Clinical Practice Guide for the Management of Dengue Hemorrhagic Fever (DHF), Siriraj Hospital

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Siriraj Med J 2007; 59: 201-205
E-journal: http://www.sirirajmedj.com

This clinical practice guidelines (CPG) was written up by the team composed of pediatric specialists in the fields of infectious diseases, critical care, hematology, and nephrology, who were experienced in treatment of children with dengue hemorrhagic fever in the Department of Pediatrics, Faculty of Medicine Siriraj Hospital. This CPG was intended to guide the house staff in order to assure the best outcome for every patient in the setting of Siriraj Hospital, a tertiary care center. This CPG may be applied for treatment in other settings but requires adaptation appropriate for the local facility. It is not intended to be the standard of care in large scale.

The definition and severity classification in this CPG are based on WHO guidelines with clarification as following:

Case definition of DHF requires that all 4 criteria are met:
1. Fever for 2-7 days (could be biphasic)
2. Evidence of bleeding tendency e.g. positive tourniquet test, petichiae, ecchymosis, purpura, hematemesis, melena, or bleeding in other site.
3. Thrombocytopenia (platelet count <100,000 cells/mm³)
4. Evidence of plasma leakage e.g. presence of pleural effusion, ascites, or hemoconcentration (increased of hematocrit of greater than 20% of baseline). In cases that baseline hematocrit is unknown, and the patient was previously healthy, the average hematocrit of normal Thai children can be use as baseline as following: 30-35% for < 2 year-old, 35-40% for 2-10 year-old, 40-45% for >10 year-old.

Severity grading of DHF is defined into 4 grades
Grade I. With above case definition criteria but the only evidence of bleeding tendency is positive tourniquet test, and there is no change in vital signs
Grade II. Similar to grade I, but with more evidence of bleeding than tourniquet test. There is no change in vital signs.
Grade III. With the above case definition, and with changes in vital signs such as tachycardia, hypotension, narrow pulse pressure.
Grade IV. Those in grade III but with profound shock and/or massive bleeding.

Confirmation of dengue virus infection
Provisional diagnosis of DHF can be made by using clinical features, CBC, and tourniquet test. Laboratory confirmation of dengue infection can be done by serology, or viral isolation, or PCR. Because of availability and cost, serology is the most common method used. Most of the time, the results of these tests are not available during critical stage, and therefore are not use to guide the treatment.
Fig 1. Management of children with suspected DHF.

Patient presents with high grade fever, flushing, no evidence of other infection or respiratory tract symptoms

- Fever < 72 hours
  - Tourniquet test
    - Symptomatic treatment
    - Follow up at around 72 hours of fever
  - Fever persists
  - Check vital signs
  - Tourniquet test
  - CBC

- Fever > 72 hours
  - Suspected DF/DHF if:
    - Tourniquet test positive if > 10 spots in an area of 1 inch diameter. (The sensitivity of diagnosing DF/DHF on day 1, 2, 3 of fever = 53% 91% and 99%, with the specificity of 76%, 78% and 74% respectively)
    - Hepatomegaly
    - CBC: Rise in Hct, low WBC, increased atypical lymphocytes, thrombocytopenia

- Treat as out-patient in case of:
  - No significant dehydration
  - No hemoconcentration
  - Able to return for follow-up until defervescent

- Out-patient treatment:
  - Paracetamol 10 mg/kg q 4-6 hr
  - Avoid aspirin or NSAID
  - Avoid other unnecessary medications e.g. antibiotics
  - In case of vomiting, may give domperidone 1 mg/kg/day in 3 divided doses
  - May give H2 blocker in cases with history or suspected gastric ulcer
  - Encourage to drink ORS or juice
  - Educate care-taker about the support care and how to detect the symptoms in critical/shock stage that usually start from day 3 of fever
  - Follow up every day until defervescent

- Hospitalize the patient in case of:
  - Significant bleeding
  - Presence of signs of shock (faint pulse, narrow pulse pressure <20 mg/Hg), or low blood pressure
  - Low urine output
  - Tachypnea, edema, presence of ascites or pleural effusion
  - Unable to take adequate oral fluid, vomiting
  - Severe abdominal pain,
  - Alteration of consciousness
  - Rise of Hct >20% of baseline or for age. Hct for normal Thai children is as follows:
    - < 2 year-old = 30-35%
    - 2-10 year-old = 35-40%
    - > 10 year-old = 46-45%
  - Unable to return for follow up

- In-patient treatment (Fig 2-3)
**Oral plus IV fluid = maintenance + deficit**

### Hemoconcentration

- **Yes**
  - Oral plus IV fluid = maintenance + 5% deficit
  - 5%D/NSS/2 for age > 1 yr or 5%D/NSS/3 for age < 1 yr
  - Monitor vital signs q 2-4 hr, urine output, and Hct q 4 hr
  - Check BUN, serum Cr
  - Oral plus IV fluid = maintenance + (if any) deficit
  - Monitor vital signs q 4 hr, urine output q 8 hr, Hct q day

- **No**
  - Oral plus IV fluid = maintenance + deficit
  - Monitor vital signs q 4 hr, urine output q 8 hr, Hct q day

**Unstable vital signs**

- **Yes**
  - Follow Figure 3

- **No**
  - Unchanged IV rate
  - Colloid if indicated

**Improvement (Hct falls)**

- **Yes**
  - Decrease IV fluid by 2 ml/kg/hr q 4 hr

- **No**
  - Unchanged IV rate
  - Colloid if indicated

**Oliguria**

- **Yes**
  - Improve IV fluid by 2 ml/kg/hr for 4 hr
  - Increase IV fluid by 2 ml/kg/hr for 4 hr
  - Or unchanged IV rate
  - Colloid if indicated

- **No**
  - Unchanged IV rate
  - Colloid if indicated

**Further improvement**

- **Yes**
  - Oral plus IV fluid = maintenance
  - Discontinue IV fluid at convalescent stage (24-48 hr after defervescence)

- **No**
  - Oral plus IV fluid = maintenance
  - Decrease IV fluid by 2 ml/kg/hr q 4 hr

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1. **Hemoconcentration:** an increase in Hct ≥ 20%
2. **Unstable vital signs:** pulse pressure ≤ 20 mmHg, hypotension, rapid and weak pulse, or capillary refill > 2 second
3. **Oliguria:** urine output < 500 mL/24 hr/1.73 m² in age > 1 yr or < 1 mL/kg/hr in age < 1 yr
4. **Colloid solutions:** e.g., plasma, FFP, Dextran 40, Haemaccel, 5% albumin
5. **Reevaluate for urinary retention and intrinsic renal failure, repeat physical exam and check lab eg., blood for BUN, Cr, electrolytes, sugar (check AST and ALT, if indicated)
6. **Use an ideal body weight (weight for height) for calculation**

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**Fig 2.** In-patient volume replacement flow chart for a patient with dengue fever or dengue hemorrhagic fever grade I-II.
**UNSTABLE VITAL SIGNS**

- Assess airway, provide O₂
- IV access (or intraosseous access if unable to establish IV in 10 min)
- Normal saline or Ringer’s lactate 10 ml/kg in 20-30 min (repeat if necessary)
- Obtain cultures, if indicated
- Blood group typing in Grade III
- Blood crossmatch in Grade IV
- Check lab²

**IMPROVEMENT**

**Stable vital signs**

- Initial IV fluid rate = 8 ml/kg/hr
  - 5%(D)NSS for age >1 yr or
  - 5%(D)NSS/2 for age < 1 yr
- Decrease IV fluid by 1 ml/kg/hr q 1-2 hr
- Monitor vital signs frequently, urine output and Hct q 4 hr

**UNSTABLE VITAL SIGNS¹**

- Yes
  - Hemoconcentration³
    - Yes
      - Follow Fig 2
    - No
      - Oliguria⁴
        - Yes
          - Hct <35% or
          - Hct decrease >5% within 4 hr
          - or >8% within 24 hr
          - Blood transfusion⁶
          - Yes
            - Stable vital signs
          - No
            - Yes
              - Yes
                - Stable vital signs
          - No
            - Yes
              - Further improvement
                - Oral plus IV fluid = maintenance
                - Discontinue IV fluid at convalescent stage (24-48 hr after defervescent)

- No
  - Hct <35% or
  - Hct decrease >5% within 4 hr
  - or >8% within 24 hr
  - No
  - Yes
    - Blood transfusion⁶

**Further improvement**

- Yes
  - Transfer to ICU
  - Chest X-ray if indicated
  - CVP monitoring
  - Bladder catheterization
  - Continue intensive care and monitoring

**Unstable vital signs**: pulse pressure ≤ 20 mmHg, hypotension, rapid and weak pulse, or capillary refill > 2 second

²Lab including blood for BUN, Cr, electrolytes, sugar, AST, ALT, albumin, coagulogram

³Hemoconcentration: an increase in Hct ≥ 20%

⁴Oliguria: urine output < 500 mL/ 24 hr./ 1.73 m² in age > 1 yr or < 1 mL/ kg./ hr in age < 1 yr

⁵Colloid eg. plasma, FFP, Dextran 40, Haemaccel, 5% albumin

⁶If no blood available at the moment, give normal saline or Ringer’s lactate 10 ml/kg/hr (do not exceed 1 hr). In case of severe bleeding, consider platelet and/or FFP if indicated.

*Use an ideal body weight (weight for height) for calculation*

**Fig 3.** In-patient volume replacement flow chart for a patient with dengue shock syndrome (dengue hemorrhagic fever grade III-IV).
Guideline for blood products transfusion in DHF

PLATELETS TRANSFUSION

Indications
1. Platelet < 10,000 /cumm
2. Platelet < 20,000 /cumm with significant coagulopathy
3. Platelet < 50,000 /cumm prior to invasive procedure
4. Platelet < 50,000 /cumm with clinical significant bleeding i.e. hematemesis, melena, epistaxis not response to local treatment, pulmonary hemorrhage, bleeding from wound, hematoma

Dosage 0.1 unit of random donors platelet/kg/dose

FRESH FROZEN PLASMA TRANSFUSION

Indications
1. Use as colloidal replacement fluid after failure of crystalloid replacement for > 2 hr, dosage not exceed 10 ml/kg/hr (max 40 ml/kg/day)
2. Use for correction of coagulopathy: liver coagulopathy, DIC, dosage 10-20 ml/kg/dose q 6-12 hr (max 40 ml/kg/day)
3. Use for plasmapheresis in hepatic failure
4. Use in combination with PRC for blood exchange transfusion or replacement of blood loss

Contraindication
1. Uncontrolled pulmonary edema
2. Congestive heart failure

PRC TRANSFUSION

Indications
1. Hct < 35 % during shock stage
2. Hct declines > 5% in less than 4 hr or > 8% in less than 24 hr Hct prior to transfusion should not exceed 40%
3. Replacement therapy for massive bleeding
4. Use with FFP for blood exchange transfusion Dosage 10 ml/kg/dose for correction of anemia or drop of Hct Replacement of continuous blood loss cc/cc

Other Coagulation factors replacement

Factor VIIa (Novo seven)*

Indications
1. Emergency life-threatening bleeding i.e. cerebral hemorrhage
2. Significant uncontrolled bleeding after maximum platelet (0.4 unit of random donors platelet/kg/day) and maximum FFP transfusion (>40 ml/kg/day)
3. Significant life-threatening bleeding and unavailable platelet and/or FFP.

* must consult hematology

INDICATION FOR INFUSION OF COLLOID SOLUTION IN PATIENTS WITH DHF

1. In patients with DHF grade III or IV who have unstable vital signs despite of bolus crystalloid solution infusion of 10 ml/kg for 2 times.
2. In patients who still have hemoconcentration or unstable vital signs and had received a large amount of crystalloid solution, i.e. more than 70%, 80%, and 100% of amount of 24-hour maintenance fluid in children <1 year-old, 1-5 year-old, and >5 year-old, respectively.
3. In patients who have difficulty of breathing due to pleural effusion or ascites, but without the condition of congestive heart failure, pulmonary edema, or hypertension.

Note. Dextran 40 should be used as first choice because of long half-life and lower cost. Fresh frozen plasma (FFP) should be used in cases with bleeding problems or coagulopathy. Haemaccel and albumin should be used if the patient cannot use dextran 40 or had received dextran 40 up to limit of recommendation (table) and still required colloid therapy.

<table>
<thead>
<tr>
<th>Colloid solution</th>
<th>Precaution</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dextran 40</td>
<td>-Caution in renal failure, thrombocytopenia, or active bleeding</td>
<td>-10 ml/kg i.v. drip in 1 hour. Can repeat but not exceed 20 ml/kg in the first 24 hour and 10 ml/kg/day afterward.</td>
</tr>
<tr>
<td>Haemaccel (Ureacrosslinked gelatin)</td>
<td>-Do not give together with citrate preserved blood</td>
<td>-10 ml/kg i.v. drip in 1 hour. Can repeat as needed.</td>
</tr>
<tr>
<td>5% Albumin</td>
<td>-Do not give in cases with congestive heart failure</td>
<td>-10 ml/kg i.v. drip in 1 hour. Can repeat but not exceed 120 ml/kg/day</td>
</tr>
</tbody>
</table>