MODULE 8D: Management of Group C – Monitoring and Management of Other Aspects of Dengue

Dengue Clinical Management

Acknowledgements
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**Group C: Monitoring and action**

Monitoring the intravascular volume and circulation is the most crucial aspect of management

Severe dengue patients should be admitted to the high dependency or intensive care area – monitor ECG, pulse oximetry ± arterial pressure

Patients may require bladder catheterization in hypotensive shock or frequent fluid boluses

Monitor the following parameters:

1. Temperature, blood pressure, pulse pressure – every 15–30 minutes until out of shock, then every 1–2 hours
2. “5-in-1 magic touch”: colour of extremities, capillary refill time, temperature, pulse volume, pulse rate (**CCTV-R**) – every 15–30 minutes until out of shock, then every 1–2 hours
3. Respiration – Excessive fluid accumulation or metabolic acidosis
4. Urine volume and specific gravity
Group C: Monitoring and action

Organ dysfunction: What do the numbers mean?

Serum electrolytes and renal function tests:
- Low sodium = due to use of hypotonic fluid or oral intake of clear fluids
- High urea = dehydration and intravascular volume depletion
- High creatinine = prolonged shock

Acid-base balance:
- Metabolic acidosis = uncorrected shock or hyperchloremia

Liver function tests:
- High glucose = too much glucose infusion or uncorrected shock
- Low glucose = poor oral intake or impaired liver function
Pearls: Group C monitoring and action

Estimate start of significant plasma leakage (from history and CBC). Project 36 and 48 hours from time of start of plasma leakage. This would be estimated time by which IVF should be discontinued.

Before this time, plasma leakage is still active. Further boluses of fluids may be required during the first 24 to 36 hours of admission.

Volume and rate of infusion should be titrated to the haemodynamic response with step-wise reduction of IVF if patient improves.

A detailed chart of all input and outputs should be maintained and reviewed regularly. Empower patients or parents to record oral intake and urine output. You must review this chart!
What does the input and output chart tell us?

Gives an important clue of where fluid is collected – extravascular or intravascular space!

Excessive fluid balance with minimal urine volume means excessive fluid accumulation (pleural effusion, ascites) – extravascular collection

- Reduce IVF if possible, if not, switch to slower colloid infusion

Excessive urine output in a stable patient means either minimal plasma leakage or too much input or both – intravascular collection

- Indicates need for more active step-wise reduction of IVF
Major Pitfall: Excessive urine output in an unstable patient indicates glycosuria – check blood glucose.

Ask:
1. Why hyperglycaemia?
2. Are you giving too much glucose?
3. Is the shock not well controlled?
4. Does the patient have diabetes mellitus?
5. Combination of the above?

It is not a good sign at all!

Action: Control blood glucose
Remove glucose from IVF
Treat shock with appropriate fluids
Continuous insulin infusion for diabetes mellitus.
Mental status remains good, even in compensated shock. Hypotensive shock can cause seizures or alternating states of drowsiness with agitation. Confusion may be caused by electrolyte imbalances – hyponatremia, hypocalcemia, hypokalemia, severe liver dysfunction or in unusual cases encephalopathy. In very rare cases, intracerebral bleeding, usually associated with trauma.

Which organ is most frequently affected in severe dengue?

*Liver enzymes are frequently elevated during the critical and recovery phases*

Alanine aminotransferase (ALT) or aspartate aminotransferase (AST) > 1000 IU/L

Supportive therapy – maintain euglycemia and adequate tissue perfusion

**Paracetamol should be discontinued during the critical phase**

What about the brain?

Mental status remains good, even in compensated shock

Hypotensive shock can cause seizures or alternating states of drowsiness with agitation.

Confusion may be caused by electrolyte imbalances – hyponatremia, hypocalcemia, hypokalemia, severe liver dysfunction or in unusual cases encephalopathy.

In very rare cases, intracerebral bleeding, usually associated with trauma.
Risks for bleeding

**Minor** mucosal bleeding: epistaxis, gum bleeding, **not uncommon**

Who are at risk of **major** bleeding?

Patients with prolonged/refractory shock*

What are the associated features?
• Hypotensive shock + renal or liver failure + severe and persistent metabolic acidosis

Who else?
• Patients taking non-steroidal, anti-inflammatory agents
• Patients with pre-existing peptic ulcer disease
• Patients receiving anticoagulant therapy
• Patients with any form of trauma, including intramuscular injection
• Menstruating patients
• Post-partum patients

*Lum, J Peds, 2002.*
Group C: Haemorrhagic complications

Where are the sites of major bleeding?

1. Gastrointestinal tract (most common site)
2. Vaginal: Menstruation
3. Vaginal: Post-partum
4. Any form of trauma:
   - Venepuncture sites
   - Chest tube insertion sites
   - Nasogastric tube insertion may cause severe epistaxis

NOTE:
1. Internal bleeding in gastrointestinal tract may not become apparent for many hours until the first black stool is passed.
2. Use oral route to pass lubricated gastric tube.
3. HCT does not become low until very significant blood loss or after IVF therapy.
Pearls: How to recognize severe bleeding

Determine if the patient has **UNSTABLE** haemodynamic status

Any **ONE** of the following:

1. Persistent and/or severe overt bleeding, regardless of the HCT level
2. A decreased HCT **after** fluid resuscitation, especially with colloids
3. Hypotensive shock with low/normal HCT **before** fluid resuscitation
4. Refractory shock
5. Persistent metabolic acidosis

Remember that clinical signs come as a “package”. Mostly likely, more than one of the above will be observed.
Group C: Emergency treatment of haemorrhagic complications

Give: 5–10 ml/kg of fresh packed red blood cells or
10–20 ml/kg of fresh whole blood at appropriate rate
Reduce colloid/crystalloid infusions, except to maintain euglycemia

What is a good clinical response?
• Improving haemodynamic state – vital signs, peripheral perfusion and urine output
• Improving acid-base balance

When should you consider repeating blood transfusion?
1. Further blood loss
2. Unstable haemodynamic state
3. No appropriate rise in HCT after blood transfusion (i.e. 3% to 4% increase in HCT for every 10 cc/kg of packed red blood cells given)
Patients with profound thrombocytopenia do not always have bleeding

Ensure bed rest and protection from trauma to reduce the risk of bleeding.

Do not give IM injections to avoid haematoma.

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

Are prophylactic platelet transfusions necessary?

Performed in some hospitals due to concerns about bleeding

Studies indicate bleeding risk not correlated with platelet count ¹,²

Does not shorten period of thrombocytopenia ³,⁴

Limited data on effectiveness of platelet transfusions to prevent bleeding complications ³,⁴,⁵

May lead to fluid overload and prolonged hospitalization ³

What is an effective way to prevent bleeding?

Prevent prolonged shock – recognize and treat it EARLY
Avoid trauma (provokes bleeding) – CVP insertion by experienced person

Pathophysiology of thrombocytopenia

Why might giving platelets not help?

1. Early bone marrow suppression

2. Peripheral immune-mediated platelet destruction via DENV binding to platelets in the presence of DENV antibody

3. Platelets aggregate on DENV-infected endothelium, resulting in platelet destruction or clearance by macrophages

4. Haemophagocytosis

Even when actively bleeding, platelet transfusion not helpful

Other complications

Fluid overload (excessive accumulation) is a major complication in dengue shock

Causes:

Increased capillary permeability (plasma leakage)

One or more of the following:
1. Excessive and/or too rapid IV fluids
2. Use of hypotonic rather than isotonic crystalloid solutions
3. Transfusion of FFP, platelet concentrates and cryoprecipitate
4. Continuation of IV fluids after plasma leakage has resolved
5. Co-morbid conditions, e.g. congenital or ischaemic heart disease, chronic lung disease, renal disease
Clinical features of fluid overload

<table>
<thead>
<tr>
<th>AS FLUID ACCUMULATION INCREASES</th>
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<tbody>
<tr>
<td><strong>Respiratory distress</strong> – rapid, shallow breathing, chest wall in-drawing, abdominal distension</td>
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<tr>
<td><strong>Late features:</strong> more severe respiratory distress – raised JVP, wheezing, hypertension, bounding pulse, abdominal pain</td>
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<td><strong>Very late features:</strong> very severe respiratory distress, Pulmonary oedema – Hypoxaemia, Heart failure – Haemodynamic instability, Cardio-respiratory failure</td>
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Case Study 1, Scenario 1

- A 40-year-old male, weight 80 kg, ideal body weight 60 kg
- Presented to emergency department on 4th day of illness. He had myalgia, headache and anorexia.
- On the 4th day, he vomited several times, had diarrhoea more than 10 times, and complained of dizziness.

Physical exam: Alert, cool extremities, coated tongue
  BP: 98/62 mmHg, PR: 116 bpm, RR: 20, temperature: 37.1°C

- Diagnosis – Hypotensive shock, most likely dengue
- FBC: Hb 18.3, TW 6.5, Plt 8, Hct 51

Given:
- Bolus crystalloid 20 ml/kg x 1 over 1 hour
- Bolus colloid 20 ml/kg x 1 over 1 hour
- 500 ml blood over 3 hours
Case Study 1, Scenario 1: 6 hours after shock presentation, chest X-ray

**6 hours after shock presentation**

Clinical assessment
- BP 134/74 mmHg, PR 94/min, good volume pulse, Warm, CRT < 2 sec, RR 25/min, 2 L O₂
- Lungs: reduced breath sounds on the right base
- I/O : 2900/700 = Positive 2200 cc

**PLASMA LEAKAGE + FLUID ACCUMULATION**
- Increased cardiothoracic ratio
- Cardiomegaly
- Congested pulmonary vessels with “bat wings”
- Domed diaphragm because of ascites
- Blunted costophrenic angle, Pleural effusion

**How were the IV fluids redistributed?**
- Work out the average urine output
- Increased intravascular compartment

**What was the acid-base?**
- pH 7.45, Bicarbonate 23.8
- Lactate 1.9 mmol/L
Case Study 1, Scenario 2
20 hours later, chest X-ray

Complained of shortness of breath and was wheezing
Clinical assessment
Alert, RR 40/min, T 37
BP 193/110 mmHg, PR 131
Lungs: generalized rhonchi
Severe pulmonary oedema

26 hours of IVF therapy
From admission
IV: 8200
Output: 2700
Balance: +5500

Acid-base?
pH 7.45, Bic 23.9
Lact 1.7 mmol/L

Work out the average urine output
Case Study 2 - 6-yr-old, 16 kg: chest X-ray

Extravascular compartment increases: Fluid accumulation

How were the administered IV fluids re-distributed?

Intravascular compartment is small

Guess her acid-base balance

pH 6.9, Bic 8.4, BE – 19,
Lactate 9.7

Work out the average urine output

Large pleural effusion

Small cardiothoracic ratio
Right heart border (right atrium) hardly visible

Why was the child intubated?

Severe metabolic acidosis worsens respiratory distress caused by fluid accumulation

BP 84/56 mmHg, HR 166/m, cold extremities, feeble pulse,
IV since admission (45 hours ago) 4,600 ml, urine 360 ml, balance +4,240 ml
Additional investigation performed on Case 2

Chest X-ray: cardiomegaly, pleural effusion, “bat wings” appearance

ECG: to exclude ischaemic changes

Arterial/Venous blood gas: to allow regular blood sampling

Echocardiogram: to assess left ventricular function, regional wall dyskinesia, ischaemic heart disease
Management of fluid overload

Determine status of intravascular volume

Track ALL fluids given since admission

PLUS

1. Concurrent haemodynamic responses
2. Concurrent hematocrit
3. Concurrent urine output – bladder should be catheterized for shock patients who require frequent boluses
4. Any other fluid/blood losses

Chest radiograph – cardiothoracic ratio, pulmonary vessels
Echocardiogram – Left Ventricle End Diastolic Diameter (if available)

Corresponding acid-base balance

Determine the phase of illness: use time of defervescence or trending of HCT, WBC or Platelet count
Management of fluid overload in a stable patient

Give oxygen immediately

Determine: Is he out of the critical phase yet? If not:

- Intravascular volume is expanded & haemodynamic status is good (Don’t act on HCT)
- End of critical phase or already in recovery phase

Carry out step-wise reduction in IVF, as per fluid algorithm
- Avoid diuretics
- Example – Case 1, Scenario 1

End of critical phase or already in recovery phase

- Stop all IV fluids
- Example – Case 1, Scenario 2
- Note the hypertension
- May require small and frequent doses of IV frusemide (0.1 to 0.5 mg/kg/dose)

What would the HCT level be?
Management of fluid overload – stopping IV fluids

Is an important milestone during the course of dengue management. Why?

Plasma leakage stops. Allows fluid in pleural and peritoneal cavities to return to intravascular compartments.

Diuresis and resolution of pleural effusion and ascites

When should IVF be stopped?

- Signs of cessation of plasma leakage:
  - Stable vital signs, peripheral perfusion and oral intake and urine output improve
  - HCT decreases in the presence of good pulse volume
  - Resolving bowel/abdominal symptoms
Management of fluid overload in an unstable patient

Give oxygen immediately

Intravascular volume is contracted & haemodynamic status is NOT STABLE, e.g. Case 2

Check haematocrit

High HCT
- Colloid infusion at 5–10 ml/kg/hr until improved. Step-wise reduce IVF.

Low or normal HCT
- Transfuse fresh whole blood or packed red cells urgently. If improved, step-wise reduce IVF (with colloid).

"contracted"
Management of fluid overload in an unstable patient

Why do patients remain unstable despite several boluses of IVF and HCT has been reduced?

- Significant overt bleeding or occult bleeding has not been corrected
- Further infusion of IV crystalloids and colloids will lead to poor outcome
- Action: Initiate fresh whole blood transfusion ASAP

If the patient remains in shock:
- Re-check HCT, and if still low, repeat blood transfusion
- Check bleeding sites – direct pressure may help, e.g. packing the nasal passage to stop epistaxis
- Slow colloid infusion may help if HCT has increased in an unstable patient.
Other issues to be managed

Hyperglycaemia – Refer to slide #6.

Hypoglycaemia – Correct with 1–2 ml/kg of Dextrose 10%, followed by glucose-electrolyte infusion to maintain euglycaemia.

Hypokalaemia – Usually occurs during recovery phase and use of diuretics. Correct by adding potassium chloride into infusion or encourage patients to drink coconut or fruit juice.

Hyperkalaemia – associated with metabolic acidosis and acute kidney injury
May resolve with correction of shock.
In AKI, treat with resonium ± a cocktail regime consisting of insulin-dextrose + calcium gluconate solution + sodium bicarbonate.
Lucy, this refers to the previous slide. Please address this, unless I have missed something that clinicians will understand. Thanks!

Administrator, 30/01/2013
Other issues to be managed (cont.)

Hypocalcaemia – usually in association with multiple blood transfusions. Correct with 10% calcium gluconate infusion.

Metabolic acidosis –
- Tissue hypoxia in shock
Action: Treat shock, metabolic acidosis corrects itself
- Hyperchloremia due to 0.9% saline or colloids
Action: Change to Ringer lactate or Hartmann’s solution

Co-infections and nosocomial infections
Action: Be vigilant and treat promptly.
Check for thrombophlebitis and remove suspicious lines.
Regular change of peripheral intravenous lines.
Supportive care and adjunct therapy

Inotropes should be used only in severe hypotension while giving fluid resuscitation to restore circulation.

Use small doses of inotropes unless proven myocarditis.

Large doses of inotropes may give a false impression of a “good” blood pressure.

Liver impairment – Avoid hepatotoxic drugs such as paracetamol and acetaminophen. Supportive care usually leads to spontaneous recovery.

Cardiac conduction defect – usually asymptomatic
Supportive care and adjunct therapy

Management of acute kidney injury

Most common organ to suffer from shock.

Oliguria and Anuria are consequences of hypoperfusion.
→Are not indications for diuretics, especially during the critical phase

The priority is to give fluid resuscitation to achieve haemodynamic stability. Urine may start to flow once stability is achieved.
Management of acute kidney injury

When to use diuretics?

- During the reabsorption phase with fluid overload
- Established oliguric AKI with haemodynamic stability

Low doses of frusemide (furosemide) may be able to coax a gentle diuresis and avert the need for dialysis. If diuresis does not happen, then renal dialysis should be considered.

Electrolyte abnormalities such as high potassium, phosphate and uric acid may exacerbate kidney injury. Potassium and phosphate binders should be considered early.

When to initiate renal dialysis?

- Should only be considered when the haemodynamic state is stable with minimal IVF + fluid overload ± metabolic acidosis
Discharge criteria

No fever for 24 – 48 hours

Improvement in clinical status
General well-being, good appetite, stable haemodynamic status, adequate urine output, no respiratory distress and no organ dysfunction

Increasing trend of platelet count (usually preceded by rising WBC)

Stable haematocrit with oral intake and off IV fluids

Rash – characteristic of dengue

Who needs to be followed up?
Follow up patients with organ impairment

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