Management of Dengue

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ไข้เลือดออก



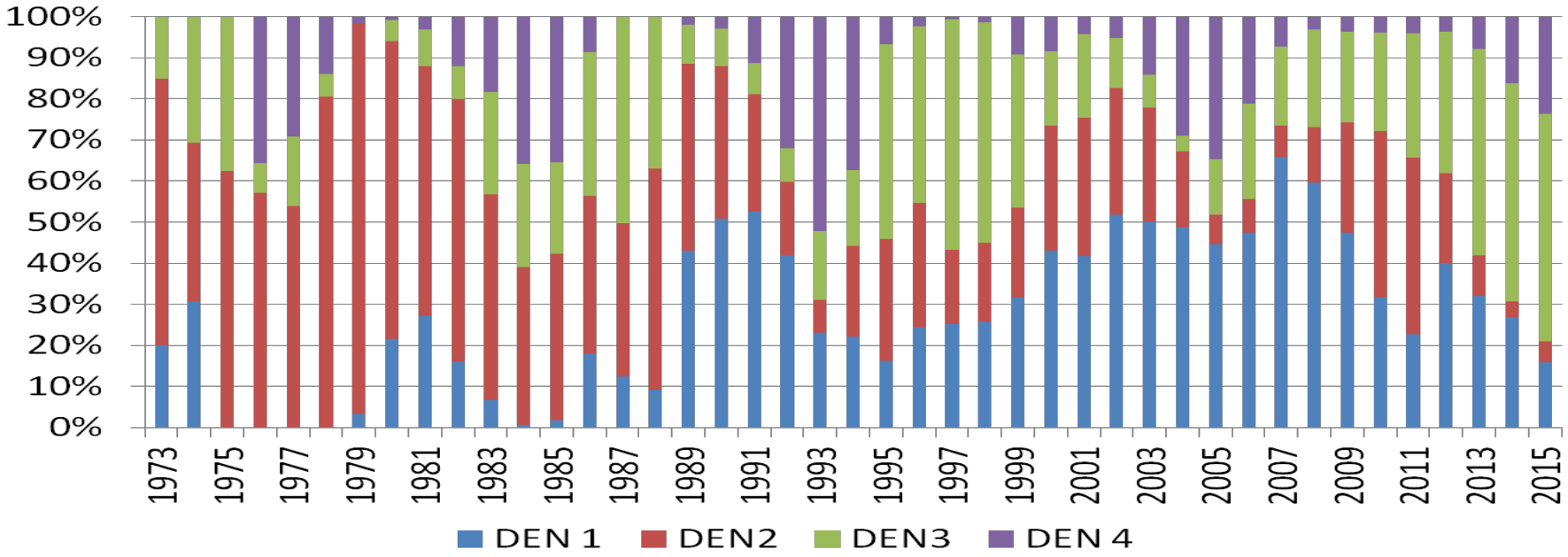
โรคที่*น่ากลัว*สำหรับคนไข้

แต่*ท้าทาย*สำหรับแพทย์

Dengue Serotypes
Queen Sirikit National Institute of Child Health 1973-2015 (April 15)

There are 4 dengue serotypes :

Dengue 1, Dengue 2, Dengue 3, Dengue 4



AFRIMS

Classifications of Dengue Infection

- **WHO 1997 (WHO Searo 2011)**
- **WHO TDR 2009**

Dengue virus infection

10,000

Asymptomatic

9,000

Symptomatic

1,000

Viral syndrome

500

Dengue fever

400

DHF

100

Plasma leakage

DHF

DSS 1-5

Expanded dengue syndrome

1.Prolonged shock: liver failure, renal failure,...Encephalopathy...

2. Co-morbidities

3. Co-infections

4. True dengue infection - encephalitis

Dengue Fever (Infection)

- **Headache**
- **Retro-orbital pain**
- **Myalgia**
- **Arthralgia/ bone pain (break-bone fever)**
- **Rash**
- **Hemorrhagic Manifestations**
- **Leukopenia (WBC < 5,000 cells/ mm3)**
- **Platelet count ≤ 150,000 cells/mm3**
- **Rising HCT 5-10%**

Diagnosis :

Tourniquet test positive + WBC ≤ 5,000 cells/cu.mm

(positive predictive value = 83%)

Dengue Hemorrhagic Fever

Clinical

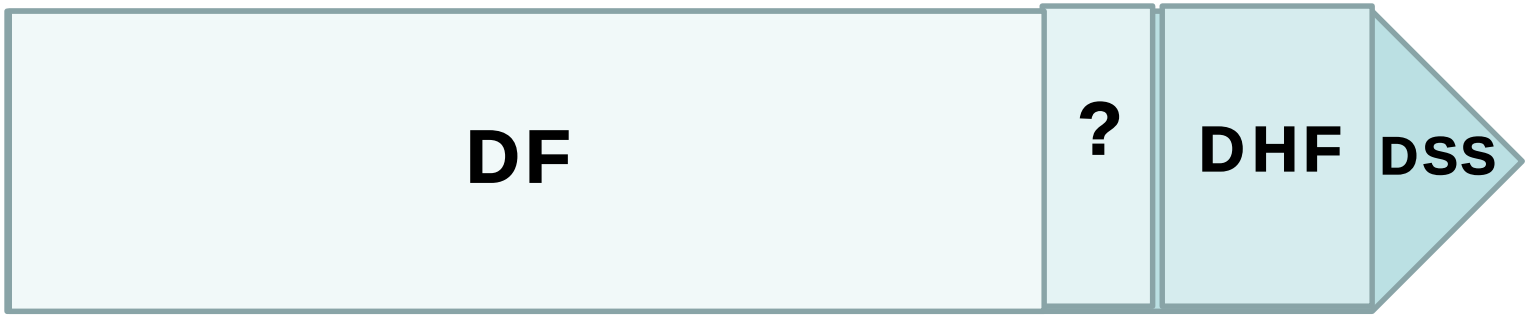
- **High, continuous fever 2-7 days**
- **Hemorrhagic manifestations: tourniquet test positive, petechiae, epistaxis, hematemesis, etc…**
- **(Liver enlargement)**
- **(Shock)**

Laboratory

- **Evidence of plasma leakage; rising Hct ≥ 20%, pleural effusion, ascites, hypoalbuminemia (serum albumin < 3.5 gm% or <4 gm% in obese patients), UTZ**
- **Platelet count ≤ 100,000 cells/ mm3.**

Note: ***Patients who have definite evidence of plasma leakage, hemorrhagic manifestations and thrombocytopenia might not be present as the exception.***

DF	DHF
• No plasma leakage • No abnormal coagulogram : PTT,TT • Thrombocytopenia – 50%	• Plasma leakage • Abnormal coagulogram : PTT, TT • Thrombocytopenia – 90%



Difference between DF and DHF

Natural course of DHF/DSS

Day 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9

Fever

Shock

Convalescence phase

Febrile phase

Critical phase

Pleural effusion, Ascites

Hematocrit

Plasma leakage

Stop leakage

Reabsorption

Fluid overload

IV fluid: NSS, DAR, DLR
Colloid: 10%Dextran-40
M+5% Deficit
(= 4,600 ml in adult)

Sometimes High Hct Increase UOP

W B C

Tourniquet test +

WBC	6,000-9,000		≤5,000				
Platelet count	200,000		<150,000	≤100,000	<50,000	< 30,000	Plt. rising
Hct	35		38	45 (rising 20%)			
Albumin				≤3.5 gm%			

(or ≤ 4 gm% in Obese or change by 0.5 gm%)

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Management targets on DHF/DSS with plasma leakage

- Among 1,000 dengue patients, probably 100 DHF with plasma leakage and 10-50 DSS (depends on early detection of plasma leakage)
- Majority of dengue patients are not severe

Hallmarks of DHF

- **Plasma leakage – rising HCT (PCV) > 20 %. pleural effusion, ascites, hypoalbuminemia (serum albumin < 3.5 gm%)**

- **Abnormal hemostasis – bleeding tendency, thrombocytopenia, prolonged PTT, Prolonged TT, prolonged PT**

The end of febrile phase

Pathophysiologic Hallmark of DHF

- **Plasma leakage – major problems**
- **Abnormal hemostasis - usually minor bleeding in early febrile phase except in those with underlying peptic ulcer or those who took NSAID, Aspirin, Steroids**

Severity of DHF

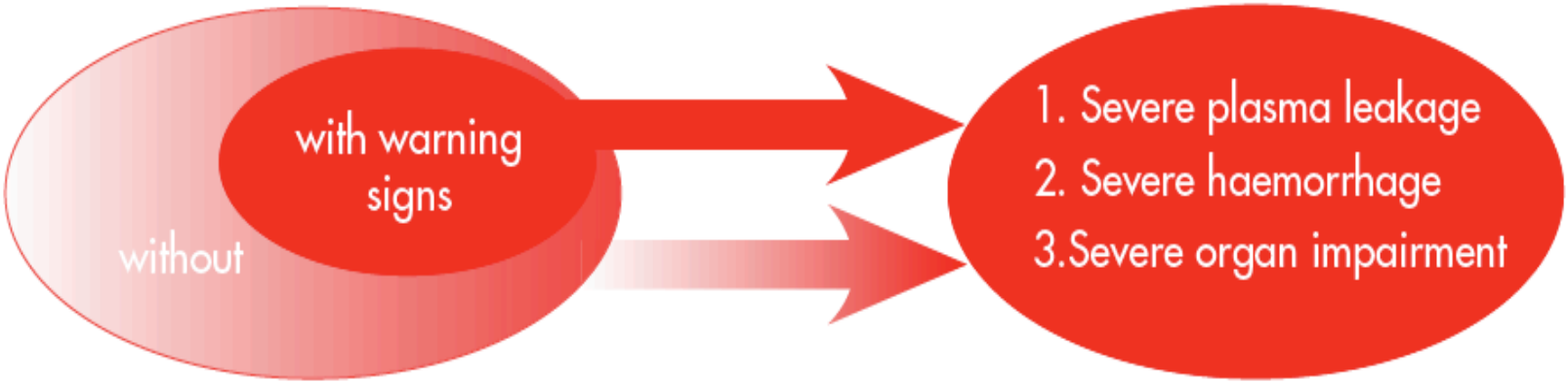
- **Grade I – No shock**
- **Grade II – No shock, spontaneous bleeding**
- **Grade III – Shock**
- **Grade IV – Profound shock (unmeasurable BP/ Pulse)**

Prolonged shock

- **> 10 hours untreated - Death!!!**
- **> 4 hours untreated**
  - **Liver failure- prognosis 50%**
  - **Liver + Renal failure - prognosis10%**
  - **3 organs failure (+respiratory failure) – Prognosis is a miracle!!!**

DENGUE ± WARNING SIGNS

SEVERE DENGUE



CRITERIA FOR DENGUE ± WARNING SIGNS

Probable dengue

live in /travel to dengue endemic area.
Fever and 2 of the following criteria:

- Nausea, vomiting
- Rash
- Aches and pains
- Tourniquet test positive
- Leukopenia
- Any warning sign

Laboratory-confirmed dengue

(important when no sign of plasma leakage)

Warning signs*

- Abdominal pain or tenderness
- Persistent vomiting
- Clinical fluid accumulation
- Mucosal bleed
- Lethargy, restlessness
- Liver enlargment >2 cm
- Laboratory: increase in HCT concurrent with rapid decrease in platelet count

*(requiring strict observation and medical intervention)

CRITERIA FOR SEVERE DENGUE

Severe plasma leakage

leading to:

- Shock (DSS)
- Fluid accumulation with respiratory distress

Severe bleeding

as evaluated by clinician

Severe organ involvement

- Liver: AST or ALT >=1000
- CNS: Impaired consciousness
- Heart and other organs

Warning signs – WHO TDR 2009

- Persistent vomiting
- Abdominal pain,
- Lethargy, restlessness
- Liver 2 cms
- Bleeding
- Rising Hct and dropping of platelet

- Non-specific, low specificity (20- 50%)
- Increase workload beyond management by existing healthcare personnel
  - 20 times at OPD
  - 3 times at IPD

Multi-country study: 18 countries
Validation study of the revised classification

1997 \ 2009	Revised not classified	Dengue without Warning Signs	Dengue With Warning Signs	Severe dengue	Total
Not Classified	23	57	159	29	268
DF	7	551	684	75	1,317
DHF	2	8	240	39	289
DSS	0	0	12	76	88
Total	32	616	1,095	219	1,962

Barniol J et al: BMC Infectious Disease 2011,11: 106

Important steps in Dengue Case management

1. Early diagnosis of dengue infections
2. Early detection of plasma leakage and proper IV fluid management
3. Detect and correct common complications: ABCS, Fluid overload
4. Management of bleeding
5. Dx & Management of unusual cases: BBH

1. Early clinical Diagnosis

- **Think of dengue in every patients who present with high fever (except in adults)**
- **High continuous fever**
- **Bleeding manifestations: petechiae, epistaxis, gum bleeding, hematemesis, melena, hematuria, hemoglobinuria, menstruation, abnormal vaginal bleeding…**
- **Ache and pain; headache, retro-orbital pain, myalgia, arthralgia/ bone pain**
- **Rash; Petechiae, MP-rash**

Early diagnosis

Non-specific signs & symtoms

Headache, retro-orbital pain, Myalgia & Joint pain

Dengue Fever

Bleeding manifestations

OPD Management of Dengue

Tourniquet test

- **Standard Winthrobe technique: (systolic + diastolic)/ 2 for 5 minutes**

- **Daisey technique: for older children > 5 years old and adult**

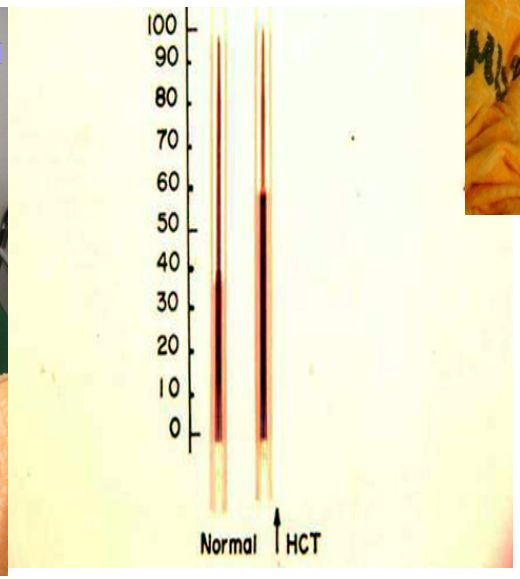
- raise pressure to 80 mmHg for 5 minutes

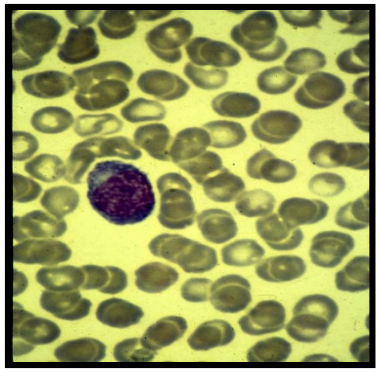
Tourniquet test ±

- **Send for CBC**
  - ❖ **At least to know baseline Hct, WBC and platelet count**
- **Give advise and Dengue brochure**
- **Ask to come for follow up: everyday from the 3rd day of illness (if possible)**

Tourniquet test = 70-90% sensitivity

CBC: WBC Platelet & Hct





WBC < 5,000 cells/ cumm.

- **- There will be no fever within the next 24 hours**
- **- In DHF/DSS patients**
  - **Entering critical period**
  - **Beginning of plasma leakage**
  - **Near to the time of shock?**

Rapid Diagnostic Tests (RDT)

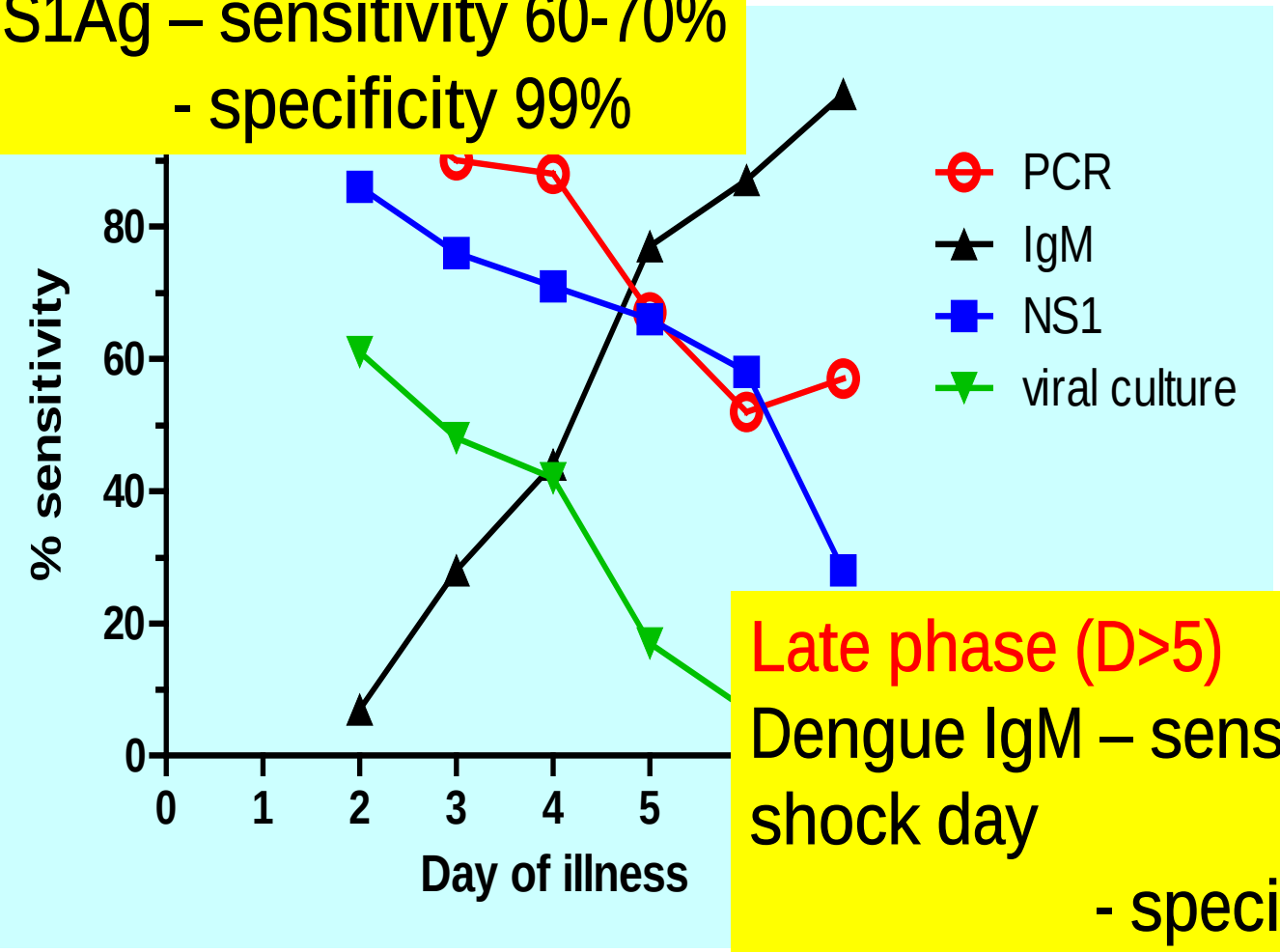
1. **NS1Ag – Early diagnosis of dengue**
2. **IgG/ IgM – ELISA, Strip Test – confirmed diagnosis**
3. **Duo or Combo + 1 + 2**
4. **Test kit : dengue, zika, chikungunya**

Dengue diagnostic options and sensitivity

Fever phase (D1-5)

NS1Ag – sensitivity 60-70%

- specificity 99%



Late phase (D>5)

Dengue IgM – sensitivity 60% on shock day

- specificity 99%

Courtesy of Armed Forces Research Institute of Medical Sciences

NS1Ag Test

- **Sensitivity ranges from 40-60% depend on the company**
- **Positive when the patients have fever**
- **The sensitivity is highest in the first day of fever (90%), then declines as fever days. By day 5 of fever the test is less sensitive and may be negative from day 6 onwards**
- **The test is likely to be positive in primary infections than secondary**
- ***Do not guide clinical management***

IgG/ IgM tests

- ***Positive after 5 days of fever***
- **IgG is more likely to be positive in secondary and past infections.**
  - **It is positive up to 1-2 years after infections.**
- **IgM is more likely to be positive in primary infections and indicates acute dengue infections.**
  - **It persists in 1-2 months**

Signs & symptoms of Dengue /Covid 19

Dengue (WHO 1997/2011)

- Fever
- Ache & pain
- Rash
- bleeding
- Non-specific
  - anorexia
  - nausea/vomiting
  - cough/running nose
  - diarrhea

Covid-19 (WHO int.)

Common

- Fever
- Cough
- Tiredness
- Loss of smell & taste
- Night sweating

Less common

- Sore throat
- Ache & pain
- Diarrhea
- Rash
- Red & irritated eyes

Serious

- Dyspnea / tachypnea
- Loss of speech or mobility or confusion
- Chest pain

Clinical that may distinguish Dengue from Covid-19

Dengue

- **Bleeding manifestations**

Covid-19

- **Loss of smell & taste**
- **Dyspnea / tachypnea**
- **Chest pain**
- **Loss of speech or mobility or confusion**

Omicron S&S

- running nose

- **Sore throat / dry cough**
- **Back pain / myalgia**
- **Fatigue / tiredness**
- **Night sweating**

Symptoms of XBB.1.16(Arcturus) in adults and children

Adults

- Fever
- Sore throat
- Runny nose
- Extreme fatigue, abdominal discomfort
- Muscle pain, and headache

Dr. Aditya S Chowti, senior consultant Internal Medicine,Fortis Hosp., Bangalore

Children

- High fever, cough, itchy conjunctivitis
- or pinkeye – without pus, but with sticky eyes
- Scratchy throat also leading to difficulty in swallowing
- Running nose, blocked nose seem to be more common symptoms in current Covid variant

Dr. Chabbra

https://www.hindustantimes.com/lifestyle/health/covid XBB.1.16 symptoms of new covid variant-Arcturus in adults-children and elderly -101681537965837.html

Lab. test

Dengue

- CBC
- Rapid diagnostic test
  - NS1 Ag
  - dengue IgM and IgG
- PCR

Covid-19

- ATK (antigen test kit)
- RT-PCR

- Risk for covid-19
- Respiratory symptoms
- Abnormal chest film

Health education for patients and families of suspected dengue cases

General care

- Reduction of fever by paracetamol and tepid sponge. Avoid aspirin and NSAID
- Promote soft diet or fruit juice, milk or electrolyte solution
- Supportive and symptomatic care

Important message

Come back to the hospital ASAP when there are:

- No clinical improvement especially when no fever of lower grade of fever
- Abdominal pain
- Vomiting
- Bleeding
- Restlessness/lethargy
- No appetite/ thirsty
- Behavior change

Warning signs

- **No improvement when there is no fever**
- **Abdominal pain**
- **Nausea/vomiting**
- **Lethargy/ Restlessness**
- **Less urine output**
- **Bleeding**

About 10-20 % of DHF/DSS patients have no warning signs

On follow up

- **Repeat the history and P.E. as before**
- **Repeat CBC**
- **Ask for follow up again until 24 hours without fever**

Indication for admission

- Very weak, cannot eat/ drink
- Bleeding
- Platelet counts < 100,000 cells/cumm./ or rising Hct 10-20%
- Clinical deterioration when defervescence
- Severe abdominal pain/ vomiting
- Shock/ impending shock
- Rapid pulse without fever
- Capillary refill time > 2 seconds
- Cold clammy skin
- Change of consciousness
- High risk patients
- Family concern

High risk patients

- Infants < 1 year of age
- Prolonged shock
- Overweight patients
- Massive bleeding
- Change of consciousness
- Have underlying diseases
- Pregnancy
- VIP

IPD Management of Dengue hemorrhagic fever and Dengue shock syndrome

Natural course of DHF/DSS

Day 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9

Fever

Shock

Convalescence phase

Febrile phase

Critical phase

Pleural effusion, Ascites

Hematocrit

Plasma leakage

Stop leakage

Reabsorption

Fluid overload

IV fluid: NSS, DAR, DLR
Colloid: 10%Dextran-40
M+5% Deficit
(= 4,600 ml in adult)

Sometimes High Hct Increase UOP

W B C

Tourniquet test +

WBC	6,000-9,000		≤5,000				
Platelet count	200,000		<150,000	≤100,000	<50,000	< 30,000	Plt. rising
Hct	35		38	45 (rising 20%)			
Albumin				≤3.5 gm%			

(or ≤ 4 gm% in Obese or change by 0.5 gm%)

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Febrile phase

- If the patients could eat and drink, no IV fluid given
- Encourage ORS 3 cc/kg/hr
- Plain water is not recommended
- If necessary, give 5% D/NSS with minimal rate

Natural course of DHF/DSS

Day 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9

Fever

Shock

Convalescence phase

Febrile phase

Critical phase

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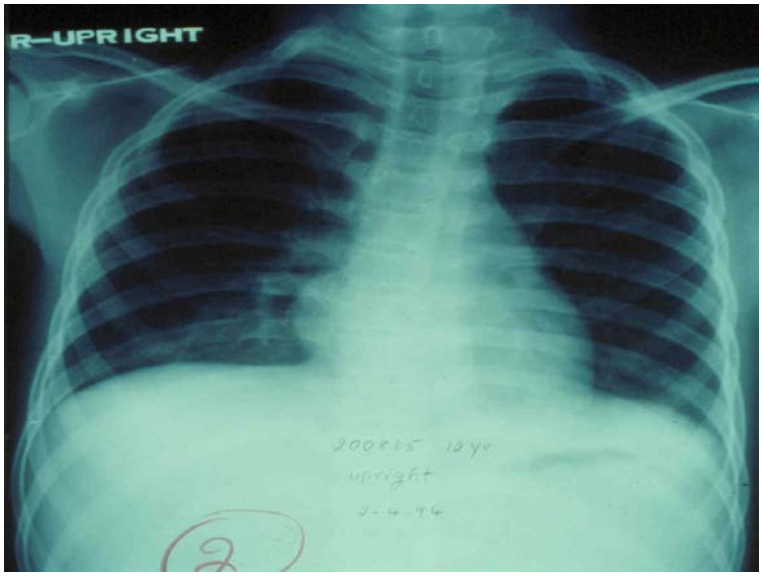
LEAKAGE PHASE

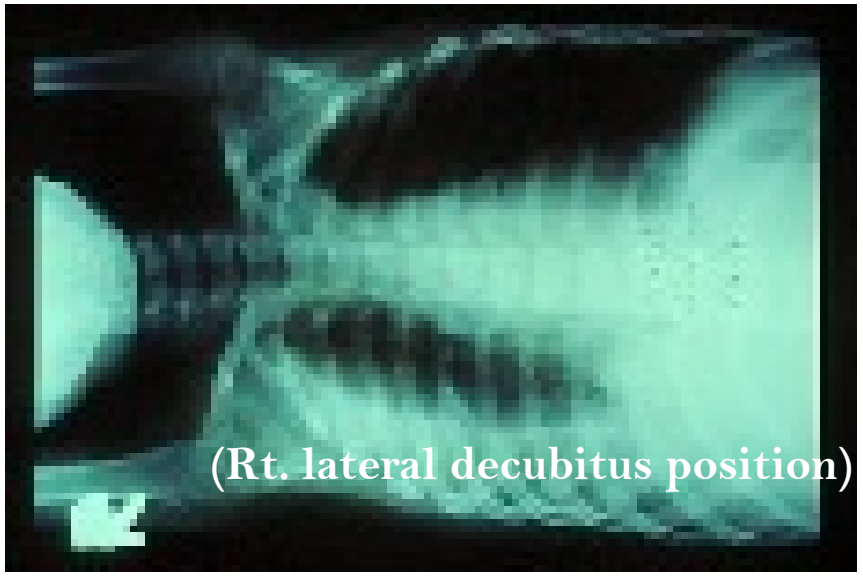
- **Rapid leakage: shock in < 24 hrs.**
  - **Morning: plt 80,000 and evening plt 30,000/mm3**
- **Slow leakage: shock > 24 hours**

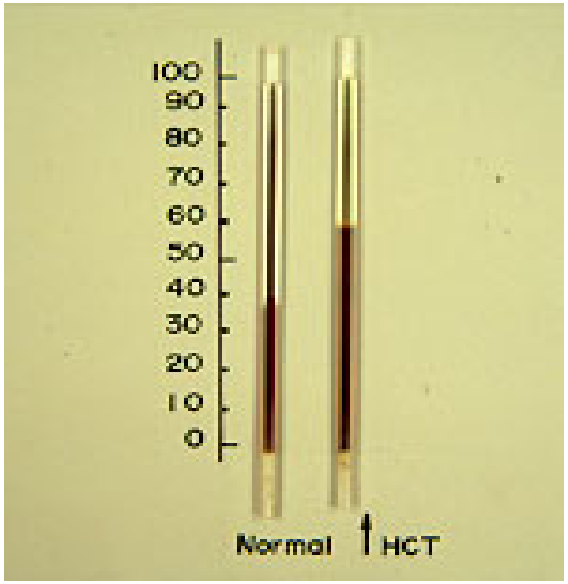
How to detect plasma leakage

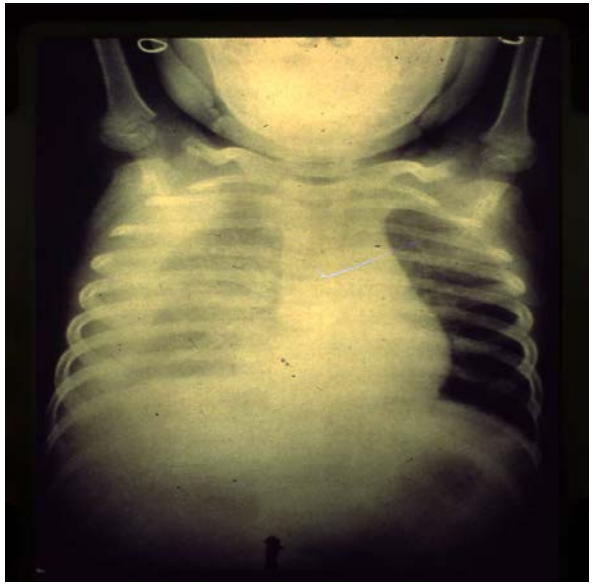
- **Fever ↓**
- **Platelet < 100,000 /cu.mm**
- **Evidence of plasma leakage**
  - **hemoconcentration ≥ 20%**
  - **pleural effusion**
  - **ascites**

Evidences of plasma leakage in DHF

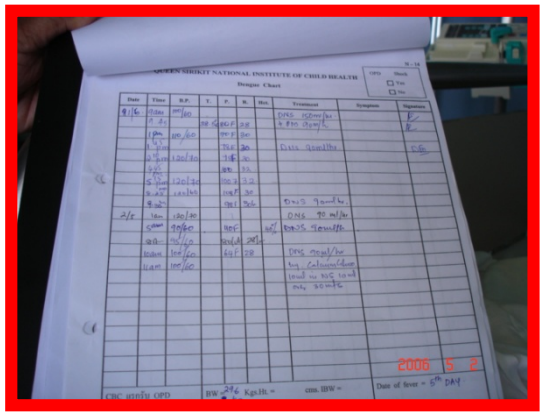


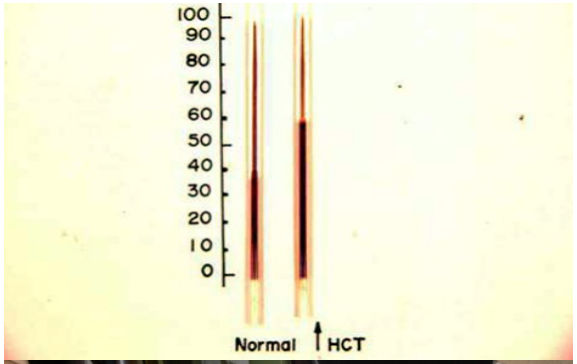






Monitoring 4 parameters





Vital signs q 2 hrs

Hct q 4-6 hours

Urine output
(0.5 – 1 ml/kg/hr)

Monitoring Chart for Dengue Patients

Instructions - Do CBC daily/bd and PCV 6 hrly. Monitor other parameters 3-4 hrly and when leaking detected monitoring every hour.

Case ▫ **Refer** ▫ **Walk in**

OPD ▫ **Shock** ▫ **Non shock**

IPD ▫ **Shock** ▫ **Non shock**

Indications to call for immediate advice

1. Pulse rate > 120/min with fever or >100/min without fever.
2. Pulse Pressure 25-20 mmHg or less (in supine position)
3. Postural drop of SBP >20mmHg.
4. Significant bleeding (Haemetemesis, Malena, Bleeding PV etc.)
5. UOP <0.5ml /Kg/hr
6. CRFT > 2 sec

Date	Time	BP	Temp	PR	RR	PP	RR	HCT (%)	Clinical/ Lab/ Treatment	Nursing Care/ Signs	INTAKE				OUTPUT		
											Blood/ rate & Amount	IV Amount	Oral	Total	Urine/ Stool	Vomit /Bleed	Total

CBC Day of Admission

Hct = **WBC =**
Plt = **Lym =**
PMN =

BW= **kgs.** **Hight =** **cms**
IBW = **kgs.**

Maintenance fluid =

M + 5% Deficit =

Date of Fever **Day of Illness**
TT
Liver
Bleeding
Epistaxis
Abdomen

Name		Age	HN	AN
	Ward	Attending Physician		

Pulse: F = Full M= Moderate W= Weak N = Not Palpable

DETECTION OF SHOCK : DIFFICULT

GOOD CONSCIOUSNESS

- No fever and rapid pulse: Impending shock?
- Narrowing of pulse pressure, e.g. 100/80, 110/90 mmHg
- Rapid/ weak pulse
- Delayed capillary filling time (>2 sec)
- Restlessness/ irritable
- Speak fowl language, rude behavior

Other causes of shock in Dengue patients

- Hypoglycemia
- Excessive vomiting
- Co-infections

Principles of IV fluid in DHF patients during leakage period

- **Isotonic salt solution: NSS, DAR, DLR with or without dextrose**
  - **Check blood sugar if given IV without dextrose**
  - **30% of DSS patients have hypoglycemia**

- **Limited amount of fluid (oral + IV) during leakage period (M +5% deficit or 4.6 L in adults)**
  - **If give more IV fluid, will cause more leakage that will interfere with respiration**

- If more volume is needed, switch to Dextran-40 (hyper-oncotic), plasma expander

IV FLUID IN CRITICAL (LEAKAGE) PHASE (PLATELET ≤ 100,000 CELLS/MM3.)

- Start Isotonic salt solution when inadequate oral intake
- Amount = Maintenance + 5%Deficit in 24-48 hours
- Shock - 24 hours
- Non-shock – 48 hours

Principles of IV fluid in DHF patients during leakage period

- **Minimal volume, just to maintain intra-vascular volume**
- **Adjust rate of IV fluid according to monitoring parameters: clinical, vital signs, Hct and amount of urine**

CALCULATION OF M + 5% DEFICIT

Maintenance:

- First 1-10 kg. = 100 ml/ kg
- 10-20 kg = 50 ml/kg
- > 20 kg = 20 ml/kg

5% Deficit = 50 ml/kg

Example: adult 50 kgs

M = (10 X 100 ml) +
(10 X 50 ml) +
(30 X 20 ml)
= 1,000 + 500 + 600
= 2,100/day = 87 ml/hr

5% D = 50 X 50 ml
= 2,500

M+5%D = 2,100 + 2,500
= 4,600/day

= 4,600/24 hr = 191.67 ml/hr
= 191.67/50 kg = 3.83 ml/kg/hr

RATE IV FLUID : COMPARE ADULT AND CHILDREN

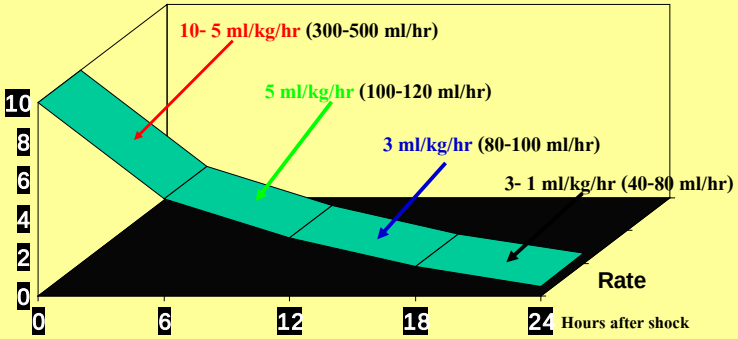
	Child (ml/kg/hr)	Adult (ml/hr)
M/2	1.5	40
Maintenance (M)	3	80
M +5%D	5	100-120
M +7%D	7	150
M + 10%D	10	300 - 500

Rate of IV fluid

Shock

Rate of IV Fluid in

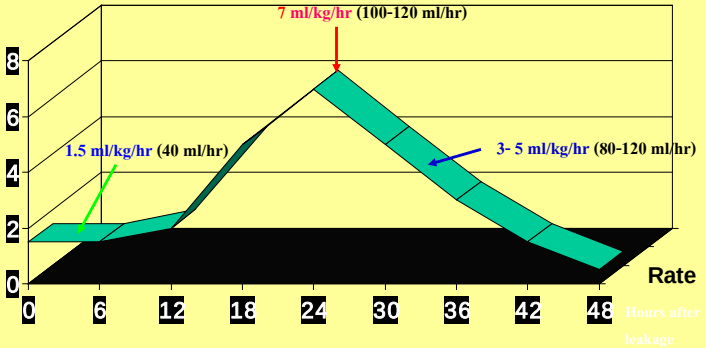
Dengue Shock Syndrome



Non-shock

Rate of IV Fluid in

Dengue Hemorrhagic Fever grade I & II



(Rate in adult)

DSS – NSS (D) 10 ml/kg/hr or 500 ml/hr in adult,
If profound shock – free flow 15-30 mins, then reduce rate

Non-shock: rate depends on degree of thrombocytopenia & rising Hct

Dextran infusion

(10% Dextran-40 in NSS)

- **Rate 10 ml/kg/hr or 500 ml in adults**
- **Dextran will bring down Hct by 10 points, but not below baseline Hct**

If Hct drops > 10 points or below baseline – Think of bleeding

- **Maximum dose per day = 30 ml/kg/day**
- **All through the course, may use up to 6 doses**
- **Aware that urine will be sticky and may not pass in reabsorption phase (need Furosemide?)**

Type of Colloidal solution used in DHF/DSS

- **Plasma expander (high osmolarity, high oncotic pressure than plasma)**
  - **10% Dextran-40 in NSS (2.7 times)**
  - **20% albumin (6 times higher)**
- **Plasma substitute**
  - **6%Dextran-70 or 6%Dextran-40**
  - **Starch**
  - **Gelatin**
  - **5% Albumin**

Indications for switching to colloidal solution

- **Signs and symptoms of fluid overload**
  - **Puffy eyelids, distended abdomen with ascites**
  - **Dyspnea/ Tachypnea**
  - **Positive lungs signs: crepitation, rhonchi, wheezing**
- **Continue rising Hct**
- **Persistent high Hct > 25-30%**
- **Too much crystalloid solutions before plasma leakage (those patients who received IV fluid early before leakage started)**

Natural course of DHF/DSS

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Shock

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Critical phase

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Hematocrit

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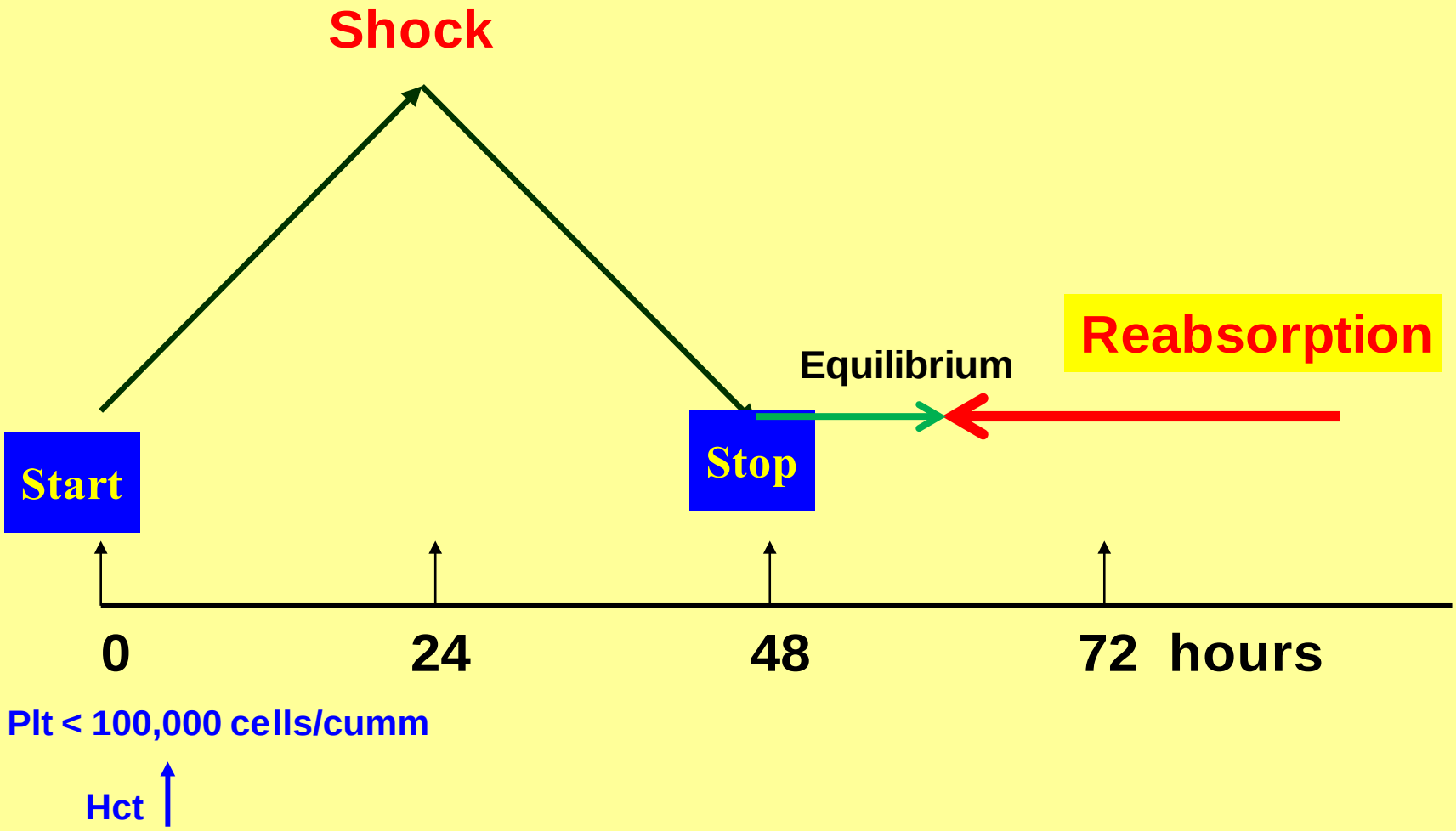
Professor Siripen Kalayanarooj

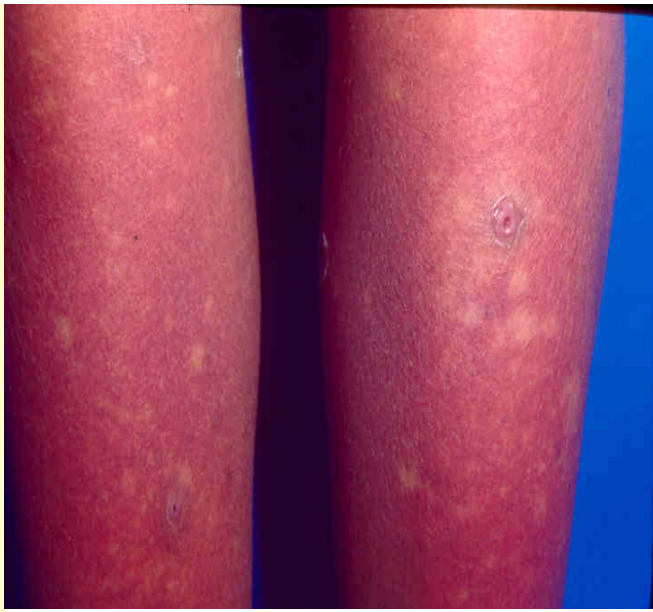
Plasma leakage : Natural course in severe cases



Convalescence phase

- **Reabsorption 8-12 hrs. after leakage is stopped**
- **Decreased the rate of IV fluid or stopped IV fluid**

- **A – appetite**
- **B – bradycardia**
- **C – Convalescence rash, itching**
- **D – Diuresis: aware of hypokalemia**



Indication for IV fluid in DHF patients

- **Entering critical period – thrombocytopenia; platelet count ≤ 100,000 and throughout plasma leakage time, 1-2 days (and 12-24 hours beyond)**

- **Shock: difficult to detect because patients are in good consciousness, able to walk and talk**

- **Not before and after stop leakage, if IV fluid is extend beyond this leakage phase, patients are at risk of fluid overload which is one of the major causes of death**

Lessons Learned

1. Early diagnosis of dengue infections

- **CBC: WBC, Platelet count, Hct - Not done, eventhough they can refer patients to be done in the nearest hospital (recommend to do CBC starts from day 3 of illness – clinical or warning signs cannot help to detect plasma leakage)**

- **No NS1Ag available but most people prefer this even though it does not guide clinicians for IV fluid management**

Lessons Learned

2. ***Early detection of plasma leakage and proper IV fluid management*** **- Major cause of fluid overload and dead**
   - **Not isotonic**
   - **Too early**
   - **Too much**
   - **Too long**
   - **No Dextran available (other colloidal solutions are not effective including albumin)**
   - **Too little - causes prolonged shock and organs failure**

Thank you!

ขั้นตอนแนะนำในการวินิจฉัยและวางแผนการรักษาโรคไข้เลือดออกในผู้ป่วยที่มีไข้ และอาศัยอยู่ในแหล่งระบาดของโรคตาม case scenario ในหนังสือเล่มนี้ คือ การประเมินผู้ป่วยตามแบบประเมินต่อไปนี้

แบบประเมินผู้ป่วยที่สงสัยว่าเป็นไข้เลือดออก วันที่_____เวลา_____Case #_____

ชื่อ_____นามสกุล_____อายุ___ปี นน.___กก. สูง___ซม. BMI___kg/m^2 HN_____ วันที่_____เวลา_____		
1	Dengue infection?	☐ Yes_____ ☐ Probable_____ ☐ No
2	DF/DHF/DSS/EDS?	☐ DF ☐ DHF _____ ☐ DSS (Date/Time of shock) _____ ☐ EDS_____
3	Clinical Phase	☐ Febrile ☐ Critical/Leakage ☐ Early Convalescence ☐ Reabsorption ☐ Hours after Shock/ leakage_____
4	High risk	☐Yes _____ ☐ No
5	Complications	☐ Yes ☐ Acidosis_____ ☐ Bleeding_____ ☐ Hypocalcemia _____ ☐ Hypoglycemia_____ ☐ Fluid overload_____ ☐ No
6	EDS	☐ Liver failure_____ ☐ Renal failure _____ ☐ Others_____ ☐ Underlying Diseases_____ ☐ Co-infection_____
7	Important Labs.	☐ Hct baseline_____ ☐ Hct (max) _____ ☐ Hct (min)_____ ☐ Urine exam ☐ blood positive ☐ RBC ____ ☐ Others_____ ☐ PLT < 100,000 /cumm. ☐ Date_____ ☐ ALB_____ ☐ AST _____ ☐ ALT_____ ☐ INR_____ ☐ Blood sugar_____ ☐ CXR_____ ☐ Others_____