DENGUE INFECTION IN LAO PDR

Douangdao Soukaloun

Mahosot Hospital, Vientiane, Lao PDR

Dengue is a systemic and dynamic disease; clinically classified into severe and non-severe forms. The illness begins abruptly and is followed by three phases; namely, the febrile, critical, and recovery phases. The non-severe forms include dengue with warning signs and dengue without warning signs.

Epidemiology of dengue infection in Lao PDR

Dengue disease is widely distributed in the whole country of Lao PDR, which consists of seven provinces. There has been a significant burden of dengue diseases over the past 4 years (Fig 1) (Khampapongpane *et al*, 2014). In 2010, there is a high burden of disease covering the whole country of Lao PDR with more than 400 cases per 100,000 population in most area of the country. In the year 2013, there was a serious epidemic of dengue infection in Lao PDR (Table 1, Fig 2) (WHO WPRO, 2013).

The most affected provinces were the Vientiane Capital and two provinces in the South, Champasak and Salavan. Only the two northern provinces had no reported cases of dengue. The number of dengue cases, from weeks 1-23 of each year, between 2007 and 2013 are shown in Table 1. It can be clearly seen that there is a sharp increase in the number of dengue cases reported in 2013–from January to June 2013–almost 8,000 cases of dengue were reported (Fig 2) (WHO WPRO, 2013).

For the first half of 2013, 31 deaths related to dengue infection had been reported. A major dengue epidemic was expected during the year of 2013 (Table 1) (WHO WPRO, 2013).

Management of dengue infection in Lao PDR

Prior to 2010, practices in Lao PDR conformed to WHO guidelines. However, after 2010, Lao PDR developed its own dengue management guidelines. There remain many formidable challenges in the clinical management of dengue in Lao PDR. Both human and financial resources are inadequate, and there is an insuffucient emergency triage system. The most common pitfall is inappropriate fluid management: either inadequate fluid resuscitation (*eg*, inadequate oral fluid during febrile stage), inadequate management during prolonged shock with unrecognised internal bleeding, or fluid overload (*eg*, intravenous fluid given for too long). Inappropiate fluid management could lead to many deaths.

The clinical course of dengue is shown in a WHO 2009 (WHO, 2009) dengue guideline (Fig 3) (WHO WPRO, 2013). After an incubation period, the illness begins very abruptly with fever, followed by three phases: febrile, critical, and recovery phases. The febrile phase manifests with high-grade fever that normally lasts for 2-7 days. During this phase, viremia oc-
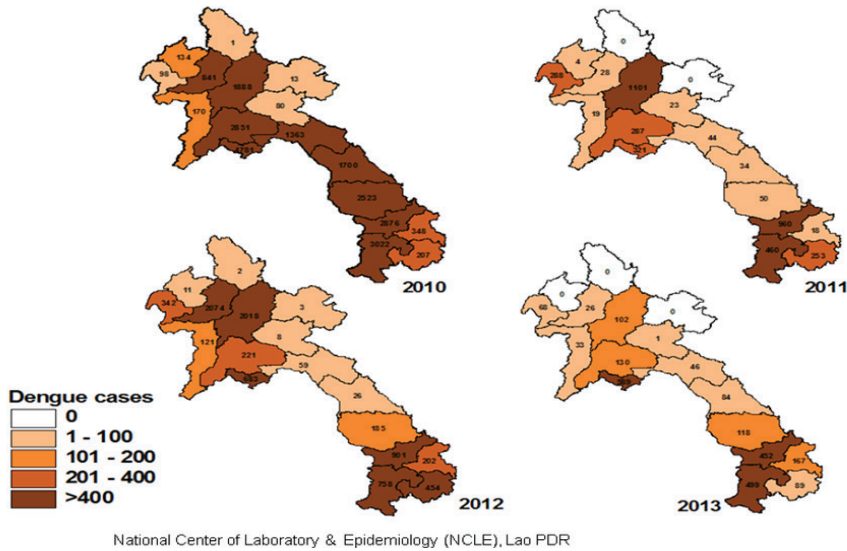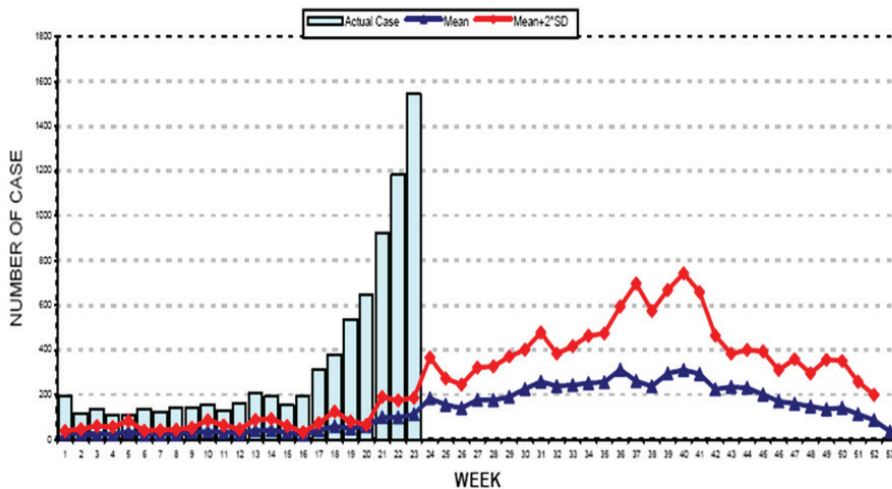
Fig 1–Distribution of dengue cases in Lao PDR during 2010-2013 (Khampa-pongpane *et al*, 2014).

Fig 2–Weekly reported number of dengue cases in Lao PDR in 2013 (WHO WPRO, 2013).

curs, and there is as of yet no immunity in the patient. At this stage platelets and the hematocrit are still normal. A common problem to occur during this phase is dehydration due to insensible losses via fever, and inadequate fluid intake. At this point young children in particular may develop febrile convulsions.

After the febrile phase, the temperature starts to decrease and the patient enters the critical phase, where there is plasma leakage. This lasts approximately

Table 1
Number of reported dengue case in Lao PDR during 2007-2013.

Year	Number of dengue cases week 1-23	Total number of dengue cases/year	Total number of death
2007	909	5,390	10
2008	1,260	4,487	21
2009	1,280	7,273	14
2010	2,521	22,890	46
2011	653	3,881	7
2012	1,048	9,952	22
2013	7,920		31

Source: National Center of Laboratory and Epidemiology (NCLE), Lao PDR (WHO WPRO, 2013).

24-48 hours, with hematocrit rising due to hemoconcentration and platelet counts dropping rapidly. In severe cases, due to plasma leakage, patients can sometimes develop shock and severe bleeding, and organ impairment, such as encephalopathy, liver failure and cardiac failure. Some patients will develop warning signs prior to severe shock and bleeding.

If the patient survives this period, they will then enter the recovery phase, where there is fluid reabsorption, and the patient is at risk of fluid overload if excessive intravenous fluid was administered beforehand. The platelet count begins to normalize at this stage, but later than the white cell count and hematocrit which normalize earlier.

The WHO 2009 revised Dengue Classification divides dengue into non-severe and severe forms. A probable dengue case is defined as a case that lives in or has travelled to a dengue endemic area, and presents with fever and at least two of the following signs and symptoms: nausea and vomiting, rash, aches and pains, a positive torniquet test, leukopenia, and any other warning signs. Warning signs that are taught to nurses, medical students, and doctors to notice are: abdominal pain or tenderness, persistent vomiting, clinical fluid accumulation, mucosal bleeding, lethargy and restlessness, liver enlargement (>2 cm below right costal margin), and an increase in hematocrit concurrent with a rapid decrease in platelet count.

Some cases of dengue, with or without warning signs, can also progress to become severe dengue. There are three types of severe dengue: severe plasma leakage, severe hemorrhage, and severe organ impairment. In severe plasma leakage the patient develops shock and has fluid accumulation with respiratory distress. Cases of severe bleeding are diagnosed as evaluated by a clinician. Severe organ involvement cases are defined as patients with AST or ALT of >1,000, impaired consciousness, or heart or other organs involvement.

The signs and symptoms of the various stages of dengue are very similar to other diseases so it is important to keep

Table 2

Recommended hemodynamic assessment for patients with dengue infection.

Parameters	Stable circulation	Compensated shock	Hypotensive shock
Conscious level	Clear	Clear	Restless, lethargy
Capillary refill time	Rapid (<2 sec)	Prolonged (>2 sec)	Very prolonged, mottled skin
Extremities	Warm and pink	Cool peripheries	Cold, clammy
Peripheral pulse volume	Good volume	Weak	Absent
Heart rate	Normal heart rate for age	Tachycardia	Severe tachycardia or bradycardia in late shock
Blood pressure	Normal blood pressure for age	Normal systolic pressure with narrowing pulse pressure Postural hypotension	Hypotension Undetectable blood pressure
Respiratory rate	Normal respiratory rate for age	Tachypnea	Hyperpnea or Kussmaul's breathing (Metabolic acidosis)
Urine output	Normal	Reduced volume	Oliguria or anuria

in mind alternate differential diagnoses as shown in the list below:

1) Flu-like syndrome: influenza, measles, chikungunya;

2) Rash: rubella, measles, scarlet fever, meningococcal infection, chikungunya, drugs;

3) Diarrhea: rotavirus;

4) Neurological manifestation: meningoencephalitis, febrile seizures;

5) Acute abdomen: acute appendicitis, acute cholecystitis, perforated viscus, diabetic ketoacidosis;

6) Shock: septic shock;

7) Leukopenia and thrombocytopenia ± bleeding: acute leukemia, malaria, leptospirosis, typhoid, typhus.

The 2009 WHO guidelines suggest a stepwise approach to dengue case management.

Step 1 : History taking and physical examination. The patient is questioned of the date of onset of fever or illness and assessed for emergency signs, such as tachypnea, hemodynamic compromise, mental compromise, their hydration status, and for other warning signs. Hemodynamic assessment is extremely important in the management of dengue cases; Table 2 illustrates what the guidelines suggest clincians note when caring for dengue patients.

Concerning laboratory tests, the most important test is the full blood count (FBC), looking at the white blood cell count, platelet count, and hematocrit. At the first visit, it is suggested an FBC be taken as
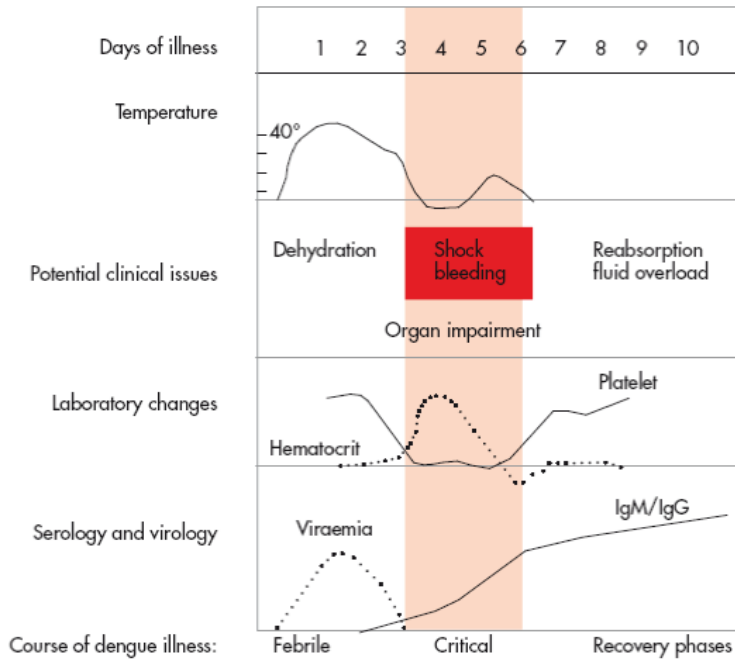
Fig 3–Clinical course of dengue disease described in WHO 2009 dengue guidelines for treatment, prevention and control (WHO, 2009).

a baseline. Other dengue diagnostic tests can be done but are unnecessary for acute management unless cases present with unusual manifestations, and are usually only helpful in confirming or refuting the diagnosis.

Step 2 : Diagnosis, assessment of disease phase and severity. With above information, the clinician is then aimed to answer the question of whether or not the index case has dengue infection, and if so, which phase and which severity it is.

Step 3 : Dengue case management and treatment. Based on the patient's classification they are then divided into three groups:

Group A, which are considered safe to send home; Group B, who need hospital admission; and Group C, who require emergency treatment and urgent referral.

Group A patients are those who are able to tolerate adequate amounts of oral fluid, pass urine at least every 6 hours, have no warning signs, have a stable hematocrit, and have no other co-existing conditions (such as children under 2 years, pregnant women, and patients with chronic diseases). They require daily review and daily blood tests (FBC, HCT until past the critical phase). The patients should be monitored for signs of disease progression, such as defervescence, rising hematocrit with concurrent rapid fall in white blood cell and platelet counts, and development of any warning signs. Patients and families should be advised to take adequate bed rest and fluid intake, paracetamol as needed, tepid sponging, to avoid steroids or NSAIDs, and
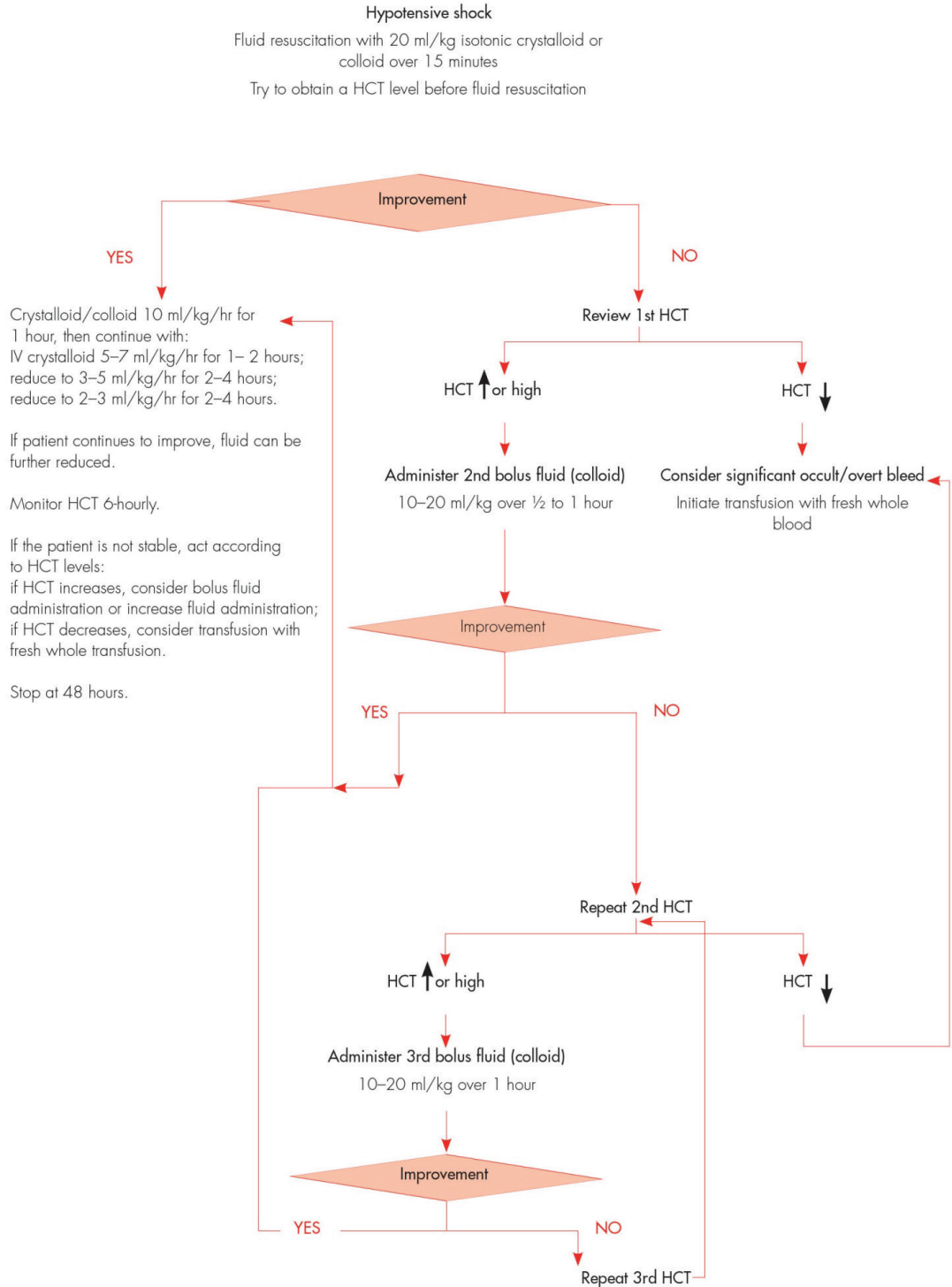
Hypotensive shock

Fluid resuscitation with 20 ml/kg isotonic crystalloid or
colloid over 15 minutes

Try to obtain a HCT level before fluid resuscitation

Improvement

YES   NO

Crystalloid/colloid 10 ml/kg/hr for
1 hour, then continue with:
IV crystalloid 5–7 ml/kg/hr for 1– 2 hours;
reduce to 3–5 ml/kg/hr for 2–4 hours;
reduce to 2–3 ml/kg/hr for 2–4 hours.

If patient continues to improve, fluid can be
further reduced.

Monitor HCT 6-hourly.

If the patient is not stable, act according
to HCT levels:
if HCT increases, consider bolus fluid
administration or increase fluid administration;
if HCT decreases, consider transfusion with
fresh whole transfusion.

Stop at 48 hours.

Review 1st HCT

HCT ↑ or high   HCT ↓

Administer 2nd bolus fluid (colloid)

10–20 ml/kg over ½ to 1 hour

Consider significant occult/overt bleed

Initiate transfusion with fresh whole
blood

Improvement

YES   NO

Repeat 2nd HCT

HCT ↑ or high   HCT ↓

Administer 3rd bolus fluid (colloid)

10–20 ml/kg over 1 hour

Improvement

YES   NO

Repeat 3rd HCT

Fig 4–Algorithm of fluid management for patient with hypotensive dengue shock.
Source: WHO, 2009.

eliminate mosquito breeding places. They are advised to return immediately if there are any clinical signs of bleeding, frequent vomiting, severe abdominal pain, drowsiness or mental confusion, pallor, clammy skin or breathing difficulties.

Group B patients are those that require admission. They are patients with warning signs, risk factors, and/or difficult social circumstances, such as patients living alone or without a reliable means of transport to a health facility. Management of these cases include monitoring of hematocrit and encouragement of oral fluid intake. Intravenous fluids should only be started if the patient is not able to take oral fluids and/or have oliguria, in which 0.9% normal saline or Ringer's Lactate should be administered, at 5ml/kg/hr for dengue with warning signs, and 3ml/kg/hr for dengue without warning signs. They should be monitored for their temperature pattern, volume of fluid intake, urine output, warning signs, and hematocrit, white cell count, and platelet count.

Group C patients require emergency treatment and urgent referral. These are cases whose features fall into the severe dengue classification as mentioned earlier, such as severe plasma leakage, severe bleeding, and severe organ impairment. The algorithm shown in Fig 4 is placed in Lao PDR to help guide healthcare workers in the fluid management of hypotensive dengue shock. Hematocrit is used as a guide of hemoconcentration and further fluid needs, and a marker of bleeding.

In conclusion, dengue infection is common in Lao PDR. The appropriate disease classification, phase of disease, and disease severity is crucial. The appropriate fluid managnment is a key of clinical management of dengue infection.

REFERENCES

Khampapongpane B, Lewis HC, Ketmayoon P. National dengue surveillance in the Lao People's Democratic Republic, 2006-2012: epidemiological and laboratory findings. *Western Pac Surveill Resp J* 2014; 5: 7-13.

World Health Organization (WHO). Dengue: guidelines for diagnosis, treatment, prevention and control. Geneva: WHO, 2009. [Cited 2011 Jul 30]. Available from: URL: http://www.who.int/rpc/guidelines/9789241547871/en/

World Health Organization, Western Pacific Regional Office (WHO WPRO). WPRO Dengue Situation Update, 10 July 2013. Manila: WHO WPRO, 2013. [Cited 2011 Jul 30]. Available from: URL: http://www.wpro.who.int/emerging_diseases/DengueSituationUpdates/en/index.html