Dengue: The Most Challenging Disease

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Global situation

- An estimated 2.5 billion people (40% of world’s population) live in over 100 endemic countries and areas where dengue viruses can be transmitted.
- Up to 50 million infections occur annually
  - DHF 500,000
  - Deaths 22,000

Multiple dengue serotypes and high frequency of dengue hemorrhagic fever at two tertiary care hospitals in Lahore during the 2008 dengue virus outbreak in Punjab, Pakistan

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Sex Distribution of Dengue Cases During 2008 Outbreak In Pakistan

- Number of Male cases: 64
- Number of Female cases: 36
Demographic Profile Of Dengue Cases During 2008 Outbreak In Pakistan

![Bar Chart]

- Age of the Patient
- No. of Cases

- 15-19
- 20-24
- 25-29
- 30-34
- 35-39
- 40-44
- 45-49
- 50-54
- 55-59
- 60-65

Note: The chart shows the distribution of cases across different age groups during the 2008 Dengue outbreak in Pakistan.
Duration of Fever Among Dengue Cases
During 2008 Outbreak In Pakistan

No. of Cases

Total Duration of Fever (days)

<table>
<thead>
<tr>
<th>Duration</th>
<th>No. of Cases</th>
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<tbody>
<tr>
<td>3</td>
<td>12</td>
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<tr>
<td>4</td>
<td>19</td>
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<td>5</td>
<td>21</td>
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<td>10</td>
<td>3</td>
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<td>11</td>
<td>3</td>
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<td>15</td>
<td>2</td>
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<tr>
<td>16</td>
<td>2</td>
</tr>
<tr>
<td>20</td>
<td>2</td>
</tr>
</tbody>
</table>

Std Dev = 2.48
Mean = 6
N = 110
Day of Presentation After Onset of Fever

Std. Dev = 2.61
Mean = 4.2
N = 110.00
### Frequency of various Hemorrhagic Manifestations

<table>
<thead>
<tr>
<th>SIGNS AND SYMPTOM</th>
<th>FREQUENCY*</th>
<th>PERCENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>110</td>
<td>100 %</td>
</tr>
<tr>
<td>Rash (Hemorrhagic)</td>
<td>57</td>
<td>51.8%</td>
</tr>
<tr>
<td>Epistaxis</td>
<td>17</td>
<td>15.5%</td>
</tr>
<tr>
<td>Retinal Hemorrhages</td>
<td>11</td>
<td>10%</td>
</tr>
<tr>
<td>Hematuria</td>
<td>10</td>
<td>9.1%</td>
</tr>
<tr>
<td>Gingival Bleed</td>
<td>9</td>
<td>8.2%</td>
</tr>
<tr>
<td>Hemoptysis</td>
<td>6</td>
<td>5.5%</td>
</tr>
<tr>
<td>Hemetemesis</td>
<td>3</td>
<td>2.7%</td>
</tr>
<tr>
<td>Vaginal Bleed</td>
<td>3</td>
<td>2.7%</td>
</tr>
<tr>
<td>Hematochezia</td>
<td>3</td>
<td>2.7%</td>
</tr>
<tr>
<td>Any hemorrhage**</td>
<td>1</td>
<td>0.9%</td>
</tr>
</tbody>
</table>

* Only 2 (3.5%) cases had severe hemorrhagic manifestations
**Dengue Serotypes**

- Total 17 patients had their viral RNA detected by RT-PCR and serotyping done.
- 10/17 were of DEN 4 serotype,
- while 5/17 were DEN 2 serotype,
- 2/17 were DEN 3 serotype,
- Three different serotypes were detected in this small number of patients.
Dengue Viral Infection (10,000)

Asymptomatic (majority) (9000)

Viral Syndrome (500)

- DF (400)
  - With bleeding

Symptomatic (1000)

- DHF (100)
  - Plasma leakage
    - DHF (98%)
    - DSS (1-2%)
  - No bleeding

Unusual dengue-expanded dengue syndrome (<<1%)
<table>
<thead>
<tr>
<th>Condition</th>
<th>DF</th>
<th>DHF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tourniquet test</td>
<td>++</td>
<td>++++</td>
</tr>
<tr>
<td>Petechiae, pur-pura</td>
<td>+</td>
<td>+++</td>
</tr>
<tr>
<td>↓WBC</td>
<td>+++++</td>
<td>+</td>
</tr>
<tr>
<td>↓platelet</td>
<td>++</td>
<td>++++</td>
</tr>
<tr>
<td>↑haematocrit</td>
<td>0</td>
<td>+++</td>
</tr>
<tr>
<td>Hepatomegaly</td>
<td>0</td>
<td>++++</td>
</tr>
<tr>
<td>Spontaneous bleeding</td>
<td>+/-</td>
<td>+</td>
</tr>
<tr>
<td>Shock</td>
<td>0</td>
<td>+</td>
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</table>
Torniquet test
DHF vs DF

Febrile Phase

Critical Phase

Recovery Phase

Febrile Phase

Critical Phase

Recovery Phase
Acute Onset high fever + Body aches
Retro-orbital pain
Flushing etc...

Viral Fever
Dengue Fever
Dengue Haemorrhagic fever

Adequate rest
Adequate oral fluids (juices and electrolyte solutions e.g. Jeewani)

Observe for warning signs
Clinical deterioration when fever subsides
Bleeding
Severe vomiting/abdominal pain
Very thirsty
Drowsy, sleeping all the time
Refuse to eat or drink
Shock / impending shock
Cold, clammy skin and extremities.
Decrease urine output or no urine for 4-6 hours.
Behavior changes e.g. confusion, restless

FBC after D2

White cell count < 5,000

Platelet count < 100,000

DF or DHF

Hospital Admission

Possible Dengue fever or Dengue Haemorrhagic fever

Repeat FBC on a daily basis

Platelet count > 100,000 but dropping

Get medical opinion to decide on hospital admission
Hospital Admission

Evidence of leaking
- Rising Hct (check Hct twice a day)
- Pleural effusions/ Ascites (by chest x-ray or ultrasound scan)
- Low albumin/ low cholesterol

Critical Phase (lasts 24 – 48 hours)
- Needs some fluid restriction (both oral / IV)
- Give only a calculated volume of fluid
- Continuous monitoring of pulse rate, blood pressure, Haematocrit, Urine output

No evidence of leaking

DHF not started leaking yet

Unusual Dengue

DF
DF or DHF?

- Important to differentiate
- Two different clinical conditions from the beginning of the illness; Though they look very similar on the first 2 days

- However badly managed DF will never become DHF (DF does not progress to DHF)
Dengue Fever (DF)

- No plasma leakage
- Plt may be decreased to <100,000 in about 50% of patients
- Leucopenia (<5000) also present
- Headache, muscle/joint/bone pain, haemorrhagic manifestations seen in both DF and DHF
- MP rash seen more in DF than DHF
Leukopenia+ Hess’s test à >80% PPV for Dengue (DF/DHF both)

Hess’s test

- When done properly it will become +Ve
- (> 10 spots)
- Do repeat tests
- Use a magnifying class
- Most useful when WBC < 5000 but platelet > 150,000/
the new guidelines for the 1\textsuperscript{st} time stressed the importance of measuring fluids that we give. Give only a calculated amount of fluid—both IV and oral!
# Fluid balance in health and dengue

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<tr>
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<tr>
<td><strong>Total intake</strong></td>
<td>3</td>
<td>3</td>
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<tr>
<td><strong>UOP</strong></td>
<td>2</td>
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<td><strong>Insensible loss</strong></td>
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Patient is in critical phase and confirmed to be DHF if ...

- Fever D 3 or beyond
- Platelet < 100,000 (WBC < 5,000)
- Evidence of plasma leak
  - Effusions: pleura/ peritoneum (CXR/ USS)
  - Hct rise of 20% from baseline
  - Low albumin/ low cholesterol
- Hemorrhagic manifestations
  - (not essential if objective evidence of plasma leak+)

Laboratory confirmation of dengue infection NOT essential
Detection of critical phase

- Defervescence
- Drowsy
- Severe abdominal pain
- Enlarged tender hepatomegally
- Rapid pulse
- Narrow pulse pressure (≤20 mmHg)
- Hypotension
- Rising Haematocrit
- Low Albumin level
- Low Cholesterol level
Haematocrit

- Rise of Hct by 20% over the baseline indicates leakage

eg: if baseline PCV 35% → 42% = 20% rise
Fluid Management in Dengue..

- Initially (During the 1\textsuperscript{st} 2 days)
  - Dengue shock is extremely rare within 1\textsuperscript{st} 2 days
  - There is NO LEAKAGE \implies Can give fluids freely
- How Much to Give?
  - \textit{GIVE THE NORMAL MAINTENANCE (M) or More as replacement if there is vomiting diarrhoea}
  - Give electrolyte solutions not plain water
Fluid Management in Dengue

- The critical phase is only 48 hrs (24-50+)
- Some fluid restriction is essential during the critical phase (24-48hrs)
- The final outcome/morbidity/mortality will largely depend on the fluid management of the critical phase
Fluid Management in Dengue...

❖ After 3rd Day

❖ May start leaking any time
❖ DONT ASK TO DRINK PLENTY OF FLUIDS
❖ SOME FLUID RESTRICTION IS USEFUL

❖ LOOK FOR SIGNS OF LEAKING & platelets dropping <100,000
WITH THE NEW GUIDELINES ... AND WITH CORRECT FLUID THERAPY

IN DENGUE THERE SHOULD BE NO WALKED IN, DEAD PATIENTS!!!

How can we achieve this?
How to time the **onset** of critical phase and predict end ....

- Have serial FBCs done during the illness, ideally from the same reliable lab.

- Beyond Day 3...when WBC is dropping below (or close to) 5000 and platelets are <150,000 and dropping do more than once/day.

- **DO FBC** – Not PCV & Platelets!!!
How to time the onset of critical phase?

<table>
<thead>
<tr>
<th></th>
<th>17th 8 am</th>
<th>18th 8 am</th>
<th>18th 8 pm</th>
<th>19th 8 am</th>
<th>19th 8 pm</th>
<th>20th 8 am</th>
<th>20th 8 pm</th>
<th>21st 8 am</th>
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<tbody>
<tr>
<td>WBC</td>
<td>3200</td>
<td>2800</td>
<td>1900</td>
<td>2900</td>
<td>3700</td>
<td>4500</td>
<td>6000</td>
<td>7000</td>
<td>7300</td>
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<tr>
<td>N %</td>
<td>53</td>
<td>41</td>
<td>31</td>
<td>26</td>
<td>25</td>
<td>31</td>
<td>33</td>
<td>43</td>
<td>58</td>
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<tr>
<td>L %</td>
<td>44</td>
<td>56</td>
<td>68</td>
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<td>73</td>
<td>67</td>
<td>66</td>
<td>55</td>
<td>41</td>
</tr>
<tr>
<td>PCV %</td>
<td>39</td>
<td>36</td>
<td>39</td>
<td>42</td>
<td>43</td>
<td>39</td>
<td>44</td>
<td>43</td>
<td>38</td>
</tr>
<tr>
<td>Plt</td>
<td>252000</td>
<td>121000</td>
<td>110000</td>
<td>61000</td>
<td>22000</td>
<td>18000</td>
<td>12000</td>
<td>8000</td>
<td>19000</td>
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Onset

End
### How to time the onset of critical phase?

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<td>18000</td>
<td>12000</td>
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<td>19000</td>
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Timing the onset of critical period

<table>
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<tr>
<th>17th</th>
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<td>8 am</td>
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<td>8 am</td>
<td>8 pm</td>
<td>8 am</td>
<td>8 pm</td>
</tr>
</tbody>
</table>
Timing the onset of critical period

- **Platelets:**
  - 17th 8 am: 7000
  - 18th 8 am: 7500
  - 18th 8 pm: 7000
  - 19th 8 am: 6500
  - 19th 8 pm: 260,000
  - 20th 8 am: 200,000
  - 20th 8 pm: 180,000
  - 21st 8 am: 160,000
  - 21st 8 pm: 140,000

- **WBC:**
  - 17th 8 am: 6500
  - 18th 8 am: 6000
  - 18th 8 pm: 5500
  - 19th 8 am: 5000
  - 19th 8 pm: 4500
  - 20th 8 am: 4000
  - 20th 8 pm: 3500
  - 21st 8 am: 3000
  - 21st 8 pm: 2000
How to confirm pt is in the critical phase?

- Look for evidence of LEAKING ➔ effusions pleural and/or peritoneal cavities

- Oedema, facial puffiness, leg/arm swelling are not suggestive of leaking but only suggest fluid overload
Look for evidence of LEAKING ➔ effusions pleural and/or peritoneal cavities

- Do not wait till these are clinically detectable
- Do USS chest/abdomen (rpt if needed)
- CXR ➔ R/lat decubitus (or PA for follow up and when clinically detectable)
- Very occasionally a very small pl effusion may be seen in pts with DF or when platelets are >100,000 but without other evidence of leaking; they will not progress (rpt CXR)
- L/sided effusion ➔ absorbing fluid?
Once in the critical phase...

Monitor properly → Pulse; BP; HCT

.....accurate values are needed for correct decision making on changes of fluid rates!

❖ Use capillary HCT (PCV) -
  ❖ What we get from FBC counts are not always good for comparison
  ❖ Venous HCT in a patient with IV fluids running can be sometimes misleading
  ❖ Except while in prolonged and profound shock Capillary HCT is the BEST - NOT VENOUS!!!
Fluid therapy...

Each patient can be managed in many different ways and with different rate and choice of IV fluids but try to master the ways of giving the ‘smoothest’ and the most ‘uneventful’ recovery for the pt

AIM: AVOID BOTH SHOCK & FLUID OVERLOAD
Fluid Management in Dengue...

Once patient is in the critical phase (24-48hrs)

TOTAL FLUIDS = MAINTENANCE + 5% DEFICIT

OVER THE ENTIRE CRITICAL PHASE (USUALLY 48 HRS)
Fluid quota for critical phase...

Calculation \( \rightarrow \text{M} + 5\% \)

Maintenance

- 1\(^{st}\) 10 kg \( \rightarrow \) 100ml/kg
- 2\(^{nd}\) 10 kg \( \rightarrow \) 50ml/kg
- Balance wt \( \rightarrow \) 20ml/kg

5% body wt = 50ml/kg

Eg: 22kg \( \rightarrow \) \((100 \times 10 + 50 \times 10 + 20 \times 2) + 50 \times 22\)

\[1540 + 1100 = 2640\text{ml}\]
Fluid Management during the critical phase

- In shock M+5% should be given over 24 h
- In non shock over 48 h
- If allocated fluid volume exceeds and shock still remains can give, but keeping in mind about the amount exceeded
- If UOP is 0.5-1 ml/ kg/h then the amount of fluid given is adequate
- If UOP is more then it suggests too much fluid
Critical Phase Fluids in DHF

- The **maximum** recommended total critical phase fluid volume for any given pt will not exceed **4600ml**

Maximum BWt 50 kg  ⇒  \[ M+5\% - (\text{maintenance} - 100\times10 + 50\times10 + 20\times30 + (50\times50)) \]

- When pt is in hospital or seen from the onset
  - When Mx begins with the onset of leaking total fluids should be given over 48 hrs.

- When Pt presents in SHOCK
  - The pt is already in the peak of leaking and has only 24 more hrs before the leaking stop. The total M+5% can here be given over 24 hrs
**IV fluids**

- Normal Saline/ Hartmann
- <6/12 may use N/2
- Dextran 40 (Dextran 40 in Saline) – Hyper-oncotic osmolarity of 310 mOsm/L. Oncotic pressure 1693 mmHg.
- Sodium Content — Dextran 40 10% in sodium chloride 0.9% provides 77 mEq of—>
- High oncotic pressure as a volume expender
- Molecular wt 10,000- 100,000(average 40,000) when given as a bolus all molecules tend to stay together
- 6% Hetastarch (voluvan)
  - osmolality -308mosm/ mol wt 100,000 – leaking less ; volume expansion –less
- *** about 60% of pts with dengue shock could be managed only with crystalloids
Blood & blood component used in DHF/DSS patients

- **Crystalloid**: 100%
- **Colloid**: 20-25%
- **Blood**: 10-15%
- **Platelet**: 0.4%

Courtesy of Prof Siripen - Thailand
Fluids that could be used as IV push for resuscitation
N saline, (FFP,) Haemaccel, gelfundin, hetastarch
If pulse/BP un-recordable give 20ml/kg fast (DHF IV)
If not (some pulse+) give 10ml/kg,
In dengue leaking is generally <10ml/kg/hr
After resuscitated change to crystalloid

**FOR INITIAL RESUSCITATION DO NOT USE DEXTRAN as its hyperosmolar nature may not open microcirculation**
Fluids during end of leaking phase...

- even if PCV is high if pt is well and pulse BP OK do not try to correct the PCV
- Reabsorption will start soon and PCV will come down.

→ WAIT
Platelet transfusion - when platelets are low may need but only in very exceptional circumstances

- (Thailand only in <0.4% of pts with DHF)
- Each platelet pack is 50-150ml \(\rightarrow\) contribute to fluid overload
- No prophylaxis plt. transfusion
- At the initial phase the platelet drop >.100,000 is due to BM suppression but later when it drops <100,000 the cause is increase platelet consumption and the BM become hypercellular with increase production
Recombinant factor VII

- 1 dose = Rs 49,750 in a 10-kgs patient (6 vials)
- No use in cases with prolonged shock and multiple organs failure
- Consider in cases with bleeding where the cause is not prolonged shock BUT other reason: peptic ulcer, trauma etc
Pts with complications ....

Usually due to
PROLONG SHOCK
FLUID OVERLOAD
Prolonged shock

- 10 hours untreated – Death!!!
- > 4 hours untreated
  - Liver failure - prognosis 50%
  - Liver + Renal failure - prognosis 10%
  - 3 organs failure (+respiratory failure) – Prognosis is a miracle!!!
Complicated DHF

- When a pt is deteriorating with no response to fluid therapy....

A: Acidosis
B: Bleeding
C: Calcium
S: Sugar
Natural course of DHF

Day 1

Fever

Hematocrit

WBC 6,000-9,000

Platelet count 200,000

Hct 35

Albumin

Cholesterol

WBC ≤5,000

Platelet count ≤100,000

Hct 38

Albumin ≤3.5 gm%

Cholesterol ≤100 mg%

Fever

WBC

Platelet count

Hct 35

Albumin

Cholesterol

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Albumin ≤3.5 gm%

Cholesterol ≤100 mg%

Fluid overload

IV fluid: NSS, DAR, DLR
Colloid: 10% Dextran, 10% Haes-steril
M+5% Deficit (= 4,600 ml in adult)

Pleural effusion, Ascites

Shock

Plasma leakage

Stop leakage

Reabsorption

Stop leakage

Reabsorption
THANK YOU!