यह कार्यक्रम स्वास्थ्य विभाग और राज्य स्वास्थ्य एवं परिवार कल्याण संस्थान (SIHFW), उत्तर प्रदेश की पहल पर उत्तर प्रदेश टेक्निकल सपोर्ट यूनिट (UPTSU) के सहयोग से हो रहा है।

Principal Secretary, Medical Health & Family Welfare, U.P.
Shri Partha Sarthi Sen Sharma

Director Administration & Director, SIHFW
Shri Shiv Sahay Awasthi

एपिसोड 18

स्वास्थ्य विभाग की पहल

शुक्रवार की शाम, डाक्टर्स के नाम

प्रदेश के जाने-माने चिकित्सकों से सीधे जुड़ें और उनके अनुभवों का लाभ उठाएँ

दिनांक : 12 जुलाई, 2024 | समय : सांय 6:00 बजे से 7:30 बजे तक

— वेबकास्ट का विषय —

डेंगू का प्रबंधन
(Management of Dengue)

वक्ता

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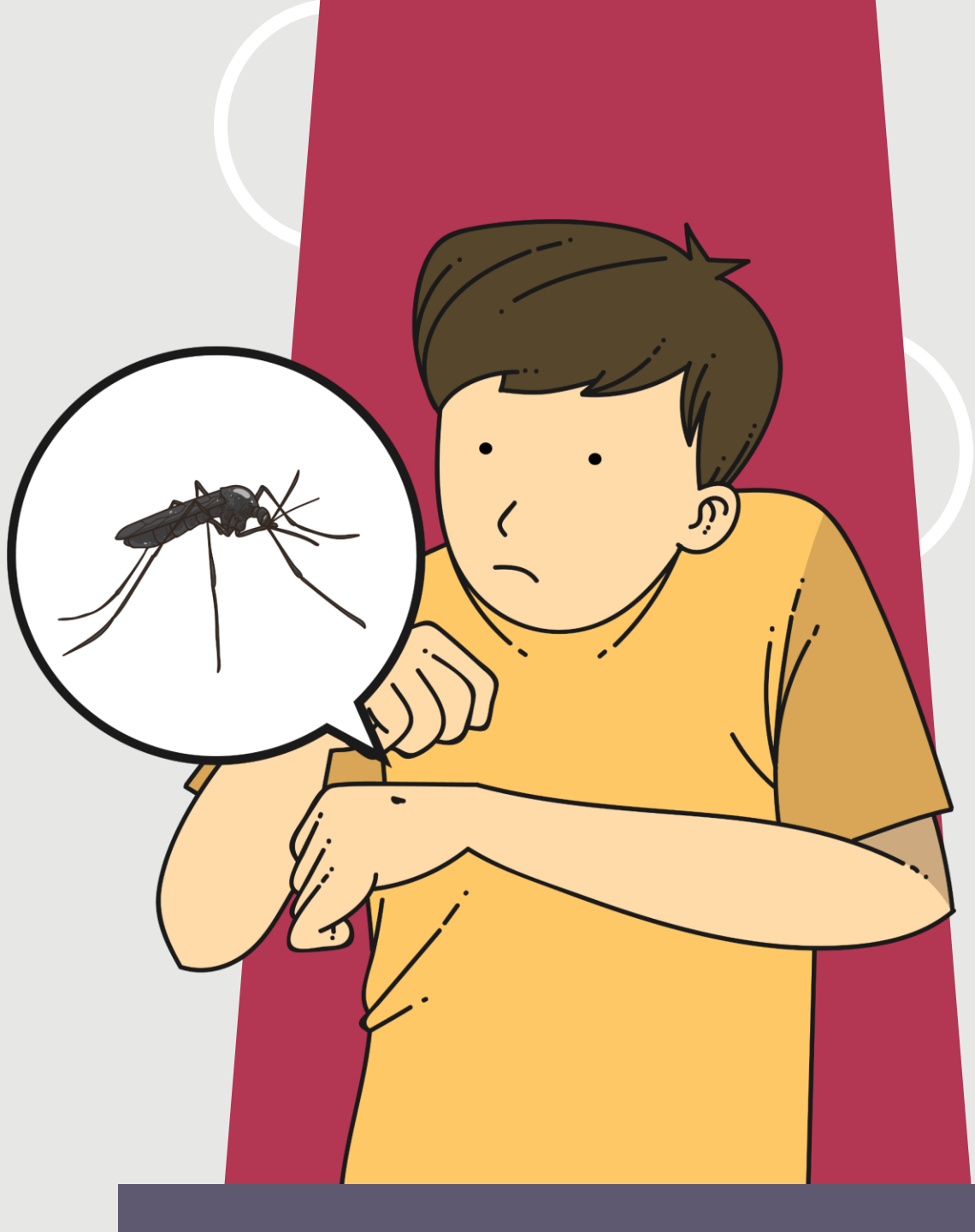
आयोजक

राज्य स्वास्थ्य एवं परिवार कल्याण संस्थान (SIHFW)
इंदिरा नगर, लखनऊ, उत्तर प्रदेश

YouTube LIVE STREAMING

ETIO PATHOGENESIS & CLINICAL MANIFESTATIONS OF DENGUE FEVER



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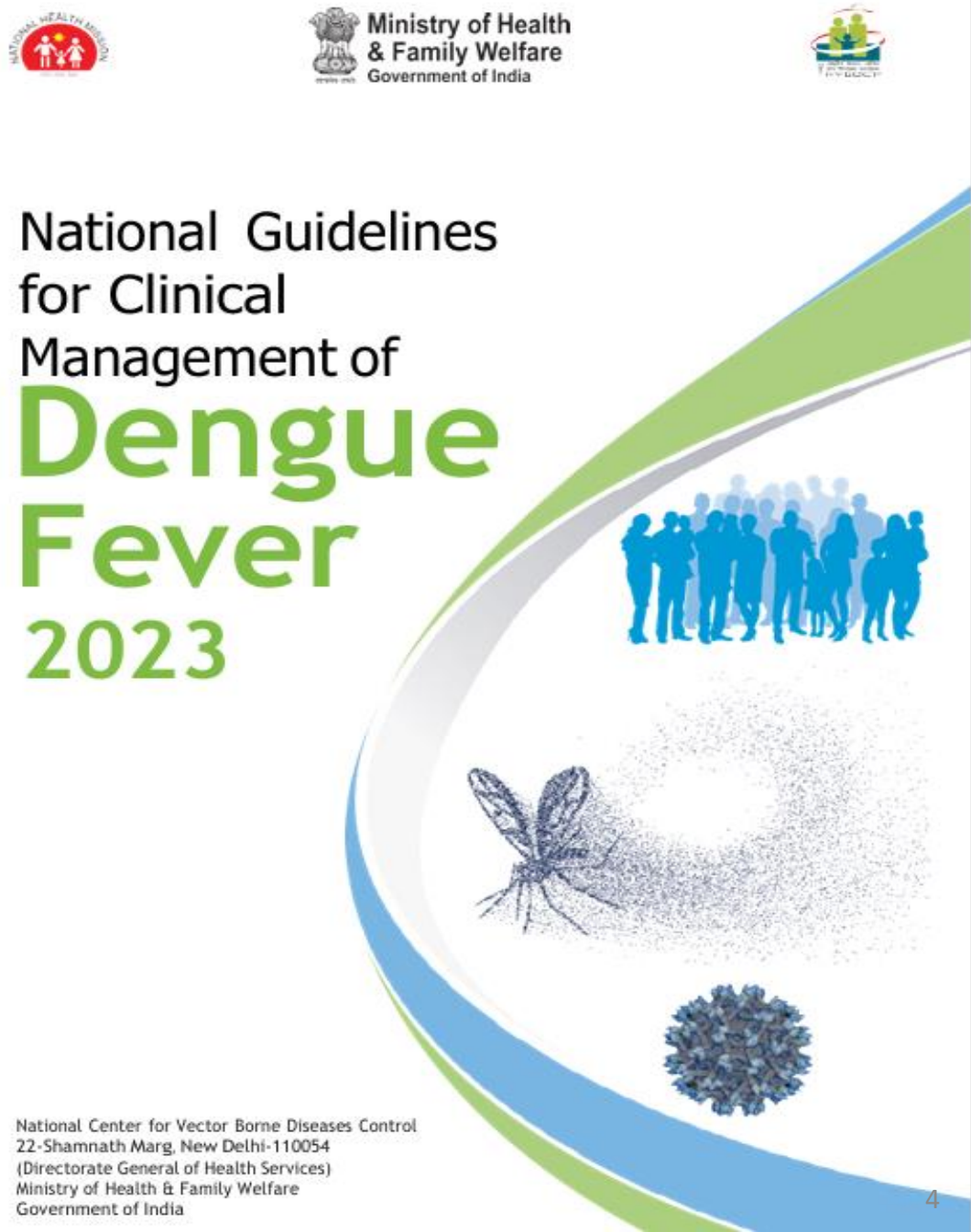
Outline

- Introduction
- Epidemiology
- Aedes Mosquito Vector
- Transmission:
- Pathogenesis
- Clinical features
- Case Classification
- Differential diagnosis

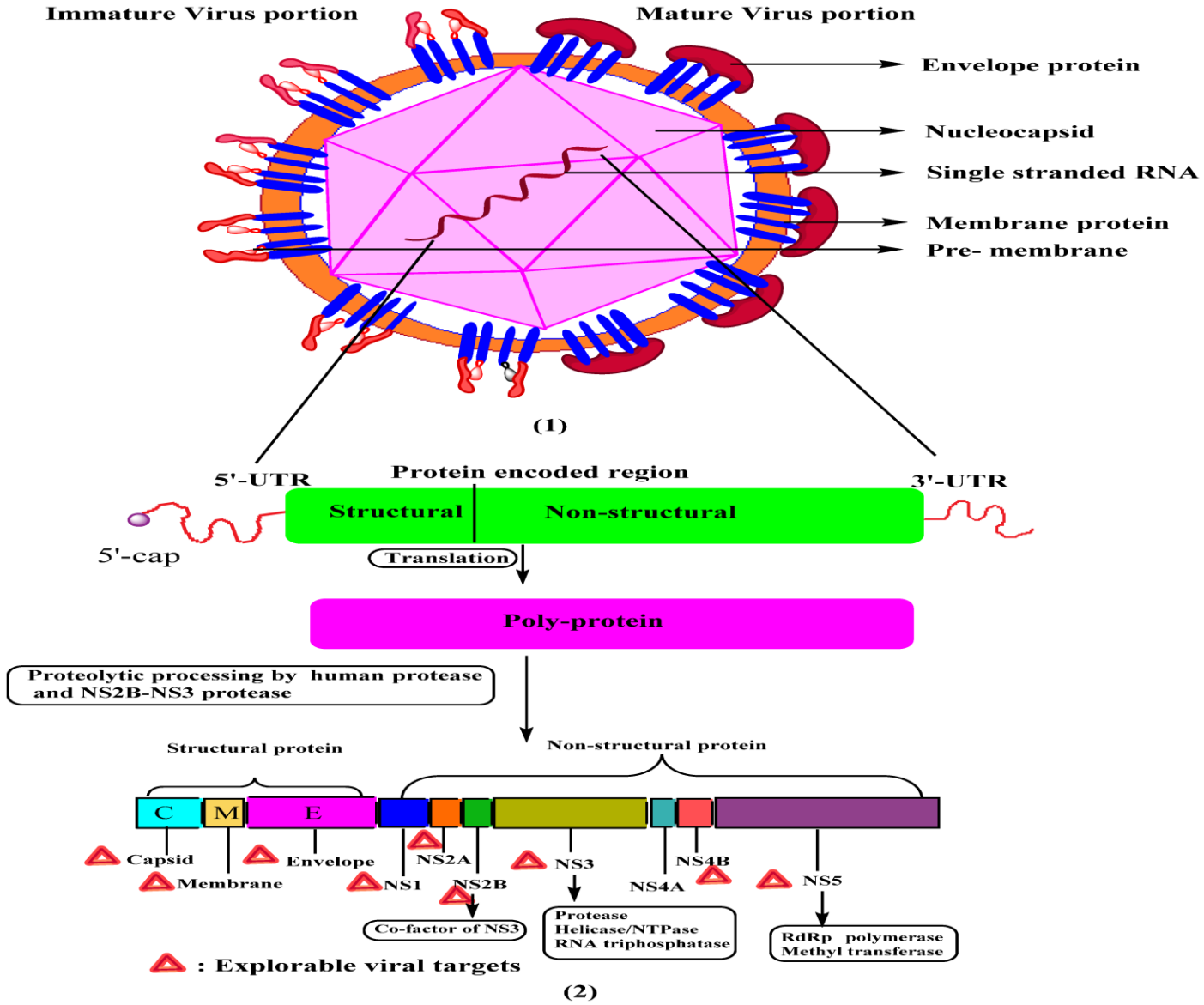


Introduction

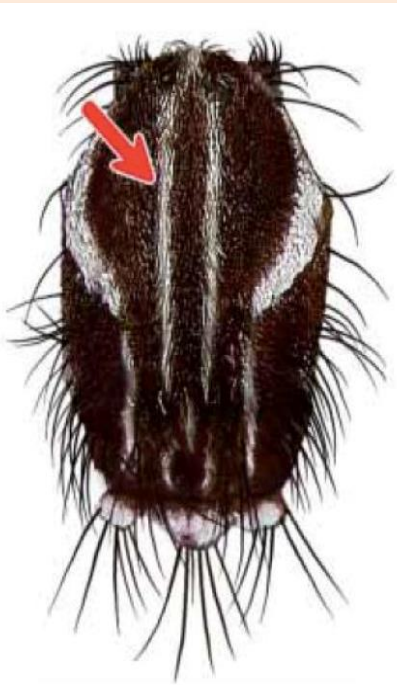
- Dengue virus was isolated first in India during 1945
- During 1996, one of the most severe outbreaks of dengue fever occurred in Delhi
- In India, till date, all States/UTs, (except Ladakh) have reported dengue cases during the last two decades (even Lakshadweep has been reporting suspected dengue cases)
- Dengue virus- single stranded RNA virus genus Flavivirus
- There are four dengue virus serotypes which are designated as DENV-1, DENV-2, DENV3 and DENV-4.
- Although all four serotypes are antigenically similar, still they are different enough to elicit cross-protection only for a few months after infection by any one of them.

Dengue virus structure

- 3 structural protein genes
- Nucleocapsid of core protein (C)
- Membrane associated protein (M)
- Envelope protein (E)
- 7 non-structural (NS) proteins - NS1, NS2A, NS2B, NS3, NS4A, NS4B and NS5



THE VECTORS…



Aedes aegypti.

Aedes albopictus.

Breeding in latex collecting cups of rubber plants

AEDES AEGYPTII

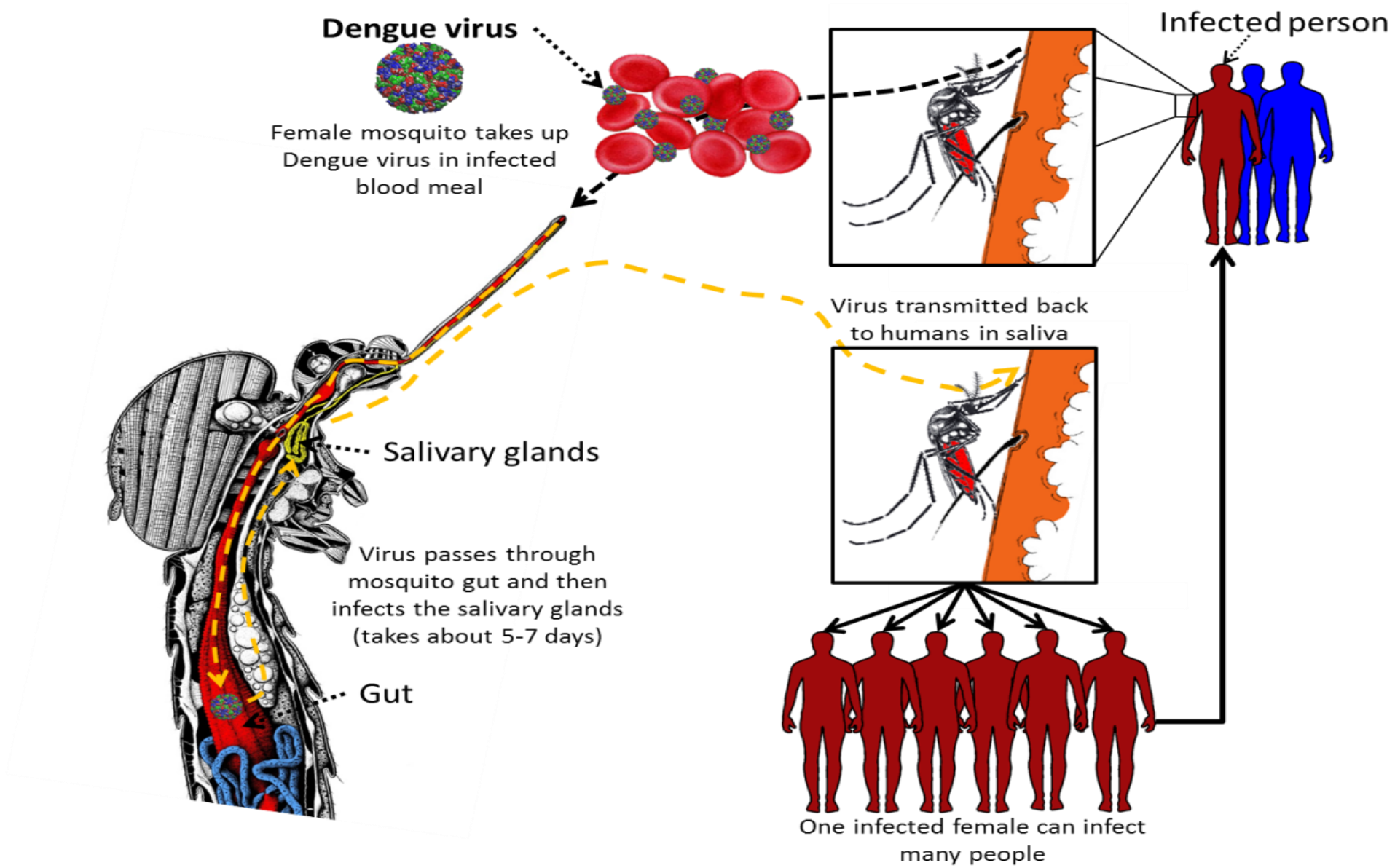
AEDES ALBOPICTUS

Aedes Mosquito

- Aedes breed in clean water collections.
- Transmission is related to rainfall and temperature. survives best between 16 - 30 degree C and a relative humidity of 60-80%
- Increased virus transmission during monsoon and post monsoon season due to high vector density.
- Outbreak typically occurs in clusters, especially in congested localities, as the flight range of these vectors is less-400 metres.
- Mosquitoes can transmit the disease to more than one person.
- Principally day biters

- Female Aedes mosquito deposits eggs singly on damp surfaces just above the water line. Under optimal conditions, the adult is emerged in seven days (after the aquatic stages in the life cycle of Ae. aegypti).
- Eggs can withstand desiccation for more than a year (can remain in viable dry condition) and emerge within 24 hours once it comes in contact with water.
- Average survival of Ae. aegypti is 30 days and Ae. albopictus is about eight weeks. During the rainy season, when survival is longer, the risk of virus transmission is greater.

Life cycle in Mosquito



Pathophysiology

Antibody-Dependent Enhancement (ADE)

- The dengue virus is initially taken up by dendritic cells.
- Host immune response targets 3 proteins- envelop protein (E), precursor membrane (pre-M), and NS1.
- Two types of antibodies are produced: neutralizing and nonneutralizing.
- The neutralizing antibodies protect against a specific serotype
- Non neutralizing antibody forms the virus antibody complex, enters the host cells, the virus replicates and generates high virus titers in the blood

Cytokine Storm

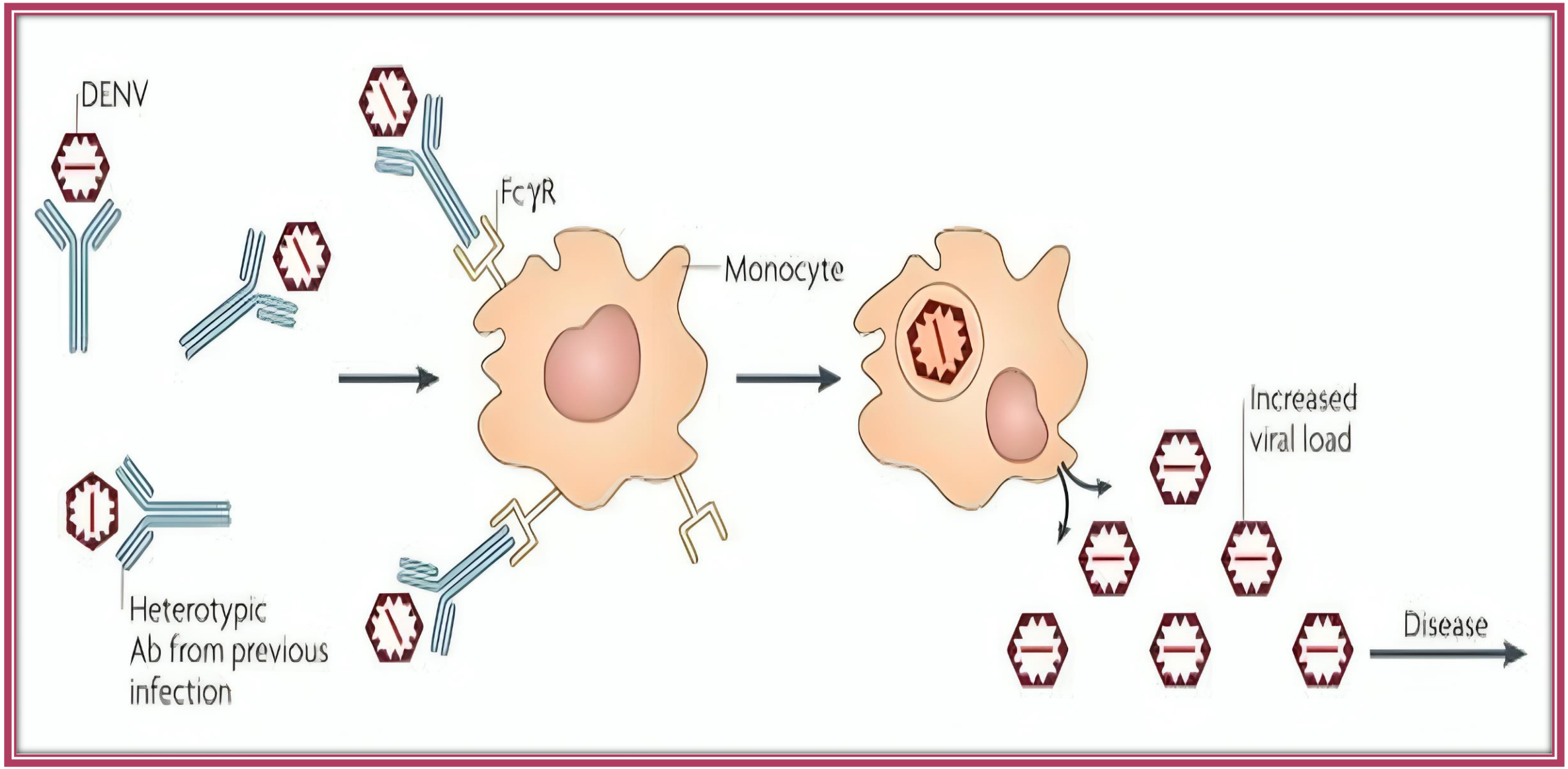
Previous infection with heterologous

Dengue serotype results in production of non protective antiviral antibodies

These Ab bind to the virion's surface

Fc receptor and focus the Dengue virus on to the target cells – macro/monocytes

Amplified response to immune system ,excess release of cytokines- interferon, TNF alpha


DENV
FcγR
Monocyte
Increased
viral load
Heterotypic
Ab from previous
infection
Disease

Vasculopathy

- Transient disturbance in the function of the endothelial glycocalyx layer
- Possible explanations include dengue virus, one of the dengue non-structural proteins, or one of the components of the immunological response to infection that might interact directly with the glycocalyx layer in such a way as to alter temporarily the characteristics of the fibre matrix.
- Heparan sulphate, an important constituent of the structure to which dengue virus can adhere, might have a role in this process.
- Anti-NS1 antibodies act as autoantibodies that cross-react with noninfected endothelial cells and platelets which triggers intracellular signaling and disturbances in capillary permeability. Plasma leakage occurs due to capillary permeability.

Coagulopathy

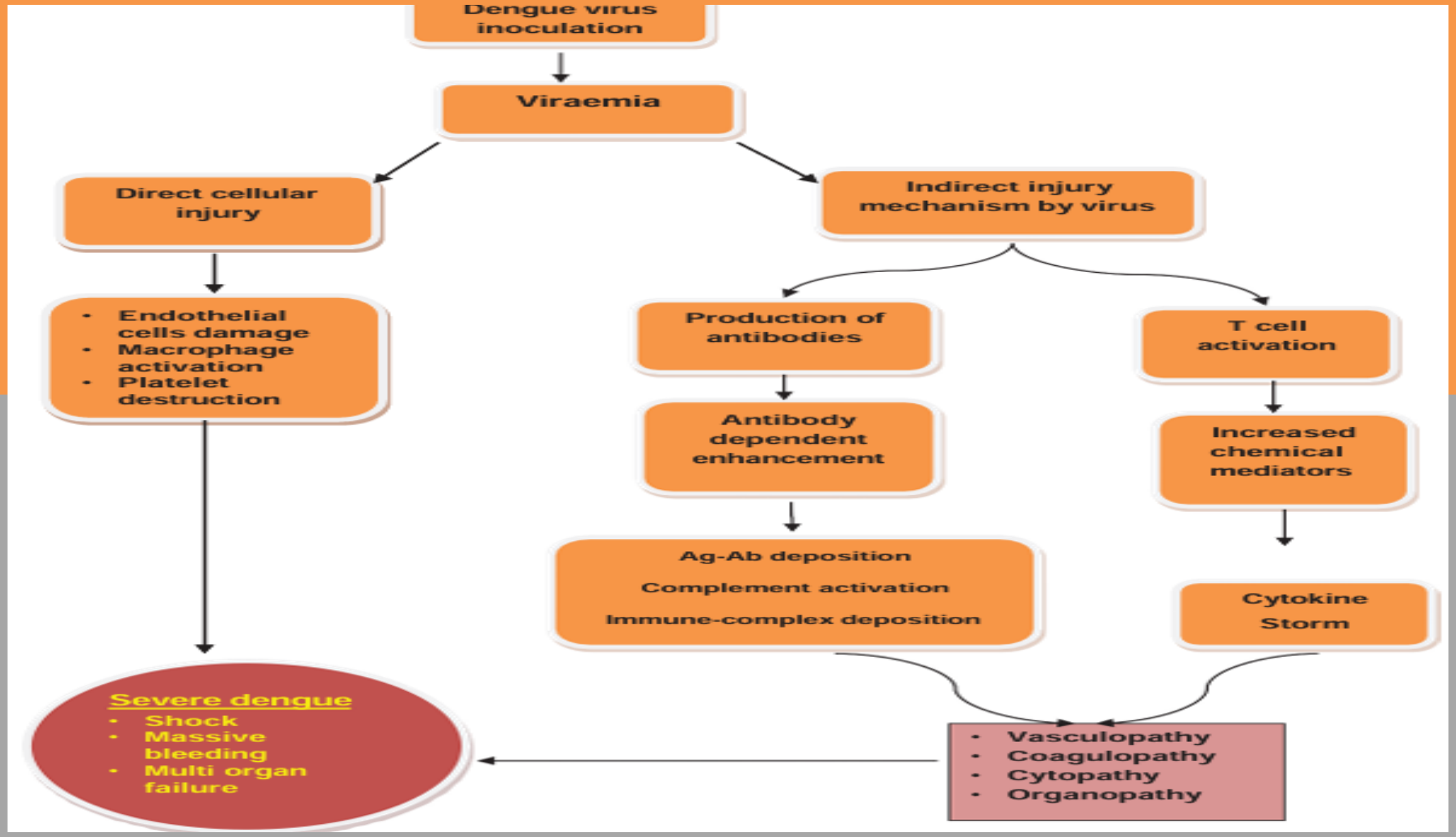
- Increased APTT
- Reduced Fibrinogen
- Reduced Platelets
- Disseminated Intravascular Coagulation (DIC)
- Enhanced fibrinolytic activity
- Release of heparan sulfate or chondroitin sulfate from the glycocalyx(molecules similar in structure to heparin that can mimic its anticoagulation function

Thrombocytopenia

Mechanisms postulated for thrombocytopenia:

1. IgM type of anti-platelet antibody
2. Anti-platelet antibodies + complements →lysis of platelets
3. Dengue viral-specific antibodies
4. Bone marrow hypocellularity
5. Destruction of platelet in the liver and spleen (peripheral sequestration)
6. Disseminated Intravascular Coagulation (DIC)
7. Cytoadherance
8. Platelet dysfunction (defect in ADP release)

Dengue Pathophysiology

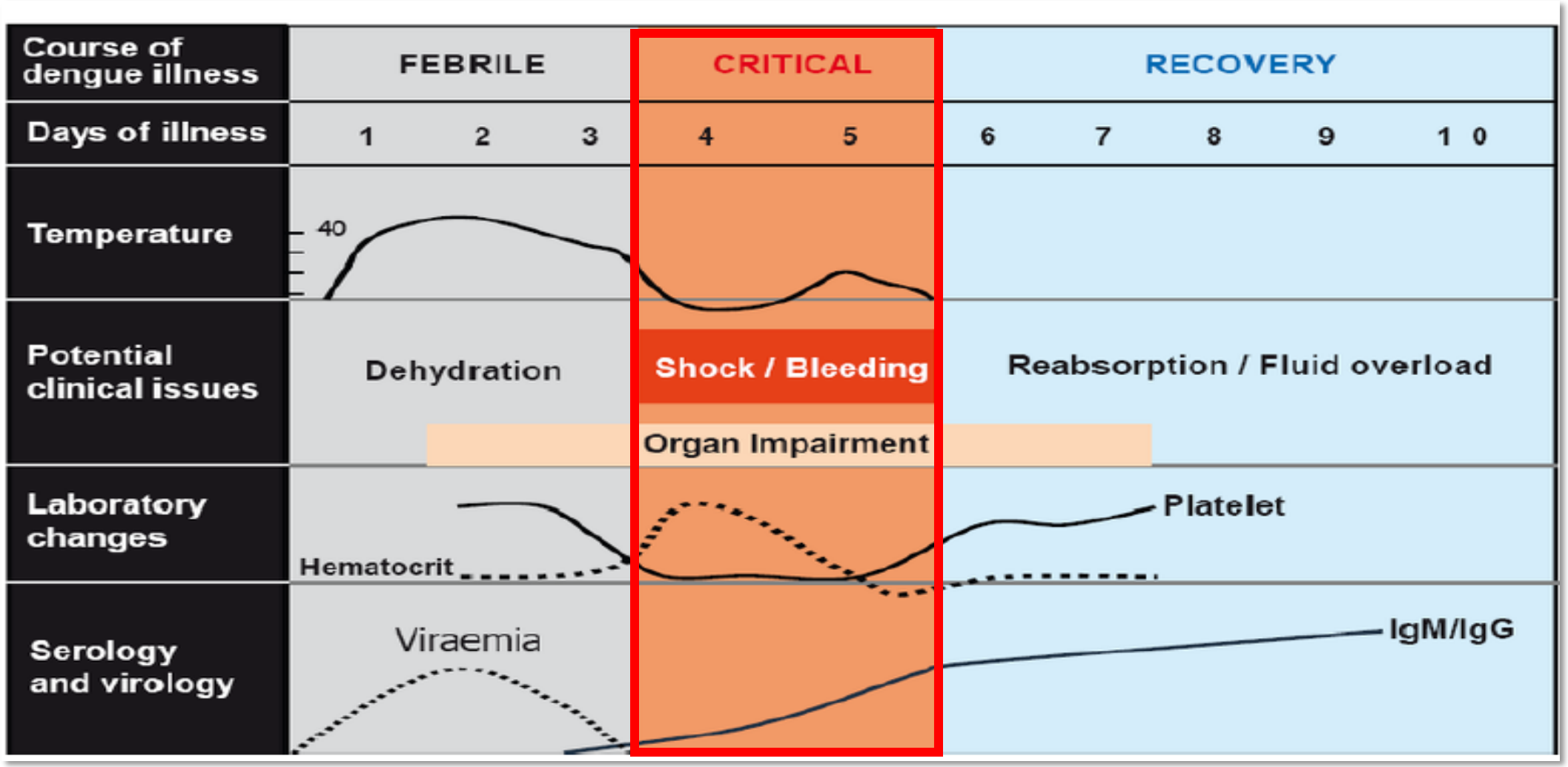


Clinical Manifestations

- Incubation period is 3-14 days(average 4-6 days)
- **Acute febrile illness of 2-7 days duration with two or more of the following manifestations:**
  - Headache
  - Retro-orbital pain
  - Myalgia
  - Arthralgia(break bone fever)
  - Rash
  - Haemorrhagic Manifestations
  - Thrombocytopenia or Leucopenia
  - Warning signs and symptoms

Phases

- Febrile, critical, convalescent / recovery phase
- Most patients do not go into critical phase and have an uncomplicated course



Febrile Phase: 2-7 days

- Early stage characterised by mild undifferentiated “flu-like” fever

  Influenza, Measles, Zika, Chikungunya, Yellow-fever, Malaria

- Fever: Acute onset high grade fever (>101.2F) with chills

1. Headache
2. Retro-orbital pain
3. Myalgia
4. Vomiting

60-70%

5. Rash
6. Skin erythema

50%

7. Photophobia
8. Generalized body ache /Arthralgia
9. Facial flushing

30-40%

- Rash is -maculopapular or rubelliform. appears after the 3 rd to 4 th day of fever and occurs over the face, neck, chest, and abdomen. It usually fades away as the fever progresses
- Occasional biphasic fever aka “saddle back fever”~ 5% cases -febrile illness remits and recurs approximately one to two days later

- Bleeding manifestations may be observed in this phase
- present with skin and mucosal bleeding
- less commonly with hematemesis, melena, heavy menstrual bleeding, epistaxis, or hematuria.
- **Physical examination-**
  - facial puffiness, conjunctival congestion
  - pharyngeal erythema
  - lymphadenopathy, and hepatomegaly
  - petechiae (on the skin and palate)
  - bruising (particularly at venipuncture sites)

- **The tourniquet test** is performed by inflating a blood pressure cuff to a point mid-way between the systolic and diastolic pressures for five minutes.
- A test is considered positive when 10 or more petechiae per 2.5sq.cm area (1 inch) are observed.
- In severe dengue, the test usually gives a definite positive result (i.e.>20 petechiae).

Critical Phase

- From the febrile phase 5-10 % of the patients may progress to the critical phase
- This phase usually begins after 3rd or 4th day of fever and may last about 24 to 48 hours.
- Vasculopathy
- Coagulopathy
- leading to plasma leakage, excessive haemoconcentration, bleeding, eventually leading to shock and organ dysfunction
    - Liver: AST/ALT>1000
    - CNS: seizures,impaired consciousness
    - Heart: myocarditis
    - Kidneys: renal failure
    - Shock

Warning symptoms and signs

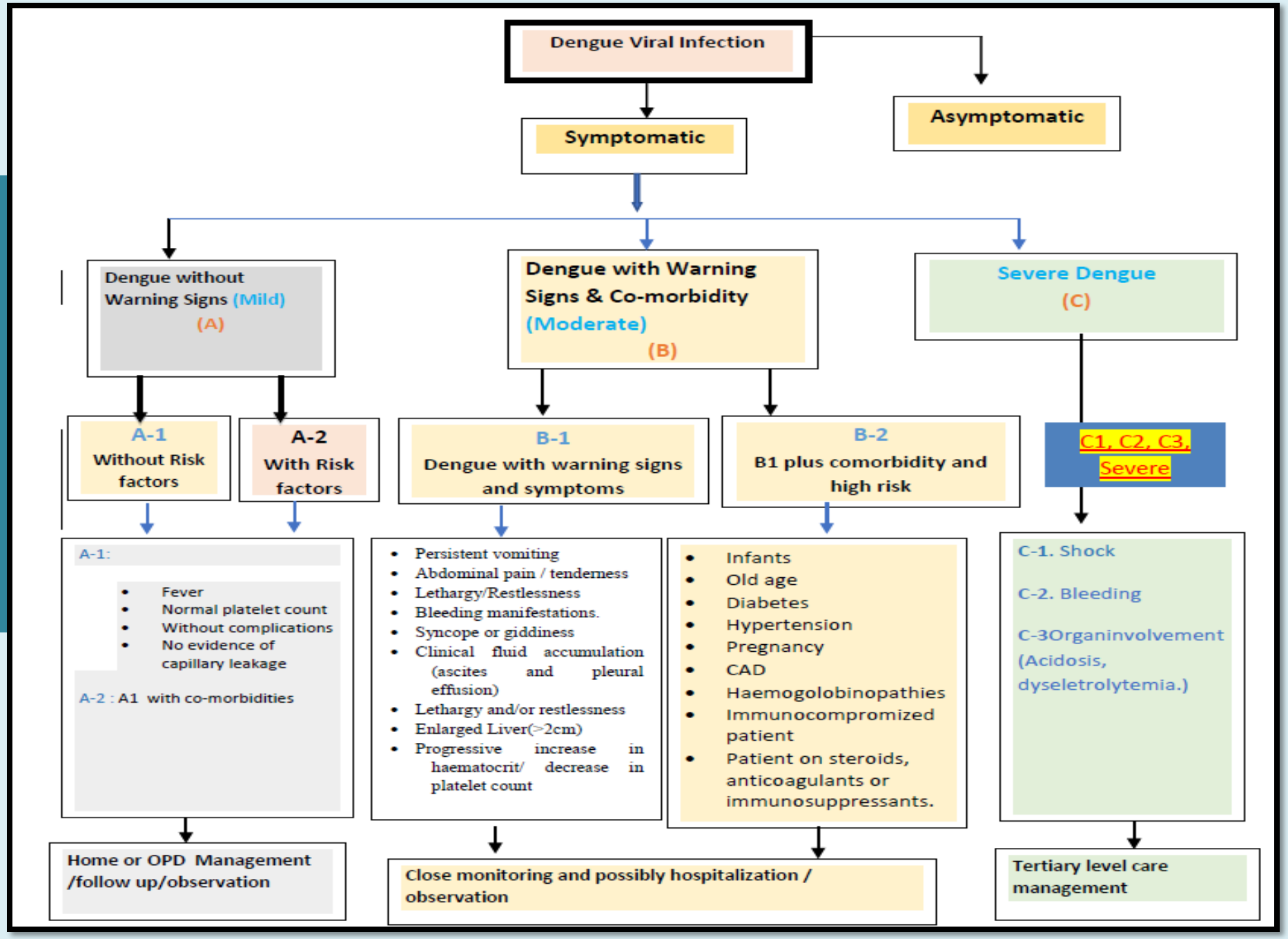
- Persistent vomiting- > 3 episodes in 1 hour or four in 6 hours
- Abdominal pain and tenderness
- Lethargy and/or restlessness
- sudden behavioral changes
- Bleeding manifestations like epistaxis, melena, haematemesis, excessive menstrual bleeding, and haematuria
- Syncope or giddiness
- Enlarged Liver(>2cm)
- Clinical fluid accumulation (ascites and pleural effusion)
- Laboratory: Progressive increase in haematocrit with a rapid decrease in platelet count

Normal Circulation	Compensated shock	Decompensated /Hypotensive shock
Normal sensorium	Normal sensorium with shock	Change of mental state – restless, combative or lethargy
Capillary refill time (<2 sec)	Prolonged capillary refill time (>2 sec)	Mottled skin, prolonged capillary refill time
Extremities are warm	Cold extremities	Cold, clammy extremities
Good volume peripheral pulses	Weak & thready peripheral pulses	Feeble or absent peripheral pulses
Normal heart rate for age	Tachycardia	Tachycardia
Normal blood pressure for age	Normal systolic pressure with raised diastolic pressure, Postural hypotension	Profound shock /unrecordable BP
Normal pulse pressure for age	Narrowing Pulse pressure (<20 mmHg)	Pulse pressure variable
Normal respiratory rate for age	Tachypnoea	Metabolic acidosis/ hyperpnoea/ Kussmaul's breathing
Urine output -normal	Urine output -reduced	Oliguria or anuria

Convalescence/ Recovery Phase

- Reabsorption of extravascular fluid into vascular compartment
- Convalescent rash characterized by confluent erythematous eruption with sparing areas of normal skin and pruritis
- Occurs after end of critical phase and lasts 2-3 days
  - General symptomatic improvement
  - Return of appetite
  - Haemodynamic stability
  - Diuresis
- Laboratory parameters: WBC counts improve, Thrombocytopenia resolves
- **Watch for Hypervolemia [owing to overzealous fluid resuscitation]**

Dengue Case Classification



Severe Dengue

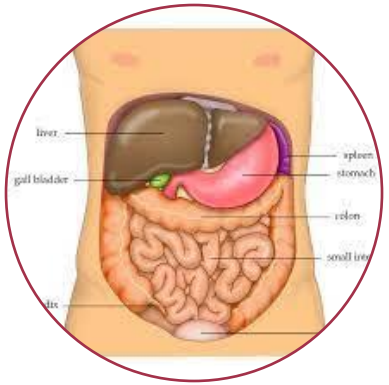
Severe forms of dengue defined by one or more of the following criteria:–

- shock or respiratory distress due to plasma leakage
- bleeding considered clinically important
- severe organ impairment (myocarditis, hepatitis, encephalitis)

Expanded Dengue Syndrome

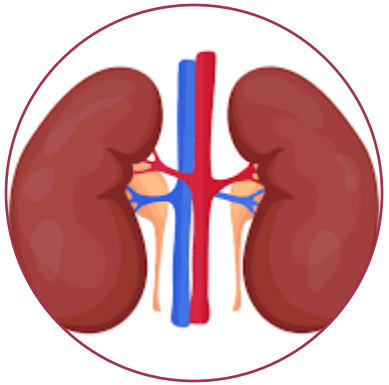
CNS involvement:

- Encephalopathy
- Encephalitis
- Febrile seizures
- Intracranial bleed
- Polyneuropathies /GB syndrome
- Transverse myelitis



GI involvement

- Acute hepatitis, fulminant hepatic failure
- Acalculus Cholecystitis
- Acute pancreatitis

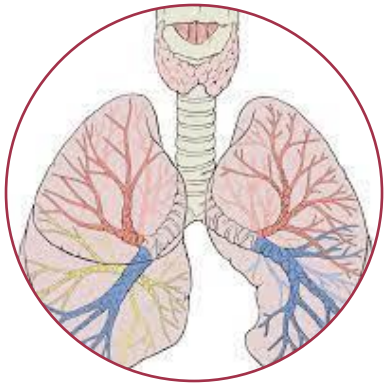


Renal involvement

- Acute renal failure
- Hemolytic uremic syndrome
- Acute tubular necrosis

Cardiac involvement

- Arrhythmia
- Myocarditis
- Pericardial effusion



Respiratory involvement

- Pulmonary edema
- ARDS
- Pulmonary hemorrhage

Eye:

- Conjunctival bleed
- Macular hemorrhage
- Visual impairement
- Optic neuritis

Other Complications

- Secondary Haemophagocytic Lymphohistiocytosis (HLH)
- Idiopathic thrombocytopenic purpura (ITP)
- Spontaneous splenic rupture

Myositis with elevated creatine phosphokinase (CPK)

- Rhabdomyolysis

Post-infectious fatigue syndrome

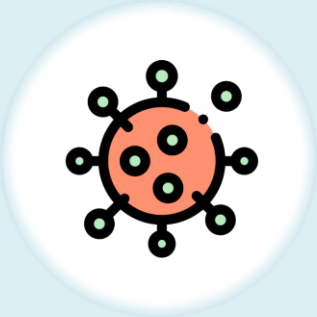
- Depression, Psychosis
- Alopecia

Case Definition

- **Probable Dengue Fever**:
- A case compatible with clinical description of dengue fever during outbreak.

  OR
- Non-ELISA based NS 1 antigen/IgM Positive (A positive test by RDT will be considered as probable due to poor sensitivity and specificity of currently available RDTs)
- **Confirmed Dengue Fever**:
- A case compatible with the clinical description (see above) of Dengue Fever with at least one of the following
  - Isolation of dengue virus (Virus culture +VE) from serum, plasma, leucocytes
  - Demonstration of IgM antibody titre by ELISA positive in single serum sample
  - Demonstration of dengue virus antigen in serum sample by NS1-ELISA
  - IgG seroconversion in paired sera after 2 weeks of four-fold increase of IgG titre
  - Detection of viral nucleic acid by polymerase chain reaction (PCR)

Differential Diagnosis



COVID-19

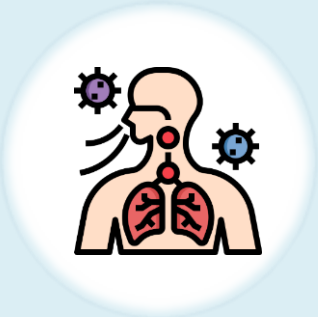
Chikungunya

Malaria

Scrub typhus

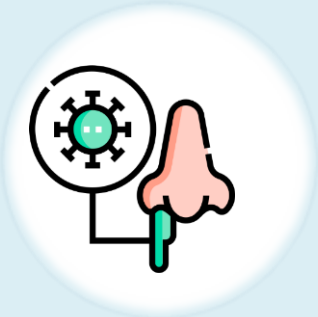
Enteric fever

Pharyngitis



Influenza

Leptospirosis



Meningococcal infection

MANAGEMENT OF DENGUE

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MD (Medicine) PDCC (CCM)

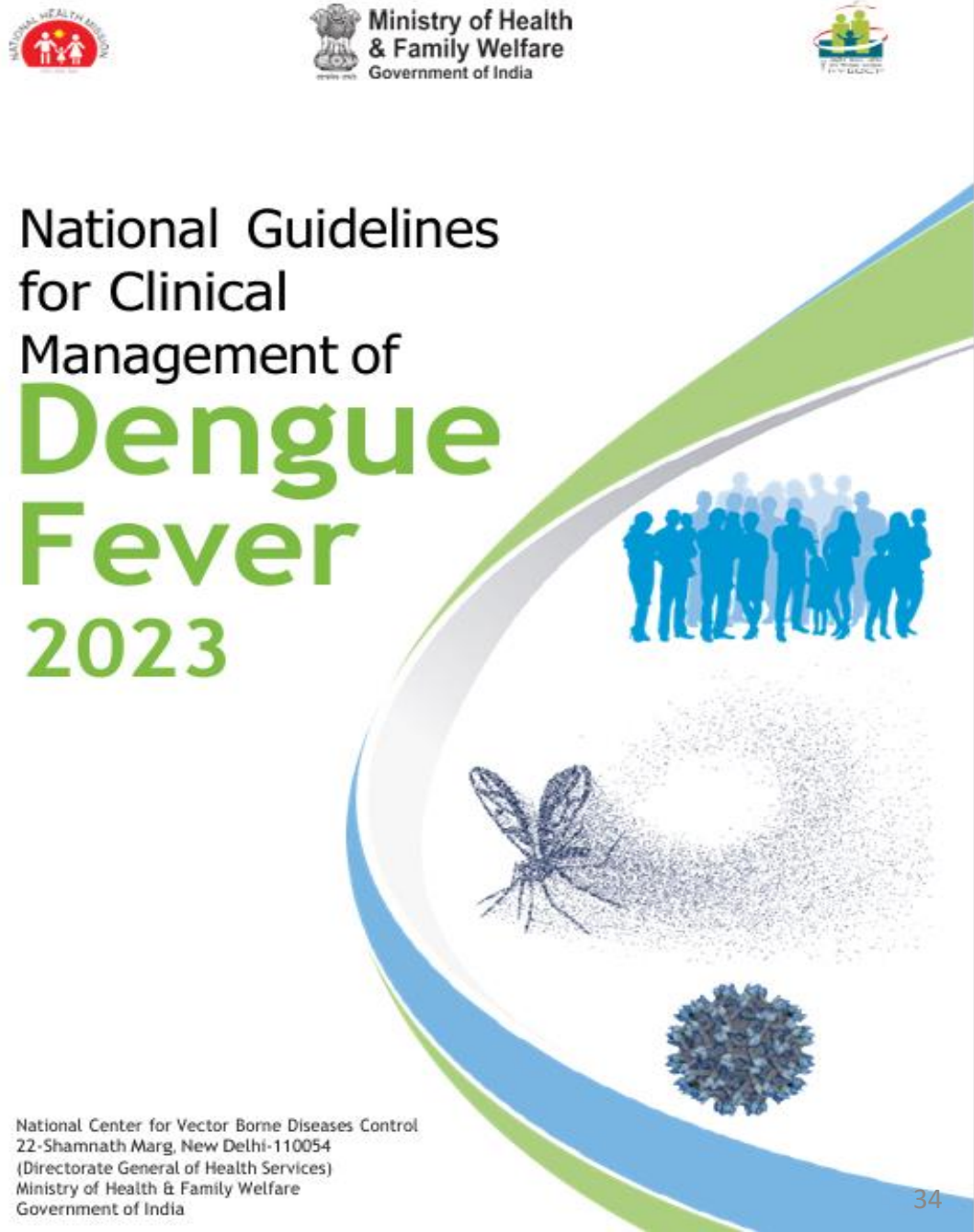
Assistant Professor

Department of Medicine

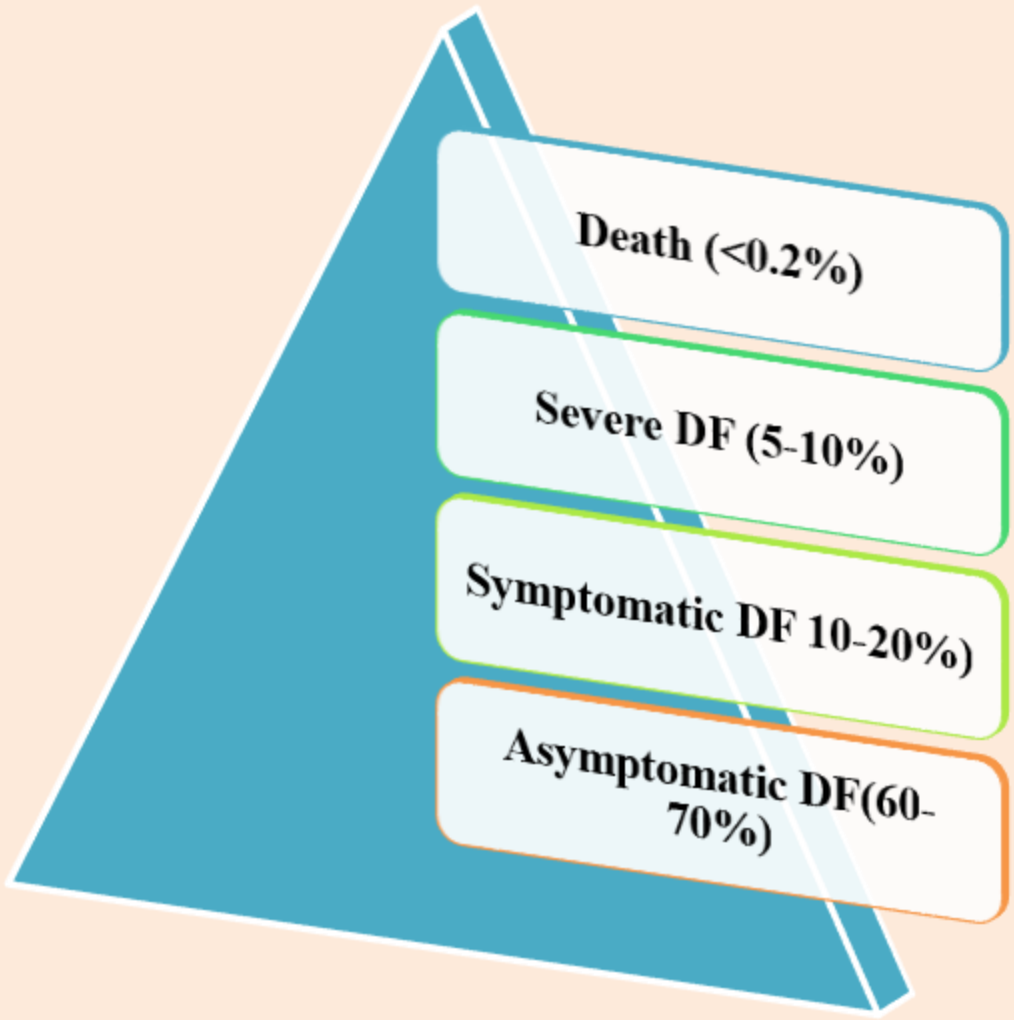
KGMU

Outline

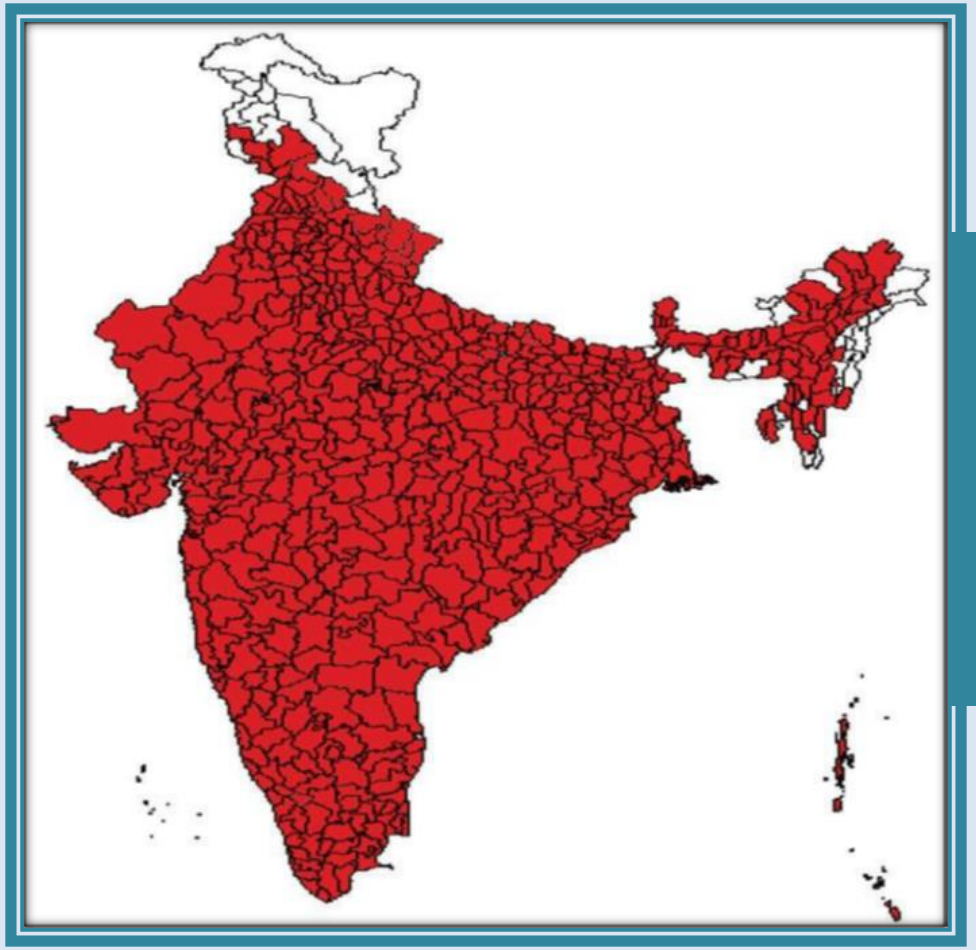
- Introduction
- Case definition
- Investigation
- Diagnosis
- Treatment
- Fluid management
- Dengue with coinfections
- Dengue with comorbidities
- Take home message



Clinical Presentation



Dengue Endemicity Map



India, till date, all States/UTs, (except Ladakh) have reported dengue cases during the last two decades.

Management of Dengue

A) Case Management

1. Diagnosis of Dengue

- Clinical diagnosis
- Laboratory diagnosis

2. Treatment

- Symptomatic management
- Specific management
- Critical care management

B) Outbreak Management

Case Definition

Probable dengue fever:

- A case compatible with clinical description of dengue fever during outbreak.

Clinical criteria of dengue:

Acute febrile illness of 2-7 days duration with two or more of the following : headache, retro-orbital pain, myalgia, arthralgia, rash, hemorrhagic manifestation

Or

- Non-ELISA based (RDT) NS 1 antigen/IgM Positive.

Confirmed Dengue Fever:

- A case compatible with the clinical description of Dengue Fever with at least one of the following
  - Virus culture +VE
  - IgM antibody by ELISA positive in single serum sample
  - Serum NS1 antigen positive by ELISA
  - IgG seroconversion in paired sera after 2 weeks of four-fold increase of IgG titre
  - Polymerase chain reaction (PCR)

Laboratory Tests

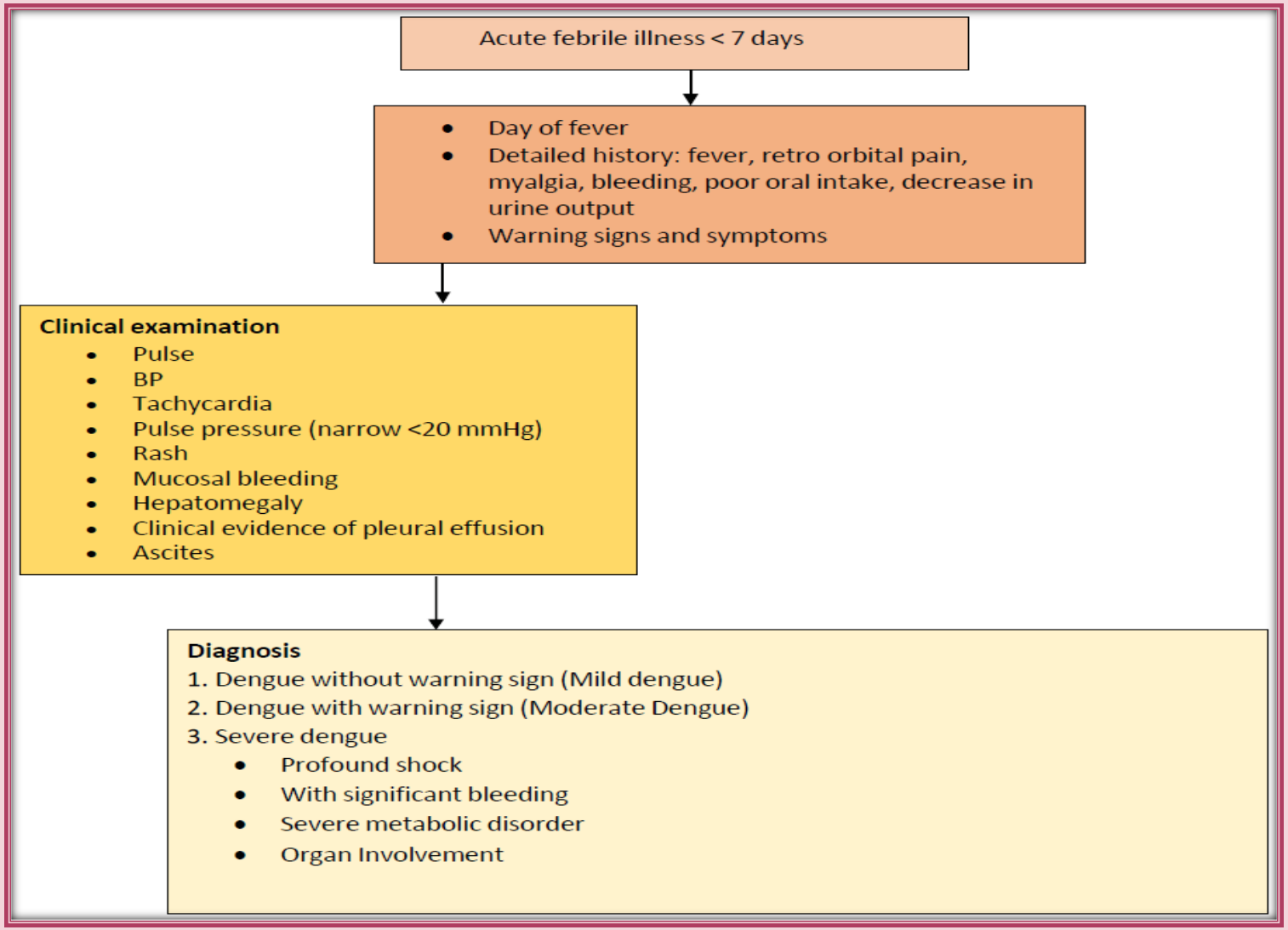
Clinical laboratory tests

- CBC– Manual platelet count , hematocrit
- Liver function tests
- Kidney function test
- Electrolytes / protein / albumin
- Urine- microscopic hematuria
- USG whole Abdomen
- CT Scan

Dengue-specific tests

- Virus isolation
- Serology
  - Antigen : NS1
  - Antibody: IgM, IgG

Approach to Diagnosis of Dengue



Days of illness

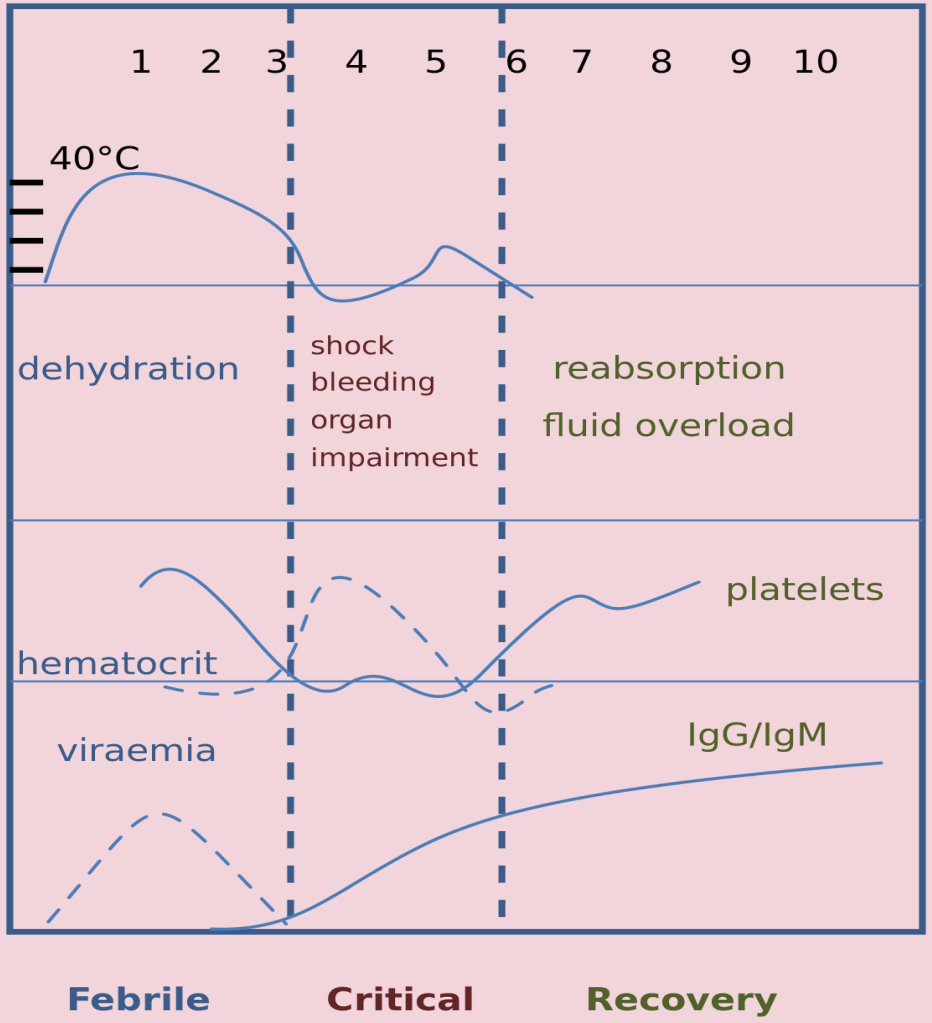
Temperature

Potential clinical issues

Laboratory changes

Serology and virology

Phases of illness



Treatment of Dengue Fever

Fluids

Antipyretics (Avoid aspirin and NSAIDS)

Rest

Monitoring

Triage of Suspected Dengue Patients

Performed by a person clinically trained in diagnosis and identification of warning signs

- Following parameters should be assessed :
  - Duration of fever
  - Presence of warning signs
  - High-risk groups (co-morbidities and co-infection)
  - Tourniquet test
  - Vital signs including temperature, blood pressure, pulse rate, respiratory rate
  - Peripheral perfusion by
    - ✓ Palpation of pulse,
    - ✓ Colour of extremities,
    - ✓ Capillary refill time
- Moderate to severe dengue patients should be referred directly to an emergency ward.

Approach to Clinical Management

Depending on the clinical manifestations, presence of warning signs and other high-risk factors, patients may be classified as following:

Mild dengue (A)

May be managed on OPD basis

Moderate dengue (B)

Observation or admission for in-hospital management

Severe dengue (C)

Require emergency treatment and urgent referral

Management of Mild Dengue Patient (Group A)

1. OPD
2. Educate about warning signs
3. Oral fluids (ORS/Coconut juice),
4. Adequate bed rest.
5. Temperature should be kept below 100°F., PCM (10 mg/kg/dose)
6. Avoid using aspirin or NSAIDs.
7. Tepid sponging of forehead, armpits, and extremities
8. Investigation (CBC, platelets , HCT)
9. Advised for follow up

WARNING SIGNS

1. Severe abdominal pain and persistent vomiting
2. Red spots patches on skin
3. Bleeding from nose and gums
4. Vomiting blood
5. Black tarry stools
6. Drowsiness or irritability
7. Pale, cold or clammy skin
8. Difficulty in Breathing

Management of Moderate and Severe Dengue

Critical period of dengue fever

- Refers to the period of plasma leakage
- Starts around the time from febrile to afebrile phase.
- Rapid fall of thrombocyte count may indicate progression of severity of disease.
- A rising haematocrit of 10% above baseline is an early objective indicator of plasma leakage.
- Intravenous fluid therapy should be started

Parameters should be monitored

- ✓ General condition, appetite, vomiting, bleeding and other warning signs and symptoms
- ✓ Peripheral perfusion assessment
- ✓ Vital signs
- ✓ Serial haematocrit should be performed at least every four to six hours
- ✓ Urine output should be recorded

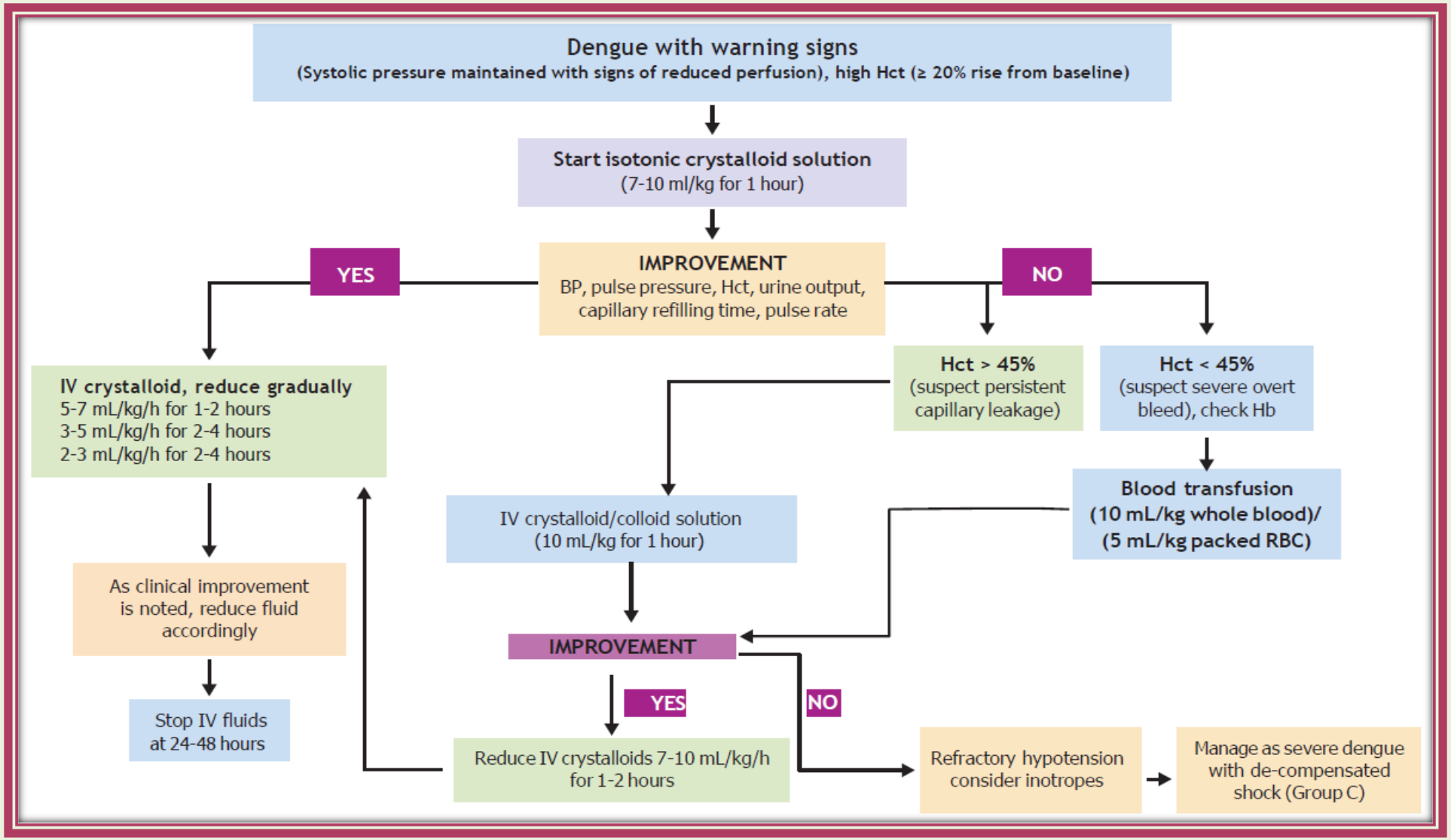
Management of Moderate and Severe Dengue

Additional laboratory investigations

Adult patients with co-morbidities/shock and/or complications

- Random blood glucose
- Blood gas analysis including lactate
- Serum electrolytes (sodium, potassium and calcium)
- Renal function tests (urea and creatinine)
- Liver function tests (AST, ALT and bilirubin)
- Coagulation profile
- Chest radiograph
- Blood Group
- Cardiac enzymes (Pro-BNP and Troponin level) / ECG
- Serum amylase and ultrasound abdomen.

Management for Moderate Dengue Patients with Warning Signs



Management of Severe Dengue (Group C)

Urgent admission and management.

Severe dengue has following characteristics:

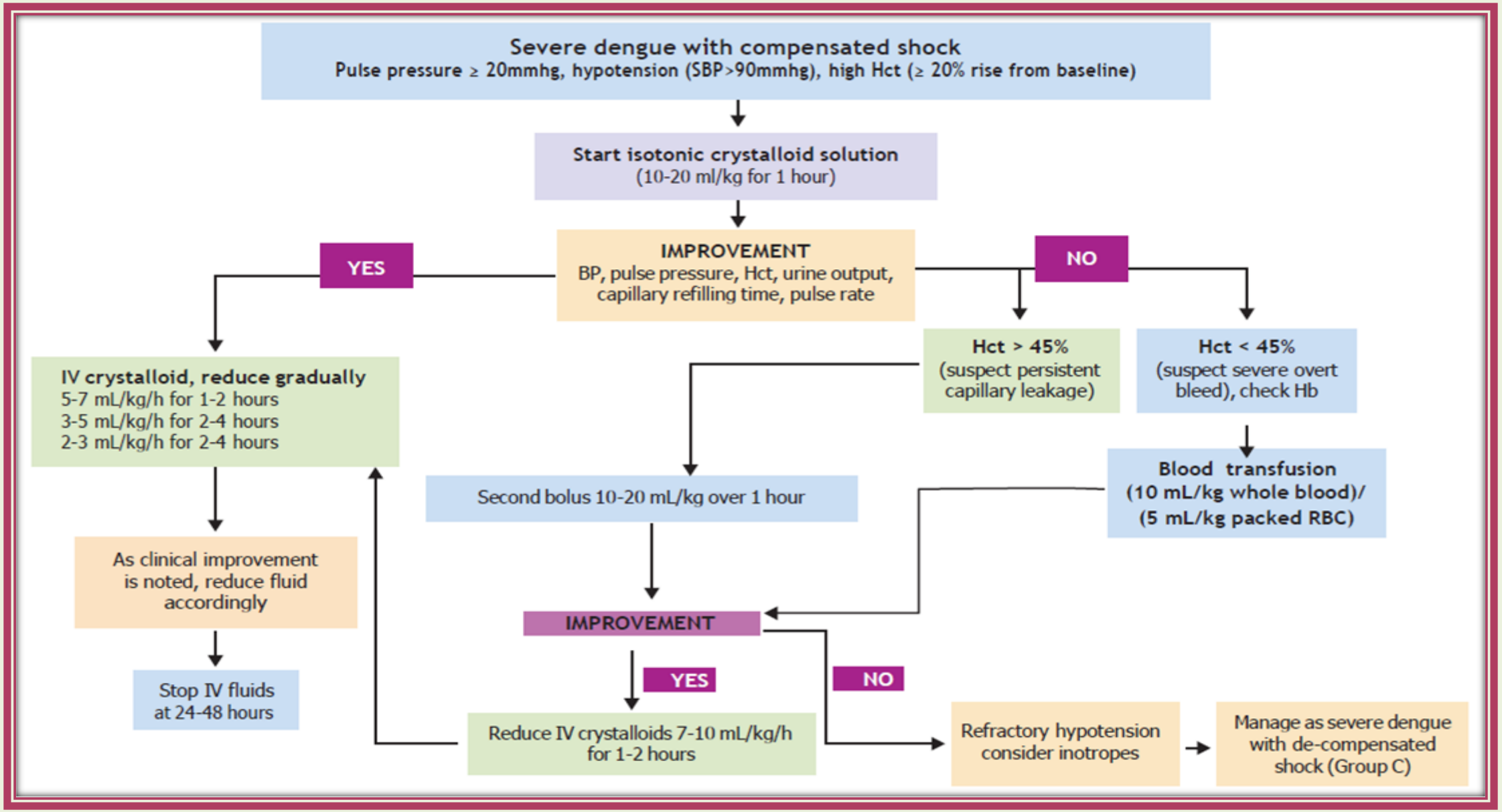
- Severe plasma leakage leads dengue shock and/or fluid accumulation with respiratory distress
- Severe haemorrhages
- Severe organ impairment hepatic damage, renal impairment, cardiomyopathy, encephalopathy or encephalitis)
- Severe metabolic abnormalities

Principles of Management of Severe Dengue:

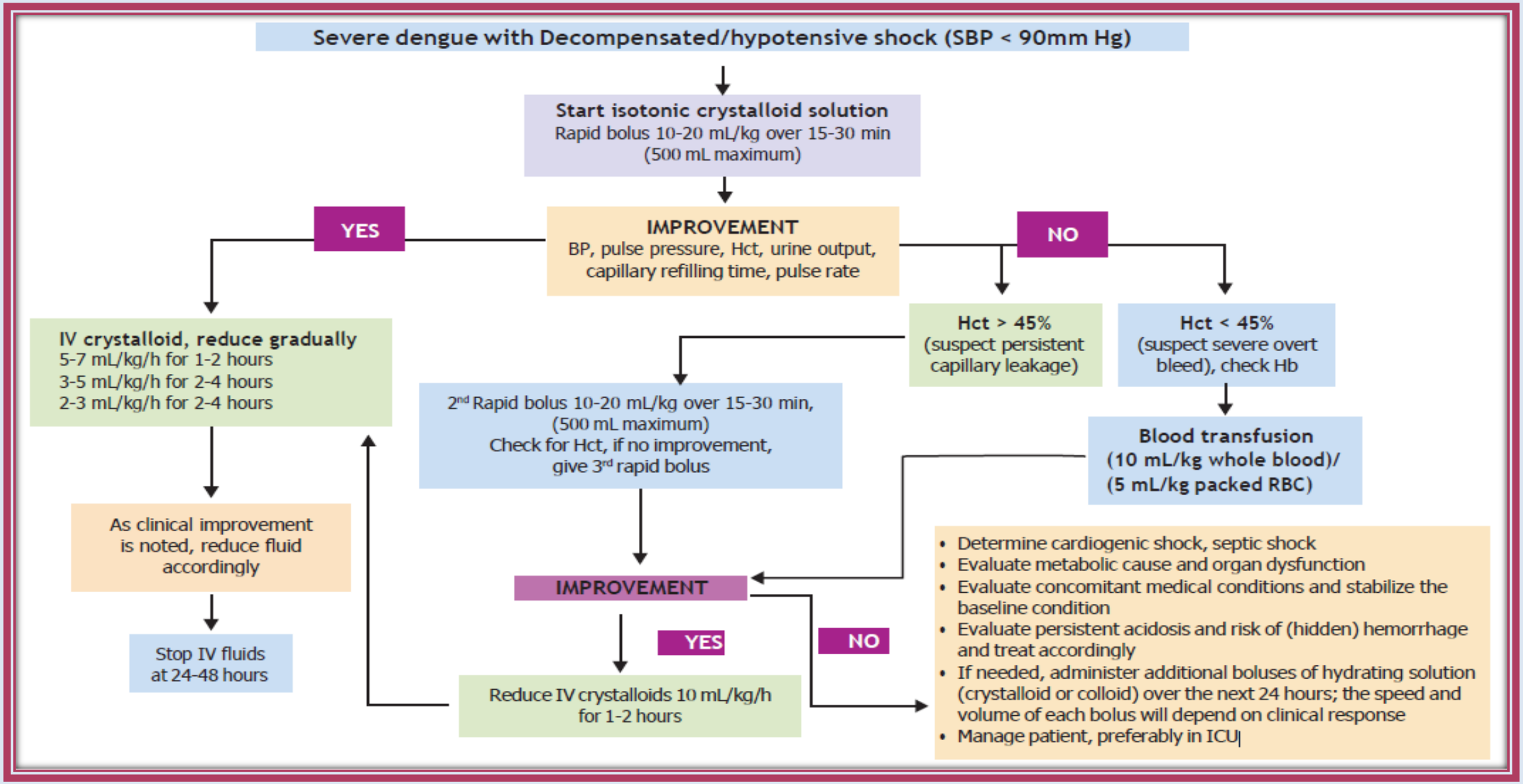
- Admission to a hospital which has blood transfusion facilities.
- Judicious IV fluid resuscitation , Prefer a crystalloid solution (0.9% NS or RL)
- Hematocrit level before starting fluid therapy
- Monitor vital signs every 5-30 min.
- Use IBW for overweight and obese patients while calculating fluid rates.

  (F: 45.5 kg + 0.91(height – 152.4 cm) , (M: 50.0 kg + 0.91(height – 152.4 cm)
- Blood group of the patient
- Blood transfusion for established or suspected severe bleeding (fall in HCT) with unexplained hypotension.

Management of dengue with compensated shock in adults



Management of severe dengue with decompensated shock



When to stop intravenous fluid therapy

Intravenous fluids reduced / discontinued when any of the following signs are present.

- Normal blood pressure, pulse and peripheral perfusion;
- Decrease in hematocrit
- Afebrile (without the use of antipyretics) for more than 24–48 hours;
- Resolving bowel/abdominal symptoms;
- Improving urine output.

Continuing intravenous fluid therapy beyond the 48 hours of the critical phase will put the patient at risk of pulmonary oedema and other complications such as thrombophlebitis

Management of Severe Haemorrhage

- Source of bleeding be identified and efforts to stop the bleeding
  - Severe epistaxis, may be controlled by nasal packing.
  - Endoscopy for internal gastrointestinal bleeding.
- Blood loss should be replaced
- 10 ml/kg of fresh whole blood or 5 ml/kg of freshly packed red cells
- Gastrointestinal bleeding: H-2 antagonists and PPI .
- Recombinant Factor 7 might be helpful

Indication of Platelet Transfusion

- Transfuse platelet only if bleeding is present
- Prophylactic platelet transfusion may be considered for counts < 10,000/cumm without bleed

Platelets

Random donor platelets (RDP):

- Prepared from whole blood
- Volume of 40-50 ml,
- Platelet content of 5.5x1010
- Shelf life of 5 days.
- Raise platelet count by 5-7 thousand in an adult and 20 thousand in pediatric patients.

Single donor aphaeresis (SDP):

- Collected by a variety of aphaeresis systems, using different protocols.
- Volume for SDP is 200-300 ml,
- Yield or platelet content of 3x1011 per bag
- Equal to 5-6 RDP.
- Regarded as the jumbo pack.
- Increase a patient's platelets count by 30-50000/ul.

Criteria For Admission of Dengue Patient to a Hospital

A. Presence of warning signs and symptoms:

- Persistent vomiting
- Abdominal pain and tenderness
- Clinical fluid accumulation (ascites and pleural effusion)
- Lethargy and/or restlessness
- Mucosal bleed (epistaxis, melena, haematemesis, menorrhagia, haematuria)
- Enlarged Liver >2cm)
- Laboratory: Progressive increase in haematocrit with rapid decrease in platelet count

B. Severe Dengue

C. Intolerance to oral administration of fluids

D. Dyspnoea

E. Hypotension and narrow pulse pressure

F. Acute Renal failure

G. Coagulopathy

H. Patient living alone or far from a health facility and without any reliable means of transport

Discharge of Dengue Patient From Hospital

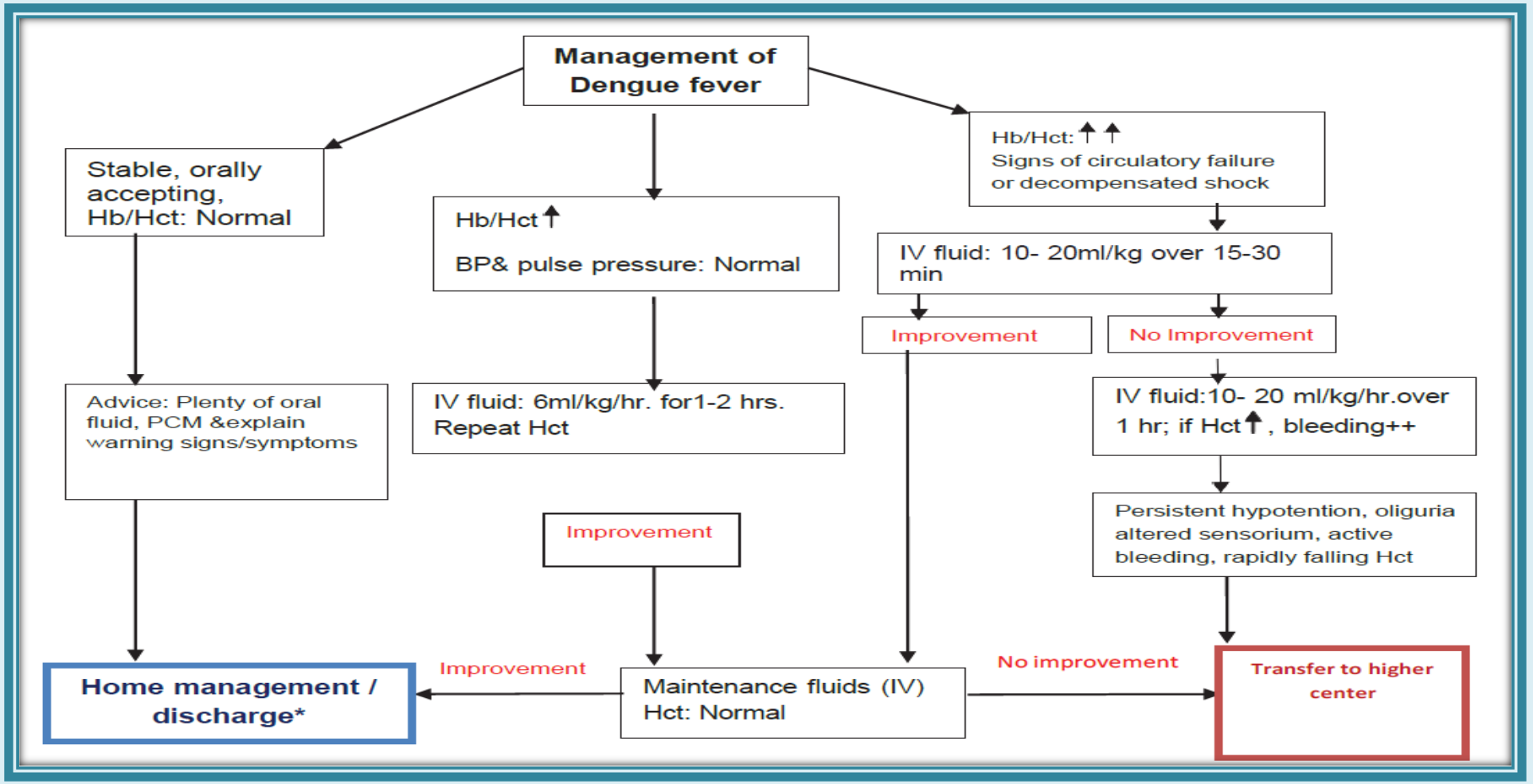
Signs of recovery of dengue patient

- Stable pulse, blood pressure and respiratory rate.
- Normal temperature.
- No evidence of external or internal bleeding.
- Return of appetite.
- No vomiting, no abdominal pain.
- Good urinary output.
- Stable hematocrit at baseline level.
- Convalescent confluent petechiae rash or itching, especially on the extremities.

Criteria for discharging patients

- Absence of fever for at least 24 hours without the use of anti-pyretic agent.
- Signs of recovery
- A minimum of 2–3 days have elapsed after recovery from shock.
- No respiratory distress from pleural effusion/ascites.
- Platelet count of more than 50,000/mm3.

Management and referral of Dengue cases at Primary Health Centre (PHC) level



Patient should be advised to come for follow-up after 24h for evaluation.
He should report to the nearest hospital immediately in case of the Warning signs

Treatment for Dengue?

- Papaya Leaf Juice
- Hot Garlic Soup
- Herbal Tea
- Red Rice
- Clove

Outbreak Management

- Space mobilization for dengue outbreak in hospital
- Staff mobilization
- Augmentation of lab. Services
- Diagnosis not required in all cases during epidemic
- Augmentation of blood bank services
- Increase of blood and blood component

Can we eradicate Dengue Fever? Mosquito

16th May National Dengue Day

- Lemon Balm (*Melissa officinalis*)
- Marigolds (*Tagetes* spp.)
- Catnip (*Nepeta cataria*)
- Basil (*Ocimum basilicum*)
- Lavender (*Lavandula angustifolia*)
- Citronella grass (*Cymbopogon nardus*)

Management of co-morbidities & co-infection with Dengue

Management of dengue in high-risk groups

Dengue with co-morbidities

- Pregnancy,
- Pediatric age group,
- Hypertension,
- Diabetes,
- Hepatitis,
- Heart diseases
- Renal diseases

Dengue with co-infections

- Tuberculosis
- HIV
- Malaria
- Chikungunya
- Enteric fever
- Scrub typhus

Dengue & Pregnancy: Challenges

Pregnancy feature	Dengue warning sign/ Severe disease feature	Challenge
Vomiting of pregnancy	Vomiting as a warning sign	Warning sign may be mistaken as hyperemesis
Hemodilution	Hemoconcentration	Dilutional anemia may mask hemoconcentration
Cardiovascular changes	Tachycardia and low BP in shock	Delay/ failure to recognize dengue shock

National Guidelines for clinical management of Dengue fever, NCVBDC 2021

Impact of Dengue on Pregnancy

Adverse pregnancy outcome

- Prone to severe manifestations and complications of dengue
- Post partum haemorrhage (10-19%)
- Increased risk of miscarriage

Adverse neonatal outcome

- Risk of vertical transmission
- Neonatal thrombocytopenia & increased risk of hemorrhage
- Preterm birth, low birth weight

1. Pavanaganga A, et al. J South Asian Fed Obstet Gynaecol. 2017
2. National Guidelines for clinical management of Dengue fever, NCVBDC 2021

Dengue & Pregnancy: Management

- Close monitoring, preferably Hospitalization
- Fluid management requires close monitoring of fluid status clinically and hematocrit
- Prophylactic platelet transfusion is not recommended
- Strict vital monitoring, frequent platelet count and coagulation profile testing
- In case of imminent delivery, patients should be transferred to tertiary care hospital (risk of obstetric hemorrhage)

Optimization of platelets	
Vaginal Delivery	> 50,000/ CC
LSCS	> 75,000/CC

Dengue Viral Hepatitis

- Impairment of liver function due to dengue viral infection.
- The AST/ALT level may be very high along with prolongation of prothrombin time.
- Hepatic complication common with preexisting conditions like chronic viral hepatitis, liver cirrhosis and hepatomegaly.
- Hepatic encephalopathy due to acute liver failure.
- Risk of severe GI bleeding leading to shock.
- Manage carefully with hepatic failure regimen
- Appropriate fluid and blood transfusion.
- PT is prolonged intravenous → vitamin K.

Cardiovascular Involvement

Dengue associated myocarditis

- Rarely cause acute myocarditis
- contribute for the development of shock.
- Cardiac complications may be seen in presence of CAD, hypertension, diabetic and valvular heart disease.
- MX of shock with IV fluid is difficult due to myocardial dysfunction.
- Patient may develop pulmonary oedema due to improper fluid management.

Dengue in coronary artery diseases and heart failure

- MX of dengue in CAD is challenging
- Antiplatelet agents which may lead to severe bleeding
- Fluid management is challenging because of risk of congestive heart failure
- Anti-platelets agent discontinued if platelet count less than one lakh or having minor or major bleeding manifestation
- Clinical characteristics such as periorbital oedema, respiratory discomfort, lung crepitation, symptoms of pleural effusion or ascites, and elevated jugular venous pressure
- Loop diuretics in patients with clinical signs of fluid overload.

Dengue and the Kidneys

- Acute Tubular Necrosis (ATN) as a result of shock
- Renal function may be reversible, if shock is corrected within a short span of time.
- Persistent shock leads to renal complications.
- Urine output monitoring is essential to assess renal involvement.
- Microscopic/ macroscopic hematuria
- Blood urea, creatinine, serum electrolyte, eGFR, and bicarbonate.

Treatment

- **Frequent** volume status assessment and **judicious** fluid administration
- Avoid fluid overload and pulmonary oedema
- **Renal replacement therapy (RRT)** may be required in:
  - Persistent volume overload
  - Refractory/severe hyperkalemia
  - Refractory acidosis
  - Uremia

CNS Involvement

Altered sensorium in dengue patient:

- shock
- electrolyte imbalance (dilutional hyponatremia or other electrolyte imbalance),
- Hypoglycemia,
- Hepatic encephalopathy
- Acute encephalopathy or encephalitis
- Difficult to clinically exclude cerebral malaria and enteric encephalopathy
- Dengue serology (IgM) in CSF to confirm dengue encephalopathy or encephalitis.
- Cerebrovascular évent

Dengue and Diabetes

- Diabetic patients may present with severe complication in dengue when target organs are involved (diabetic retinopathy, neuropathy, nephropathy, vasculopathy, cardiomyopathy and hypertension).
- Hyperglycemia may require insulin therapy for better management.
- Before starting the treatment, a reference hematocrit level must be determined
- Fluid replacement with caution and under the supervision

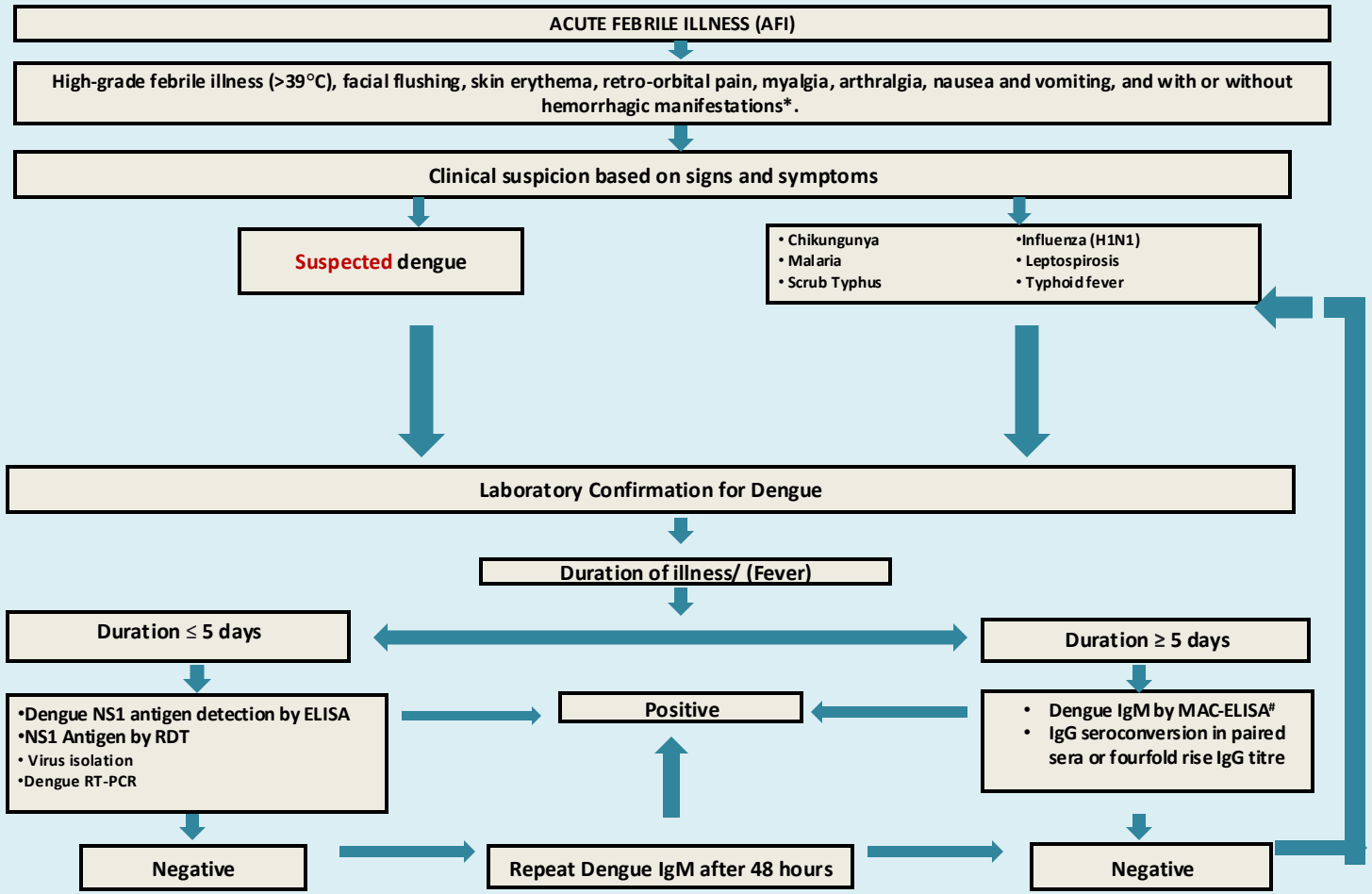
Dengue with Co-infections

Dengue & other acute febrile illness

- **Differentiating** other co-infections **on clinical grounds alone is difficult**
- Hence having a **high index of clinical suspicion** for co-infection is essential
- Mixed infections are not uncommon
- The clinical presentations may be similar in few cases of coinfection, but majority of them present with **more severe manifestations and complications**

1. Begam NN, Kumar A, et al. Drug Discov Ther. 2021;15(3):130-138.
2. Mandage R, Soneja M, Acharya P. Emerg Infect Dis. 2020 Aug;26(8):1645-1653.

Diagnostic approach to suspected dengue cases



- * Haemorrhagic manifestations include petechiae, purpura, gum or nasal bleeding, gastrointestinal bleeding, haematuria, menorrhagia and positive tourniquet test.
- ** Depending on the availability of the test, RT-PCR ;Real –time reverse transcriptase-polymerase chain reaction; CBNAAT; Cartridge-based nucleic acid amplification test ; RAT ; Rapid antigen test)
- # IgM capture enzyme-linked immunosorbent assay (MAC-ELISA)

Dengue & COVID-19

- About 70 – 80% of COVID-19 and dengue cases are asymptomatic
- A large portion of the co-infected population may be asymptomatic for both the diseases
- Challenges to distinguish COVID-19 from dengue at the time of initial presentation
- Management dilemma if both diseases are severe

The National Guidelines for Dengue case management during COVID-19 pandemic, NCVBDC 2020

Case classification of co-infection

1. Asymptomatic co-infection
2. Symptomatic co-infection
    i. Predominant Corona Viral Diseases (P-CVD)
    ii. Predominant Dengue Viral Disease (P-DVD)
    iii. Co-dominant co-infection (CD-CI)

The National Guidelines for Dengue case management during COVID-19 pandemic, NCVBDC 2020

Dengue and COVID-19 co-infection- challenges in management

Management	Dengue	COVID
Fluids	Drug of choice	Can worsen oxygenation in ARDS
Anticoagulation	Increases risk of bleeding	Recommended treatment to prevent & treat thrombosis
Corticosteroids	No definite role, contraindicated in viremic phase, can increase risk of GI bleed	Drug of choice in moderate & severe cases

The National Guidelines for Dengue case management during COVID-19 pandemic, NCVBDC 2020

Take Home Message

- The guideline are useful for proper diagnosis, management and referral of cases from primary health care centre to higher centre .
- No role of prophylactic platelet transfusion above 10000.
- Fluid management is very crucial.
- High risk groups need to be monitored closely
- Co-infections not uncommon in Dengue
- High index of suspicion (clue: severe symptoms, pattern of organ involvement)

Key Points

Manage critical phase with appropriate volume

– Don’t under transfuse

– Don’t over transfuse

Meticulous monitoring during critical phase

Prognosis

- Dengue fever is mostly a self-limiting disease.
- Mortality may increase in severe dengue cases.
- Early recognition of shock is of paramount importance.
- Recovery is fast and majority recover completely in 24-48 hours.
- Prognosis is grave in patients with prolonged shock
- Other adverse correlates of outcome include:
  - ✓Encephalitis,
  - ✓DIC,
  - ✓Myocarditis,
  - ✓Fulminant hepatitis
  - ✓ ARDS.

Compatibility testing not required for platelet concentrates

- Although platelet concentrates from donors of the identical ABO group and the patient can have the components of choice and should be used as far as is possible.
- However, administration of non identical ABO platelet transfusions are also an acceptable transfusion practice in particular, when platelet concentrates are in short supply.

b. Similarly, RhD-negative platelet concentrates should be given, where possible, to RhD-negative patients, particularly to women who have not reached the menopause.

If RhD-positive platelets are transfused to RhD-negative woman of childbearing potential, it is recommended that anti-D should be given.

A dose of 300 IU of anti-D should be sufficient to cover six SDP or 30 RDP RhD – positive platelets within a 6-week period.

c. Standard Dose for adults is 5-6 units of Random Donor Platelets or One unit of Aphaeresis platelets. For Neonates/ Infants the dose of the platelets should be 10- 15ml/kg of body weight.

Thank You