MODULE 4: Clinical Course of Disease

Dengue Clinical Management

Acknowledgements

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Clinical course of dengue

Dengue is a systemic and dynamic disease.

Dengue is NOT a platelet count disease
Clinical course of dengue

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*

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

**Recovery phase** – commences when plasma leakage resolves
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<th>Days of illness:</th>
<th>0</th>
<th>1</th>
<th>2</th>
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<td>Phases of dengue:</td>
<td>Febrile</td>
<td>Critical</td>
<td>Recovery</td>
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Adapted from WCL Yip, 1980 by Hung NT, Lum LCS, Tan LH
Phases of dengue:

- Febrile
- Critical
- Recovery

6 Key features:

1. Temperature
   - Defervescence
   - Bi-phasic/Saddle back picture
   - Subnormal temperature

Virology and Serology

Adapted from WCL Yip, 1980 by Hung NT, Lum LCS, Tan LH
Days of illness:  0  1  2  3  4  5  6  7  8  9  10

Phases of dengue:

6 Key features:

1. Temperature

Laboratory changes

4. WBC
5. Platelet
6. HCT

Virology and Serology

Adapted from WCL Yip, 1980 by Hung NT, Lum LCS, Tan LH
Phases of dengue:
- Febrile
- Critical
- Recovery

6 Key features:
1. Temperature
2. Oral intake
3. Urine output
4. WBC
5. Platelet
6. HCT

Potential clinical issues:
- Dehydration
- Shock
- Bleeding
- Capillary permeability

Laboratory changes:
- Viraemia
- IgM/IgG
- Platelet
- WBC
- Haematocrit

Key features:
1. Temperature
2. Oral intake
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Adapted from WCL Yip, 1980 by Hung NT, Lum LCS, Tan LH
Vignette of febrile phase

- Usually lasts 2 to 7 days
- High temperature; may be modified by antipyretics
- Common symptoms: myalgia, headache, retro-orbital pain, aches, rash
- Difficult to differentiate dengue from viral febrile illness
- Normal CBC in first 1 to 2 days of fever

Quality of life may be affected¹
- Changes in behaviour and mood
- Inability to focus and concentrate on work and self-care

Children

Nausea and vomiting may be prominent

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. Mucosal bleed
4. Lethargy; restlessness
5. Liver enlargement >2cm
6. Clinical fluid accumulation

**Laboratory Warning Signs**
1. Leukopenia
2. Rapid decrease platelet count
3. Rising haematocrit
Pearls and pitfalls: abdominal pain

What is “significant” abdominal pain?

- Severe enough to be patient’s chief complaint
- Could be mistaken as surgical condition

What does significant abdominal pain signify?

Severe abdominal pain is associated with increased vascular permeability and/or shock in the defervescence phase.

Pitfall:

Tense abdomen due to ascites + liver congestion can cause abdominal pain;

**Consider fluid overload instead!**

If IV fluid therapy increases, this can cause acute pulmonary oedema
Pearls: persistent vomiting

What is persistent vomiting?

- Three or more times per day
- Patient is not able to tolerate oral fluid.

What does persistent vomiting signify?

Important sign of plasma leakage
Pearls: lethargy

When is lethargy is more than usual?

- Patient is confined to bed for most of the day.
- Patient sleeps most of the time.
- Patient is uninterested in food or television.
- Patient is too weak to walk to toilet.

Remember: restlessness = severe shock + cerebral hypoperfusion
Pearls: mucosal bleeding

Mucosal bleeding

Mucosal bleeding = warning of more severe manifestations

Fluid accumulation

Volume of fluid accumulation
= severity of vascular permeability + fluid therapy

Mild fluid accumulation: undetectable
Pearls: laboratory warning signs

Leucopenia

- Occurs 24 hours before rapid decrease in platelet count
- Not predictive of plasma leakage
- Good indicator that patient could have dengue

Rapid decrease in platelet count + rising trend in haematocrit

- Occur shortly before or at defervescence
- May precede changes in blood pressure and pulse pressure
- Indicate an increase in vascular permeability

**NOTE:** Changes in haematocrit may be masked by IV fluid therapy
What happens during the critical phase?

- Increased vascular permeability
- Significant plasma leakage
- Development of warning signs
- Deterioration in patient’s condition

How long does plasma leakage last? 24 – 48 hours

What could happen without treatment? Death

Shock occurs when critical volume of plasma is lost through leakage. Shock is often preceded by warning signs. Body temperature may be sub-normal when shock occurs. The total white cell count may increase (instead of leukopenia) in patients with severe bleeding at this stage.
Do all dengue patients enter critical phase?

**NOT all patients will experience the critical phase**

Clinical course of patient without significantly increased vascular permeability:
- Fever subsides → general condition improves and appetite recovers
- May have leukopenia
- Mild to moderate thrombocytopenia
Vignette of recovery phase

What happens in recovery phase?

Vascular permeability reverts to normal
→ Gradual reabsorption of extravascular fluid in next 48 to 72 hours

Clues to progression from critical phase to recovery phase

Clinical clues:
1. Improvement in general well-being and stable haemodynamic status
2. Diuresis
3. Biphasic fever
4. May have bradycardia
5. Isles of white in the a sea of red

Laboratory clues:
1. HCT stabilizes.
   HCT may lower due to dilutional effect of reabsorbed fluid (haemodilution).
2. WBC usually starts to rise soon after defervescence.
3. **Thrombocytopenia persists longer than leucopenia.**
# Summary of clinical problems during each phase

## Febrile Phase
- **Dehydration**

  Contributing factors:
  1. Poor oral intake from anorexia and nausea
  2. Insensible fluid loss from high fever

- **High fever → Neurological disturbances**
  1. Hallucination
  2. Febrile seizures

## Critical Phase
- **Plasma leakage → hypovolaemia and shock**

- **Severe haemorrhage**

- **Organ impairment to liver, kidneys and other organs**

## Recovery Phase
- **Hypervolaemia with fluid overload because of inappropriate fluid management**
When to consider severe dengue?

Severe dengue is defined by one or more of the following:

1. Severe plasma leakage
2. Severe bleeding
3. Severe organ impairment

Severe manifestations of dengue are related to severe plasma leakage

→ Reduced organ perfusion and tissue hypoxia
→ Organ impairment
When to consider severe dengue?

1. Severe plasma leakage
   - Patient has hypovolaemic shock
   - Patient has respiratory distress due to fluid accumulation: either pleural effusion or ascites

2. Severe bleeding
   - Patient remains in **shock** despite IV isotonic crystalloid solution and the **hematocrit is decreasing**
   - Bleeding can be occult and not recognized in a timely manner; important to do frequent vital signs and **monitor hematocrit**
   - Bleeding usually occurs in the gastrointestinal tract, and only rarely in the brain
   - Severe bleeding exacerbates shock

Severe bleeding has been observed in adults who had **no or only mild** plasma leakage
When to consider severe dengue?

3. Severe organ impairment

Consequences of hypovolaemic shock

It is defined as one of the following:

- Alanine aminotransferase (ALT) or aspartate aminotransferase (AST) > 1000 IU/L
- Impaired consciousness
- Impaired cardiac function – raised cardiac enzymes with reduced left ventricular function

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

**Severe impairment of organs** such as liver, kidneys and brain has been observed in patients with **only mild or no plasma leakage** or after the critical phase of dengue.*

Pearls and pitfalls: dengue shock

Dengue shock presents as a physiologic-time continuum

Compensated shock in the early stage (normal or elevated blood pressure) → Decompensated shock in the late stages (hypotension & unrecordable blood pressure)

Stable → Warning signs → Compensated shock → Hypotensive shock → Cardiac arrest

Identification and treatment of **early shock** will improve clinical outcome.

**Delayed treatment** leads to a clinical course complicated by severe bleeding and organ impairment.

Severe bleeding will exacerbate the shock state and if unrecognized will cause refractory and irreversible shock with a very poor outcome.

**Pitfall: Why is it easy to miss dengue shock?**

Even in the severe shock state, the patient appears deceptively normal or “stable” with a lucid conscious level.

A careful physical examination is critical to recognizing a patient in shock before the stage of cardiovascular collapse.