Fluid balance in the critically ill child with dengue – Too much too little?

Professor Lucy Lum
Universiti Malaya
ASMIC 2018
21-23 Sept
## Dengue Cases Reported in the Week 36/2018
(2nd September until 8th September 2018)

<table>
<thead>
<tr>
<th>No.</th>
<th>States</th>
<th>No. of dengue cases and deaths reported</th>
<th>Cumulative dengue cases until week 36/2018</th>
<th>Cumulative dengue cases until week 36/2017</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Cases</td>
<td>Deaths</td>
<td>Cases</td>
</tr>
<tr>
<td>1</td>
<td>Perlis</td>
<td>5</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>2</td>
<td>Kedah</td>
<td>21</td>
<td>0</td>
<td>35</td>
</tr>
<tr>
<td>3</td>
<td>P. Pinang</td>
<td>144</td>
<td>0</td>
<td>112</td>
</tr>
<tr>
<td>4</td>
<td>Perak</td>
<td>33</td>
<td>0</td>
<td>38</td>
</tr>
<tr>
<td>5</td>
<td>Selangor</td>
<td>874</td>
<td>1</td>
<td>913</td>
</tr>
<tr>
<td>6</td>
<td>WP KL &amp; Putrajaya</td>
<td>202</td>
<td>1</td>
<td>148</td>
</tr>
<tr>
<td>7</td>
<td>N. Sembilan</td>
<td>41</td>
<td>1</td>
<td>32</td>
</tr>
<tr>
<td>8</td>
<td>Melaka</td>
<td>20</td>
<td>0</td>
<td>13</td>
</tr>
<tr>
<td>9</td>
<td>Johor</td>
<td>92</td>
<td>0</td>
<td>111</td>
</tr>
<tr>
<td>10</td>
<td>Pahang</td>
<td>20</td>
<td>0</td>
<td>13</td>
</tr>
<tr>
<td>11</td>
<td>Terengganu</td>
<td>20</td>
<td>0</td>
<td>13</td>
</tr>
<tr>
<td>12</td>
<td>Kelantan</td>
<td>71</td>
<td>0</td>
<td>61</td>
</tr>
<tr>
<td>13</td>
<td>Sarawak</td>
<td>12</td>
<td>0</td>
<td>16</td>
</tr>
<tr>
<td>14</td>
<td>Sabah</td>
<td>71</td>
<td>1</td>
<td>72</td>
</tr>
<tr>
<td>15</td>
<td>WP Labuan</td>
<td>1</td>
<td>0</td>
<td>2</td>
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</tbody>
</table>

**CFR** 0.22 in 2017  
0.15 in 2018
Lecture Contents:

• Dynamic disease – Self-limiting capillary leak syndrome

• Phases of fluid resuscitation

• Targets and evaluation of fluid responsiveness

• Strategic management of Re-shock
After the incubation period, the illness begins abruptly.

It is characterized by 3 phases:

**Febrile phase** – commences at symptom onset

**Critical phase** – commences around time of defervescence* - **PLASMA LEAKAGE**

* Defined as when body temperature drops to less than 38°C and remains below this level.

**Recovery phase** – commences when **plasma leakage resolves**
Pathophysiology of Severe Dengue

- Timing of severe manifestations at height of inflammatory host response suggest immune driven phenomenon
Endothelium-glycocalyx complex

Dengue shock: Rapid capillary leak of smaller proteins such as albumin into interstitial spaces
Fluid flux = \( (P_c - P_{is}) - \sigma (\pi_c - \pi_{is}) \)

= Hydrostatic pressure – \( \sigma \) (oncotic pressure)

\( \propto \) Hydrostatic pressure
Fluid accumulation with respiratory distress*

- Age < 15 years – AHR 3.85
- Referral from an inpatient facility
- Longer Duration of IV fluid therapy – AHR 1.66 per additional day
- Amount of IVF in the preceding 24 hours – AHR 1.18 per 10 ml/kg
- IV fluid bolus in the preceding 24 hours – AHR 2.9.

- Each were independent risks factors

*Vascular leakage in dengue – clinical spectrum and influence of parenteral fluid therapy, 2016, TMIH
### Why the need to balance carefully –

<table>
<thead>
<tr>
<th>Too much fluid</th>
<th>Too little fluid</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Vascular leak syndrome</td>
<td>• Prolonged shock</td>
</tr>
<tr>
<td>• Fluid accumulation – respiratory distress</td>
<td>• Organ impairment</td>
</tr>
<tr>
<td>• More organ impairment</td>
<td>• Severe bleeding – can be difficult to recognize</td>
</tr>
<tr>
<td>• Bleeding tendencies and peripheral destruction of platelets – chest drains may cause bleeding</td>
<td>• Refractory shock</td>
</tr>
</tbody>
</table>
Indications of IV fluid therapy

- Resuscitation Therapy
- Rehydration Therapy – Deficit
- Replacement Therapy – on-going abnormal losses
- Maintenance Therapy – “Just enough” IV fluid for metabolic rate – Oral + Parenteral
Stages of fluid resuscitation:

- Rescue
- Stabilization
- Optimization
- De-escalation

Four phases of intravenous fluid therapy: a conceptual model
E. A. Hoste, BJA 2014
### Four phases of intravenous fluid therapy: a conceptual model

E. A. Hoste, BJA 2014

<table>
<thead>
<tr>
<th></th>
<th>Rescue</th>
<th>Optimization</th>
<th>Stabilization</th>
<th>De-escalation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Principles</strong></td>
<td>Life-Saving</td>
<td>Organ rescue</td>
<td>Organ support</td>
<td>Organ recovery</td>
</tr>
<tr>
<td><strong>Goals</strong></td>
<td>Correct shock</td>
<td>Optimize and</td>
<td>Aim for zero or negative fluid</td>
<td>Mobilize fluid accumulated – negative fluid</td>
</tr>
<tr>
<td></td>
<td>(Macrocirculation) maintain tissue</td>
<td>balance</td>
<td>balance</td>
<td>balance</td>
</tr>
<tr>
<td><strong>Time</strong></td>
<td>Usually minutes</td>
<td>Hours</td>
<td>Days</td>
<td>Days to weeks</td>
</tr>
<tr>
<td><strong>Phenotype</strong></td>
<td>Severe shock</td>
<td>Unstable</td>
<td>Stable</td>
<td>Recovering</td>
</tr>
<tr>
<td><strong>Fluid therapy</strong></td>
<td>Rapid boluses</td>
<td>Titrate fluid</td>
<td>Minimal maintenance infusion only if</td>
<td>Oral intake if possible. Avoid unnecessary i.v.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>infusion,</td>
<td>oral intake inadequate</td>
<td>fluids</td>
</tr>
<tr>
<td></td>
<td></td>
<td>conservative use</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Volumes</strong></td>
<td>10 to 20 ml/kg</td>
<td>5 - 8 ml/kg</td>
<td>Maintenance fluid</td>
<td>Reduce / discontinue IV</td>
</tr>
</tbody>
</table>
Group C: Emergency treatment – Summary

**Compensated shock** (systolic pressure maintained + reduced perfusion)

- **Start isotonic crystalloid therapy**
  - 5–10 ml/kg/hr (adult) or
  - 10–20 ml/kg (child) for 1 hour

  → **Improved**
  → **REASSESS**

- **Step-wise reduction of IV crystalloids**
  - 5–7 ml/kg/hr for 1–2 hours
  - 3–5 ml/kg/hr for 2–4 hours
  - 2–3 ml/kg/hr for 2–4 hours

  → **Further boluses may be required**

- **Clinical improvement or improved oral intake, reduce fluids step-wise**

  → **Stop IV fluids at 24–48 hours**

**Hypotensive shock**

- **Start isotonic crystalloid or colloid therapy**
  - 10–20 ml/kg (adult) or
  - 20 ml/kg (child) over 15–30 min

  → **REASSESS**

- **Step-wise reduction of IV crystalloids**
  - 5–7 ml/kg/hr for 1–2 hours
  - 3–5 ml/kg/hr for 2–4 hours
  - 2–3 ml/kg/hr for 2–4 hours

  → **Further boluses may be required**

- **Clinical improvement or improved oral intake, reduce fluids step-wise**

  → **Stop IV fluids at 24–48 hours**

* Reassess the patient’s clinical condition: vital signs, pulse volume, capillary refill time and temperature of extremities; decide on the situation. ** Colloids are preferable if the patient has already received several boluses of crystalloid.
Fluid titration in compensated dengue shock

IV Fluid management (mL/kg/hr)

- **Rescue**: 10 ml in 1 hour
- **Optimization**:
  - 5-8 ml in 2-3 hours
  - 4-7 ml in 4-7 hours
  - 3-5 ml in 8-11 hours
- **Stabilization**: 2-4 ml in 12-24 hours
- **De-escalation**: 2-4 ml in 24-48 hours
- **STOP**: > 48 hours
Fluid titration in hypotensive dengue shock

- **Rescue**: 20 ml (15 min)
- **Optimization**: 10 - 15 ml (1 hr)
- **Stabilization**: 7 - 10 ml (2 - 3 hr)
- **De-escalation**: 5 - 7 ml (4 - 7 hr)
- **Stop**: 3 - 5 ml (8 - 11 hr)
- **48 h**: 3 - 4 ml (12 - 24 hr)
- **25 - 36 h**: 1 - 3 ml (24 - 48 hr)
6 yr-old, Admitted on Day 5 of illness,

Vomiting 6 times, Temp 37°C, HR 168/min. At admission, HCT 36%. Encouraged oral fluids, no IV drip

14 hrs later:
Poor perfusion,
HCT increased to 47%

Bolus 20 ml/kg saline over 1 hr,

Post bolus, still poor perfusion; Repeat HCT 47%

Supine A-P CXR, post bolus 20 ml/kg saline

How would you manage at this stage?
**Group C: Emergency treatment – Summary**

**Compensated shock** (systolic pressure maintained + reduced perfusion)

- Start isotonic crystalloid therapy 5–10 ml/kg/hr (adult) or 10–20 ml/kg (child) for 1 hour
- Step-wise reduction of IV crystalloids:
  - 5–7 ml/kg/hr for 1–2 hours
  - 3–5 ml/kg/hr for 2–4 hours
  - 2–3 ml/kg/hr for 2–4 hours
- Further boluses may be required
- Clinical improvement or improved oral intake, reduce fluids step-wise
- Stop IV fluids at 24–48 hours

**Increasing or high HCT**

- Crystalloids (2nd bolus) or colloids** 10–20 ml/kg/hr for 1 hr
- If improved:
  - Reduce IV crystalloids to 7–10 ml/kg/hr for 1–2 hours
  - Continue step-wise reduction of IVF

**Check haematocrit**

**Not improved**

- If Improved:
  - Reduce IV crystalloids to 7–10 ml/kg/hr for 1–2 hours
  - Continue step-wise reduction with crystalloids

**Increasing or high HCT**

- Colloids** 10 ml/kg for 30–60 min
- If improved:
  - Reduce IV crystalloids to 7–10 ml/kg/hr for 1–2 hours
  - Continue step-wise reduction with crystalloids

**Compensated shock**

**Hypotensive shock**

- Start isotonic crystalloid or colloid therapy 10–20 ml/kg (adult) or 20 ml/kg (child) over 15–30 min

**Try to obtain CBC, HCT, GXM & other bloods before fluid resuscitation**

**Increasing or high HCT**

- IV crystalloid or colloid 10 ml/kg/hr for 1 hours
- Step-wise reduction of IV crystalloids:
  - 5–7 ml/kg/hr for 1–2 hours
  - 3–5 ml/kg/hr for 2–4 hours
  - 2–3 ml/kg/hr for 2–4 hours
- Further boluses may be required
- Clinical improvement or improved oral intake, reduce fluids step-wise
- Stop IV fluids at 24–48 hours

* Reassess the patient’s clinical condition: vital signs, pulse volume, capillary refill time and temperature of extremities; decide on the situation.
** Colloids are preferable if the patient has already received several boluses of crystalloid.
Colloid therapy in dengue shock

When should colloids be given?

- Hypotensive shock\(^1,2,3\)
- **Re-shock** – 2nd or 3rd shock and onwards
- After >20 to 30 ml/kg of crystalloids
- HCT does not decrease after crystalloid administration in shock state

**NOTE:** If **NO** clinical improvement with **REDUCED HCT**, suspect **significant occult bleeding**

**DOSE:** Limited to 30 to 50 ml/kg/day

**Fluid-sparing strategy**

**Chest x-ray, Case 2 - 16 kg**

**FLUID ACCUMULATION:**
Extra-vascular compartment increases
Intravascular compartment is small

**Large Pleural Effusion**

Small cardio-thoracic ratio
Right heart border (Right Atrium) is hardly visible

Severe metabolic acidosis worsens respiratory distress caused by fluid accumulation

**What other investigations that will guide fluid management?**

Hematocrit – 36%, Platelet – 6

**BP 84/56 mmHg, HR 166/m, cold extremities, feeble pulse**
**IV since admission (45 hours ago) 4600 ml, Urine 360 ml, Balance +4240 ml**

pH 6.9, Bic 8.4, BE – 19,
Lactate 9.7
* Reassess the patient's clinical condition: vital signs, pulse volume, capillary refill time and temperature of extremities; decide on the situation.

** Colloids are preferable if the patient has already received several boluses of crystalloid.
Clinical and laboratory data and outcome of severe hemorrhage in dengue shock syndrome

<table>
<thead>
<tr>
<th>Clinical/laboratory data</th>
<th>Group 1 (significant hemorrhage)</th>
<th>Group 2 (no/mild hemorrhage)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)°</td>
<td>7.0 (0.3–12.0)</td>
<td>6.0 (0.2–11.7)</td>
<td>.801</td>
</tr>
<tr>
<td>Hypotension (%)</td>
<td>68.1</td>
<td>37.8</td>
<td>.010</td>
</tr>
<tr>
<td>Mottling (%)</td>
<td>45.0</td>
<td>22.0</td>
<td>.027</td>
</tr>
<tr>
<td>Encephalopathy (%)</td>
<td>63.3</td>
<td>28.3</td>
<td>.002</td>
</tr>
<tr>
<td>Liver failure (%)</td>
<td>63.6</td>
<td>22.0</td>
<td>.000</td>
</tr>
<tr>
<td>Abnormal glycemia (%)</td>
<td>61.9</td>
<td>17.4</td>
<td>.000</td>
</tr>
<tr>
<td>Duration of shock (h)°</td>
<td>12.0 (2.0–24.0)</td>
<td>4.0 (0.0–10.2)</td>
<td>.000</td>
</tr>
<tr>
<td>Platelet count at admission (×10^9/L)°</td>
<td>60.5 (7.0–219.0)</td>
<td>61.0 (11.5–187.9)</td>
<td>.902</td>
</tr>
<tr>
<td>Hematocrit at admission (%)</td>
<td>39.5 (14.0–64.0)</td>
<td>45.0 (31.3–60.0)</td>
<td>.032</td>
</tr>
<tr>
<td>Lowest platelet count°</td>
<td>17.0 (7.0–90.0)</td>
<td>22.0 (5.3–99.5)</td>
<td>.227</td>
</tr>
<tr>
<td>Prothrombin time ratio°</td>
<td>2.16 (1.0–4.0)</td>
<td>1.19 (1.0–2.4)</td>
<td>.000</td>
</tr>
<tr>
<td>Partial thromboplastin time (s)°</td>
<td>120.0 (48.5–200.0)</td>
<td>72.2 (36.8–182.8)</td>
<td>.001</td>
</tr>
<tr>
<td>Serum creatinine (μmol/L) at admission°</td>
<td>198.0 (448.0–938.0)</td>
<td>74.0 (24.5–637.7)</td>
<td>.022</td>
</tr>
</tbody>
</table>

*Data shown are median (2.5–97.5 percentile).
Number of deaths was 6 of 22 for group 1; none for group 2 (P = .001).

J Pediatr 2002;140:629-31
Multivariate logistic regression analysis of clinical and laboratory features of severe hemorrhage in dengue shock syndrome

<table>
<thead>
<tr>
<th>Clinical and laboratory features</th>
<th>Odds ratio</th>
<th>95% CI</th>
<th>β</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Encephalopathy</td>
<td>0.01</td>
<td>0.00–41.89</td>
<td>-4.40</td>
<td>.289</td>
</tr>
<tr>
<td>Mottling</td>
<td>0.08</td>
<td>0.00–15.50</td>
<td>-2.50</td>
<td>.350</td>
</tr>
<tr>
<td>Hypotension</td>
<td>2.28</td>
<td>0.18–28.19</td>
<td>0.08</td>
<td>.521</td>
</tr>
<tr>
<td><strong>Duration of shock</strong></td>
<td><strong>2.11</strong></td>
<td><strong>1.13–3.92</strong></td>
<td><strong>0.75</strong></td>
<td><strong>.019</strong></td>
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<tr>
<td>Hematocrit at admission</td>
<td><strong>0.72</strong></td>
<td><strong>0.55–0.95</strong></td>
<td><strong>-0.33</strong></td>
<td><strong>.020</strong></td>
</tr>
<tr>
<td>Liver failure</td>
<td><strong>1.8 × 10^4</strong></td>
<td><strong>0.50–6.80 × 10^8</strong></td>
<td><strong>9.83</strong></td>
<td><strong>.067</strong></td>
</tr>
<tr>
<td>Renal failure at admission</td>
<td>1.44</td>
<td>0.10–249.90</td>
<td>0.37</td>
<td>.889</td>
</tr>
<tr>
<td>Prothrombin time ratio</td>
<td>0.10</td>
<td>0.00–46.89</td>
<td>-2.30</td>
<td>.454</td>
</tr>
<tr>
<td>Abnormal glycemia</td>
<td>2.71</td>
<td>0.22–33.68</td>
<td>1.00</td>
<td>.437</td>
</tr>
<tr>
<td>Partial thromboplastin time</td>
<td>1.03</td>
<td>0.98–1.07</td>
<td>0.03</td>
<td>.262</td>
</tr>
</tbody>
</table>
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

Group and **CROSS MATCH** for all dengue SHOCK (esp Hypotensive) patients at admission

Urgent Transfusion of Fresh blood
Monitoring of hemodynamic responses to IV fluid boluses – fluid responsiveness

Frequent assessment – Targets and Safety limits

- Clinical assessment
- Hematological & Biochemical: Serial Hct, lactate (Yacoub et al, 2017), SvO$_2$
- Radiological – point of care ultrasound (POCUS) of IVC (Finnerty et al, 2017)
- Left ventricle end diastolic volume (LVEDd)

- Fluid balance & Fluid accumulation

- Fluid overload – increased mortality, prolonged ventilation and acute kidney injury

Alobaidi, et al, JAMA Pediatr 2018
Payen et al, Crit Care 2008
Vaara et al, Crit Care 2012
## Prevention of Fluid overload in dengue

### Causes
- *Cumulative balance > 100 ml/kg
- IV fluid therapy in Febrile phase
- Recurrent shock – crystalloids
  Not changing to colloid solution
- Transfusion of platelet count, FFP
- Delayed recognition of shock
  Delayed recognition of bleeding
- Continuation of IV fluid beyond critical phase

### Prevention
- Oral or minimal IV fluid during febrile phase
- Frequent assessment
- Recognise early shock
- Change to colloid early
- Suspect occult bleeding
- Urgent blood transfusion
- Step-wise reduction of IV Infusion
- Stop IV infusion by 48 hours

*[(Total Fluid Intake – Total Fluid Output in Liters) / Adm Weight in Kilograms] × 100.*
**Summary of IV fluid therapy in dengue**

**Inadequate**
- Hypovolaemia
- Compensated shock
- Hypotensive shock
  - Bleeding
  - DIC
  - Multi-organ failure

**JUST ENOUGH**
- Improved circulation and tissue perfusion
  - Capillary refill <2 seconds
  - Normal heart rate
  - Normal blood pressure
  - Normal pulse pressure
  - Urine 0.5ml/kg/hr
  - ↓ HCT to normal
  - Improving acid-base

**Excessive**
- Fluid overload:
  - Pulmonary oedema
  - Respiratory distress
  - Worsening pleural effusion and ascites
  - Clinical deterioration
More research need ...

- The fluid-overloaded dengue shock syndrome
- Recurrent shock - What is the most suitable fluid?
- What is the most suitable colloid solution
- Is starch solution that bad?
- What is the role of oral fluids during the critical phase?
Thank you for your attention!
Transition from febrile phase to critical phase

- Usually day 4 to day 7 of illness
- Could be as early as day 3 or as late as day 7 or 8
- Coincides with defervescence

Development of warning signs:
Identify dengue patients already in shock or at risk of developing shock

**Clinical Warning Signs**

1. **Severe abdominal pain**
2. **Persistent vomiting**
3. **Lethargy; restlessness**
4. Mucosal bleed
5. Liver enlargement >2cm
6. Clinical fluid accumulation

**Laboratory Warning Signs**

1. Leukopenia
2. Rapid decrease platelet count
3. Rising haematocrit
• *Alle Dinge sind Gift, und nichts ist ohne Gift, allein die Dosis macht dass ein Ding kein Gift ist.*

All things are poison, and nothing is without poison, the dosage alone makes it so a thing is not a poison.
Summary of Proactive Measures

• Team training – knowledge, rehearse skills; from triage to ICU team – recognition, monitoring, fluid therapy.

• Dengue Shock: Minute-to-minute evaluation and decision-making to achieve and then maintain hemodynamic equilibrium

• Co-morbid conditions could be worse than the dengue illness

• Handover from one team to another, across departments: Gaps in continuity of care - Change of work shift, on-call team
• In patients with vascular leakage, IV fluid therapy can aggravate fluid accumulation and lead to respiratory distress
Fluid therapy and phases of dengue

**Incubation period**

**Febrile Phase**
- Viraemia: headache, nausea, anorexia, myalgia, body ache and rash,

**Critical Phase**
- Resus Fluid + Oral + IV therapy

**Recovery Phase**
- Oral fluid therapy

Fluid therapy
- Oral fluid therapy

Days
0 1 2 3 4 6 8 10