Incorporating the Revised Dengue Guidelines in General Pediatric Practice

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Case 1

- A 4-year old boy, previously healthy
- Brought to the ER for the following:
  - High grade fever (T max 39.5 ^{o}C) for 2 days
  - Poor appetite, vomiting and body malaise
- Pertinent PE:
  - Vital Signs: CR = 128/min, RR = 28/min, T= 39.2 ^{O}C, BP = 90/60 Weight= 15 kgs
  - (+) Flushed skin
  - Hyperemic throat but (-) exudates
  - Rest of the PE findings normal.
  - (-) Tourniquet test

Initial CBC:
Hgb 110 g/L
Hct 0.33
WBC count 4.0 x 10^{9},
seg 0.35, lym 0.70,
platelet cnt 160,000 U/L

- **Is this patient a Dengue Suspect?**

☑ YES

❑ NO

References

WHO. Dengue Guidelines for Diagnosis, Treatment, Prevention and Control. New edition 2009. WHO/HTM/NTD/DEN/2009.1

Administrative Order No. 2012-0006. DOH Revised Dengue Clinical Case Management Guidelines 2011.

PPS Revised Guidelines on Fluid Management of Dengue Fever and Dengue Hemorrhagic Fever 2012

WHO TDR Handbook for Clinical Mangement of Dengue 2012.

New Dengue Case Classification

Probable Dengue Fever

Lives in or travels to dengue-endemic area, with fever, plus any two of the following:

- **Headache**
- **Body malaise** ✓
- **Myalgia**
- **Arthralgia**
- **Retro-orbital pain**
- **Nausea, Vomiting** ✓
- **Anorexia** ✓
- **Diarrhea**
- **Flushed skin**
- **Rash (petechial rash, Hermann's sign)**
- **Tourniquet test positive**

AND

- **Laboratory test, at least CBC (leukopenia *with or without* thrombocytopenia)** ✓
- ***and/or*** **Dengue NS1 antigen test or dengue IgM antibody test (optional tests)**

DOH /PPS Revised Dengue Clinical Case Management Guidelines 2011

New Dengue Case Classification

Confirmed Dengue Fever

- **Viral culture isolation**
- **PCR**

DOH/PPS Revised Dengue Clinical Case Management Guidelines 2012

New Dengue Case Classification

Dengue with Warning Signs

Live in or travels to dengue-endemic area, with fever lasting for 2-7 days, plus any one of the following:

- **Abdominal pain or tenderness**
- **Mucosal bleeding**
- **Clinical signs of fluid accumulation**
- **Persistent vomiting**
- **Lethargy, restlessness**
- **Liver enlargement**
- **Decreased or no UO within 6 hours**
- **Laboratory: increase in Hct *and/or* decreasing platelet count**

DOH/PPS Revised Dengue Clinical Case Management Guidelines 2012

New Dengue Case Classification

Severe Dengue

Lives in or travels to a dengue-endemic area with fever of 2–7 days and any of the above clinical manifestations for Dengue with or without warning signs, *plus* any of the following:

<u>Severe plasma leakage</u>, leading to:

- **Shock**
- **Fluid accumulation with respiratory distress**

<u>Severe bleeding</u>

<u>Severe organ impairment</u>

- **Liver: AST or ALT ≥ 1000**
- **CNS: e.g., seizures, impaired consciousness**
- **Heart: e.g., myocarditis**
- **Kidneys: e.g., renal failure**

DOH/PPS Revised Dengue Clinical Case Management Guidelines 2012

How should the patient be classified?

A. Dengue without warning signs

B. Dengue with warning signs

C. Nonsevere dengue

D. Severe Dengue

Manifestations of Dengue Virus Infection

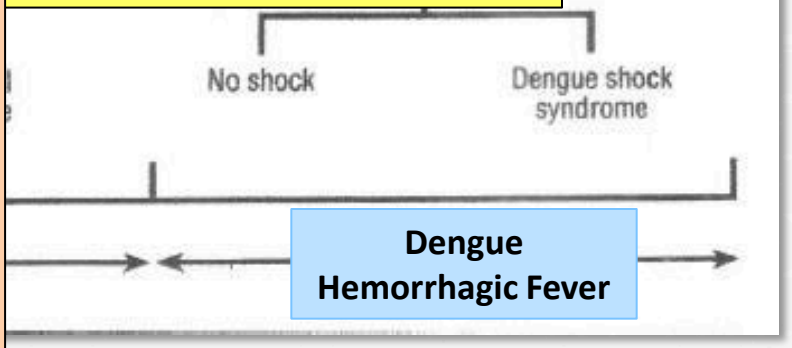
DENGUE HEMORRHAGIC FEVER (DHF)

The following must ALL be present:

1. **Fever, or history of fever, lasting for 2-7 days**
2. **Hemorrhagic tendencies evidenced by at least one of the following:**
   - **(+) Tourniquet Test**
   - **Petechiae, ecchymosis, purpura**
   - **Bleeding from the mucosa, GIT, injection sites or other locations**
   - **Hematemesis or melena**
3. **Thrombocytopenia (≤ 100,000 cells/mm^3)**
4. **Evidence of plasma leakage due to increased vascular permeability, manifested by at least one of the following:**
   - **↑Hct ≥ 20% above average for age, sex, and population**
   - **↓Hct following volume replacement treatment ≥ 20% of baseline**
   - **Signs of plasma leakage, i.e. pleural effusion, ascites and hypoproteinemia**

wing:

280, a
body test on a
pecimen



Technical Advisory Committee. Dengue hemorrhagic fever: diagnosis, treatment, prevention, and control. Geneva: World Health Organization, 1997.

Challenges in Using the WHO Case Classification for DHF

- **Rigidity of definitions - all four DHF criteria must be present**
  - **Dengue with severe hemorrhage, without plasma leakage[1,2]**
  - **Dengue with Shock without fulfilling all four DHF criteria**
    - **14-22% of those with shock did not fulfill all four criteria considered necessary for a diagnosis of DHF by the WHO [3,4.5]**
  - **Dengue with organ dysfunction**
- **Low sensitivity of criteria in detecting DHF**
  - **Many DSS do not have platelet count <100,000 [1]**
  - **Hemorrhagic tendency do not reliably differentiate DF and DHF[2]**
  - **↑HCT not seen after IVF therapy, in patients with poor perfusion, severe bleeding, anemia [1]**

1. Bandyopadhyay S et al. Trop Med Int Health 2006; 2. Gupta et al. J Infect Dev Ctries 2010; 3. Phuong et al. Am. J. Trop. Med. Hyg 2004;; 4.Setiati et al. BMC Infectious Diseases 2007, 5. Alexander N et al. Trop Med Int Health 2011.

Challenges in Using the WHO Case Classification for DHF

- **Many cases cannot be classified using the WHO 1997 classification**
  - **Many cases that could not be classified by the previous WHO classification system are classified as having unusual manifestations [1, 2]**
- **Assumption that DF means mild disease [2]**
  - **DF may present with unusual hemorrhage**

1. Alexander N et al. Trop Med Int Health 2011; 16(8): 936–9;
2. Bandyopadhyay S et al. Trop Med Int Health 2006;11:1238-1255

Consequences of Inconsistency of WHO Case Classification

- Does not consistently capture cases of severe and life-threatening dengue which do not fulfil all criteria for DHF
- Classifies all patients in whom the requisite four criteria are not demonstrated as having DF by default
  - If fever and significant plasma leakage are documented, patients are classified as DHF even without bleeding or thrombocytopenia
- A formal DHF diagnosis is often only possible late in the evolution of the infection
- Clinicians develop a variety of loose and incommensurable interpretations to allow prompt institution of appropriate management
- Underdiagnosis and under-reporting of DHF cases where DHF misclassified as DF
- Poor case management resulting in fatal outcomes

Bandyopadhyay S et al. Trop Med Int Health 2006;11:1238-1255

Multicentre prospective study on dengue classification in four South-east Asian and three Latin American countries

- Prospective observational study conducted from 2006-07 by the DENCO Study Group sponsored by the WHO-TDR
- Included patients with clinically suspected dengue recruited at 11 hospitals in 7 countries in SE Asia and Latin America
- 1734 dengue cases: 1568 (90%) confirmed and 166 (10%) highly suggestive
- Applying the existing WHO system, 47/210 (22%) of patients with shock did not fulfil all the criteria for DHF: 27 classified as DF and 20 unclassifiable
- However, no three-tier revision could adequately described the different severity groups
- Inclusion of readily discernible complications (shock/severe vascular leakage/severe bleeding/severe organ dysfunction) was necessary to devise a system that identified patients requiring major intervention with sufficient sensitivity and specificity to be practically useful.

Alexander N et al. Trop Med Int Health 2011; 16(8): 936–948.

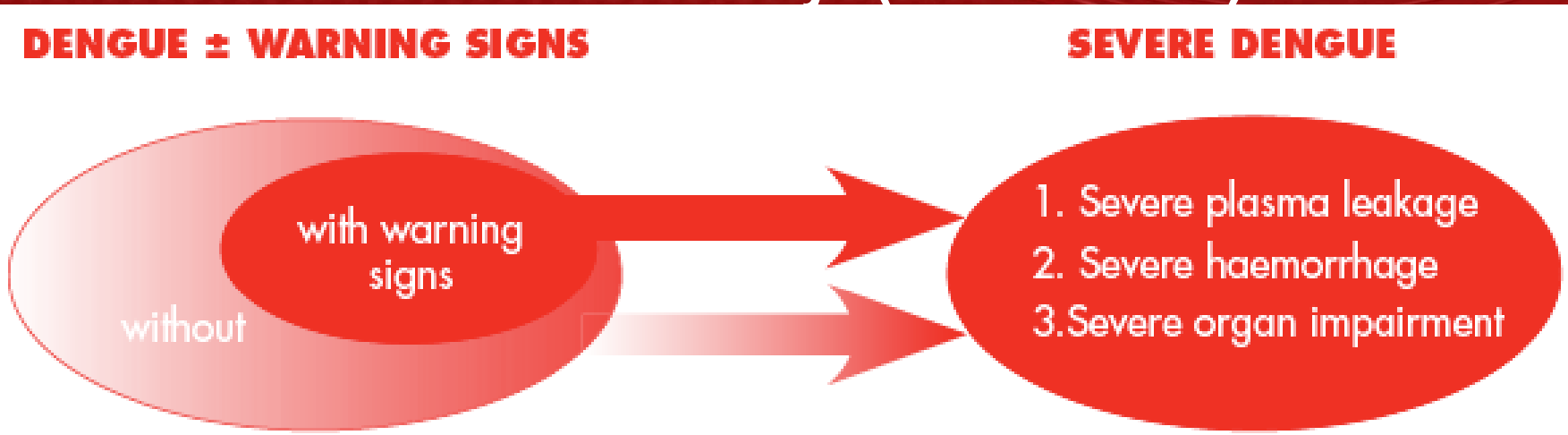
Comparison of WHO Standard Classification with Revised Classification to Distinguish Cases requiring Intervention

Classification	Sensitivity	Specificity
WHO Standard Classification (1997)	76%	54%
Revised WHO Classification (2009)	95%	97%

- Multivariate analysis showed that the following were significantly increased risk for severe disease: abdominal pain or tenderness, lethargy, mucosal bleeding and a decrease in platelet count.
- At the WHO-sponsored expert review meeting, there was general agreement that a new system based on these results and comprising two entities, 'Dengue' and 'Severe Dengue', should be incorporated into the new WHO guidelines (WHO 2009)
- Further refinements remain necessary with respect to risk prediction and for application in specific areas of pathogenesis research.

Alexander N et al. Trop Med Int Health 2011; 16(8): 936–948.

Suggested Dengue Case Classification and Levels of Severity (WHO 2009)



CRITERIA FOR DENGUE ± WARNING SIGNS

Probable dengue
live in /travel to dengue endemic area.
Fever and 2 of the following criteria:
- Nausea, vomiting
- Rash
- Aches and pains
- Tourniquet test positive
- Leukopenia
- Any warning sign

Laboratory-confi rmed dengue (important when no sign of plasma leakage)

Warning signs*
- 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

*(requiring strict observation and medical intervention)

CRITERIA FOR SEVERE DENGUE

Severe plasma leakage leading to:
- Shock (DSS)
- Fluid accumulation with respiratory distress

Severe bleeding as evaluated by clinician

Severe organ involvement
- Liver: AST or ALT >=1000
- CNS: Impaired consciousness
- Heart and other organs

Revised Dengue Classification (DOH 2011)

Probable Dengue

Lives in or travels to dengue-endemic area, with fever, plus any two of the following:

- Headache
- Body malaise
- Myalgia
- Arthralgia
- Retro-orbital pain
- Anorexia
- Nausea
- Vomiting
- Diarrhea
- Flushed skin
- Rash (petechial, Hermann's sign)

AND

- Laboratory test, at least CBC (leukopenia with or without thrombocytopenia) and/or dengue NS1 antigen test or dengue IgM antibody test (optional).

Lab-confirmed Dengue

- Viral culture isolation
- PCR

Warning Signs

- Abdominal pain or tenderness
- Persistent vomiting
- Clinical signs of fluid accumulation
- Mucosal bleeding
- Lethargy, restlessness
- Liver enlargement
- Laboratory: increase in hematocrit and/or decreasing platelet count

1. **Severe plasma leakage** *leading to*
   - Shock (DSS)
   - Fluid accumulation with respiratory distress
2. **Severe bleeding**
3. **Severe organ involvement**
   - Liver: AST or ALT ≥ 1000
   - CNS: e.g., seizures, impaired consciousness
   - Heart: e.g., myocarditis
   - Kidneys: e.g., renal failure

DOH Revised Dengue Clinical Case Management Guidelines 2011

WHO Dengue Case Definition (1997) compared with the New PPS/DOH Dengue Case Definition and Classification

WHO Case Definition of Dengue and Levels of Severity (1997, 2011)

Case Definition for DENGUE FEVER

Probable:

- An acute febrile illness with ≥ 2 of the following:
- Headache
- Retro-orbital pain
- Arthralgia
- Rash
- Hemorhagic manifestations
- Leukopenia
- AND
- Supportive serology (a reciprocal HI antibody titer ≥1280, a comparable IgG assay ELISA titer or (+) IgM antibody test on a late or acute convalescent phase serum specimen

NEW Case Classification and Levels of Severity (DOH 2011)

Case Definition for DENGUE W/O WARNING SIGNS

Probable dengue:

Lives in or travels to dengue-endemic area, with fever, plus any two of the following:

- Headache
- Body malaise
- Myalgia
- Arthralgia
- Retro-orbital pain
- Nausea, Vomiting
- Anorexia
- Diarrhea
- Flushed skin
- Rash (petechial rash, Hermann's sign)
- Tourniquet test positive

AND

- Laboratory test, at least CBC (leukopenia ***with or without*** thrombocytopenia)
- ***and/or*** Dengue NS1 antigen test or dengue IgM antibody test (optional tests)

WHO Dengue Case Definition (1997) compared with the New PPS/DOH Dengue Case Definition and Classification

WHO Case Definition of Dengue and Levels of Severity (1997, 2011)

Case Definition for DENGUE HEMORRHAGIC FEVER (DHF)

The following must ALL be present:

1. **Fever/ history of fever, lasting for 2-7 days, occasionally biphasic**
2. **Hemorrhagic tendencies evidenced by at least one of the following:**
   - **(+) TT**
   - **Petechiae, ecchymosis, purpura**
   - **Bleeding**
   - **Hematemesis or melena**
3. **Thrombocytopenia (≤100,000 cells/mm^3)**
4. **Evidence of plasma leakage due to increased vascular permeability, manifested by at least one :**
   - **↑ Hct ≥ 20% above average for age, sex, popn**
   - **↓Hct ≥ 20% of baseline ff volume replacement**
   - **Signs of plasma leakage, i.e. pleural effusion, ascites and hypoproteinemia**

NEW Case Classification and Levels of Severity (DOH 2011)

Case Definition for DENGUE WITH WARNING SIGNS

Lives in or travels to dengue-endemic area, with fever lasting for 2-7 days, plus any one of the following:

- **Abdominal pain or tenderness**
- **Persistent vomiting**
- **Clinical signs of fluid accumulation**
- **Mucosal bleeding**
- **Lethargy, restlessness**
- **Liver enlargement**
- **Laboratory: increase in Hct *and/or* decreasing platelet count**
- **Decreased or no UO within 6 hours**

WHO Dengue Case Definition (1997) compared with the New PPS/DOH Dengue Case Definition and Classification

WHO Case Definition of Dengue and Levels of Severity (1997, 2011)

DHF Grade 1

Fever accompanied by non-specific constitutional signs and symptoms such as anorexia, vomiting, abdominal pain; the only hemorrhagic manifestation is a (+) tourniquet test and/or easy bruising

DHF Grade 2

Spontaneous bleeding in addition to manifestations of grade 1 patients usually in the form of skin or other hemorrhages (mucocutaneous, gastro-intestinal)

DHF Grade 3 (DSS)

Circulatory failure manifested by rapid, weak pulse and narrowing of PP or hypotension, with the presence of cold clammy skin and restlessness

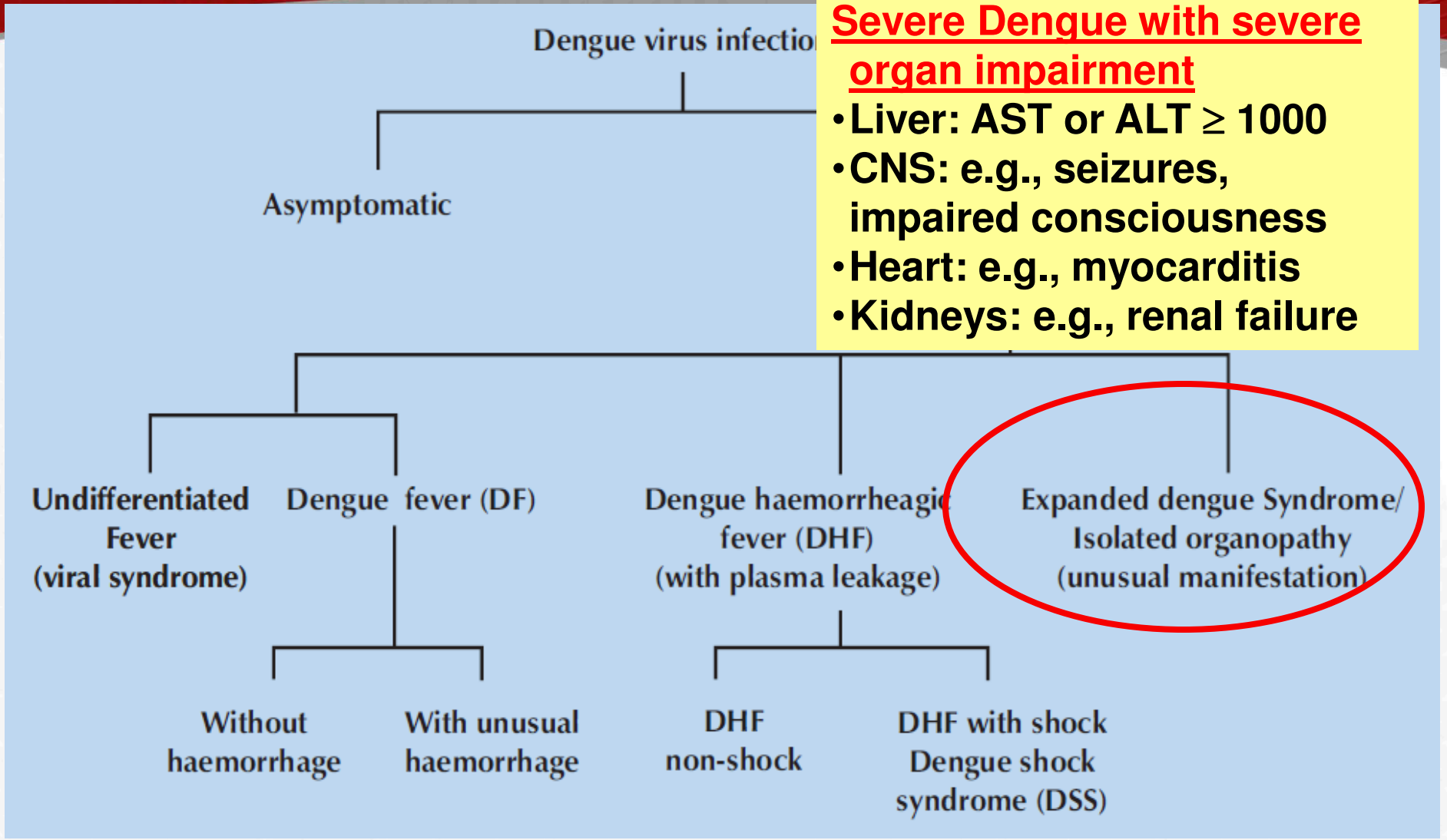
DHF Grade 4 (DSS)

Profound shock with undetectable BP or pulse

NEW Case Classification and Levels of Severity (DOH 2011)

- **Case Definition for SEVERE DENGUE**
- Lives in or travels to a dengue-endemic area with fever of 2–7 days and any of the above 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

Manifestations of Dengue Virus Infection



Severe Dengue with severe organ impairment

- **Liver: AST or ALT ≥ 1000**
- **CNS: e.g., seizures, impaired consciousness**
- **Heart: e.g., myocarditis**
- **Kidneys: e.g., renal failure**

WHO SEARO 2011. Comprehensive Guidelines for Prevention and Control of Dengue and Dengue Haemorrhagic Fever. *Revised and expanded edition*

Dengue Surveillance

2,103 Patients enrolled
1,809 (86%) Lab-confirmed dengue

Age distribution of laboratory-confirmed dengue cases

Pediatric Age				Total
Agegroup (years)	**N = 137**	**N=657**	**N=1015**	**N=1809**
< 1	0 (0.0)	8 (1.2)	25 (2.5)	33 (1.8)
1 - 2	2 (1.5)	18 (2.7)	90 (8.9)	110 (6.1)
*** 3 – 5**	**20 (14.6)**	**107 (16.3)**	**275 (27.1)**	**402 (22.2)**
*** 6 – 10**	**53 (38.7)**	**215 (32.7)**	**401 (39.5)**	**669 (37.0)**
*** 11 – 15**	**61 (44.5)**	**191 (29.1)**	**224 (22.1)**	**476 (26.3)**
16 - 18	1 (0.7)	118 (18.0)	0 (0.0)	119 (6.6)
Median	10.54	10.46	7.29	8.70

* 85.5% of dengue cases from these age group

Duration from onset of fever to admission

Duration of Fever	JBL N = 137 n (%)	WVMC N = 657 n (%)	DMC N = 1015 n (%)	Total N = 1809 n (%)
1 day	4 (2.9)	54 (8.2)	17 (1.7)	75 (4.1)
2 days	10 (7.3)	87 (13.2)	32 (3.2)	129 (7.1)
3 days	38 (27.7)	158 (24.1)	216 (21.3)	412 (22.8)
4 days	42 (30.7)	143 (21.8)	314 (30.9)	499 (27.6)
5 days	27 (19.7)	99 (15.1)	241 (23.7)	367 (20.3)
6 days	5 (3.7)	54 (8.2)	113 (11.1)	172 (9.5)
1 week	8 (5.8)	41 (6.2)	61 (6.0)	110 (6.1)
> 1 week	3 (2.2)	21 (3.2)	21 (2.1)	45 (2.5)

70% were admitted to the hospital when fever was on its 3rd to 5th day of illness

Lab-confirmed dengue cases

Diagnostic test				Total
PCR, number tested	**182 (100.0)**	**798 (100.0)**	**1121 (99.8)**	**2101 (99.9)**
Positive	123 (67.6)	530 (66.4)	670 (59.8)	* **1323 (63.0)**
Subtype of RT-PCR Positive Cases[a]				
Dengue-1	36 (29.3)	20 (3.8)	220 (32.8)	276 (20.9)
Dengue-2	28 (22.8)	* **346 (65.1)**	57 (8.5)	431 (32.5)
Dengue-3	* **54 (43.9)**	122 (23.0)	* **311 (46.4)**	* **487 (36.8)**
Dengue-4	4 (3.3)	24 (4.5)	70 (10.5)	98 (7.4)
IgM				
Number Tested	182 **(100.0)**	797 **(99.9)**	1116 **(99.4)**	2095 **(99.6)**
Positive	105 (57.7)	447 (56.1)	914 (81.9)	* **1466 (70.0)**
IgG				
Positive	81 (44.5)	411 (51.6)	761 (68.2)	* **1253 (59.8)**

RITM Lab-confirmed cases 2010-2011

	2010	2011	2012	Total
PCR				
Total no of samples/ No of samples tested	182/165	210/178		
No of positive	**101 61.2%**	**87 48.9%**		
No of negative	**64 38.8%**	**91 51.1%**		
Serotype				
1	**30.7%**	**48.3%**		
2	**19.8%**	**11.5%**		
3	**43.6%**	**37.9%**		
4	**3.0%**	**2.3%**		

What laboratory tests confirm the diagnosis of Dengue?

A. Dengue viral culture

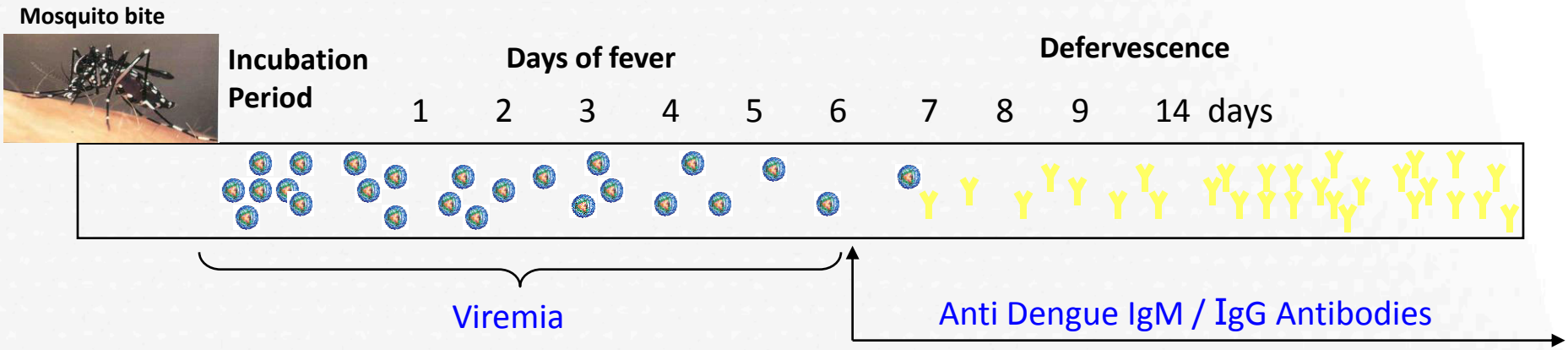
B. Dengue NS1 test

C. Dengue PCR

D. Dengue serology

Laboratory Diagnosis of Dengue Infection

The right test at the right time!



- viral culture
- RT-PCR
- NS1 Ag test

- Dengue IgM/IgG (EIA, Dot blot, Dipstick, Immunoblot, Immunochromotography)

How should patients with Dengue without warning signs but with signs of dehydration be managed?

A. Send home on oral rehydration fluids

B. Admit for oral rehydration fluids

C. Admit to the wards for IV fluid therapy

D. Admit to the ICU for IV fluids

GROUP A: Patients Who May Be Sent Home

- **Patients with ALL of the following:**
  - **Able to tolerate adequate volumes of oral fluids**
  - **Pass urine at least once every 6 hours**
  - **Do not have any of the warning signs, particularly when fever subsides**
  - **Normal hematocrit (≤40%) and normal platelet count (≥150,000)**
- **Ambulatory patients should be monitored daily for disease progression decreasing WBC, defervescence, warning signs until out of the critical period**
- **Advice to return immediately to the hospital if they develop any of the warning signs.**

Dengue Guidelines for Diagnosis, Treatment, Prevention and Control. 2009. WHO/HTM/NTD/DEN/2009.1

ACTION PLAN : GROUP A (Home Care)

ORS

- Reduced osmolarity ORS (contains Na 50-75 mmol/L)
- No sports drinks or fluids containing high sugar/glucose
- Plain water will cause electrolyte imbalance

Paracetamol

- Use appropriate dosages for children
- Not more than 4g for adults
- Do not give aspirin, ibuprofen or other NSAIDs
- Tepid sponging
- Antibiotics are not necessary

Dengue Home Care Card & Advice on when to return to hospital

- Bed rest
- Fluids
- Fever management
- Warning signs: bleeding, freq vomiting, abdominal pain, drowsiness, mental confusion or seizures, pale, cold or clammy hands and feet, difficulty in breathing, decreased or no UO within 6 hours

GROUP B: Patients Who Should Be Referred For In-hospital Management

- Patients with any warning sign present
- No warning sign present but with any of the following:
  - Co-existing conditions that may make dengue or its management more complicated, i.e. pregnancy, infancy, old age, obesity, DM, renal failure, chronic hemolytic diseases
  - Social circumstances, i.e. living alone, living far from a health facility without reliable means of transport

ACTION PLAN : DENGUE WITHOUT WARNING SIGNS (In-Hospital Mx)

Encourage ORS

IVF 0.9% saline or LR at maintenance rate, if ORS not tolerated

ORS after a few hours of IVF therapy

Fluid Management for Patients Admitted Without Warning Signs and Without Shock

- **IVF(Isotonic solutions) : D_5 LRS, D_5 Acetated Ringers, D_5 NSS/ D_5 0.9 NaCl**
- **For infants < 6 mos old, D5 0.45 NACl* is preferred if available. Do NOT use hypotonic fluids (e.g.D5 0.3NaCl)**
- **Computation of Maintenance IVF**
  - **Caloric-expenditure method (Holliday-Segar Method)**
  - **Calculation Based on Weight**
- **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 requirement (TFR).**

*** D5 0.45 NaCl is prepared by mixing equal volumes of D5 0.9 NaCL and D5W**

Calculation of Maintenance IVF Infusion

Holliday-Segar Method [1]

ABW (Kg)	TFR (ml/day)
3 -10	100 ml/kg
> 10-20	1,000 ml + 50 ml/kg for each kg > 10 kg
> 20	1,500 ml + 20 ml/kg for each kg > 20 kg

Ludan Method [2]

ABW (Kg)	TFR (ml/kg/day)
> 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

1. Holliday MA, Segar WE. Maintenance need for water in parenteral fluid therapy. Pediatrics 1957; 19:823.

2. Ludan A. Chapter 41: Pediatric Fluid and Electrolyte Therapy. In *Textbook of Pediatrics and Child Health*. Fourth edition. 2000:1485-1499

Calculation of Total Fluid Requirement (TFR) in Patients with Mild Dehydration but Not in Shock

Total Fluid Requirement

Maintenance IVF

PLUS

Fluids for Mild Dehydration *

*Volume of Fluid for Mild Dehydration	
Infant (≤ 12 mos)	**50 ml/kg**
Older Child or Adult (age >12 mos)	**30 ml/kg**

- **The computed TFR is given <u>over 24 hours</u>**
- **Constant, periodic reassessment is needed.**
- **Fluid rate should be adjusted according to the clinical condition, vital signs, urine output and hematocrit levels**

ACTION PLAN : DENGUE WITHOUT WARNING SIGNS (In-Hospital Mx)

- **Periodic assessment needed for appropriate fluid adjustment**
- **Monitor clinical parameters and correlate with Hct**
- **Avoid over- and under hydration**
- **Decrease IVF anytime based on clinical assessment**
- **If with signs of deterioration ⇨ see Mx for Compensated or Hypotensive Shock**

- **Monitor:**
  - **Temperature pattern**
  - **Volume of fluid intake and losses**
  - **Urine output (volume and frequency)**
  - **Warning signs**
  - **CBC (HCT, WBC, platelet count), HGT or capillary blood glucose (CBG)**

Case 2

- A 15-year old adolescent girl
- Brought to the ER for the following:
  - High grade fever (T max 40.0 ^{O}C)
  - Weakness, headache, poor appetite, vomiting, poor appetite
- Pertinent PE:
  - Flushed skin, weak-looking, dry lips
  - CR = 120/min, RR = 32/min, T= 37.4 ^{O}C, BP = 90/60; Weight = 40 kg
  - (+) Hepatomegaly w/ tenderness on right subcostal area
  - On auscultation: ↓ breath sounds on right lower lung field
  - CRT 4 seconds

Initial CBC:
Hgb 110 g/L
HCT 0.33
WBC count 4.0 x 10^{9}
seg 0.35, lympho 0.70
platelet cnt 160,000 U/L

What is the most probable diagnosis for this patient?

A. Dengue without warning signs

B. Dengue with warning signs

C. Severe dengue with compensated shock

D. Severe dengue with uncompensated shock

Hemodynamic Assessment: Continuum of Hemodynamic Changes

Parameters	Stable Circulation	Compensated shock	Hypotensive shock
Sensorium	Clear and lucid	Clear and lucid	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 &thready	Feeble or absent

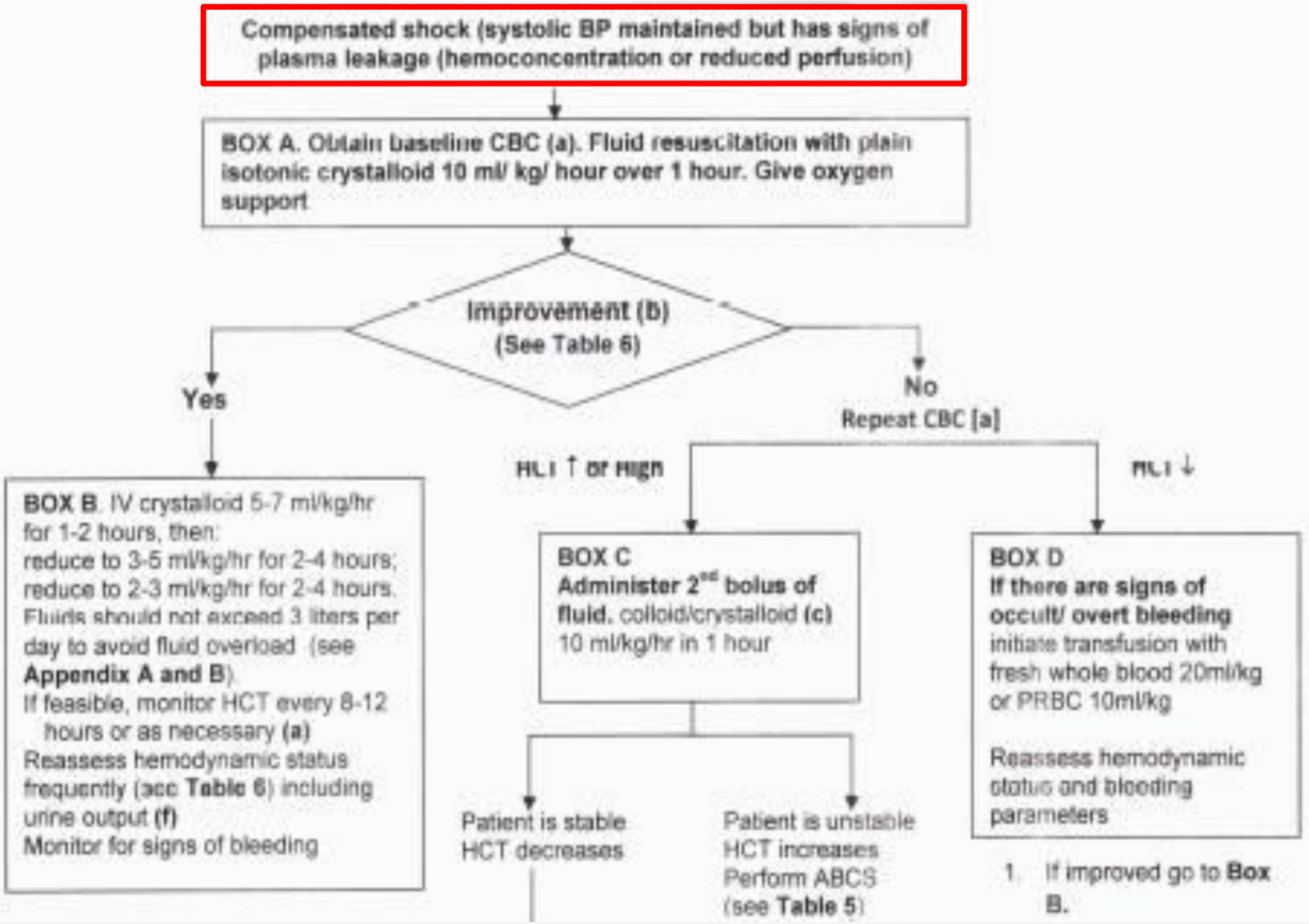
**Note: shock can be missed if you do not touch the patient*

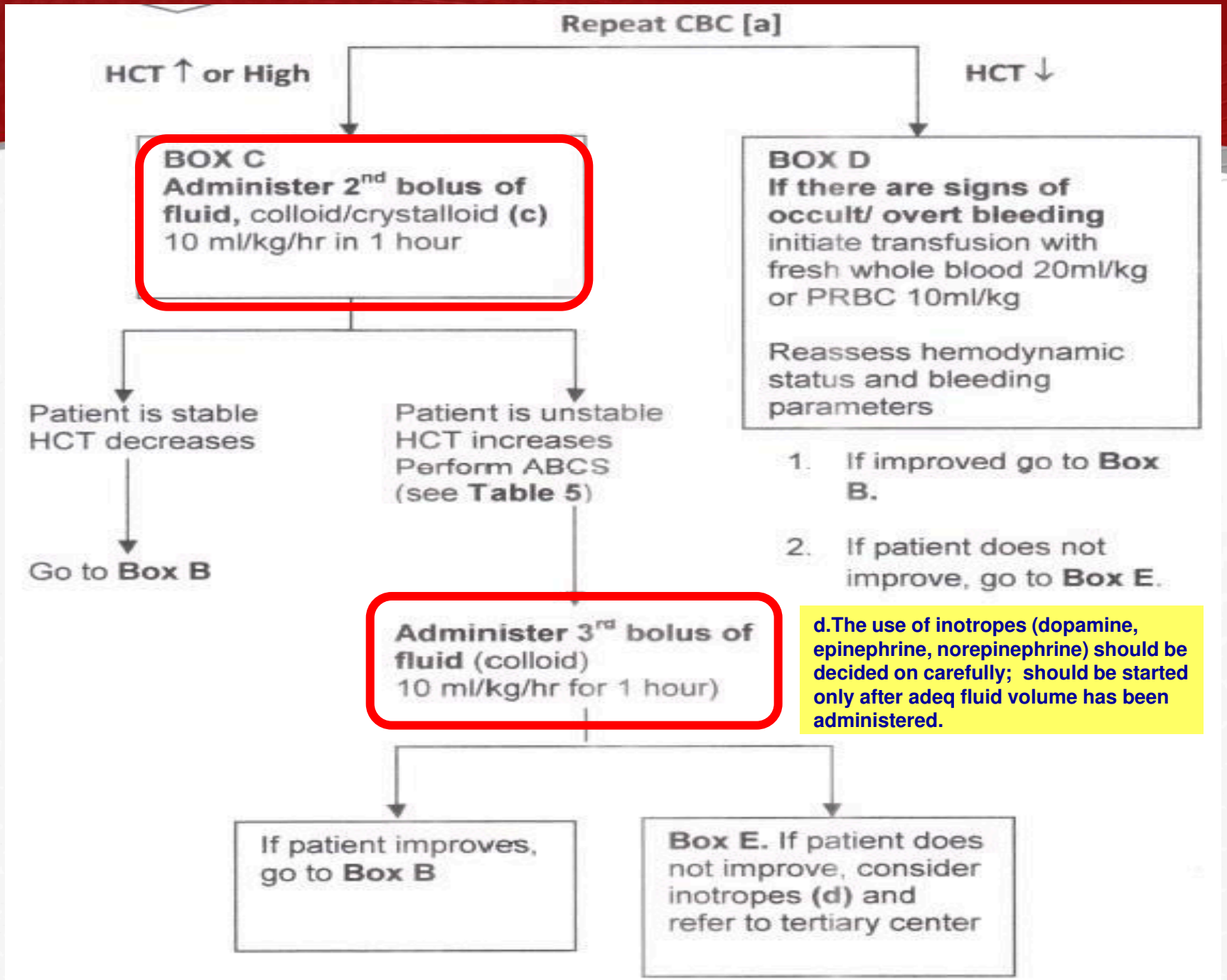
Hemodynamic Assessment: Continuum of Hemodynamic Changes

Parameters	Stable Circulation	Compensated shock	Hypotensive shock
Heart rate	Normal heart rate for age	Tachycardia	Severe tachycardia with bradycardia in late shock
Blood pressure	Normal blood pressure for age Normal pulse pressure for age	Normal systolic pressure but rising diastolic pressure Narrowing pulse P Postural hypotension	Narrowed pulse pressure (<20 mmHg) Hypotension Unrecordable BP
Respiratory rate	Normal respiratory rate for age	Tachypnea	Metabolic acidosis/ hyperpnea/ Kussmaul's breathing

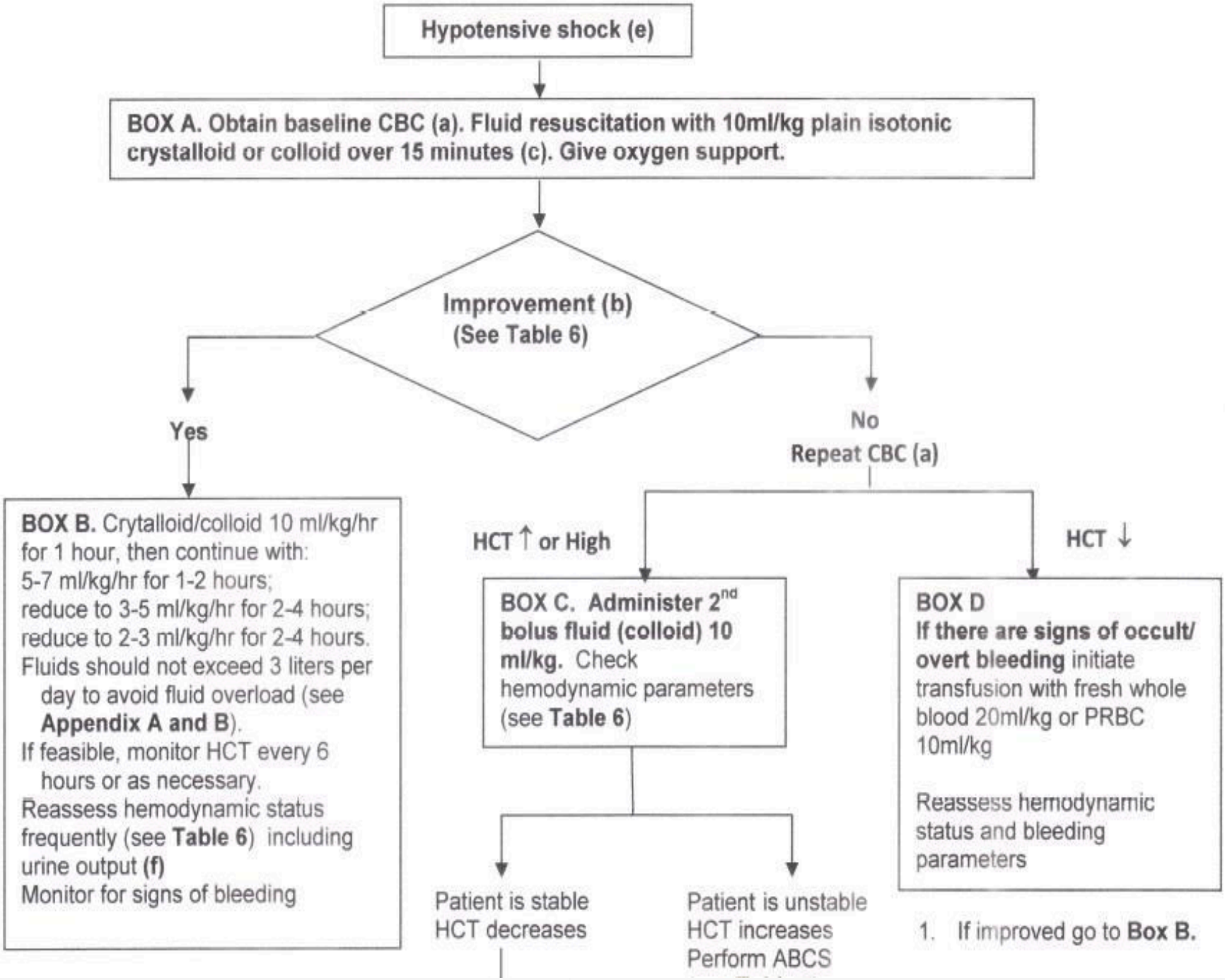
How should patient with Dengue and shock be managed?

A. IV fluid bolus using isotonic crystalloid 20 cc/kg x 10 minutes
B. IV fluid bolus using isotonic crystalloid 10 ml/ kg/ hour over 1 hour
C. IV fluid bolus using albumin 20 cc/kg x 10 minutes
D. IV fluid bolus using colloid solution 10 ml/ kg/ hour over 1 hour

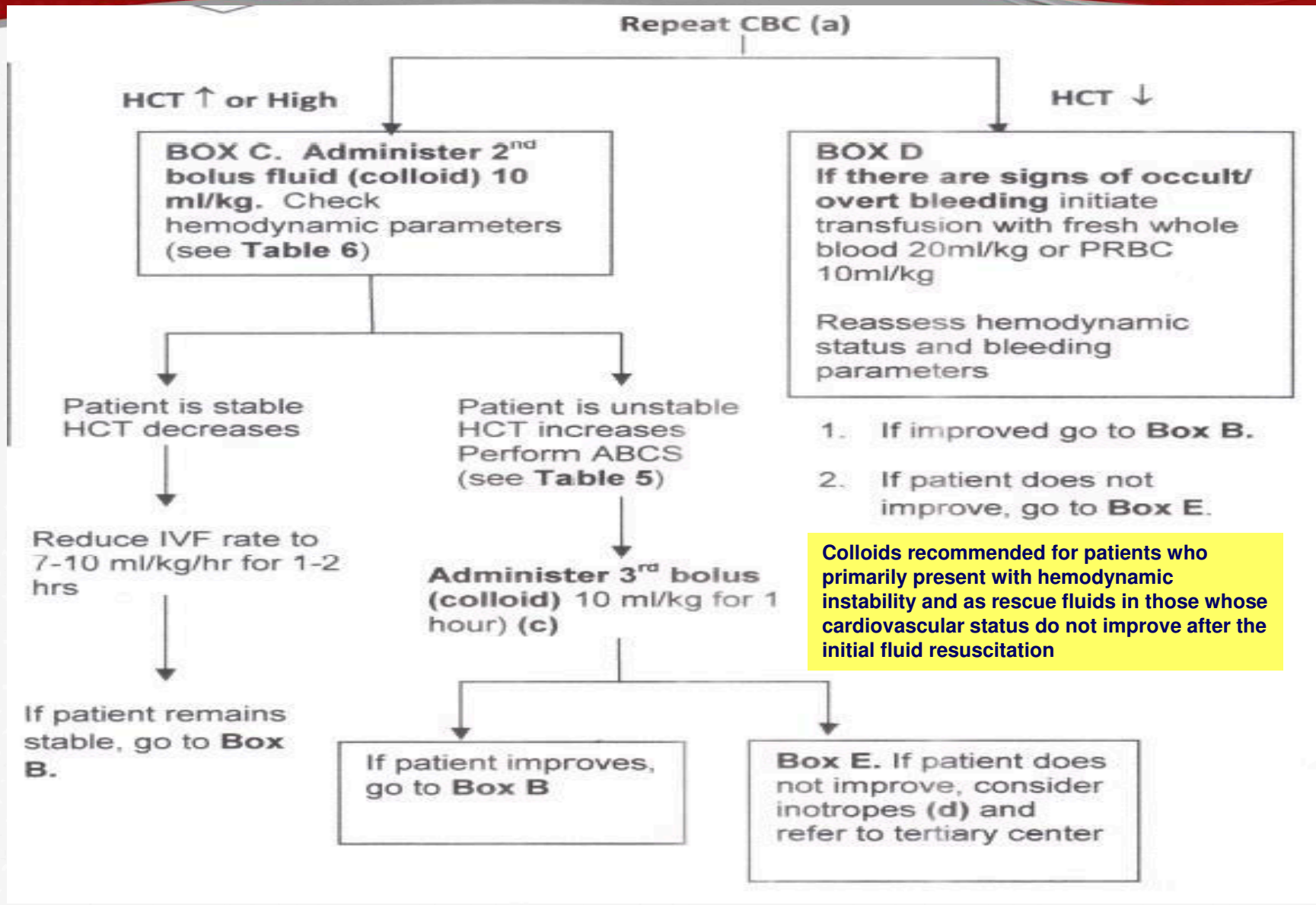

Compensated shock (systolic BP maintained but has signs of plasma leakage (hemoconcentration or reduced perfusion)
BOX A. Obtain baseline CBC (a). Fluid resuscitation with plain isotonic crystalloid 10 ml/ kg/ hour over 1 hour. Give oxygen support
Improvement (b) (See Table 6)
Yes
No
Repeat CBC [a]
HCT ↑ or High
HCT ↓
BOX B. IV crystalloid 5-7 ml/kg/hr for 1-2 hours, then:
reduce to 3-5 ml/kg/hr for 2-4 hours;
reduce to 2-3 ml/kg/hr for 2-4 hours.
Fluids should not exceed 3 liters per day to avoid fluid overload (see Appendix A and B).
If feasible, monitor HCT every 8-12 hours or as necessary (a)
Reassess hemodynamic status frequently (acc Table 6) including urine output (f)
Monitor for signs of bleeding
BOX C
Administer 2nd bolus of fluid, colloid/crystalloid (c) 10 ml/kg/hr in 1 hour
BOX D
If there are signs of occult/ overt bleeding initiate transfusion with fresh whole blood 20ml/kg or PRBC 10ml/kg
Reassess hemodynamic status and bleeding parameters
Patient is stable
HCT decreases
Patient is unstable
HCT increases
Perform ABCS
(see Table 5)
1. If improved go to Box B.



d.The use of inotropes (dopamine, epinephrine, norepinephrine) should be decided on carefully; should be started only after adeq fluid volume has been administered.


Hypotensive shock (e)
BOX A. Obtain baseline CBC (a). Fluid resuscitation with 10ml/kg plain isotonic crystalloid or colloid over 15 minutes (c). Give oxygen support.
Improvement (b) (See Table 6)
Yes
No
Repeat CBC (a)
BOX B. Crytalloid/colloid 10 ml/kg/hr for 1 hour, then continue with:
5-7 ml/kg/hr for 1-2 hours;
reduce to 3-5 ml/kg/hr for 2-4 hours;
reduce to 2-3 ml/kg/hr for 2-4 hours.
Fluids should not exceed 3 liters per day to avoid fluid overload (see Appendix A and B).
If feasible, monitor HCT every 6 hours or as necessary.
Reassess hemodynamic status frequently (see Table 6) including urine output (f)
Monitor for signs of bleeding
HCT ↑ or High
HCT ↓
BOX C. Administer 2nd bolus fluid (colloid) 10 ml/kg. Check hemodynamic parameters (see Table 6)
BOX D
If there are signs of occult/ overt bleeding initiate transfusion with fresh whole blood 20ml/kg or PRBC 10ml/kg
Reassess hemodynamic status and bleeding parameters
Patient is stable
HCT decreases
Patient is unstable
HCT increases
Perform ABCS
1. If improved go to Box B.

No Improvement after Fluid Resuscitation with Plain Isotonic Crystalloid



Crystalloids vs Colloids

Crystalloids (Ringer's lactate or 0.9 NaCl solutions)

- Should be used as first line in fluid resuscitation in Moderately Severe (Compensated) Dengue Shock.
- Safe and as effective as colloid solutions (dextran, starch, or gelatin) in reducing recurrence of shock and mortality.
- Comparable to colloids in terms of total amount of fluids used in resuscitation and rescue fluid

Colloids (gelatin-, dextran-, and starch-based)

- Associated with ↑risk of allergic reactions & new bleeding manifestations; more expensive.
- Insufficient data to ascertain advantage of one type of fluid in cases of Severe Dengue Shock (DHF grade IV) or Hypotensive (Uncompensated) Shock
- May be used in patients who primarily present with HEMODYNAMIC INSTABILITY and as RESCUE FLUIDS in those whose cardiovascular status do not improve after the initial fluid resuscitation.

Crystalloids

Crystalloid	Advantage	Disadvantage
0.9% saline ["normal" saline]/NSS	• Suitable option for initial fluid resuscitation	• Repeated large vol of 0.9% NaCl may lead to hyperchloremic acidosis • Hyperchloremic acidosis may aggravate or be confused w/ lactic acidosis from prolonged shock • When se Cl- level exceeds N range, change to LR advised
Ringer's Lactate	• Lower Na+ (131mmol/L) and Cl- (115mmol/L) contents and osm(273mOsm/L) • Not suitable for resuscitn of patients w/ severe hypoNa+ • suitable solution after 0.9 NaCl has been given and the se Cl-l has exceeded the N range.	• LR should be avoided in liver failure and patients taking metformin where lactate metabolism may be impaired.

Colloids

Colloid	Advantage	Disadvantage
Dextran-based	• Less risk of allergic reaction	• Dextrans may bind to von Willebrand factor/Factor VIII complex and impair coagulation the most • Dextran 40 can potentially cause an osmotic renal injury in hypovolemic patients • Allergic reactions, e.g. fever, chills and rigors been observed in Dextran 70
Gelatin-based	Least effect on coagulation among all the colloids	• Highest risk of allergic reactions,

Findings

- Hypoalbuminemia in 67 % of adults and 87% of children.

de Castro R et al, Am J Trop Med 2007

Findings

- Hypoalbuminemia in 76% of adult patients with DHF.

Itha, Nat J Ind 2005

Clinical Implication

- Increases the sensitivity in the diagnosis of DHF.

Brito, Braz J Trop Med 2007

Centeno, Am J Trop Med 2008

Clinical Implication

- May be a sign of hemoconcentration.

Shepherd, 2012

Therapeutic Implication

- No advantage of colloids vs crystalloids in the management of shock.

Perel, P. WHO Sec. 2010

Patient became unstable and did not respond after 1 dose of crystalloids and 2 doses of colloids. What laboratory test should be done for a patient with Dengue with shock?

A. Order for arterial blood gas (ABG)

B. Coagulation profile (PT, PTT)

C. Serum calcium

D. Blood glucose

Laboratory investigations (ABCS) for patients with profound shock, complications, or no clinical improvement in spite of adequate

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

WHO-SEA Comprehensive guidelines for prevention and control of dengue and dengue haemorrhagic fever. Revised & expanded ed . 2011

Going back to the second case...

- After 6 hours, the patient suddenly developed abdominal enlargement, sudden pallor
- Vital signs: CR 140/min, RR 40/min, T 36.8 ^{o}C, BP 80/60.
- On auscultation : (+) progression in the pleural effusion with decrease in breath sounds in both lung fields extending up to te interscapular area (+) occasional crackles.
- Laboratory tests :
  - CBC: Hgb 11 g/L, Hct 0.37, WBC 3.0 x 10^{9}, seg 0.28, lympho 0.70, platelet count 120,000 U/L.
  - PT: patient 13 seconds (control 12seconds)
  - PTT: 65 seconds (control 37 seconds); INR not taken
-

Is blood transfusion indicated for this patient? If blood transfusion is indicated, what blood component should be transfused?

A. Packed RBC

B. Fresh whole blood

C. Platelet concentrate

D. Fresh frozen plasma

BLOOD TRANSFUSION

Transfusions should be given only when there are definite and established indications and in practically all cases component therapy should be utilized.

AABB 2003

What is happening ????

- Decrease in Hct
- Decrease in Platelet Count
- Prolonged PTT

What is happening ???

- Abdominal Enlargement and Pain
- Pallor

BLEEDING !!!

ABNORMAL HEMOSTASIS

- Consumptive coagulopathy is NOT the major cause of BLEEDING but rather the profound shock and intractable acidosis.

- Fibrinogen is the most severely affected clotting factor

BLOOD TRANSFUSION

- PRBC or FWB if with significant bleeding such as melena.
- PRBC or FWB if with decreasing Hct inspite of IVF
- Platelet concentrate if < 50,000 with bleeding
- DIC – cryoprecipitate (1 bag/ 5kg) or FFP (10-20 ml/kg)

PPS 2008 GUIDELINES

- In massive bleeding such as hematamesis, FWB, PRBC, and plasma may be used.
- Once DIC sets in, cryoprecipitate, FFP, and platelet concentrate may be used.

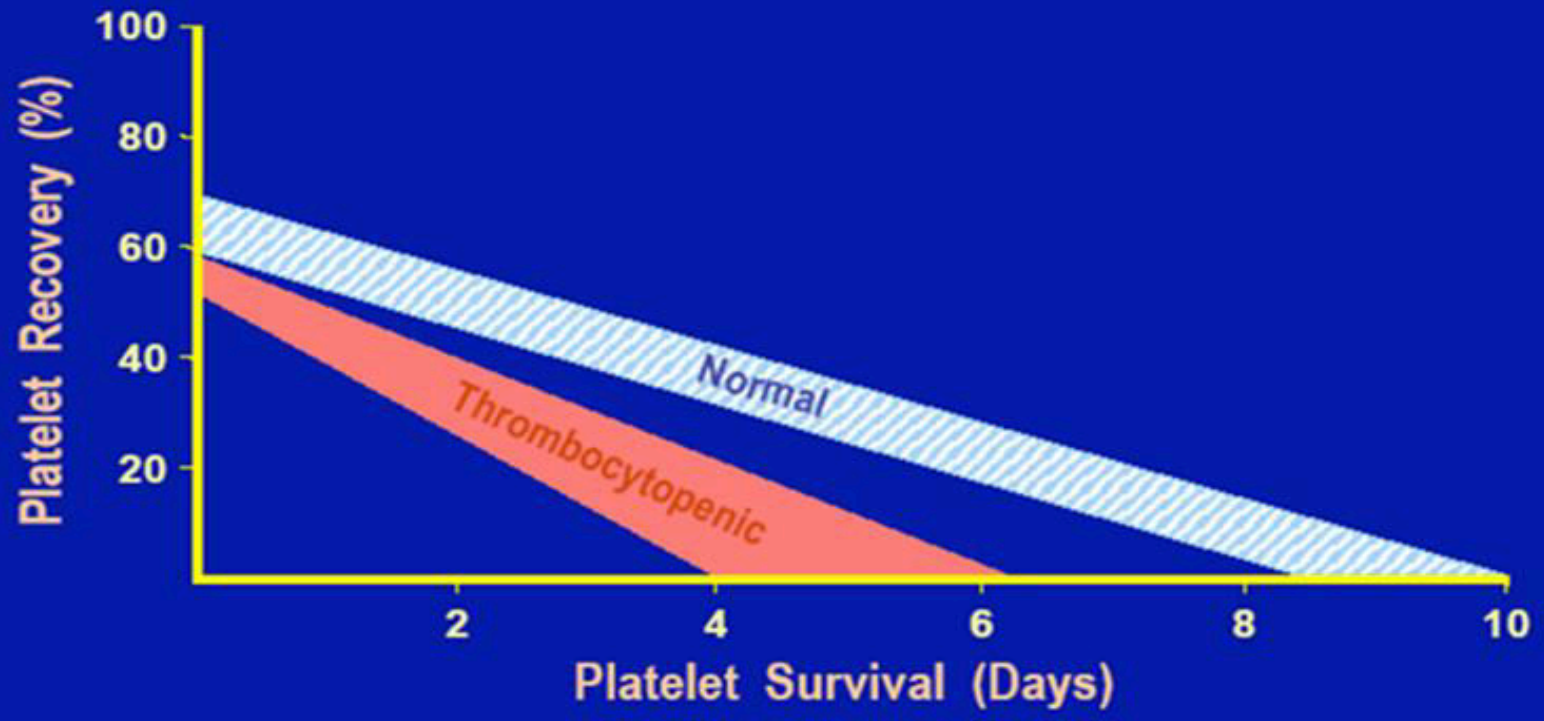
Level of Evidence: **Class 2**

Grade of Recommendation: **A**

THROMBOCYTOPENIA

- Kavath et al – DHF with platelets of < 50,000 had a 6x higher mortality rate.
- Krishnamuti, S – bleeding without shock is due to platelet abnormalities rather than coagulopathy.

PLATELET RECOVERY AND SURVIVAL IN NORMALS AND THROMBOCYTOPENIC PATIENTS



Slichter & Harker; *Clin Hematology* 7:523, 1978.

Platelet Transfusion Therapy

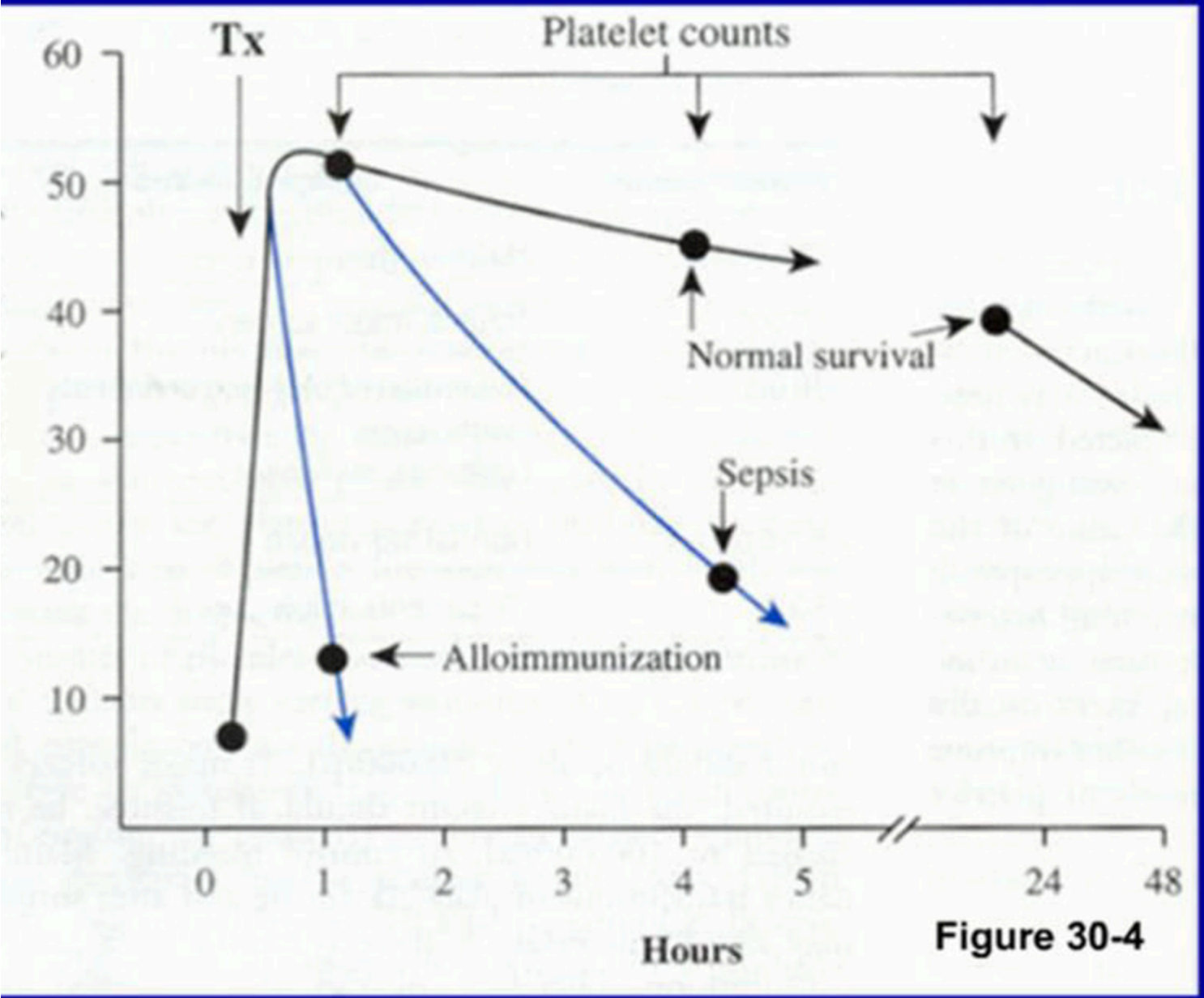


Figure 30-4

Hillman and Ault, Hematology in Clinical practice, pg. 330, 2002

e demographic characteristics, clinical and laboratory data on the day the platelet count reased to <20×103 platelets/μL, and clinical outcomes for patients with acute dengue infection who did or did not receive prophylactic platelet transfusion.

Variable	Patients given platelet transfusion (n = 188)	Patients not given platelet transfusion (n = 68)	P
Demographic characteristics			
Age, years	40 (22–64)	39 (22–58)	.54
Male sex	144 (77)	45 (66)	.11
Dengue diagnosis			
Dengue hemorrhagic fever	4 (2)	2 (3)	.66
Positive results of PCR	124 (66)	46 (68)	.88
Test results positive for IgG	60/86 (70)	24/32 (75)	.65
Preexisting medical conditions			
Diabetes mellitus	11 (6)	2 (3)	.52
Hypertension	18 (10)	5 (7)	.80
Hyperlipidemia	9 (5)	1 (1)	.30
Ischemic heart disease	0 (0)	0 (0)	1.00
Clinical features			
Fever	46 (24)	22 (32)	.26
Headache	13 (7)	3 (4)	.57
Myalgia/arthralgia	27 (14)	12 (18)	.56
Eye pain	1 (1)	0 (0)	1.00
Anorexia	17 (9)	4 (6)	.61
Nausea	21 (11)	6 (9)	.82
Vomiting	17 (9)	5 (7)	.80
Diarrhea	14 (7)	3 (4)	.57
Rash	27 (14)	8 (12)	.68
Temperature, °C	37.5 (36.6–39)	37.2 (36.5–39.4)	.09
Temperature ≥38°C	62 (33)	12 (18)	.02
Systolic blood pressure, mm Hg	115 (95–140)	110 (95–130)	.01
Diastolic blood pressure, mm Hg	70 (50–87)	70 (50–85)	.12
Systolic blood pressure <90 mm Hg	0 (0)	1 (1)	.27
Pulse pressure, mm Hg	45 (30–70)	40 (30–60)	.03
Pulse, beats/min	70 (55–93)	70 (60–94)	.84
Pulse <60 beats/min	18 (10)	2 (3)	.11
Abdominal tenderness	3 (2)	0 (0)	.57
Pleural effusion or ascites	0 (0)	0 (0)	1.00
Laboratory results			
Hematocrit, %	45.7 (36.7–52.1)	44.9 (35.4–50.3)	.24
Hematocrit >50%	23 (12)	4 (6)	.17
Leukocyte count, $\times 10^3$ leukocytes/μL	3.4 (1.7–7.2)	3.6 (1.7–8.2)	.46
Leukocyte count <3.3 × 10^3 leukocytes/μL	86 (46)	26 (38)	.32
Platelet count, $\times 10^3$ platelets/μL	15 (7–19)	15 (8–19)	.87
Clinical outcomes			
Any bleeding	1 (1)	2 (3)	.17
Platelet increment the next day, $\times 10^3$ platelets/μL	7 (−7 to 50)	11 (−4 to 41)	.26
Time to platelet count ≥50 × 10^3 platelets/μL, days	3 (1–4)	3 (1–5)	.59
Length of hospital stay, days	6 (4–8)	5 (4–7)	.09
Death	1 (1)	0 (0)	1.00

NOTE. For dichotomous variables, data are no. (%) of patients; for continuous variables, data are median (5th–95th percentiles).

Lye D C et al. Clin Infect Dis. 2009;48:1262-1265

PPS 2008 GUIDELINES

Preventive transfusion has NO ROLE in the treatment of DHF.

Level of Evidence: Class 2

Grade of Recommendation: A

Points of Emphasis

GOOD PRACTICE	BAD PRACTICE
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
Administration of paracetamol for high fever if the patient is uncomfortable	Administration of acetylsalicylic acid (aspirin) and ibuprofen
Obtaining HCT level before and after fluid boluses	Not knowing when HCT levels are taken w/ respect to fluid therapy

Points of Emphasis

GOOD PRACTICE	BAD PRACTICE
Clinical assessment of the hemodynamic status before and after each fluid bolus	No clinical assessment of patient with respect to fluid therapy
Interpretation of HCT levels in the context of fluid administered and hemodynamic assessment	Interpretation of HCT levels independent of clinical status
Giving IVF volume just sufficient to maintain effective circulation during the period of plasma leakage for severe dengue	Excessive or prolonged IVF administration for severe dengue

Points of Emphasis

GOOD PRACTICE	BAD PRACTICE
IVF, frequency of monitoring and HCT measurement adjusted according to the patient's condition	Fixed IVF rate, unchanged frequency of monitoring and HCT measurement during entire hospitalization for severe dengue
Close monitoring of blood glucose	Not monitoring blood glucose
Discontinuation or reducing fluid therapy once hemodynamic status stabilizes	Continuation and no review of intravenous fluid therapy once hemodynamic status stabilizes