Case of Dengue Complicating Pregnancy

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somi Society of Obstetric Medicine, India & FERNANDEZ HOSPITAL Health Care for Women & Newborn

Case Details

- Mrs JD
- 29 yrs, BMI 26
- G2A1
- Spontaneous conception
- Booked case
- Presented at 38 weeks with fever since morning

History of Presenting Illness

- **Fever – High grade with chills, intermittent**
- **Cough and cold**
- **Myalgia**

History of Presenting Illness

- No h/o – chest pain / abdominal pain/ vomiting/ headache/ bone or joint pains/ burning micturition / bowel disturbance
- No h/o bleeding from any site
- No c/o decreased fetal movements/ leaking / bleeding pv

Obstetric history

- G1 – spontaneous miscarriage at 8 wks in 2008
- 2012- work up for infertility, hystero-laprascopy done – normal findings
- G2- PP, spontaneous conception

History of Present Pregnancy

- Booked at 5 weeks
- Regular Antenatal checkup (ANC) visits
- Diagnosed as GDM at 11 weeks – on diet control
- Rest ANC profile – normal
- <u>Scans</u>

NT – low risk, TIFFA – normal,

Growth Scan (31 wks) - AGA

- **Past medical history / family history – not contributory**

Examination

- General – looking ill with fever, dehydration
- Temp- 100F, PR-110/min, BP-80/70, RR- 20/min
- No icterus/petechiae/lymphadenopathy/edema
- Systemic- unremarkable
- Obstetric – Uterus relaxed, FHR +

Investigations

Hb – 12.8%

PCV – 37.3% (normal)

WBC – 7,700/cumm

Plt - 1.06 lakhs/cumm

LFT – WNL

CUE – WNL

Urine C/S – sterile

Malarial Parasite- negative

IMPRESSION –

Viral fever ?

Dengue ? Flu

Management

- Early warning chart
- Hydration (crystalloids @ 100 ml/hr)
- Diabetic diet
- Paracetamol
- Platelet count monitoring daily
- Counseled for SDP(single donor platelet) donor screening; RDPs (random donor platelet)reserved

Platelet Count Trend

8/10 (D1)	9/10 (D2)	10/10 (D3)	11/10 (D4)	12/10 (D5)	13/10 (D6)	14/10 (D7)
1.06	96,000	94,000	85,000	34,000	18,000	16,000

DENGUE IgM and IgG – negative when sent on 3rd day,
when repeated on 7th day - positive

Fetal Evaluation

- NST – reactive
- Scan – AGA(average for gestational age) , polyhydramnios
- DFKC(daily fetal kick count), FHR(fetal heart rate)monitoring 2 hrly

Course in the Hospital

- Fever subsided on second day of admission
- Developed itching and flushing of palms on day 5 of fever
- Donor bled and SDP kept on agitator when Platelet count touched 18,000 (no petechiae)

Course in the Hospital

- **Spontaneous labour next day (day 7 of fever)**
- **Lab Parameters**

  Hb- 14.1%

  PCV – 40.9%

  Plt count – 16,000 later 13,000

  PT/APTT/INR – normal

Intra-partum Details

- Emergency LSCS for Presumed fetal compromise
- General Anesthesia
- 1 unit SDP given intra-op
- Blood loss average
- Intra-peritoneal drain kept

Baby Details

- Baby boy, 3.12 kg, 08/08/09
- Dengue IgM and IgG positive
- Asymptomatic

Post operative Period

- Uneventful
- Day 0 POD- Platelet count 17,000/cumm

  Coag profile - Normal
- Supportive measures
- Platelet count monitored 6th hrly : 34,000 – 58,000
- Day 3 POD – 2.27 lakhs/cumm
- Drain removed on 4th POD
- Abdominal wound healthy
- Discharged on day 5 POD

Case Summary

- G2A1, 38 weeks, GDM on diet, presenting with fever, myalgia and thrombocytopenia
- Diagnosed as Dengue (IgM and IgG positive after 7 days of fever)
- Managed with early warning chart, hydration and daily platelet counts
- SDP screened and RDP reserved

Case Summary

- Set into spontaneous labour but needed Emergency LSCS for Fetal compromise with good fetal outcome
- 1 unit SDP given intra-op
- Baby screened for Dengue and found to be IgM and IgG positive but asymptomatic

Fernandez Data – 2010 To 2014

- ***TOTAL 45 CASES***
- **26 – delivered at FH; 19 – outside**
- **1st trimester – 6**

  2nd trimester – 9

  3rd trimester - 30

Platelet counts and Transfusion

Platelet count	Number
<10,000	3
10,000-50,000	20
50,000 – 1 lakh	7
1-1.5 lakhs	10
Normal	5

LOWEST PLATELET COUNT – 6,000/cumm

- **11 - Platelet transfusion**
  - **3 – platelet count < 10,000**
  - **7 - Intrapartum**
  - **1 - Epistaxis**

26 – Delivered at FH

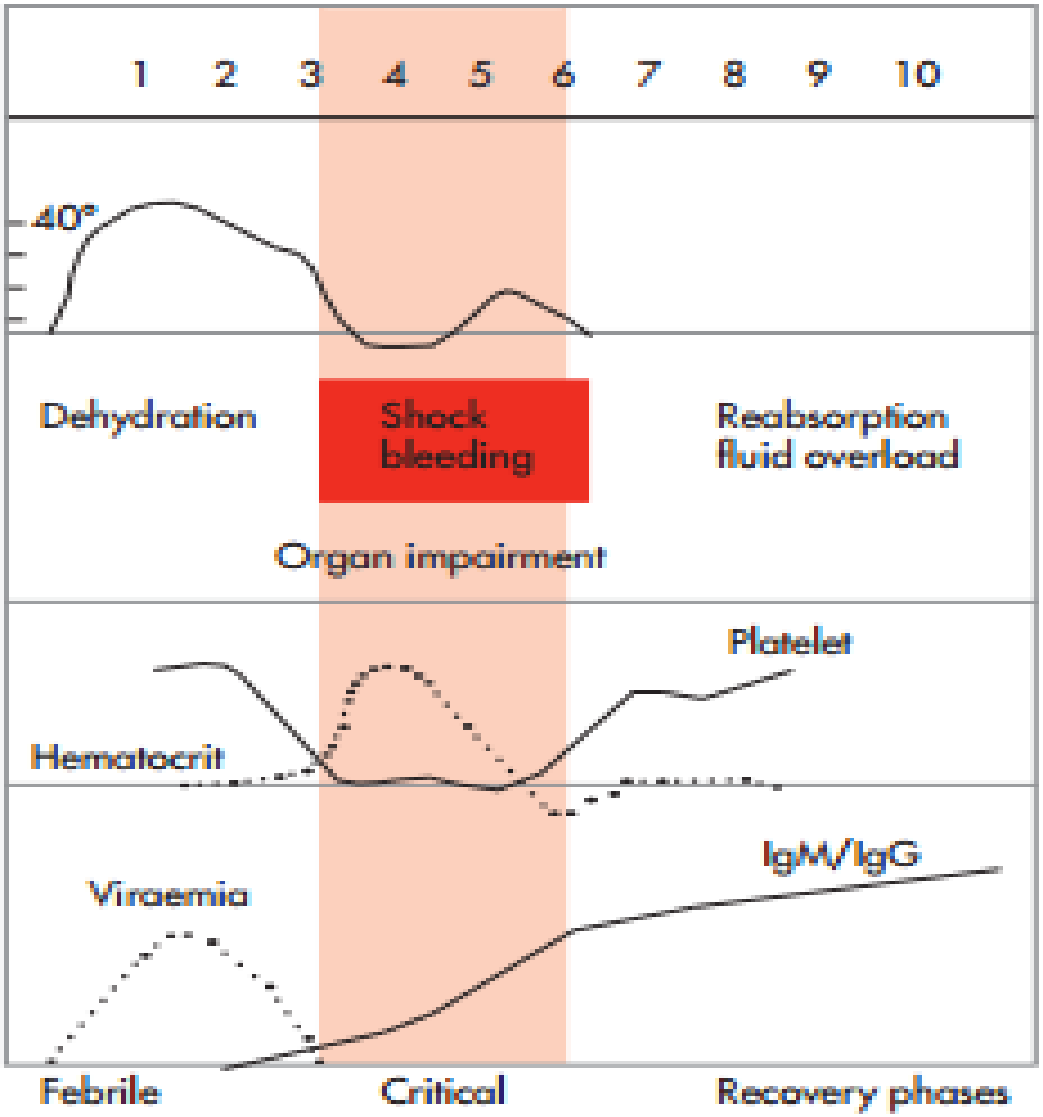
- 1 IUFD(intra uterine fetal deaths)
- 7 preterm deliveries (32 – 36 weeks)
- 4 SGA babies
- 1 neonatal dengue positive

Discussion

Presentation of Dengue

- Type I- Febrile illness – flu like symptoms, rash, no typical features
- Type 2- Classical Dengue fever – Severe headache, retro-orbital pain, congestion of eyes, severe bone pains (break-bone fever)
- Type 3-Dengue Hemorrhagic fever (DHF) – hemorrhagic manifestations like petechiae, plasma leak as evidenced by rising hematocrit and third space collection
- Type 4- Dengue shock Syndrome (DSS) – signs of shock and MODS

Course of Dengue Illness



Critical Phase

- **Progressive leukopenia followed by a rapid decrease in platelet count usually precedes plasma leakage.**
- **At this point patients without an increase in capillary permeability will improve, while those with increased capillary permeability may become worse as a result of lost plasma volume. The degree of plasma leakage varies.**

Critical Phase

- Pleural effusion and ascites may be clinically detectable depending on the degree of plasma leakage and the volume of fluid therapy. Hence chest x-ray and abdominal ultrasound can be useful tools.
- The degree of increase above the baseline haematocrit often reflects the severity of plasma leakage

Dengue Shock Syndrome

- **Shock occurs when a critical volume of plasma is lost through leakage. Usually takes place around defervescence, usually on day 4 or 5 (range days 3–7) of illness. Often preceded by warning signs. (see next slide)**
- **The body temperature may be subnormal when shock occurs.**

Dengue Shock Syndrome

- With prolonged shock→ organ hypoperfusion →progressive organ impairment, metabolic acidosis and disseminated intravascular coagulation→severe haemorrhage →haematocrit to decrease;total white cell count may increase in patients with severe bleeding
- Severe organ impairment such as severe hepatitis, encephalitis or myocarditis and/or severe bleeding may also develop without obvious plasma leakage or shock

- Those who deteriorate will manifest with warning signs. This is called dengue with warning signs
- Warning signs:
  - Clinical Abdominal pain or tenderness
  - Persistent vomiting
  - Clinical fluid accumulation
  - Mucosal bleed
  - Lethargy, restlessness
  - Liver enlargement >2 cm
  - Laboratory Increase in HCT concurrent with rapid decrease in platelet count

- Cases of dengue with warning signs will probably recover with early intravenous rehydration.
- Some cases will deteriorate to severe dengue
- Uniquely, in dengue shock, the diastolic pressure rises towards the systolic pressure and the pulse pressure narrows as the peripheral vascular resistance increases due to compensation initially.
- Patients in dengue shock often remain conscious and lucid.
- The inexperienced physician may measure a normal systolic pressure and misjudge the critical state of the patient.
- Finally, when there is decompensation, both pressures disappear abruptly.
- Prolonged hypotensive shock and hypoxia may lead to multi-organ failure and an extremely difficult clinical course

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

Severe Dengue Criteria

- **Fever of 2–7 days plus any of the following features:**
  - **There is evidence of plasma leakage, such as:**
    - high or progressively rising haematocrit;
    - pleural effusions or ascites;
    - circulatory compromise or shock (tachycardia, cold and clammy extremities,
    - capillary refill time greater than three seconds, weak or undetectable pulse,
    - narrow pulse pressure or, in late shock, unrecordable blood pressure.

Severe Dengue Criteria

- There is significant bleeding
- There is an altered level of consciousness (lethargy or restlessness, coma, convulsions)
- There is severe gastrointestinal involvement (persistent vomiting, increasing or intense abdominal pain, jaundice)
- There is severe organ impairment (acute liver failure, acute renal failure, encephalopathy or encephalitis, or other unusual manifestations, cardiomyopathy)
- or other unusual manifestations

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

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

Effects in Pregnancy

- Studies have shown increase in miscarriages, preterm labour and low –birth weight babies (due to effects of febrile illness not dengue virus per se)
- No increase in maternal mortality. Morbidity more with DSS
- No increased severity of course of dengue due to pregnancy
- Chances of vertical transmission upto 5.6%

Diagnosis of Dengue

- **Clinical suspicion if fever not responding even after 3-4 days ; or fever with leucopenia,thrombocytopenia**
- **Laboratory tests**
  - **First week – PCR test, NS1 antigen**
  - **After 7 to 10 days – Dengue IgM and IgG**

Interpretation of Tests

- Diagnosis may require a combination of tests because the body's immune system produces varying levels of antibodies over the course of the illness.
- IgM antibodies are produced first and tests for these are most effective when performed at least 7-10 days after exposure.
- Levels in the blood rise for a few weeks, then gradually decrease.
- After a few months, IgM antibodies fall below detectable levels.
- IgG antibodies are produced more slowly in response to an infection. Typically, the level rises with an acute infection, stabilizes, and then persists long-term.
- Individuals who have been exposed to the virus prior to the current infection maintain a level of IgG antibodies in the blood that can affect the interpretation of diagnostic results.

Molecular Testing (Polymerase Chain Reaction- PCR)

- Detects genetic material of dengue virus in blood up to 5 days after symptom onset (fever).
- It is generally considered the most reliable means of diagnosis, but the test is not widely available.
- A negative result on a PCR test may indicate that no infection is present or that the level of virus is too low to detect, as may happen if the test was performed in the 5-day window period during which the virus is present at low levels in the sample collected for this test.
- If very recent exposure is suspected, repeating the test at a later time (after 5days) may be warranted

Following table summarizes results that may be seen with antibody testing

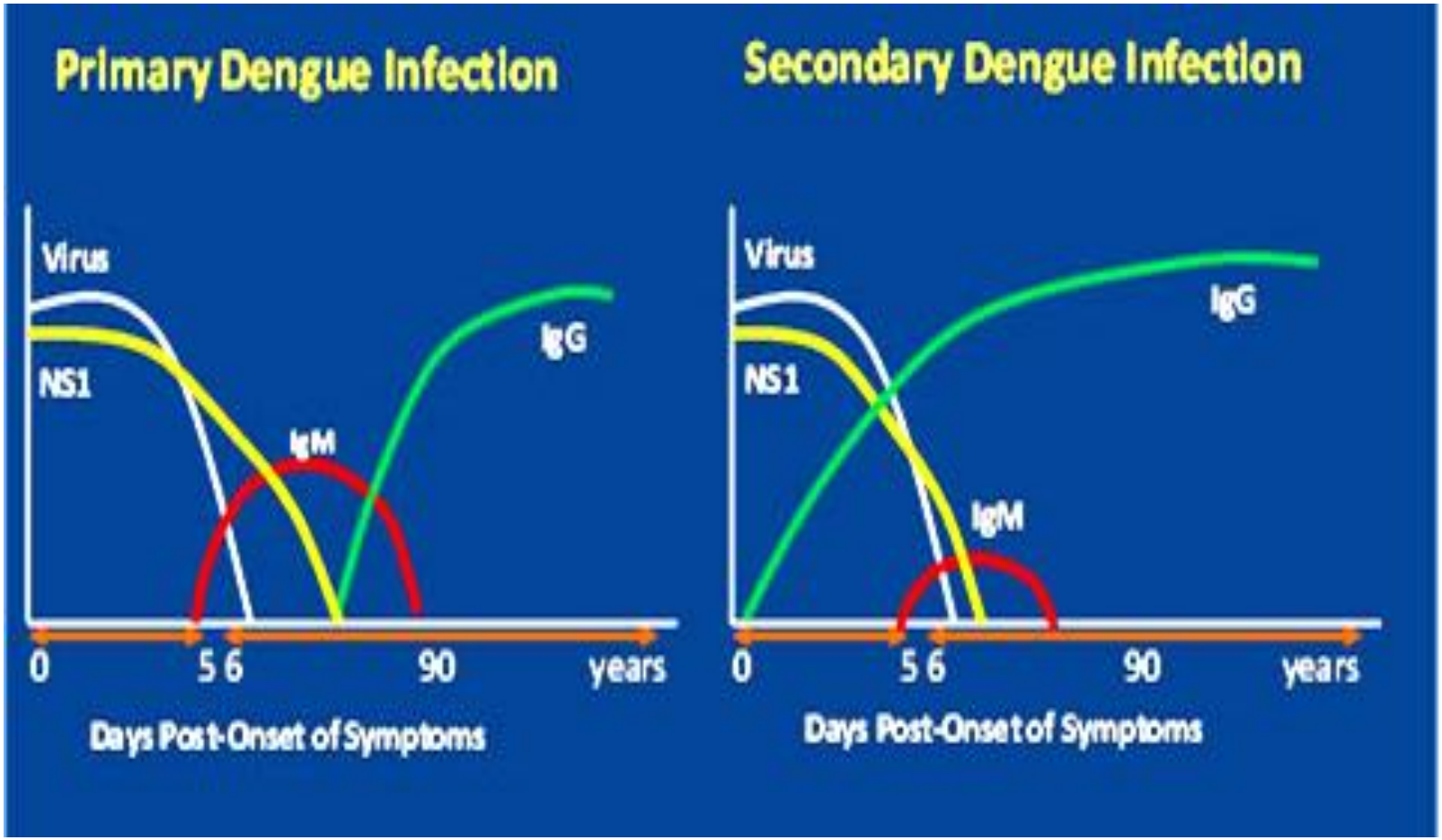
IgM Result	IgG Result	Possible Interpretation
Positive	Negative	Current infection
Positive	Positive	Current infection
Low or negative or not tested	Four-fold increase in samples taken 2-4 weeks apart	Recent infection
Low or negative	Positive	Past infection
Negative	Negative	Too soon after initial exposure for antibodies to develop or symptoms due to another cause

Possible Interpretation

- **Positive IgM and IgG tests for dengue antibodies detected in an initial blood sample mean that it is likely that the person became infected with dengue virus within recent weeks.**
- **If the IgG is positive but the IgM is low or negative, then it is likely that the person had an infection sometime in the past. If the dengue IgG antibody titer increases four-fold or greater (e.g., titer of 1:4 to a titer of 1:64) between an initial sample and one taken 2 to 4 weeks later, then it is likely that a person has had a recent infection.**
- **Negative tests for IgM and/or IgG antibodies may mean that the individual tested does not have a dengue infection and symptoms are due to another cause, or that the level of antibody may be too low to measure. The person may still have a dengue infection – it may just be that it is too soon after initial exposure to the virus to produce a detectable level of antibody.**

Dengue NS1 Ag Test

- **The dengue virus non-structural antigen non-structural protein 1 (NS1) that develops right at the beginning of the feverish period and before the appearance of dengue IgM and/or IgG is emerging as a suitable option for dengue diagnosis *(Am J Trop Med Hyg. 2010 Sep; 83(3):696-9.)*.**
- **Consequent to a multi-country evaluation of two commercially available NS1 enzyme-linked immunoabsorbent assay (ELISA) assays, a combination of NS1 and IgM detection in samples during the first few days of illness was recommended to increase overall dengue diagnostic sensitivity *(Negl Trop Dis. 2010 Aug 31; 4(8):.)*.**
- **The NS1 Ag is positive as early as day 1 of fever.**



- **Samples with a negative IgG in the acute phase and a positive IgG in the convalescent phase of the infection are primary dengue infections.**
- **Samples with a positive IgG in the acute phase and a 4 fold rise in IgG titer in the convalescent phase (with at least a 7 day interval between the two samples) is a secondary dengue infection.**

Management

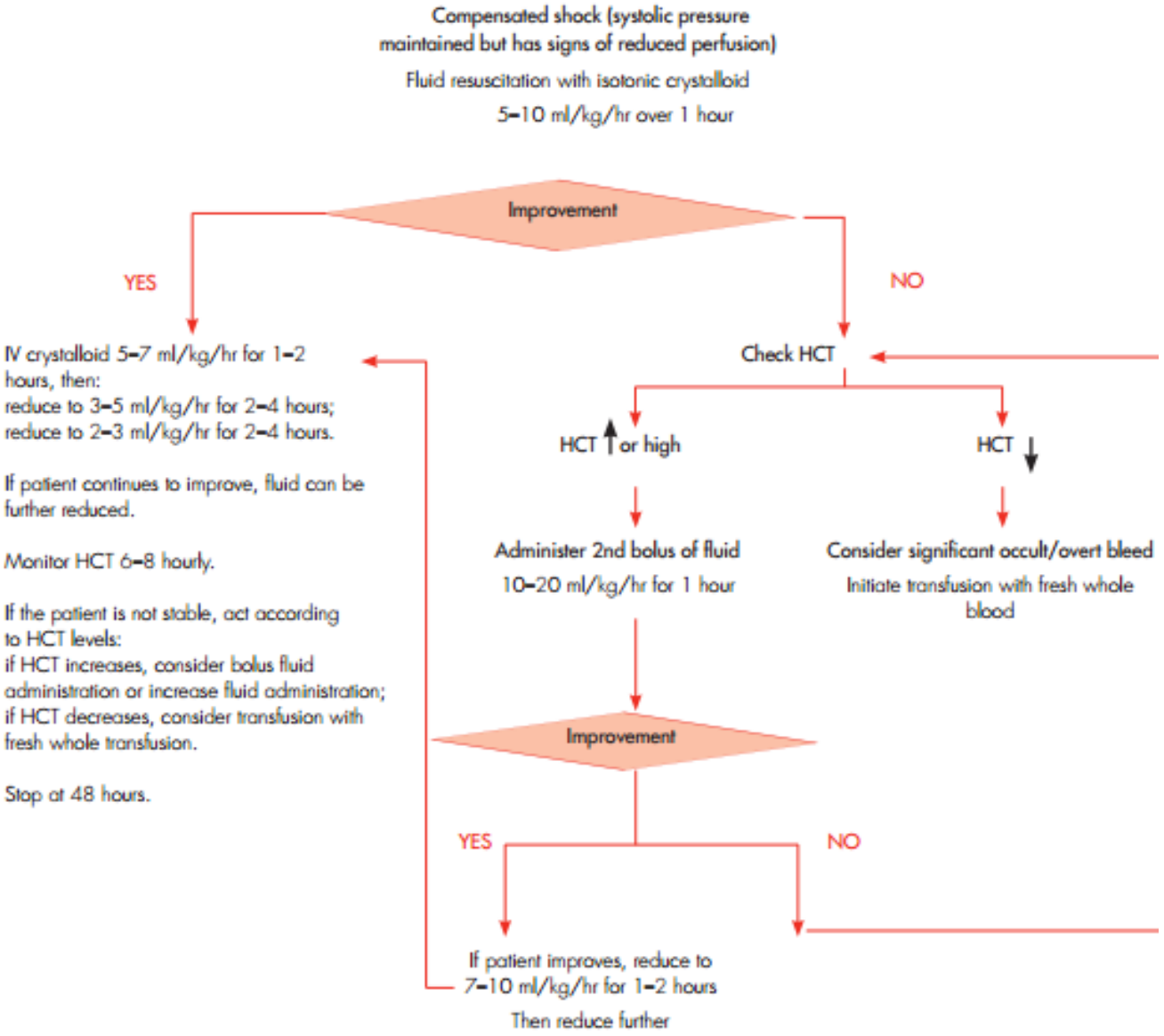
Table 2.2 A stepwise approach to the management of dengue

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

Hospital Monitoring

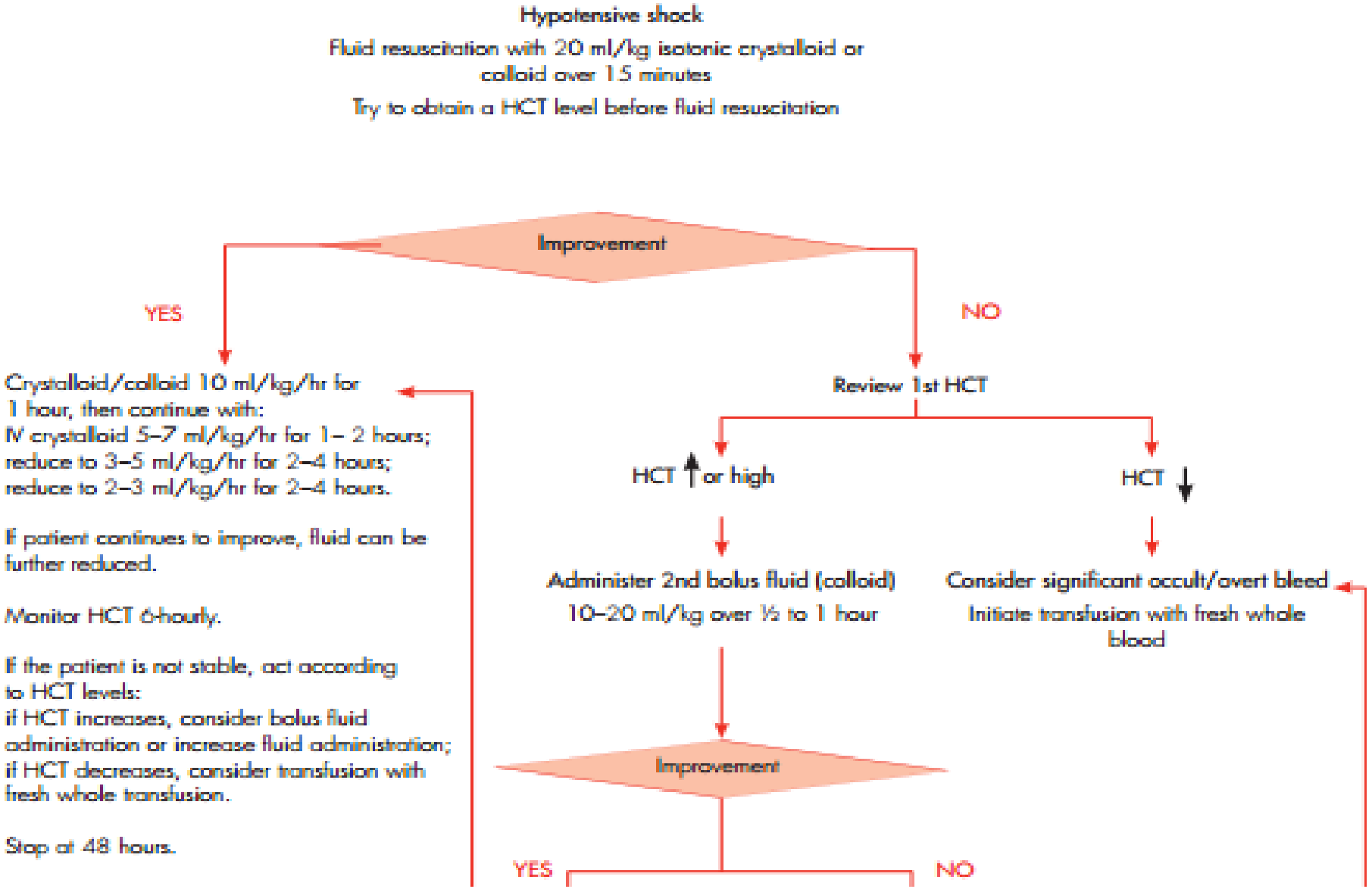
- Early warning chart
- Serial platelet counts (daily, repeat when in active labour or intervention planned)
- Hematocrit
- Look for s/s of worsening like hemorrhagic manifestations, shock

Figure 2.2 Algorithm for fluid management in compensated shock



HCT = haematocrit

Figure 2.3 Algorithm for fluid management in hypotensive shock



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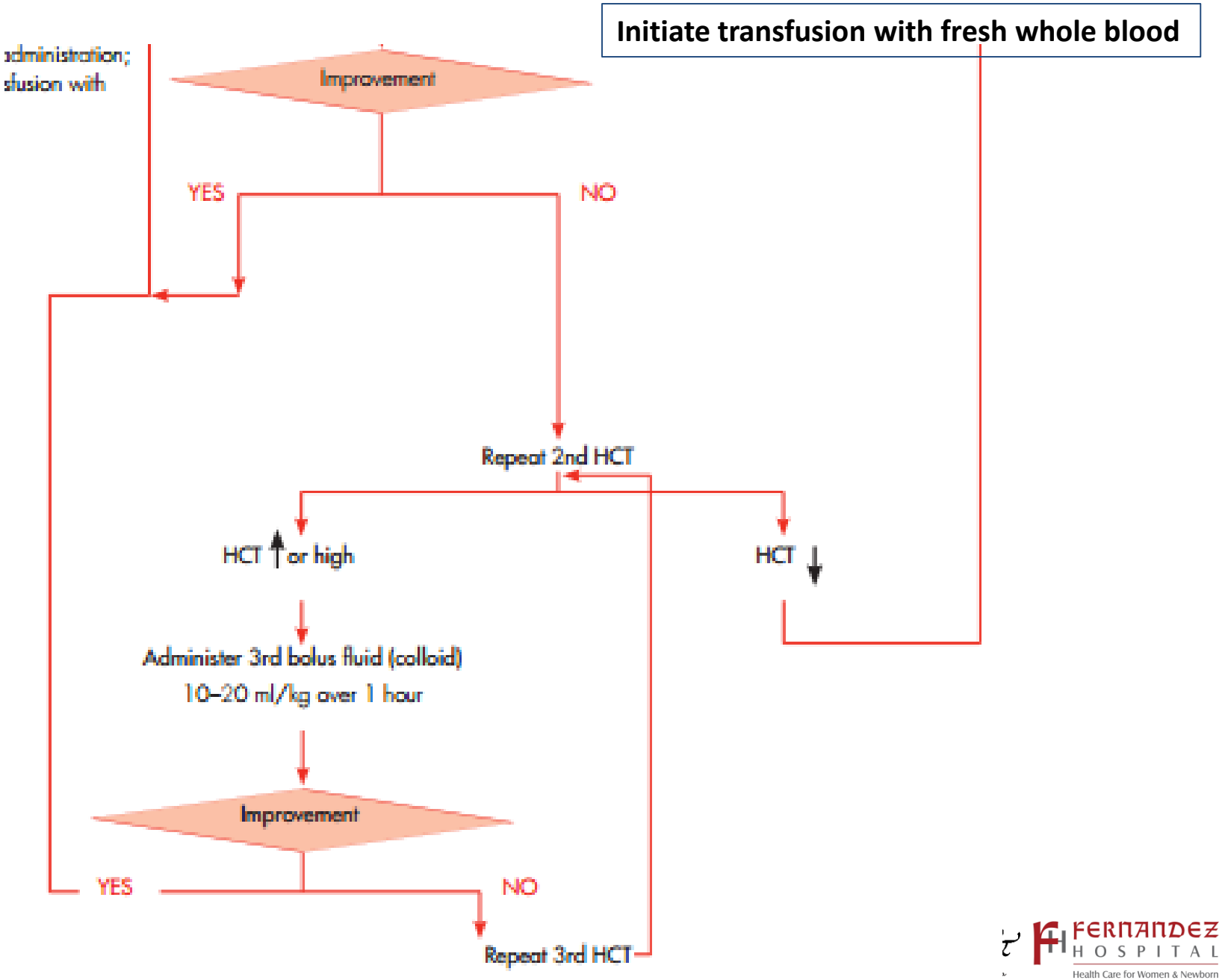

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Bleeding in Dengue

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

- Note that haematocrit of <30% as a trigger for blood transfusion, as recommended in the Surviving Sepsis Campaign Guideline (15), is not applicable to severe dengue.
- The reason for this is that, in dengue, bleeding usually occurs after a period of prolonged shock that is preceded by plasma leakage.
- During the plasma leakage the haematocrit increases to relatively high values before the onset of severe bleeding.
- When bleeding occurs, haematocrit will then drop from this high level. As a result, haematocrit levels may not be as low as in the absence of plasma leakage.

Blood Transfusion

- Give 5–10ml/kg of fresh-packed red cells or 10–20 ml/kg of fresh whole blood at an appropriate rate and observe the clinical response.
- It is important that fresh whole blood or fresh red cells are given.
- Oxygen delivery at tissue level is optimal with high levels of 2,3 di-phosphoglycerate (2,3 DPG).
- Stored blood loses 2,3 DPG, low levels of which impede the oxygen-releasing capacity of haemoglobin, resulting in functional tissue hypoxia.
- A good clinical response includes improving haemodynamic status and acid-base balance.

Counselling

- Assurance of patient and family
- To educate about symptoms that indicate worsening; also to report if any bleeding
- Avoid unnecessary platelet transfusions as it won't benefit the patient; infact may add to risk of sepsis from transfusions

Delivery

- Most may set into spontaneous labour. Hence the need to watch for preterm labour
- To repeat platelet counts at the start of active labour or before any intervention
- To have donors screened for SDP. If not available reserve RDPs
- General Anaesthesia preferred if severe thrombocytopenia present
- To watch for coagulopathy and keep blood products ready

Vertical Transmission

- Studies have shown upto 5.6% chances of vertical transmission hence neonatologists need to be alerted before delivery about maternal disease.
- Screening of newborn for NS1 antigen or dengue IgM
- Affected newborns can have a spectrum of manifestations from asymptomatic to hemorrhagic fever
- Monitoring and conservative management

Preventive Measures

- Patient education about spread of dengue
- Aedes aegypti mosquito infests stagnant water that collects in pots of plants or tyres. Water in bird baths and plant pots or drip trays should be changed at least twice each week. Pet's water bowls need to be emptied daily.
- Use of mosquito repellents not only at night time as it is a day biter especially around dawn and dusk.
- Cover water containers in the house to prevent fresh egg laying.

Preventive Measures

- Have infants sleep under bed nets during the day.
- Wear protective clothing (full sleeves shirts & full pants during day time).
- Use tight-fitting screens/wire mesh on doors and windows.
- Clogged gutters and flat roofs that may have poor drainage need to be checked regularly.
- Vaccine trials are ongoing in research projects

- There are four serotypes of the dengue virus.
- There is no cross-protective immunity to all dengue viruses when you are exposed to one serotype.
- In addition, a subsequent infection with a dengue fever virus is usually associated with more severe disease.

Government Notification format (for communicable diseases like Dengue)

S.No	Patient Name	Age & Sex	Complete Address with Phone No.	Prov. Diag.	Relevant Lab Inves.	Final Diag.	Date of Adm.	Date of Dis.	Date of death (if, any)

We at Fernandez hospital have a system where infection control nurse is made aware of any case of communicable disease admitted to the hospital. She collects the necessary information and sends to admin department who in turn mail it to health authorities as per the regulations

Clinical practice points

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

Textbox H. Calculations for normal maintenance of intravenous fluid infusion

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

4 mL/kg/h for first 10 kg body weight

+ 2 mL/kg/h for next 10 kg body weight

+ 1 mL/kg/h for subsequent kg body weight

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

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

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

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

(17)

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

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

Notes:

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

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

Who weblink address for Dengue guidelines for diagnosis, treatment, prevention and control: 2009

- **http://whqlibdoc.who.int/publications/2009/9789241547871_eng.pdf**