Abstract
A guide to the medical management of dengue for reducing its case-fatality rate as experienced in Singapore is furnished. The mortality from dengue in Singapore is low and most cases recover uneventfully. However, complacency and under-estimation of the disease does occur. It is important to recognize the symptoms of severity and understand the patho-physiology that leads to dengue shock syndrome (DSS). A protocol giving indications of platelet transfusion will guide appropriate usage. Patients should be informed prior to platelet transfusion as to its possible dangers. In our experience, with good initial appropriate support in a stable patient, platelet transfusion is seldom needed till the platelets fall below 10,000/mm$^3$. DSS is reversible if appropriately treated with fluids and plasma infusion to reverse the osmotic permeability gradient due to hypoalbuminaemia. Severe pulmonary oedema causes adult respiratory distress syndrome (ARDS). The lung effusions and hypotension must be differentiated from other causes of shock and pulmonary oedema. Correction of acid-base balance and internal bleeding if present, recognition and appropriate treatment of sepsicaemia and pneumonia, and avoiding fluid overload usually result in recovery. Nosocomial and mycoplasma pneumonias, not uncommonly, complicate severe ARDS. Fatalities are often from these unrecognized infections.

Keywords: DHF, DSS, management, guidelines, Singapore.

Introduction
In recent years dengue has been a major international health problem with high levels of dengue fever/dengue haemorrhagic fever (DF/DHF) in the WHO Western Pacific Region. Malaysia had 19,544 cases (1997), Philippines 12,811 cases (1997), Viet Nam 108,000 cases (1997), Australia 165 cases (Dec.’97–May ’98), Fiji 24,780 cases (Dec.’97–May ’98) and Singapore 5,285 cases with 153 being imported in 1998$^{(1)}$ and in 1999, 1355 dengue cases with 217 imported$^{(2)}$. There has been a resurgence in 1998 and in 2001. Fatality varied from 1%-4% in this Region.
Around sixty million cases occur annually with 30,000 fatalities worldwide\(^3\). The changing climate pattern due to the El Nino weather phenomenon is thought to be the cause\(^4\). Tourists travelling in the region often visit Singapore and fall ill, while others from neighbouring countries seek medical treatment in Singapore. The critically ill are transported there by international air emergency services.

The fact that there are no antibiotics or antiviral drugs for dengue and most patients recover has, in my opinion, led to complacency and under-estimation of the disease. Not recognizing the symptoms of its severity and ignorance of the pathophysiology of dengue that leads to DSS, further contribute to complacency in its treatment.

**Diagnosis criteria**

**DF/DHF**

- Abrupt onset of high fever, continuous and lasting 2-7 days, headache, myalgia and arthralgia.
- Haemorrhagic manifestations including any of the following:
  - Positive tourniquet test
  - Petechiae, purpura, ecchymosis
  - Epistaxis, gum bleeding
  - Haematemesis and/or melaena
- Enlargement of liver
- Thrombocytopenia (100,000/mm\(^3\) or less)
- Haemoconcentration (haematocrit increased by 20% or more)

The presence of the first two clinical criteria plus thrombocytopenia and haemoconcentration are sufficient to establish the clinical diagnosis of DHF.

**Dengue shock syndrome (DSS)**

- All the above criteria, plus
- Shock as manifested by rapid and weak pulse with narrowing of pulse pressure (< 20mmHg regardless of pressure levels) or hypotension with cold, clammy skin and restlessness.

(Based on “Dengue Haemorrhagic Fever: Diagnosis, Treatment, Prevention and Control”, WHO, 1997)

**Pathophysiology**

In DHF/DSS the severity is due to the increase in vascular permeability leading to plasma loss from the vascular compartment. This vascular permeability may show as pleural effusion and ascites on clinical examination and can be confirmed by radiology and ultrasound.

Hypoalbuminaemia contributes to the problem. The face and legs may also be oedematous. In severe cases there is a reduction in the plasma volume of >20%. Disseminated intravascular coagulation (DIC) occurs and causes thrombocytopenia, prolonged prothrombin and partial thromboplastin times (PT/PTT), decreased fibrinogen levels and increased
fibrinogen degradation products. Thrombocytopenia is also due to bone marrow depression.

**Clinical manifestations**

Early clinical signs and symptoms that suggest possible progression to DHF/DSS are high fever, severe muscle ache, arthralgia, anorexia, vomiting, epigastric pain, abdominal distension, diarrhoea, headache, eyeball discomfort, dyspnoea, tachycardia, a rapid fall in platelet count of 25% - 50% or more per day and a falling blood pressure.

During the early stage, a chest X-ray may show evidence of pleural effusion mainly on the right side, but could be bilateral with pulmonary oedema. An ultrasound of the abdomen may show an oedematous gall bladder or ascites.

Low platelet is manifested by easy bruising or bleeding. In severe cases hypotension leads to DSS generally after the third day of the illness with the patient having cold extremities, rising haematocrit, restlessness, oliguria, tachycardia, abdominal pain and narrowing of pulse pressure (<20 mm Hg) as warning signs. If the shock is not corrected it becomes refractory and the patient may die from a gastro-intestinal haemorrhage within 24 hours, and often may be mentally alert till just before death.

**Essentials of management**

- Do not underestimate the illness. Take a good history.
- Recognize and look for the danger signs as (mentioned above) of severe dengue infection.
- Monitor the patient regularly for changes in clinical condition, i.e. blood counts, PT/PTT, haematocrit, electrolytes, acid base balance, liver function tests, pulse, temperature and blood pressure. Rapidly-dropping blood counts may need monitoring 3-4 times daily and blood pressure should be taken every 2 hours.
- Exclude other causes of febrile illness, e.g. malaria, typhoid, typhus, liver abscess, leptospirosis, meliodosis, drug allergy, HIV, lymphoma, septicemia, etc. A blood culture must be done.
- A serological test, if done early, may be negative, but if suggestive symptoms are present, dengue should still be suspected. A PCR (polymerase chain reaction), if available, detects the infection earlier.
- Hospitalization should be considered if the patient shows symptoms of severe dengue, especially nausea, vomiting and diarrhoea, a falling platelet count below 100,000 mm$^3$ or less, bleeding from gastro-intestinal or uro-gential tract or a persisting high haematocrit despite fluid replacement.

**Principles of management**

Prognosis depends on early recognition and prompt treatment of shock with rapid replacement of plasma loss with fluids,
electrolyte solutions, plasma or plasma expanders. Adjust intravenous fluids administration according to vital signs, haematocrit and urine output. With early correction of electrolytes, metabolic disturbance and acidosis with sodium bicarbonate, DSS and intravascular coagulation is prevented.

Do not mistake DSS for other causes of shock, e.g. myocarditis; ECG and echocardiogram will assist in the diagnosis.

**Indications for platelet transfusion**

(a) Stable patients with platelet counts <10,000/mm$^3$.

(b) Patients with platelet counts <20,000/mm$^3$ with minor bleeding.

(c) Patients with platelet counts 50,000/mm$^3$ with significant bleeding.

(Information regarding potential risks and benefits should be given to the patient before administration of platelets and other blood products.)

DF/DHF usually responds to symptomatic treatment. Antipyretics can be given for fever >39°C, together with cooling procedures, e.g. ice-packs on the head and neck. Avoid salicylates, it can cause gastritis, gastric bleeding, acidosis or Reyes syndrome (fatty liver and encephalopathy) in children. Paracetamol can be given, or if the patient is vomiting Voltaren suppositories. Antacids are prescribed for epigastric pain and antiemetics for vomiting. Rehydration may be needed. If there is significant bleeding, blood transfusion can be given and Vitamin K1 added. Platelets may be needed if thrombocytopenia is severe.

DSS patients are best monitored in the intensive care unit, given oxygen, a central venous pressure line (CVP) inserted if possible, and a urinary catheter for urine output to guide fluid replacement. A strict intake and output chart should be observed. Blood gases, ECG, chest X-ray, electrolytes, serum albumen and blood counts should be monitored.

Respiratory failure commonly supervenes due to pulmonary oedema and patient may develop respiratory failure needing respirator assistance. Correct hypotension with intravenous fluids, e.g. dextro-saline, dextran, haemacell, etc., as well as a vasopressor, e.g. dopamine. If unsuccessful and hypoalbuminaemia is severe, give sufficient plasma or plasmanate to correct the low serum albumen. This will reverse the osmotic gradient to prevent further fluid extravasation and correct hypotension. Nosocomial respiratory tract and mycoplasma pneumoniae infections are not uncommon in hospitalized patients with pulmonary oedema. They should be given appropriate antibiotics. Septicaemias, if present, must be treated. Diuretics may need to be used to promote urine flow and excrete excess fluid. Recovery from DSS usually occurs with these emergency procedures if done urgently, but should hypotension persist despite a falling haematocrit, internal bleeding should be considered.

Intravenous fluids should be discontinued when haematocrit drops to 40% with vital signs being stable, urine output
satisfactory and patient feels better. With recovery at this stage reabsorption of extravasated plasma occurs. Pulmonary oedema and cerebral oedema can occur if more fluid is given.

Patients can be discharged if afebrile, have normal blood pressure for 48 hours, are able to eat, are not breathless, have good urine output and platelet count more than 50,000 mm$^3$ with stable blood counts and haematocrit.

**Conclusion**

Dengue is a multisystem disease, but with good medical care and public health control, deaths can be further reduced. Fatalities are increased due to the unfamiliarity of DSS shock treatment, unrecognized pneumonia and septicaemia. A guide to its management should be available in hospitals.

**References**