYD-Tetravalent Dengue Vaccine (Dengvaxia) was first introduced in the country through a school-based immunization of Grade 4 students, 9 years and above, in all public elementary schools in Regions 3, 4A and NCR. It was then followed by a community-based immunization in Cebu Province of Region 7 and in 4 cities in NCR. A total of 830, 000 individuals were vaccinated in these programs, excluding those vaccinated by the private sector.

In November 29, 2017, Sanofi released an update which confirmed that Dengvaxia provides persistent protective benefit against dengue fever in those who had prior Dengue infection. However, for those not previously infected by dengue virus, more cases of severe disease could occur following vaccination upon a subsequent dengue infection in the longer term.

II. OBJECTIVE

This issuance shall provide technical guidance to health workers on the diagnosis, referral, and management of Dengvaxia-vaccinated individuals who acquired dengue infection.

III. SCOPE

This issuance shall apply to the Department of Health (DOH) - Central Office, Regional Offices, DOH-ARMM, Philippine Health Insurance Corporation (PhilHealth), public hospitals, private hospitals & clinics, Health Centers/ Rural Health Units (RHUs), other government agencies, LGUs and communities.

IV. DEFINITION OF TERMS

1. **Fluid resuscitation**- is a strategy in which larger volumes of fluids (e.g. 10-20 ml/kg boluses) are administered for a limited period of time under close supervision, to evaluate the patient's response and to avoid the development of pulmonary edema.

2. **Rapid Diagnostic Test (RDT)-** a collection of reagents and other materials for in-vitro diagnosis, intended to be used for detection of either antigen or antibody from clinical samples, usually blood, within a shorter period.

3. **Dengue Non-structural protein 1 (NS1) RDT**- is a rapid test used to detect the Dengue virus non-structural protein 1 antigen in human serum, plasma or whole blood to suggest early acute dengue infection.

4. **Dengue IgM/IgG RDT**- is a rapid test used to detect IgM or IgG antibodies to Dengue virus in human serum, plasma or whole blood. The presence of IgM antibodies to Dengue Virus (DV) is consistent with acute-phase infection, while IgG antibodies become detectable on 3 to 7 days following infection and may remain detectable for up to 6 months or longer following disease resolution.

5. **Homecare card-** an important checklist reminder given to suspect dengue patient before leaving the health facility.

6. **Plaque Reduction Neutralization Test (PRNT)**- considered to be the "gold standard" to characterize and quantify circulating level of anti-DENV neutralizing antibody (NAb).

V. GENERAL GUIDELINES

1. All Dengvaxia vaccinees shall be identified and issued with a Dengvaxia identification card.
2. All Dengvaxia vaccinees shall be monitored for any possible dengue infection and other diseases in a span of five years or more.
3. Monitoring and assessment of dengue signs and symptoms shall be a shared responsibility among health workers, school teachers and parents.
4. Capacity building of health workers, school teachers, parents, private practitioners and other concerned stakeholders in the early recognition of dengue infection , proper home care management of mild infections, and triaging for referral shall be one of the priorities of DOH; and shall be achieved through inter-agency collaboration and public-private partnership.
5. Children and communities shall be educated on dengue to empower them in their own care and prepare them to seek medical care at the right time, avoid self-medication, identify warning signs and symptoms, etc.
6. All health centers/RHUs shall be capacitated to detect early dengue infection using the Dengue NS1 RDT. The Dengue NS1 RDT shall be recognized as primary screening test that shall be provided to all health centers/RHUs, public hospitals and/or PhilHealth-accredited private hospitals for free.
7. Dengvaxia vaccinees with symptomatic dengue infection shall be prioritized to receive laboratory and medical services in all health centers/ RHUs, public hospitals and PhilHealth-accredited hospitals.
8. The two-way referral system from school or community to the nearest health center/ RHU, public hospital or private hospital shall be strengthened.
9. Clinical assessment, laboratory diagnosis, referral and management of dengue vaccinees with dengue infection shall be in accordance with Administrative Order (AO) No. 2012-006: Revised Dengue Clinical Case Management Guidelines 2011, with minor updates and revisions as discussed in the specific guidelines of this AO.

VI. SPECIFIC GUIDELINES

A. Identification of Dengvaxia vaccinated individuals

1. All Dengvaxia-vaccinated individuals under the school-based and community-based immunization program, shall be validated by the respective schools, health centers/ RHUs; and shall be issued with vaccination cards (Refer to Annex 1: Dengvaxia Identification Card).
2. Individuals who received Dengvaxia from private physicians and private schools shall be registered to the health center/ RHU nearest to their place of residency.
3. Private physicians and private schools shall provide lists of Dengvaxia-vaccinated individuals) to the Municipal Health Office (MHO)/ City Health Office (CHO) nearest to their place.
4. The name of the child shall be validated from the Dengvaxia masterlist. If the child is not listed in the masterlist, the old identification card, or the patient record duly signed by the administering physician shall be used as proof of identification.
5. The Dengvaxia card shall be presented upon consultation to avail laboratory and medical services.

B. Assessment and Diagnosis

1. Individuals with chief complaints similar to signs and symptoms of dengue shall be immediately asked regarding previous history of vaccination.
2. If an individual is confirmed to have been vaccinated with Dengvaxia and exhibited signs and symptoms of dengue, prioritization shall be done to rule out possible dengue infection (Refer to Annex 2: Guide to Stepwise Approach to Assessment of Dengue).
3. Dengue patient shall be categorized according to level of severity and case definitions as follows:

a) dengue without warning signs:

i. suspect dengue

- patient who received at least one dose of the vaccine, with acute febrile illness of **1-7** days duration plus **two** of the following: headache, body malaise, retro-orbital pain, myalgia, arthralgia, anorexia, nausea, vomiting, diarrhea, flushed skin, rash (petechial, Hermann's sign)

ii. probable dengue

- a suspect case plus laboratory test: Dengue NS1 antigen test and at least CBC (leukopenia with or Without thrombocytopenia) and/or dengue IgM antibody test.

iii. confirmed dengue

- a suspect case or probable case with positive result from viral culture **and/or** Polymerase Chain Reaction (PCR).

b) dengue with warning signs

- a patient who received at least one dose of dengue vaccine, with acute febrile illness of 1-7 days plus any of the following:
  - abdominal pain or tenderness

- persistent vomiting
- clinical fluid accumulation (ascites)
- mucosal bleeding
- lethargy or restlessness
- liver enlargement > 2 cm
- increase in haematocrit concurrent with rapid decrease in platelet count

c) severe dengue

severe plasma leakage leading to

- shock (DSS)
- fluid accumulation with respiratory distress

severe bleeding

as evaluated by clinician

severe organ impairment

- Liver: AST or ALT >=1000
- CNS: e.g. seizures, impaired consciousness
- Heart and other organs (e.g. myocarditis, renal failure)

4. Case classifications and duration of illness shall be the basis to request for laboratory test (Refer to Annex 3 Dengue Patient Diagnosis and Referral Algorithm). Descriptions of tests as follows:

Test	Description	Remarks
1.Dengue NS1 RDT	• Requested between 1-5 days of illness • Used to detect dengue NS1 virus antigen during early phase of acute infection • Test is free in health centers and selected public and private hospitals	Must be done
2.Other tests: -Total White Blood Cell (WBC) count -Platelet -Hematocrit	• Routinely used in health centers and hospitals as standard dengue diagnostic tests • Determine trends of decreasing WBC, decreasing platelet and increasing hematocrit • Requested on the first visit	Must be done
3.Dengue IgM/IgG RDT	• Requested beyond five days of illness • Used to detect dengue antibodies during the acute late stage of dengue infection (IgM) and to determine previous infection (IgG) • May give false positive result due to antibodies induced by dengue vaccine • May cross react with other arboviral diseases such as Chikungunya and Zika • DOH augmentation is limited to selected government hospitals only	May be done

5 6. The Dengue NS1 RDT can be used in combination with Dengue IgM/IgG RDT. The combination test is supported only by the Department of Health at the hospital level. Results can be interpreted as follows:

Rapid Diagnostic Test (RDT)			Interpretation
NS1 Ag	Dengue IgG/IgM		
	IgM	IgG	
+	+	-	Acute early infection
-	+	-	Primary dengue infection
+	+	+	Secondary dengue infection
-	+	+	Acute dengue infection, secondary infection
+	-	-	Acute primary, early phase
-	-	-	May mean that individual does not have dengue infection; otherwise, the level of antigen and antibody may be too low to measure

6 7. For dengue with warning signs and severe dengue other tests and procedures can done depending on discretion of the attending physician.

7 8. Three (3) ml of blood samples shall be collected (two sets-one on admission, one before discharge) and shall be submitted to the Research Institute for Tropical Medicine (RITM) for the following tests:

a) Polymerase Chain Reaction (PCR) -used to confirm dengue virus.
b) Plaque Reduction Neutralization Test (PRNT)- is the gold standard to characterize and quantify circulating level of anti-DENV neutralizing antibody (NAb).

C. Referral

1. Referral of dengue patient from the health center/RHU to hospital shall be based on the following criteria (1) severity of disease and (2) phase of dengue infection. Phases of dengue infection shall guide the health worker according to the following:

a) **Febrile Phase**
- Usually lasts **2-7 days**
- Mild haemorrhagic manifestations like petechiae and mucosal membrane bleeding (e.g nose and gums) may be seen.
- Difficult to distinguish dengue with other non-dengue febrile diseases thus a positive tourniquet test increases the probability of dengue.
- Oral Rehydration Solution shall be used as needed to keep the body hydrated.
- Observe for the following:
  - Signs of dehydration and neurological disturbances
  - High fever that may cause seizures in young children
  - Warning signs

Note: Monitoring of warning signs is crucial to recognize its progression to critical phase.

b) **Critical Phase**

- This is the phase when patient can either improve or deteriorate.
- **Defervescence** is known as the period in which the body temperature (fever) drops to **almost normal** (between 37.5 to 38°C).
- Those who will improve after defervescence will be categorized as **Dengue without Warning Signs**, while those who will deteriorate will manifest warning signs and will be categorized as **Dengue with Warning Signs** or some may progress to **Severe Dengue.**
- Regularly monitor the body temperature to determine when the patient reaches defervescence.

> **Note: When warning signs** occur, **severe dengue** may follow near the time of defervescence which usually happens between **24 to 48 hours.**

i. Patient shall be brought immediately to the hospital if any of the following occurs: no clinical improvement, deterioration around the time of defervescence, severe abdominal pain, persistent vomiting, cold and clammy extremities, lethargy or irritability/restlessness, bleeding (i.e black stool or coffee-ground vomiting), no passing of urine for more than 4-6 hours.

ii. Use the following criteria to decide when to transfer the patient to the emergency unit:

- Early presentation with shock (on day 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)

c) **Recovery Phase**

- Happens in the next **48 to 72 hours** after critical phase in which the body fluids go back to normal.
- Patients' general well-being improves, appetite returns, gastrointestinal symptoms abate, haemodynamic status stabilizes and diuresis ensues.
- Some patients may have classical rash of "isles of white in the sea of red" or generalized pruritus.
- The WBC usually starts to rise soon after defervescence but the normalization of platelet counts typically happens later than that of WBC.

2. Patient shall be referred using the dengue vaccine referral form template (see Annex 5 Dengue Vaccine Referral Form Template) and through the dengue fast lane established in hospitals. Summary of referral actions are as follows:

Phase of Infection	Severity of Disease	Action
1. Febrile	Without Warning Signs	-Shall be managed at the health center or hospital out-patient
	With warning signs	-Shall be immediately referred to the nearest hospital for admission
2.Critical	Without warning signs	-Shall be managed at the health center or hospital out-patient
	With warning signs	Shall be immediately referred to the hospital for admission
	Severe Dengue	-Shall be immediately referred to the emergency unit
3.Recovery Phase	With warning signs	-Shall be stabilized first before transferring to the nearest government hospital if initially admitted in the private hospital
	Severe Dengue	-Shall be stabilized as needed -No need to transfer

3. Hospitals shall ensure the availability of dengue fast lanes and hospital beds for dengue patients referred in the hospital.
4. There shall be a designated area in the hospital to cohort dengue patients and closely monitor those who will shock.
5. Doctors and nurses shall be trained on Revised Dengue Clinical Management Guidelines to equip them to recognize high-risk patients and institute appropriate monitoring and treatment.

D. Management and Treatment

Classification and guidelines based on management and treatment of dengue patient are as follows:

1. **Group A- patients who may be sent home**
   a) These are patients who:
      - Are able to tolerate adequate volumes of oral fluids
      - Pass urine atleast every 6 hours
      - Do not have any of the warning signs particularly when the fever subsides.
      - Have stable haematocrit
   b) Refer to Annex 6: Group A- Action Plans For Patient Who May Be Sent Home

2. **Group B- patient who should be referred for in-hospital management**

   a) Patients shall be referred immediately to in-hospital management if they have the following conditions:
      -Warning signs
      -Without warning signs but with co-existing conditions that may make dengue or its management more complicated (such as pregnancy, infancy, old age, obesity, diabetes mellitus, hypertension, heart failure, renal failure,

chronic haemolytic diseases such as sickle- cell disease and autoimmune diseases, etc.)
-Social circumstances such as living alone or living far from health facility or without a reliable means of transportation.
-The referring facility has no capability to manage dengue with warning signs and/or severe dengue.

b) These patients shall be referred and admitted for in-hospital management using the dengue patient referral form (refer to Annex 5: Dengue Referral Form Template).
c) Refer to Annex 7: Group B- Action Plans For Patient Without Warning Signs But With Co-Existing Conditions.
d) Refer to Annex 8: Group B- Action Plans For Other Dengue Patients Without Warning Signs Who Are Admitted But Without Shock.
e) Refer to Annex 9: Group B- Action Plans For Patients Without Warning Signs.

3. **Group C- patient with severe dengue requiring emergency treatment and urgent referral**

a) These are patients with severe dengue who require emergency treatment and urgent referral because they are in the critical phase of the disease and have the following:
   - 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)

b) Patients in Group C shall be immediately referred and admitted in the hospital **within 24 hours.**
c) All patients with severe dengue shall be referred by the health center/ RHU to a hospital with access to blood transfusion facilities.
d) Fluid resuscitation shall be clearly separated from simple fluid administration. Judicious intravenous **fluid resuscitation** is the essential and usually sole intervention required. The goals of fluid resuscitation include:
   - Improving central and peripheral circulation- i.e. decreasing tachycardia, improving BP and pulse volume, warm and pink extremities, a capillary refill time < 2 seconds
   - Improving end-organ perfusion- i.e. achieving a stable conscious level (more alert or less restless), and urine output $\geq$ 0.5 ml/kg/hour or decreasing metabolic acidosis.

e) Refer to Annex10: Group C-Treatment For Patient Admitted To Hospital With Compensated Shock
f) Refer to Annex 11: Group C- Treatment For Patient Admitted To The Hospital With Hypotensive Shock (in profound shock; undetectable pulse and BP)
g) Refer to Annex12: Treatment of Haemorrhagic Complications

4. Patient shall be discharged if all of the following conditions are present:
   - No fever for at least 48 hours
   - Improvement in clinical status (general well-being, appetite, hemodynamic status, urine output and no respiratory distress)

- Increasing trend of platelet count
- Stable haematocrit without IVF

VII. ROLES AND RESPONSIBILITIES

A. Department of Health

1) Infectious Disease Prevention and Control Division (IDPCD), Disease Prevention and Control Bureau (DPCB)

a) Develops guidelines, policies, standards for diagnosis, referral and management of dengue infection.
b) Provides Dengue NS1 RDT in all DOH Regional Offices.
c) Coordinates with Logistics Management Division (LMD) on the distribution of NS1 RDT and other dengue commodities to all DOH Regional Offices.
d) Coordinates with RITM for the External Quality Assurance (EQA) of Dengue NS1 RDT.
e) Monitors and evaluates the implementation of dengue diagnostic tests, referral and case management guidelines.

2) Expanded Program on Immunization (EPI), Women, Men and Children Health and Development Division (WMCHDD)

a) Oversee the overall implementation of dengue vaccination program.
b) Provide masterlist of vaccinees.
c) Disseminate guidelines to all DOH Regional Offices EPI coordinators and concerned stakeholders.

3) Epidemiology Bureau

a) Oversees the implementation of Dengvaxia enhanced Adverse Event Following Immunization (AEFI) surveillance at the local, sub-national and national levels.
b) Collects AEFI reporting forms, analyze reports and submit to Family Health Office, DPCB, Family Health Office (FHO), Food and Drug Administration (FDA) and to Secretary of Health as needed.
c) Provide report to the Dengue Prevention and Control Program, FHO, DPCB and Secretary of Health as needed.
d) Convenes the National AEFI Committee for the causality assessment of reported AEFI cases.

4) Health Promotion and Communication Service

a) Develops Dengvaxia identification card.
b) Develops Homecare Card for distribution to public hospitals, private hospitals/clinics and health centers/ RHUs.
c) Develops dengue diagnosis, referral and case management advocacy, communication plan and IEC materials for distribution to DOH Regional Offices and health centers/RHUs.

5) Logistics Management Division (LMD) shall be responsible for timely delivery and adequate supply of logistics including NS1 RDT to various regional and local offices.

6) **Bureau of Local Health System Development (BLHSD)** shall ensure the preparedness and acceptance of various local government units for the diagnosis, referral and management of Dengvaxia vaccinated individuals who may acquire dengue infection.

7) **Health Human Resource Development Bureau (HHRDB)**
   a) Provide assistance in the development of training modules/ learning materials and conduct of capacity building of health workers, teachers, parents, other stakeholders and community on dengue patient care, referral and management.
   b) Establish a directory and partnership with academe and other learning institutions to disseminate and provide trainings for this AO.
   c) Develop learning materials/ courses with academe and other learning institutions.

8) **Department of Health - Regional Offices (DOH-RO)**
   a) Conduct capacity building of health workers, teachers and other stakeholders on the diagnosis, referral and management of Dengvaxia -vaccinated individuals.
   b) Enter through a Memorandum of Agreement (MOA) with private hospitals and clinics for the payment scheme of vaccinees who may be admitted due to dengue infection.
   c) Ensure the availability of Dengue NS1 RDT in all public hospitals, RHUs, and selected private hospitals.
   d) Monitor and evaluate the implementation of these guidelines.
   e) Regularly analyse data and submit report to DOH Central Office Dengue Program, FHO, LMD, Epidemiology Bureau and HPCS.

9) **Research Institute for Tropical Medicine**
   a) Serves as the national reference laboratory for dengue.
   b) Performs dengue confirmatory tests such as PCR, PRNT and IgM/IgG ELISA.
   c) Performs Dengue NS1 RDT External Quality Assurance (EQA).
   d) Regularly analyses data and submits report to Dengue Program, Epidemiology Bureau and Secretary of Health as needed.

10) **PhilHealth** shall develop a payment scheme including an outpatient package for Dengvaxia-vaccinated individuals.

11) **DOH and Local Government Hospitals**
   a) Recognize the result of Dengue NS1 RDT from RHUs.
   b) Prioritize the admission of referred Dengvaxia vaccinated individuals from RHUs, schools, private clinics and private hospitals.
   c) Manage dengue patients and ensure No Balance Billing policy among vaccinees.
   d) Submit report to DOH Epidemiology Bureau, DOH Regional Office and PhilHealth.

12) **Philippine Blood Center** shall ensure the availability of blood and blood products for dengue patients whenever blood transfusion is needed.

13) **Local Government Units (LGUs)**
   a) Ensure the adoption and implementation of this Administrative Order to health centers/ RHUs nationwide.

b) Collaborate with DOH to ensure that the LGU health workers are capacitated on the early identification of dengue patient, referral and management.
c) Collaborate with DOH to identify and report implementation gaps of this AO and develop and implement smart solutions.
d) Coordinate with DOH for needed technical assistance to strengthen the two-way referral mechanism from health centers/ RHUs to public or private hospitals.
e) Coordinate with DOH for needed technical assistance to develop local public-private partnership to synergize resource for dengue referral and management.

14) Health Center/ Rural Health Units (RHUs)

a) Closely coordinate with public schools, private schools and the community to identify and monitor Dengvaxia vaccinated individuals.
b) Shall dispense Dengvaxia identification card to all validated Dengvaxia vaccinated individuals.
c) Serve as the primary health facility to immediate diagnose dengue through Dengue NS1 RDT and provide management and HOMECARE CARD to mild dengue infections.
d) Guide teacher and parents to refer vaccinated individuals from primary health facility to government and/ or private hospitals as needed.

15) Private Hospitals

a) Collaborate with Department of Heath (DOH) to provide laboratory and medical services for Dengvaxia vaccinated individuals.
b) Accept admission of referred Dengvaxia vaccinated individuals from RHUs, schools, private clinics and private hospitals in accordance with DOH policies.
c) Submit report to DOH Epidemiology Bureau, DOH Regional Office and PhilHealth.

16) Department of Education

a) Closely coordinate with health centers/ RHUs in the identification and monitoring of Dengvaxia vaccinated individuals.
b) Collaborate with DOH and health centers/ RHUs to capacitate school teachers and parents on dengue diagnosis, referral and management.

IX. REPEALING CLAUSE

All order and other issuances inconsistent with this administrative order are hereby revised, modified or rescinded accordingly. All other provisions of existing issuances which are not affected by this order shall remain valid and in effect.

X. EFFECTIVITY CLAUSE

This Administrative Order shall take effect immediately upon approval.

FRANCISCO T. DUQUE III, MD, MSc
Secretary of Health

Annex 1: Dengvaxia Identification Card

No. _____

DENGUE IMMUNIZATION

IDENTIFICATION CARD

DOH

ID NUMBER

NAME

SCHOOL :

GRADE : SEX :

ADDRESS :

NAME OF PARENTS/ GUARDIAN :

CONTACT NUMBER :

Dengue Immunization Record

Doses	Date Given	Place Given (If Hospital/ RHU/Private Clinic)
1		
2		
3		

ANO ANG DAPAT GAWIN KAPAG NAKITAAN NG SINTOMAS NG DENGUE ANG INYONG ANAK?

- Dalhin kaagad at ipakonsulta sa pinakamalapit na health center o ospital ang inyong anak sa unang araw pa lang nang pagkakaroon ng mataas na lagnat upang maiwasan ang komplikasyon.
- Iwasan ang pag-inom ng gamot na hindi inireseta ng doktor.
- Kakaunti lang sa mga nagkaka-Dengue ang nagiging grabe o severe.
- Panatilihing malusog ang katawan ng mga bata sa tamang nutrisyon.

If symptoms persist, immediately bring the child to nearest health facility.

ISSUED BY/ DATE ISSUED

DOH HOTLINE: (02) 711-1001 (02) 711-1002 0920-1107498 0915-7725621

Annex 2: Guide for Stepwise Approach to Assessment of Dengue

Step I – Overall assessment	
I.1	History, including symptoms, past medical and family history
I.2	Physical examination, including full physical and mental assessment
I.3	Investigation, including routine laboratory tests and dengue-specific laboratory tests
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 (1): - be sent home (Group A) - be referred for in-hospital management (Group B) - require emergency treatment and urgent referral (Group C)

Step 1: Overall Assessment

5.1 History

- Date of onset of fever/ illness
- Quantity of oral intake
- Assess for warning signs
- Diarrhea
- Seizures, impaired consciousness, behavioural changes
- Urine output (frequency, volume and time of last voiding)
- Other important relevant histories:
    - Familymembers or neighbors with dengueor travel to dengue-endemic areas
    - Co-existing conditions such as infancy, pregnancy, obesity, diabetes milletus, hypertension, etc.
    - Jungle trekking and swimming in waterfall (consider leptospirosis, typhus, malaria)
    - Recent unprotected sexual or drug use behaviour (consider acure HIV seroconversion illness)

5.2 Physical Examination

- Assess mental state and Glascgow Coma Scale (GSC) score
- Assess hydration status
- Assess hemodynamic status
- Look out for tachypnea/acidotic hreathing/ pleural effusion
- Check for abdominal tenderness/ hepatomegaly/ ascites
- Examine for rash and bleeding manifestations

- Perform tourniquet test (repeat if previously negative or there is no bleeding manifestation)

5.3 Investigation (Laboratory Diagnosis)

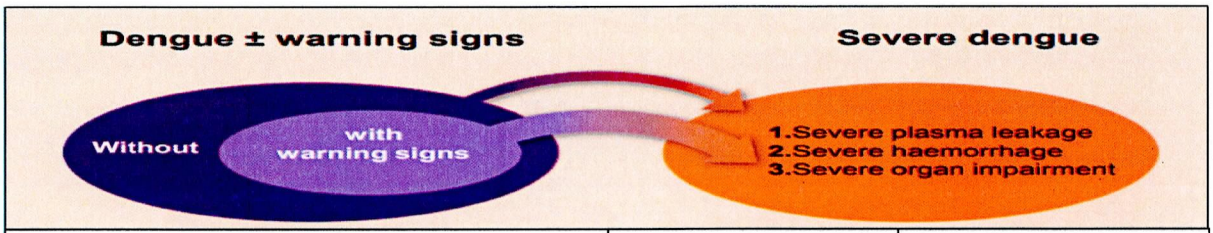
- **Dengue diagnostic tests**
  - Dengue NS1 RDT
  - Dengue IgM/IgG

- **Complete Blood Count (CBC)**
  - CBC should be done at the first visit to establish baseline data of WBC, platelet and hematocrit

Step 2: Assessment of Disease Phase and Severity

Determine:

- Is it dengue? (without warning signs. with warning signs, severe)
  (suspect, probable, confirmed)
- Which phase of dengue?(febrile/critical/ recovery)
- Are there warning signs?
- What is the hydration and hemodynamic status?
- Does the patient require admission?



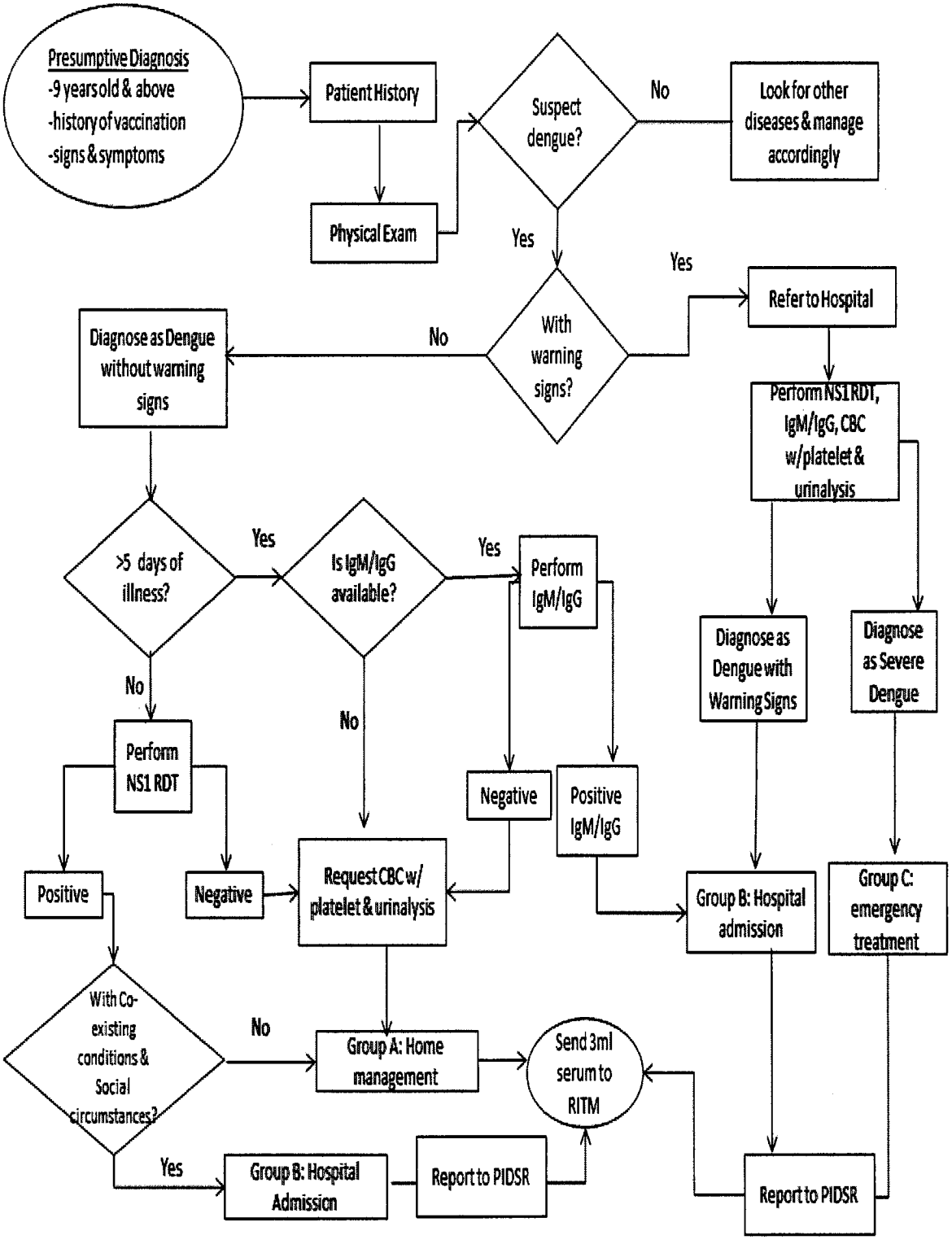
Dengue without warning signs			Dengue with warning signs	Severe dengue
Suspect	**Probable**	**Confirmed**		
Received at least 1 dose of dengue vaccine with fever for **1-7** days duration plus **two** of the following: headache, body malaise, retro-orbital pain, myalgia, arthralgia, anorexia, nausea, vomiting, diarrhea, flushed skin, rash (petechial, Hermann's sign).	A suspect case plus laboratory test: Dengue NS1 antigen test and at least CBC (leukopenia with or Without thrombocytopenia) or dengue IgM antibody test (optional).	A suspect case or probable case with positive result from viral culture **and/or** Polymerase Chain Reaction (PCR) **and/or** Nucleic Acid Amplification Test- Loop Mediated Amplification Assay (NAAT-LAMP) and/ or Plaque Reduction Neutralization Test (PRNT)	A vaccinee, who received at least one dose of dengue vaccine, with acute febrile illness of 1-7 days plus any of the following: abdominal pain or tenderness, persistent vomiting, clinical signs of fluid accumulation (ascites), mucosal bleeding, lethargy or restlessness, liver enlargement, increase in haematocrit and/or decreasing platelet count.	A vaccinee, who received at least one dose of dengue vaccine, with acute febrile illness of 1-7 days duration and any of the clinical manifestations for dengue with or without warning signs, plus any of the following: **severe plasma leakage leading to** shock fluid accumulation with respiratory distress **severe bleeding** **severe organ impairment** Liver: AST or ALT ≥ 1000 CNS: e.g. seizures, impaired consciousness Heart: e.g. myocarditis Kidneys: e.g. renal failure

Step 3: Management

a. Disease notification
b. Management decisions- depending on the clinical manifestations and other circumstances, patient may:

- be sent home (Group A);
- be referred for in-hospital management (Group B)
- required emergency treatment and urgent referral (Group C)

Annex 3: Dengue Patient Diagnosis and Referral Algorithm



Annex 4: Dengue Homecare Card

DENGUE HOME CARE CARD

Part I

Your child or family member might have dengue. It is important for you to carefully monitor them at home for the next 1-7 days.

1. What should be done?
   - Keep your body HYDRATED because this will save your life.
   - Your first aid is Oral Rehydration Solution (ORESOL), drink it as follows:

Calculation of Oral Rehydration Fluids Using Weight (Ludan Method)

Body Weight (kg)	ORS to be given
> 3-10	100 ml/kg/day
> 10-20	75 ml/kg/day
> 20-30	50-60 ml/kg/day
> 30-60	40-50 ml/kg/day

Source: Ludan A. Chapter 41: Pediatric Fluid and Electrolyte Therapy. *Textbook of Pediatrics and Child Health*. del Mundo F, Estrada FA, Santos-Ocampo PD, Navarro XR, editors. Manila: JMC Press. Fourth edition. 2000:1485-1499

   - You can also take water, milk, coconut water, rice water, fruit juice in moderation
   - Do not take too much SPORTS drink due to its high osmolarity which may cause danger
   - Too much plain water alone may cause electrolyte imbalance
   - Monitor the volume and frequency of your urine. This will guide you and your physician to know if your body is well hydrated.

   - Adequate bed rest is important to keep your body healthy.
   - Take paracetamol not more than 3 grams/day for adult and give paracetamol for children accordingly.
   - Tepid sponging can be done to lower down fever.
   - Use insect repellent and wear long clothes to prevent the dengue virus from spreading from you to other members of your household through mosquito bites.
   - Remove mosquito breeding places in and outside the home.

2. **What should be avoided?**
   - Do not take aspirin (acetylsalicylic acid), mefenamic acid, ibuprofen or other NSAIDS or steroids.
   - Antibiotics are not necessary
   - If you have already taking these medications, consult your doctor.

3. **What is important?**
   - Constantly monitor your body temperature and look out for **defervescence.**
   - Defervescence is known as the period in which the body temperature (fever) drops to **almost normal** (between 37.5 to 38°C). This happens between 3-7 days of illness.

- Those who will improve after defervescence can stay at home, while those who will deteriorate must be immediately taken to the hospital.
- Constantly monitor warning signs.

4. What is critical?

If any of the following warning signs are observed, you must be immediately taken to the nearest hospital within **24 hours:**

- Bleeding
  - red spots or patches on the skin
  - bleeding from nose or gums
  - vomiting blood
  - black- coloured stools
  - heavy menstruation/ vaginal bleeding
- Frequent vomiting or not being able to drink
- Severe abdominal pain
- Drowsiness, mental confusion or seizures
- Pale, cold or clammy hands and feet
- Difficulty in breathing
- Posture dizziness
- No urine output for 4-6 hours

In case of emergency, contact me: Name :_____

Phone number :_____

DENGUE HOME CARE CARD

Part II

For patient/relative: Urine Output Monitoring Table

Time (hh:mm)	Volume (ml)						
	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
ex. 8:00am	10ml						

For physician/health worker: Laboratory Result Monitoring Table

Date/ Time	Laboratory Result						
	NS1 antigen	IgM/IgG	PCR	PRNT	Hct	WBC	Platelet

Annex 5: Dengue Referral Form Template

Dengue Vaccine Referral Form

Name of Receiving Unit:_____
Address:_____

Name of Patient: _____ **Age:**____ **Sex**_____ **ID No.** _____
Last Name First Name M.I.

Address of Patient: _____
No. Street Barangay

_____
City/ Municipality Province

Vital Signs:_____ **BP:**____ **Temp:**____ **RR:**____ **PR:**____ **Weight:** ____ **Height:**_____ **BMI:**_____

Pertinent Findings:_____
_____

Intervention/Laboratory Work ups:_____
_____

Impression:_____

Reason for Referral:_____

Name of Referring Unit:_____ **Date:**_____

Address:_____ **Time:**_____
Contact No:_____ **Email address:**_____
Name of Physician:_____ **Signature:**_____

Dengue Vaccine Referral Reply Slip

From:_____ **Date:**_____ **Time:**_____
To:_____ **Address:**_____
Name of Patient:_____
Action/s Taken:

_____ Admitted	____ For Follow-up
_____ Sent Home	____ For Observation
_____ Against Medical Advice	____ Reffered to other facility
_____ Died	____ Others, specify:_____

Name of Physician:_____ **Signature:**_____

Annex 6: Group A- Action Plans For Patient Who May Be Sent Home

1. Patient shall be instructed to take Oral Rehydration Solution (ORS), coconut water, fresh fruit juices, etc to replace fluid loss from fever and vomiting.
2. Give Oral Rehydration Solution (ORS) based on weight as follows:

Calculation of Oral Rehydration Fluids Using Weight (Ludan Method)	
Body Weight (kg)	ORS to be given
> 3-10	100ml/kg/day
> 10-20	75 ml/kg/day
> 20-30	50-60 ml/kg/day
> 30-60	40-50 l/kg/day

3. Osmolarity or ORS containing sodium maybe be reduced from 45 to 60 mmol/liter.
4. Patients shall be instructed to avoid sport drinks and commercially carbonated drinks.
5. Patient shall be instructed to monitor urine output and volume. Sufficient oral fluid intake should result in a urinary frequency of atleast 4-6 times per day.
6. Paracetamol can be prescribed to high fever if the patient feels uncomfortable. The recommended dose is 10 mg/kg/dose, not more than 3-4 times in 24 hours in children and not more than 3g/day in adults.
7. Patients with ≥ 3 days of illness shall be reviewed for disease progression (decreasing WBC & platelet count, increasing haematocrit, defervescence & warning signs) until they are out of the critical period.
8. Relatives or caregivers shall be instructed to bring the patient immediately to the hospital if any of the following occurs: no clinical improvement, deterioration around the time of defervescence, abdominal pain, persistent vomiting, cold and clammy extremities, lethargy or irritability/ restlessness, bleeding (e.g. black stools or coffee-ground vomiting), shortness of breath, not passing urine for more than 4-6 hours.
9. Patient shall receive a Homecare Card before leaving the health facility and shall be instructed to return as necessary.
10. Patient shall report back to the health facility after seven days.

Annex 7: Group B- Action Plans for Patient Without Warning Signs But With Co-Existing Conditions

1. Patient shall be encouraged to take oral fluids. If not tolerated, intravenous therapy shall be started using 0.9% NaCl (saline) or Ringer's Lactate with or without glucose at the appropriate maintenance rate (see table below).

Table 1. Normal maintenance fluid per hour can be calculated based on the following* (Equivalent to Holiday-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 patient calculate normal maintenance fluid based on ideal body weight (IBW) using the following formula:

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

2. The ideal body weight shall be used for calculation of fluid infusion for obese and overweight patients.
3. The fluid infusion shall be revised frequently since patient may be able to take oral fluids after a few hours of intravenous therapy.
4. The minimum volume required to maintain good perfusion and urine output shall be used.

Note: Intravenous fluids are usually needed for only 24-48 hours.

Annex 8: Group B- Actions For Other Dengue Patients Without Warning Signs Who Are Admitted ButWithout Shock

1. Isotonic solutions (D5 LRS, D5 Acetated Ringers, D5 NSS/ D5 0.9NaCl) are appropriate.
2. Maintenance IVF shall be computed using the caloric-expenditure method (see table 1 and below).

Table 2.Calculation of Maintenance Intravenous Fluid Infusions (Holiday and Segar Method)

Body Weight (kg)	Total Fluid Replacement (ml/day)
0-10	100 ml/kg
>10-20 kg	1,000 ml + 50 ml/kg for each kg >10 kg
>20 kg	1,500 ml + 20 ml/kg for each kg > 20 kg

3. If the patient shows signs of mild dehydration but is NOT in shock, the volume needed for mild dehydration is added to the maintenance fluids to determine the total fluid replacement (TFR) using the formula:

TFR= Maintenance IVF+ Fluids as for Mild dehydration

*where the volume of fluid for mild dehydration is computed as follows:

Infant	50 ml/kg
Older Child or Adult	30 ml/kg

4. One-half of the computed TFR shall be given in 8 hours and the remaining one-half shall be given in the next 16 hours.

Sample computation for a 10 kg patient with dengue and mild dehydration:

Step 1: Compute for Total Fluid Replacement:
TFR= maintenance fluid + fluid for mild dehydration
= (100x10) +(50x10kg)
= 1000+500
= 1500 ml

Step 2: Compute one-half of TFR
TFR/2 = 1500 ml/2 =750ml

Step 3: Volume to be given in the first 8 hours:
= 750 ml in 8 hours
= 93 ml/hour for 8 hours

Step 4: Volume to be given in the next 16 hours
= 750 ml in 16 hours
=46 ml per hour for 16 hours

5. Periodic assessment is needed so that fluid may be adjusted accordingly.
6. Clinical parameters should be monitored closely and correlated with the haematocrit. This will ensure adequate hydration, avoiding under and over hydration.
7. The IVF rate may be decreased anytime as necessary based on clinical assessment.
8. If the patient shows signs of deterioration, follow Management for Compensated or Hypotensive Shock, whichever is applicable.
9. All admitted Group B patients without warning sings should be monitored by health workers for the following:
    - Temperature pattern
    - Volume of fluid intake and losses
    - Urine output- volume and frequency
    - Warning signs
    - Hematocrit, WBCs and platelet counts

Annex 9: Group B- Action Plans for Patients With Warning Signs

Remember:

- Rapid fluid replacement in patients with warning signs is the key to prevent progression to the shock state.
- Judicious volume replacement by IVF therapy from this early stage may modify the course of severity of disease.
- The following actions shall be applied to infants, children and adults:

1. Obtain a reference haematocrit before fluid therapy begins.
2. Give only isotonic solutions such as 0.9% NaCl (saline), Ringer's Lactate, Hartmann's solution.
    - Start with 5-7 ml/kg/hr for 1-2 hours, then reduce to 3-5 ml/kg/hour for 2-4 hours, and then reduce to 2-3 ml/kg/hour or less according to the clinical response (see table below)

Table 14. Hourly Maintenance Fluid Regime for Overweight or Obese Patients

Estimated Ideal Body Weight (kg)	Normal Maintenance fluid (ml/hr)*	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.			

3. Reassess the clinical status and repeat the haematocrit.
4. 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.
5. If there are worsening of vital signs and rapidly rising haematocrit, increase the rate to 5-10 ml/kg/hours for 1-2 hours.
6. Reassess the clinical status, repeat haematocrit and review fluid infusion rates accordingly.
7. 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 to 48 hours.
8. 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 is/are adequate or
   - Haematocrit decreases below the baseline value in a stable patient
9. Patients with warning signs should be monitored by health worker until the period of "risk" is over.
10. A detailed fluid balance should be maintained.
11. Parameters that should be monitored include:
    - Vital signs and peripheral perfusion (1-4 hourly until the patient is out of critical phase)
    - Urine output (4-6 hourly)
    - Hematocrit (before and after fluid replacement, then 6-12 hourly)
    - Blood glucose
    - Other organ functions (such as BUN, creatinine, AST/ALT, or as indicated)
12. Antibiotics are not indicated unless concomitant infection is confirmed.

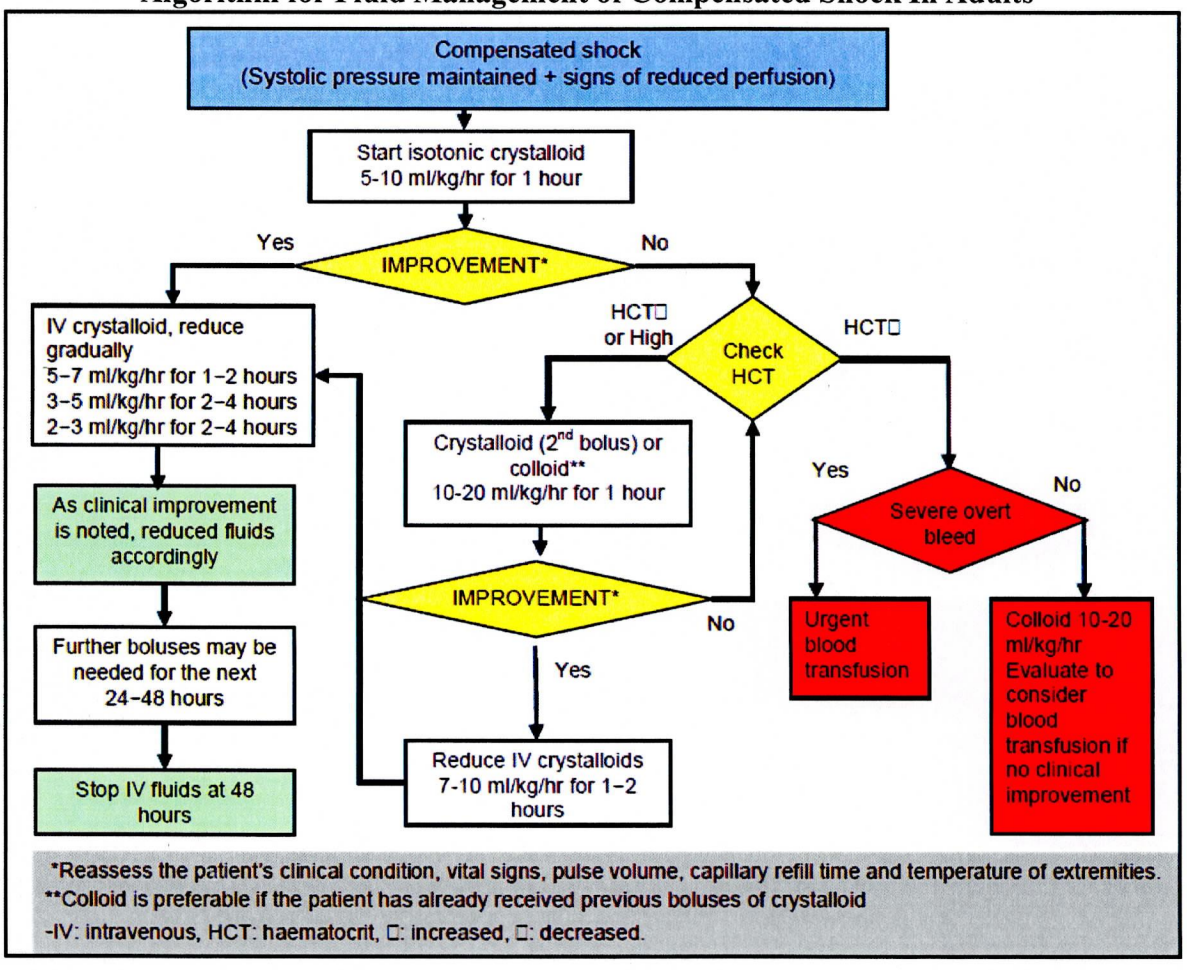
Annex 10: Group C- Treatment of Patients Admitted to the Hospital With Compensated Shock

1. A reference haematocrit shall be obtained before starting an IVF therapy.
2. Start intravenous fluid resuscitation with isotonic crystalloid solutions at 5-10 ml/kg/hr over 1 hour in adults and 10-20 ml/kg/hour over one hour in infants and children. Then reassess the patient's condition (vital signs, capillary refill time, haematocrit, urine output) and decide depending on the situation:

   b) If the condition of **adult** patient improves, intravenous fluids should be gradually reduced to,
      - 5-7 ml/kg/her 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 reduction depends on hemodynamic status and can be maintained for up to 24-48 hours.
   - Consider reducing intravenous fluid earlier if oral fluid intake improves. The total duration of intravenous fluid therapy should not exceed 48 hours

Algorithm for Fluid Management of Compensated Shock In Adults

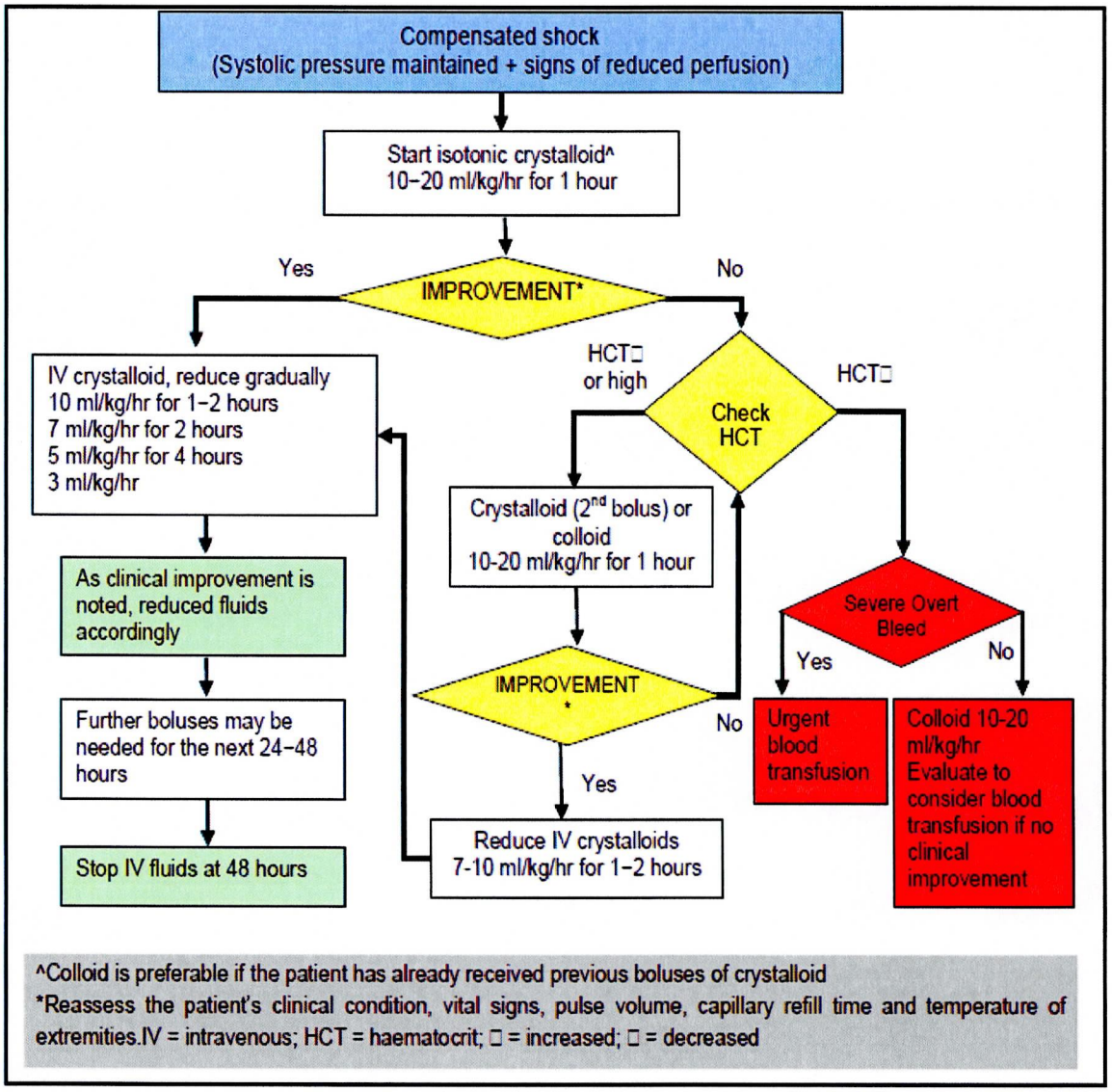


c) If the condition of the **infant** or **child** patient improves, intravenous fluids should be reduced to,

- 10 ml/kg/hour for 1-2 hours; then to
- 7 ml/kg/hour for 2 hours;
- 5 ml/kg/hour for 4 hours and then to
- 3 ml/kg/hour that can be maintained for up to 24-48 hours

- Further reduction depends on hemodynamic status and can be maintained for up to 24-48 hours.
- Consider reducing intravenous fluid earlier if oral fluid intake improves. The total duration of intravenous fluid therapy should not exceed 48 hours.

Algorithm for Fluid Management of Compensated Shock In Infants and Children



3. If vital signs are **still unstable (shock persists),** check the haematocrit after the first bolus.

a) **In adults**:

1. If the haematocrit increases or is still **high** (i.e. haematocrit >50%)
   - Repeat a second bolus of crystalloid/colloid solution at 10-20 ml/kg/hour for one hour.
   - After this second bolus, if there is improvement continue with crystalloid solution and reduce the rate to 7-10 ml/kg/hour for 1-2 hours, then continue to reduce as above.

2. If haematocrit decreases compared to the initial reference haematocrit (especially if the repeat haematocrit is below the baseline, for example < 35-40% in adult females, < 40-45% in adult males), and the patient still has unstable vital signs, this may indicate bleeding.
   - Look for severe bleeding
   - Cross-match fresh blood or fresh packed red cells and transfuse if there is severe overt bleeding
   - If there is no bleeding, give a bolus of 10-20 ml of colloid, repeat clinical assessment and determine the haematocrit level.
   - Physician in charge should carry out a review to consider blood transfusion (Refer to Annex 12: Treatment For Haemorrhagic Complications)

b) **In infants and children:**

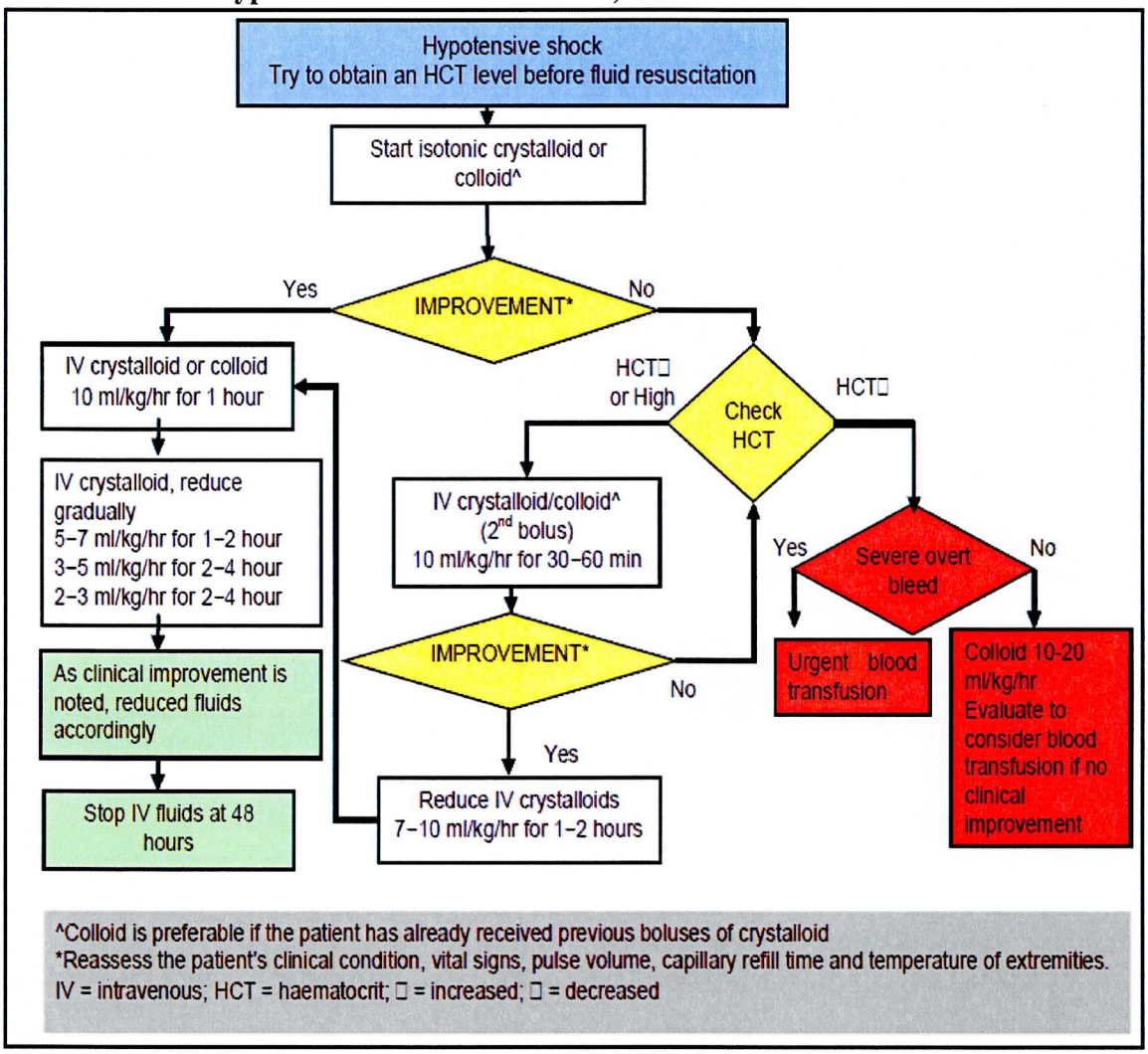
1. If the haematocrit **increases or still high**,
   - Change to colloid solution at 10-20 ml/kg/hour.
   - After the initial dose, reduce the rate to 10 ml/kg/hour for 1 hour, then reduce to 7 ml/kg/hour.
   - As mentioned above, change to crystalloid when the patient's condition improves.

2. If the haematocrit **decreases** compared to the initial reference haematocrit (especially if the repeat haematocrit is below the baseline, for example, <35-40%), and the patient still has **unstable vital signs**, this may indicate bleeding. Observe the following:
   - Look for severe bleeding
   - Cross-match fresh whole blood or fresh packed red cells and transfuse if there is severe overt bleeding
   - If there is no bleeding, give a bolus of 10-20 ml/kg of colloid over 1 hour, repeat clinical assessment and determine haematocrit level.
   - Physician in-charge should carry out a review to consider blood transfusion.

4. For all patients, further boluses of crystalloid or colloidal solutions may need to be given during the next 24 to 48 hours.

Annex 11: Group C- Treatment for patients admitted to the hospital with <u>Hypotensive Shock (in profound shock; undetectable pulse and BP)</u>

Algorithm for Fluid Management In Hypotensive Shock- In Infants, Chidren and Adults



1. For all patients (infant, children and adults) with hypotensive shock should be managed more vigorously.
2. For all patient (infants, children and adult), initiate IVF resuscitation with crystalloid or colloid solution at 20 ml/kg as a bolus given over 15 minutes to bring the patient out of shock as quickly as possible.
3. Colloids may be preferred choice if BP has to be restored urgently (i.e. those with pulse pressure less than 10 mmHg). Colloids have shown to restore the cardiac index and reduce the level of haematocrit faster than crystalloids in patients with intractable shock.
4. The intra-osseous route should be attempted if peripheral venous access cannot be obtained.

5. If the **patient's condition improves:**
   - Give a crystalloid/ colloid infusion of 10 mg/kg for 1 hour
   - Then continue with crystalloid infusion and gradually reduce to,
     5-7 ml/kg/ hour for 1-2 hours, then to;
     3-5 ml/kg/hour for 2-4 hours, and finally to;
     2-3 ml/kg/hour (or less), which can be maintained for up to 24-48 hours
   - Consider reducing intravenous fluid earlier if oral fluid intake and urine output improve.
   - The total duration of intravenous fluid should not exceed 48 hours.
6. For all patients, **if vital signs are still unstable** (i.e. shock persists), review the haematocrit obtained before the first bolus.

   - If the **haematocrit was normal** or low (<30-35% in infants, <35-40% in children and adult females, <40-45% in adult males), this may indicate bleeding. Consider the following:
     - Look for severe bleeding. Cross-match fresh whole blood or fresh packed red cells and transfuse if there is severe overt bleeding.
     - If there is no bleeding, give a second bolus of 10-20 ml/kg of colloid over 30 minutes to 1 hour, repeat clinical assessment and haematocrit level plus a review of senior staff to consider blood transfusion (see treatment for haemorrhagic complications).
   - If the **haematocrit was high** compared to the baseline value (if not available, use population baseline)
     - Change intravenous fluid to colloid solutions at 10-20 ml/kg as a second bolus over 30 minutes to 1 hour.
     - After the second bolus, reassess the patient
     - If the condition improves, reduce the rate to 7-10 ml/kg/hour for 1-2 hours, then change back to crystalloid solution and reduce the rate of infusion as mentioned above.

7. If the condition is still **unstable**, repeat the haematocrit after the second bolus.
   - If the **haematocrit decreases** compared to the previous value (<35% in infants, <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.
   - 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 1 hour. After this dose, reduce the rate to 7-10 ml/kg/ hour for 1-2 hours, then change back to crystalloid solution and reduce the rate of infusion as mentioned above when the patient condition improves. If the condition is still unstable, repeat the haematocrit after the third bolus.

8. Further boluses of fluid 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. Patient with severe dengue should be admitted to the high-dependency or intensive care area and be managed by the Physician in Charge.

Clinicians who take care of dengue shock infants should remember that an infant with a low baseline haematocrit of 30%, presenting with dengue shock and a haematocrit of 40%, is relatively more haemoconcentrated than another child with a baseline value of 42% and haematocrit of 50% at the time of shock.

9. Patients with dengue shock should be monitored frequently until the danger period is over.
10. A detailed fluid balance of all inputs and outputs should be maintained.
11. Parameters to be monitored include:
    - Alertness and comfort levels
    - Vital signs
    - Peripheral perfusion (every 15–30 minutes until the patient is out of shock then 1–2 hourly).

12. 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.
13. If previously not detectable, pleural effusion and ascites should be detectable after fluid boluses. Monitor their effects on breathing.
14. If resources are available for blood gas and/or lactate analysis, capillary or venous blood should be sampled for repeated analysis to monitor changes in the circulation during fluid replacement.
15. For severe cases not responding to fluid resuscitation on several attempts, admit to a high dependency unit/ICU.
16. Monitoring of ECG and pulse oximetry should be available in the intensive care unit.
17. Urine output should be checked regularly (each hour until the patient is out of shock, then every 1–2 hours). A continuous bladder catheter enables close monitoring of urine output. The first urine volume after bladder catheterization should be discarded because the duration in the bladder is unknown. Thereafter, an acceptable urine output would be about 0.5 ml/kg/hour.
18. Haematocrit should be monitored (before and after fluid boluses until stable, then 4–6 hourly).
19. In addition, there should be monitoring of: blood glucose (before fluid resuscitation and repeat as indicated); arterial or venous or capillary blood gases; lactate; total carbon dioxide/bicarbonate (every 30 minutes to 1 hour until stable, then as indicated); and other organ functions (such as renal profile, liver profile, coagulation profile) before resuscitation and as indicated.

Notes:
Interpretation of hematocrit: *Changes in the hematocrit are a useful guide to treatment. However, it must be interpreted in parallel to the hemodynamic status, the clinical response to fluid therapy and the acid-base balance.*

For examples:
A rising or persistently high hematocrit:

- *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*
- *With stable hemodynamic status and adequate urine output, do not require extra IVF. 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 hematocrit:

- *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*
- *Together with stable hemodynamic status and adequate urine output indicate hemodilution and/or re-absorption of extravasated fluids; IVF must be discontinued immediately to avoid pulmonary edema*

Annex 12: Treatment Of Hemorrhagic Complications

1. Mucosal bleeding may occur in any patient with dengue but if the patient remains stable with fluid resuscitation/replacement, this should be considered as a minor issue. The bleeding usually improves rapidly during the recovery phase.
    - In patients with profound thrombocytopenia, ensure strict bed rest and protection from trauma to reduce the risk of bleeding.
    - Do not give intramuscular injections to avoid hematoma.

Note: Prophylactic platelet transfusions for severe thrombocytopenia in otherwise haemodynamically stable patients are not necessary.

2. If major bleeding occurs, it is usually from the gastrointestinal tract, and/or per vagina in adult females because of hypermenorrhoea. Internal bleeding may not become apparent for many hours until the first black stool is passed.
3. Watch for patients at risk of developing severe bleeding, those who:

    - Have profound/prolonged/refractory shock;
    - Have hypotensive shock and multi-organ failure 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.

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

4. Severe bleeding should be recognized in the following situations:

    - Persistent and/or severe overt bleeding in the presence of unstable haemodynamic status, regardless of the haematocrit level;

- A decrease in haematocrit after boluses of 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 inappropriately low/normal haematocrit;

5. Blood transfusion should be given as soon as severe bleeding is suspected or recognized with particular attention to prevent fluid overload.
   - Blood typing and cross matching before blood transfusion.
   - If possible, attempts should be made to stop bleeding if the source of bleeding is identified e.g. severe epistaxis may be controlled by nasal adrenaline packing.
   - If blood loss can be quantified, this should be replaced. If not, give aliquots of 5–10 ml/kg of fresh -packed red cells or 10–20 ml/kg of fresh or fairly fresh whole blood (FWB) at an appropriate rate and observe the clinical response.
   - A good clinical response includes improving hemodynamic 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.
   - Although there is little evidence to supports the practice of transfusing platelet concentrates and/or fresh-frozen plasma for severe bleeding in dengue, they may be give judiciously.
   - Great care should be taken when inserting a nasogastric tube or bladder catheters that may cause severe haemorrhage. A lubricated orogastric tube may minimize the trauma during insertion. The insertion of a Central Venous Catheter should be done by an experienced person with ultra-sound guidance.

Annex 13 The Role of Inotropes

1. The use of inotropes should be decided on carefully and it should be started after adequate fluid volume has been administered.

   - To calculate the AMOUNT of **Dopamine** to be added to 100 ml of IV base solution:

$$\textbf{mg of Dopamine} = \frac{\text{6 x desired dose (mcg/kg/min)}}{\text{desired fluid rate (ml/hr.)}} \times \text{weight (kg)}$$

   - To calculate the VOLUME of drug to be added to 100 ml of IV base solution:

$$\textbf{ml. of Dopamine} = \frac{\text{mg of drug (determined using formula above)}}{\text{concentration of drug (mg/ml)}}$$

   - Preparation of Dopamine: 40 mg/ml; 80 mg/ml

2. Other vasopressors in dengue shock:
   - **Epinephrine**

Preparation: 1:10,000
Dose: 0.1 to 1 ug/kg per minute by IV/IO infusion (titrate to the desired effect) 52

- **Norepinephrine**
  Stock dose: 1 mg/ml
  Dose: 0.1 to 2 ug /kg per minute by IV/IO infusion (titrate to the desired effect)