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Dengue: a guide to diagnosis and management

Resume module

This module provides a thorough overview of the topic with a test of your knowledge at the end.

Learning outcomes

At the end of this learning module, you should have an improved knowledge and understanding of:

The epidemiology and pathogenesis of dengue

The clinical manifestations of dengue

How to manage uncomplicated and complicated dengue fever.

Contributors:
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Peer reviewed by:
OC Abraham

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Accreditor	credit	Accreditation statement
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Resume module

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BMJ Learning

Dengue: a guide to diagnosis and management

Welcome

Learning outcomes

At the end of this learning module you should have an improved knowledge and understanding of:

- The epidemiology and pathogenesis of dengue
- The clinical manifestations of dengue
- How to manage uncomplicated and complicated dengue fever.

Contributors: Surendra K Sharma, Abhenil Mittal, Siddharth Jain

Peer review: OC Abraham

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BMJ Learning

Dengue: a guide to diagnosis and management

About this module

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Why we wrote this module

Dengue fever is currently the most common arboviral illness in the world. Despite being a self limiting viral illness, it remains an important cause of morbidity and mortality. Important knowledge gaps in recognising and managing the disease exist, especially at the primary healthcare level.

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Dengue: a guide to diagnosis and management

Introduction: what is dengue?

Dengue is a self limiting vector borne febrile illness caused by the dengue virus. Recent decades have witnessed an emergence and re-emergence of dengue epidemics in the form of larger, more severe, and more frequent outbreaks, even in previously unaffected areas. Dengue, which was considered primarily a disease of the tropics and the subtropics (especially Asia and Latin America) is now endemic in more than 100 countries. WHO estimates [1] that about 50% of the world's population is at risk of dengue. Dengue fever was ranked by WHO as the fastest growing vector borne viral illness in 2013.[2]

Clinical tips

- Fluids form the mainstay of treatment of dengue fever: Oral fluids should be encouraged whenever possible. Intravenous fluids should be used judiciously and for the shortest possible period of time
- The differential diagnoses of acute febrile illness with thrombocytopaenia are wide; other diseases with similar manifestations should be kept in mind while treating patients
- Patients should be referred to a specialist centre without delay if they develop complications like major bleeding or organ impairment
- In a patient with dengue fever who has a sudden drop in haematocrit, the possibility of internal bleeding should be considered and packed red blood cells should be transfused

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Dengue: a guide to diagnosis and management

Epidemiology

Global scenario

About 390 million dengue infections occur annually (95% confidence intervals 284 to 528 million). Of these, 96 million patients develop clinical manifestations.[3] This is much higher as compared to the WHO estimate of 50 to 100 million infections per year.[1] According to a recent study, 3.9 billion people (about 50% of world's population) in 128 countries are at risk of being infected with dengue virus.[4] Around 500 000 people with dengue require hospitalisation each year, a large majority of which are children.[1] About 2.5% of the total number affected die.[1 (https://app.elucidat.com/projects/build_view_wrapper/57c6abfeefa15/57c6aee017605#)]

The disease burden of dengue is expected to increase in the near future due to factors like climate change, globalisation, travel, international trade, socioeconomics, settlement, and viral evolution. Prior to 1970, only nine countries had experienced major outbreaks, while today dengue has become endemic in over 100 countries.

The year 2015 was important in this as there were many large outbreaks across various countries, from re-emergence in areas like Japan and the Pacific Island countries to emergence in European nations.[1 (https://app.elucidat.com/projects/build_view_wrapper/57c6abfeefa15/57c6aee017605#)] The alarming feature of these outbreaks was a trend toward an increasing number of infections (as well as more severe infections). This is likely due to hyperendemicity of dengue virus serotypes in many countries.

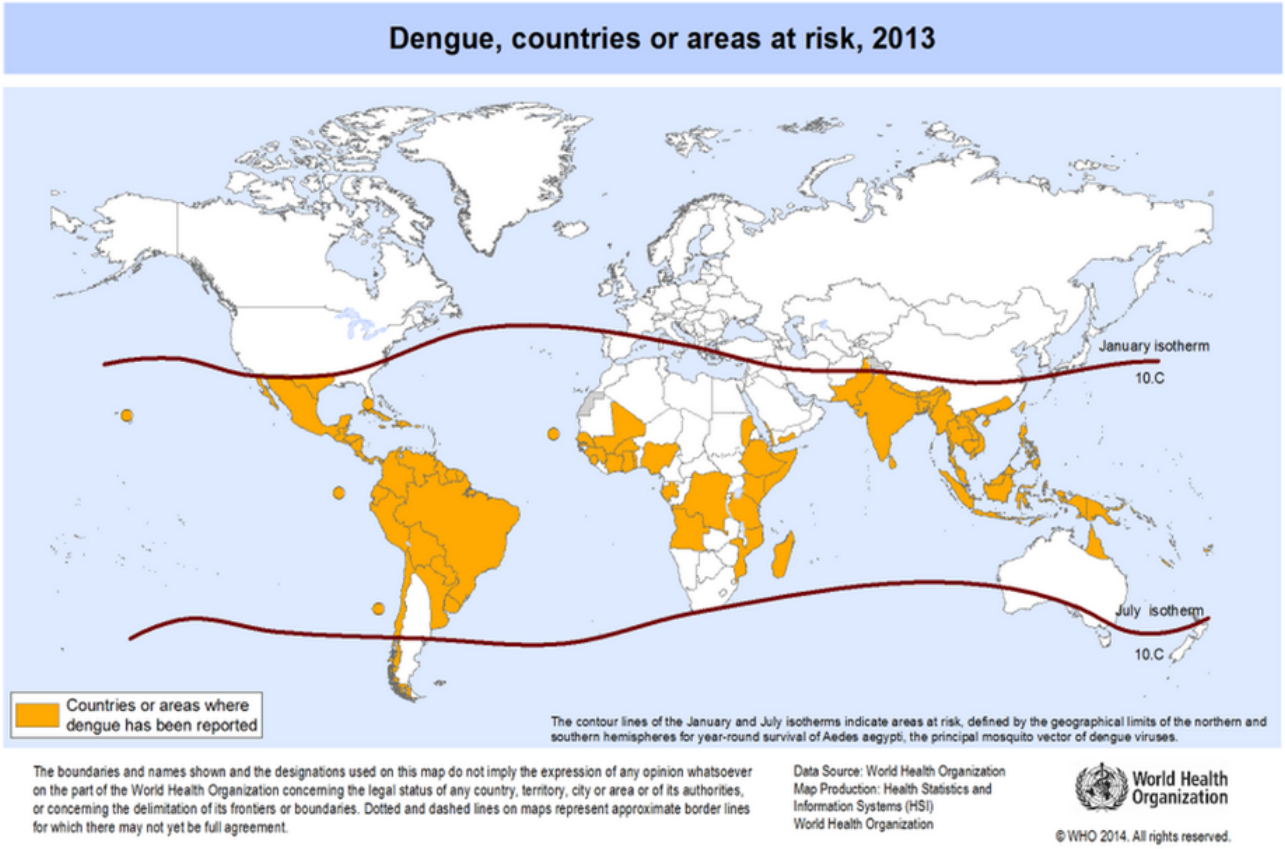

Figure 1: Areas at risk of dengue fever (Reproduced with permission from WHO)

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Module Outline

Dengue: a guide to diagnosis and management

The Indian scenario

Dengue epidemiology in India has been difficult to assess due to inadequate disease surveillance, lack of awareness, and under-reporting. As a tropical country, India has long been endemic with dengue, but its epidemiology has witnessed a major change over time. Outbreaks have been reported at regular intervals from almost all parts of India.

Certain areas such as Delhi are witnessing increasing frequency of outbreaks and have now become hyperendemic. All the four serotypes (DENV1-4) have been reported in India, with changes in the leading serotype responsible for the outbreak. The fifth serotype, which was first reported from the forests of Malaysia, has not yet been reported from India. In 2015, Delhi recorded its worst outbreak since 2006 with around 16 000 infections reported.[5] For the first time, National Dengue Day was observed in India on 16th May 2016, with the objective of increasing community awareness on the prevention of dengue.

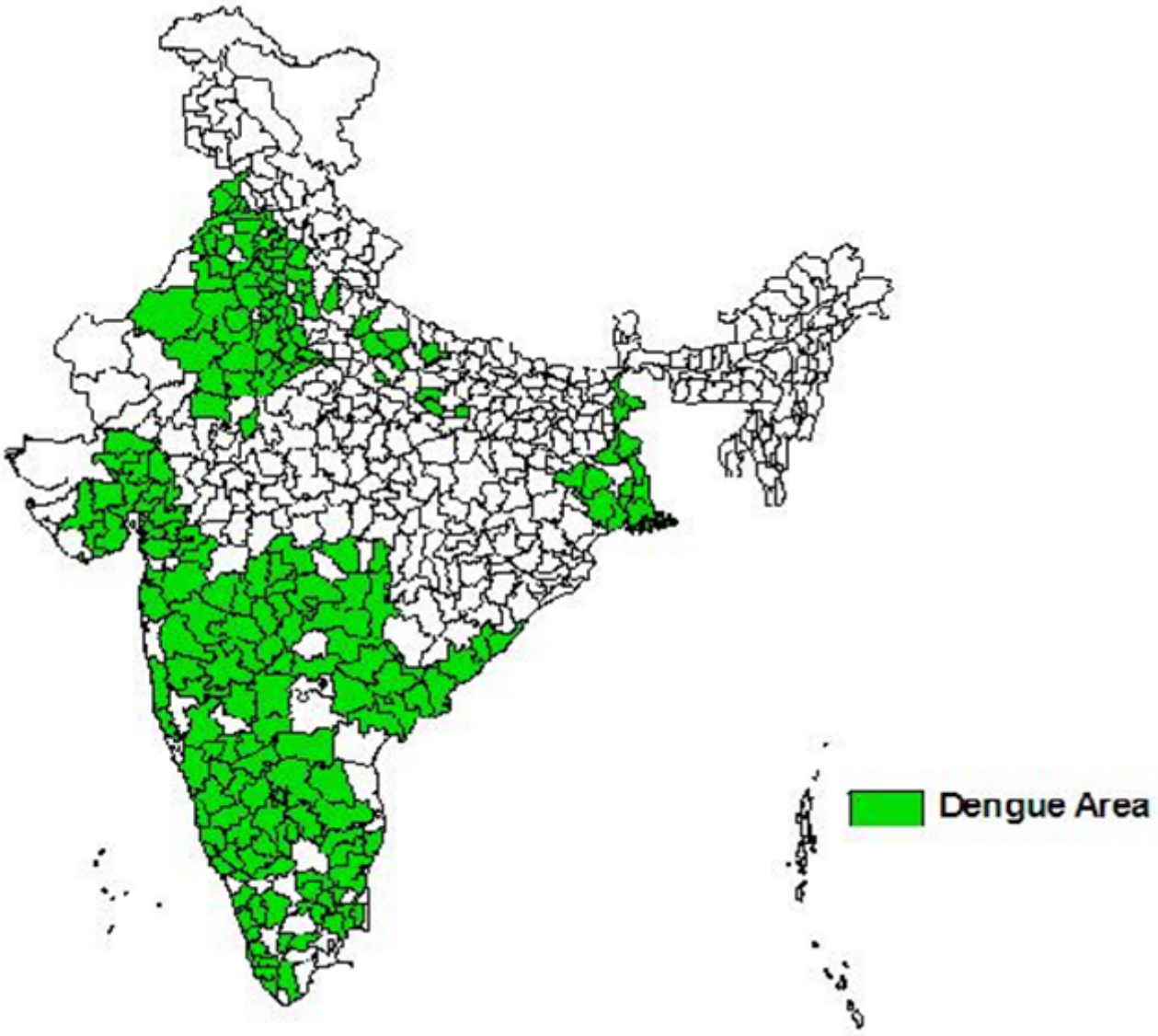

Figure 2: Areas at risk of dengue fever (India) [5] (Acknowledgement: National Vector Borne Disease Control Program, Ministry of Health and Family Welfare, Government of India)

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Dengue: a guide to diagnosis and management

Dengue vector and transmission

(i) Agent

Dengue virus is a single stranded RNA virus belonging to the family *flaviviridae* with four distinct but closely related serotypes (DENV1 to DENV4). A fifth serotype was isolated and reported in October 2013 by researchers from Texas at the Third International Conference on Dengue and Dengue haemorrhagic fever.[6] This has a predominantly sylvatic cycle. A sylvatic cycle is the fraction of the organism's life cycle which is spent cycling between wild animals and vectors with humans as incidental or dead end hosts. This makes it difficult to contain the disease. Infection by one serotype produces lifelong immunity against re-infection by that serotype. However, cross-protection from re-infection with a different serotype is partial and only temporary. In fact, re-infection by another serotype generally leads to a more severe illness.

(ii) Vector

Dengue fever is transmitted by the bite of the female *Aedes* mosquito (most commonly *Aedes aegypti*, less commonly *Aedes albopictus*). This vector also transmits Zika virus, chikungunya, and yellow fever. The *Aedes aegypti* breeds mostly in man made containers of clean, stagnant water and has a flight range of about 400 metres. The mosquito predominantly bites during the day, with peak biting periods occurring after dawn and before dusk.

Aedes albopictus, a secondary dengue vector, is fast spreading from Asia to North America and Europe, predominantly due to trade and the mosquito's inherently high adaptability and tolerance to low temperature.

(iii) Environmental factors

The *Aedes* mosquito is extremely sensitive to environmental changes. Variables like temperature, rainfall, and atmospheric humidity are critical to the mosquito's survival and development. Additionally, high temperatures reduce the time required for the virus to replicate (extrinsic incubation period), thus facilitating transmission. Although sporadic dengue outbreaks are seen throughout the year, a peak is often seen during the monsoon months.

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Dengue: a guide to diagnosis and management

Pathophysiology of dengue fever

There is now evidence to suggest that endothelial dysfunction may play an important role in pathogenesis.[7] Dengue virus does not directly infect endothelial cells; binding of the virus NS1 antigen to heparin sulfate may lead to transient disruption in the glycocalyx thereby leading to increased permeability to proteins like albumin. The presence of albuminuria in patients with severe dengue infection strengthens this hypothesis. However, major gaps still exist in our understanding of these manifestations.

The following groups of patients are at risk of severe infection [7 (https://app.elucidat.com/projects/build_view_wrapper/57c6abfeefa15/57c6b23a9e154#)]:

- Younger age
- Females
- High body mass index (BMI)
- Subsequent infection by a different serotype. This is linked to antibody dependent enhancement (ADE) of virus infection. After a person is infected with dengue they then develop an immune response to that dengue subtype. The immune response produces antibodies to that subtype's specific surface proteins that prevent the virus from binding to macrophage cells (the target cell that dengue viruses infect) and gaining entry. However, if another subtype of dengue virus infects the individual, the virus will activate the immune system to attack it as if it was the first subtype. The immune system is tricked because the four subtypes have similar surface antigens. The antibodies bind to the surface proteins but do not deactivate the virus. The immune response attracts numerous macrophages which the virus then proceeds to infect because it has not been deactivated. This situation is referred to as antibody dependent enhancement (ADE) of a viral infection
- Major histocompatibility complex (MHC) class I variants.

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Dengue: a guide to diagnosis and management

WHO Classification of dengue fever

1. Dengue with or without warning signs
2. Severe dengue

Patients are considered to have a likelihood of dengue fever if they have lived in or travelled to dengue endemic areas with fever and two of the following [9]:

- Nausea and vomiting
- Rash
- Body ache
- Positive tourniquet test
- Leucopenia
- Any warning sign.*

*** Warning signs include:**

1. Abdominal pain or tenderness
2. Persistent vomiting
3. Evidence of third space fluid accumulation
4. Mucosal bleeding
5. Lethargy/restlessness
6. Hepatomegaly 2 cm
7. Increase in haematocrit with rapid fall in platelet count.

Severe dengue is suggested by any one of the following:

- Severe plasma leakage leading to:
  - Shock
  - Third space fluid accumulation with respiratory difficulty (pleural effusion, ascites)
- Severe bleeding
- Severe organ impairment
  - Liver: AST or ALT 1000 IU/l
  - CNS: impaired consciousness
  - Cardiac or other major organ involvement

Dengue: a guide to diagnosis and management

Phases of typical dengue infection

Febrile phase

Critical phase

Recovery phase

Phases of dengue infection are illustrated in figure 3.

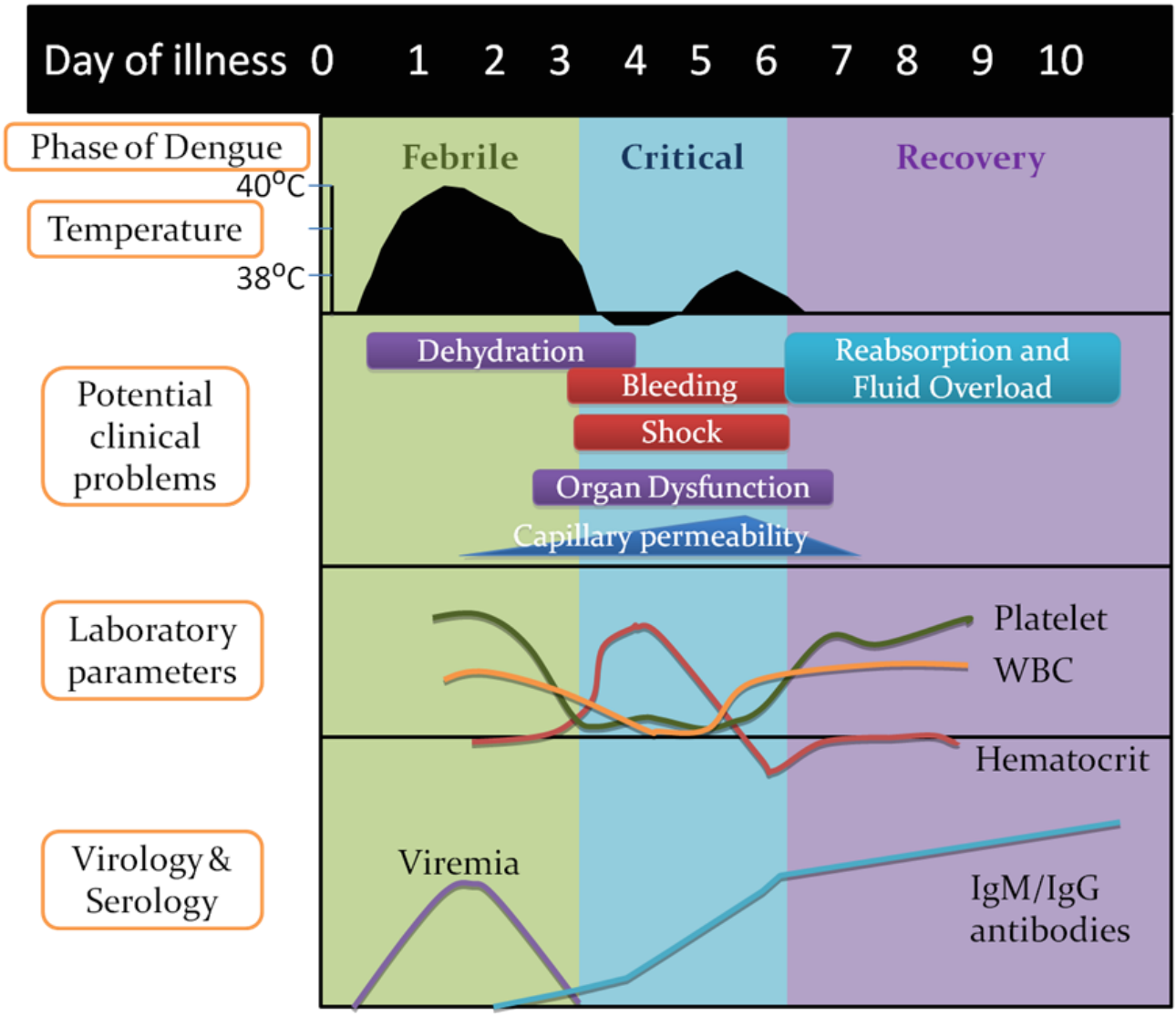

Figure 3: Phases of dengue infection [9]

(Adapted from World Health Organization: Dengue Hemorrhagic Fever: Diagnosis, Treatment, Prevention and Control. Third Edition. Geneva, WHO/TDR, 2009)

Dengue: a guide to diagnosis and management

Clinical case scenario 1

A 22 year old female came to the emergency room with complaints of fever for four days along with epistaxis for one day. Her initial evaluation revealed thrombocytopaenia of 25 000/mm^3 and haematocrit of 50%. NS1 antigen was positive so a diagnosis of severe dengue was made. Ultrasound showed splenomegaly (spleen size of 19 cm) and mild ascites.

Four hours after admission she started complaining of severe generalised abdominal pain. Her abdomen was tender on palpation with rebound tenderness. She developed hypotension with fall in haematocrit to 35%. FAST (focussed assessment with sonography in trauma) showed presence of free fluid in Morrison's pouch.

What is the most probable diagnosis?

Spontaneous splenic rupture

Rare manifestations [11]

Occur mostly during the critical phase and can affect any major organ system. These include:

Gastrointestinal/hepatic	• Acalculous cholecystitis • Hepatitis/ fulminant liver failure • Acute pancreatitis
Respiratory	• Acute respiratory distress syndrome (ARDS) • Alveolar haemorrhage
Renal	• Acute kidney injury • Haemolytic uraemic syndrome
Cardiac	• Myocarditis • Pericarditis • Conduction abnormalities

Neurological	• Encephalitis • Aseptic meningitis • Intracranial thrombosis/haemorrhage • Neuropathy/Guillain–Barre syndrome • Myelitis
Musculoskeletal	• Myositis • Rhabdomyolysis
Lymphoreticular	• Spontaneous splenic rupture • Lymph node infarction • Haemophagocytic lymphohistiocytosis

Initial evaluation (click to expand)

Laboratory parameters (click to expand)

Note: Malaria test kit is a point of care immunochromatographic test that differentiates between *Plasmodium falciparum* and *Plasmodium vivax* as the causative agent. It is sensitive, accurate, and can detect low levels of parasitaemia.

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Module Outline

Dengue: a guide to diagnosis and management

Clinical case scenario 2

A 45 year old man with chronic alcohol dependency disorder is brought by his relatives to the emergency room with complaints of fever for the past few days (exact duration unknown). Laboratory tests reveal that he has thrombocytopaenia with elevated haematocrit and evidence of gall bladder wall oedema on ultrasound. You suspect dengue fever.

Which laboratory investigation would you use to confirm your diagnosis?

Confirmation of an infection with dengue [13]

- During the febrile phase:
  - Viral nucleic acid detection by means of RT-PCR
  - Non-structural protein (NS1) antigen detection by ELISA (sensitivity of 90% in primary infection and 60 to 70% in secondary infection, specificity has been found to be close to 100% in almost all studies for various commercially available NS1 kits) [14]
- Serological diagnosis:
  - Detection of IgM by ELISA is possible only after four days of onset of illness; however, rising titre in paired sera (at a gap of about two to four weeks) is confirmatory
  - Single time detection in patients with compatible clinical features is considered as solid evidence of infection
  - IgM/IgG optical density ratio 1.2 helps to differentiate primary from secondary infection
  - Possible confounding factors include infection with related flaviviruses like Zika virus and Japanese encephalitis virus.

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Dengue: a guide to diagnosis and management

Clinical case scenario 2: question 2

The patient had a recent history of travel to Gangotri, North India and had coexisting jaundice with decreased urine output.

Which illness would you like to rule out?

Differential diagnoses of dengue [13]

Disease	Clinical features	Laboratory parameters
Malaria	High grade fever with splenomegaly is the usual manifestation, evidence of plasma leakage favours dengue.	Peripheral smear shows malaria parasite, thrombocytopaenia may be present in both vivax and falciparum malaria.
Enteric fever	Low to moderate grade fever in step ladder pattern with relative bradycardia and splenomegaly.	Leucopenia is common, thrombocytopaenia is rare; Widal test/blood culture gives the diagnosis.
Chikungunya	Symmetric arthritis of small and large joints, which can be persistent and disabling. Rash is more common in chikungunya.	May have leucopenia and thrombocytopaenia but lymphopaenia is more prominent in chikungunya and thrombocytopaenia is mild.
Leptospirosis	History of travel to high risk areas along with concurrent hepatic and renal dysfunction in the form of jaundice and decreased urine output is more common; evidence of plasma leak suggests dengue.	May be coexistent with dengue, MAT–ELISA is the confirmatory test; thrombocytopaenia and deranged liver and renal function tests are common.
Scrub typhus	Presence of eschar at the site of tick bite in 60 to 70% of patients, hepatic and renal dysfunction in the form of jaundice and decreased urine output is more common; evidence of plasma leak suggests dengue.	Positive IgM ELISA for scrub typhus clinches the diagnosis; thrombocytopaenia and deranged liver and renal function tests are common and may be coexistent with dengue.

Meningococcemia	Wide pulse pressure with bounding pulses and warm extremities with absence of warning signs.	Blood culture grows meningococcus, smear from the petechial rash shows diplococci.
Viral haemorrhagic fevers (Crimean Congo haemorrhagic fever and Hanta fever)	Presentation similar, pathogenesis differs and classic febrile to critical phase transition is not seen, history of contact present.	Diagnosis made by specific serology; leucopenia and thrombocytopaenia are common.
Acute immune thrombocytopaenic purpura	May present as acute febrile illness with thrombocytopaenia, which does not respond to supportive management.	Giant platelets on peripheral smear may give a clue to the diagnosis.
Yellow fever (not seen in India)	Not endemic in Asia, clinical features similar; liver dysfunction more prominent in yellow fever	Liver function tests (LFTs) almost always deranged and prominent; thrombocytopaenia rare.
Influenza	Prominence of URTI symptoms in influenza.	Nasal/nasopharyngeal swab positive for influenza virus PCR.
Adenovirus infection	URTI symptoms with cervical adenopathy, bleeding is rare.	May have leucopenia, thrombocytopaenia is rare.
Systemic lupus erythematosus/other autoimmune diseases	More acute presentation with high fever favours dengue.	Positivity for ANA/dsDNA and other autoimmune markers, immune thrombocytopaenia is common.

Key: URTI, upper respiratory tract infection; MAT-ELISA, microscopic agglutination test- enzyme linked immunosorbent assay; ANA, anti-nuclear antibody; dsDNA, double stranded deoxyribonucleic acid.

in this patient, we would like to do a MAT-ELISA for leptospira, a peripheral smear for malaria parasite; and look for any tick bite mark/eschar on the body.

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Dengue: a guide to diagnosis and management

Clinical case scenario 2 question 3

Let us continue with our patient in case scenario 2. The patient had a blood pressure of 80/50 mmHg on the second day of hospitalisation and he was given a bolus of normal saline. There was initial improvement and intravenous fluids were stepped down. However, on the fourth day of admission the patient developed hypotensive shock with sudden decrease of haematocrit which does not respond to two boluses of saline.

What will be your next step in this situation?

Management of fluid status and the role of haematocrit

When to start intravenous fluids?

- In the critical phase for 24 to 48 hours to reverse haemoconcentration
- When there are features of shock
- In the febrile phase if oral intake is inadequate

What fluids to be used?

- Isotonic solutions like Ringer's lactate and normal saline are ideal
- Colloid solutions like dextran and albumin are used in indications specified below

Which intravenous fluids to be avoided?

- Hypotonic saline, fresh frozen plasma, dextrose containing fluids (5% dextrose, dextrose normal saline)

When are colloids given?

- In refractory shock a bolus of colloids 20 to 30 ml/kg can be given if haematocrit does not increase after two boluses of crystalloids
- Dose: 10 to 20 ml/kg/hour bolus to 30 to 50 ml/kg/day

When to stop intravenous fluids?

- Monitor haematocrit and vital signs and reduce fluids in a step by step manner
- Discontinue immediately if patient has good volume pulse with hypertension or pulmonary oedema
- Forty-eight hours after abatement of fever
- Improving urine output

How much fluid to give and how fast?

- Compensated shock: 5 to 10 ml/kg over one hour
- Hypotensive shock: 10 to 20 ml/kg over 15 to 30 minutes
- Maintenance fluids according to Holliday–Segar formula
  - 4 ml/kg/hour for first 10 kg body weight
  - 2 ml/kg/hour for next 10 kg body weight
  - 1 ml/kg/hour for each kg body weight after 20 kg

Obese patients should receive fluids according to their ideal body weight (IBW).

Note: IBW (kg) = 50 + 2.3 (height in inches - 60) for males. 45.5 + 2.3 (height in inches - 60) for females. This formula is applicable to persons who are taller than 60 inches (152 cm).

Use of haematocrit to guide fluid therapy

Algorithm of inpatient management (group B)

Algorithm of inpatient management (group C)

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Module Outline

BMJ Learning

Dengue: a guide to diagnosis and management

Clinical case scenario 2 question 4

The patient was immediately transfused packed red blood cells after he became hypotensive. He then improved and became afebrile on day seven of his hospital stay. However, you forgot to discontinue his intravenous fluids and the next day you notice that he has developed respiratory distress.

When you examine him you find bilateral basal crepitations with hypoxemia and elevated jugular venous pressure. What do you think happened?

Management of fluid overload

Usually due to over enthusiastic fluid resuscitation along with redistribution of leaked fluid back into the circulation.

- Immediately stop intravenous fluids
- Furosemide 0.1 to 0.5 mg/kg/dose used two or three times daily or as a continuous infusion of 0.1 mg/kg/hour (if out of critical period)
- Oxygen therapy
- Transfer to intensive care unit, if facilities exist

Management of bleeding complications

Management principles

Note: Indian guidelines (NVBDCP) versus WHO guidelines. Indian guidelines differ slightly from the WHO guidelines, as follows:

- NVBDCP guidelines recommend prophylactic platelet transfusion at platelet counts 10 000/mm^3, whereas WHO states no evidence of benefit of prophylactic platelet transfusion
- From a management point of view, Indian guidelines classifies dengue into mild, moderate, and severe infection, whereas WHO categorises it into group A, B, and C
- Fluid boluses advocated by Indian guidelines in patients with shock are slightly lower than those advocated by WHO, probably due to the smaller body habitus of the Indian population.

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Dengue: a guide to diagnosis and management

Clinical case scenario 3

A 45 year old homeless male came to the emergency room with history of fever for two days without any localising symptom. On evaluation he was found to have mild thrombocytopaenia of 0.1 million/mm^3 and no other warning signs. His NS1 antigen was positive.

What is the next best step in management?

Admit for observation

Group A: send home

Criteria: presence of all of the following:

- Adequate oral intake
- Passing urine every six hours
- No warning signs
- Haemodynamically stable with stable haematocrit.

Management:

1. Oral fluids: Oral rehydration solution (ORS), fruit juices, lemon water, buttermilk, coconut water, and soft drinks
2. Paracetamol for fever (3 g/day as a maximum)
3. Guidance and proper counselling to patients and their caregivers
4. Daily follow-up with haematocrit and platelet count and assessment of warning signs

Group B: inpatient care

Criteria: presence of any of the following:

- Warning signs
- Coexisting conditions: diabetes mellitus, uraemia, pregnancy, extremes of age
- Social circumstances: Lives alone or far away with no reliable transport

Management:

1. Inpatient care
2. Monitor haematocrit and haemodynamic stability with judicious use of intravenous fluids

Group C: admit to intensive care unit (ICU) (if available)

Criteria: Any feature of severe dengue according to WHO classification mentioned above warrants admission to ICU.

Management:

Emergency treatment in intensive care unit with blood transfusion (if indicated) and urgent fluid resuscitation.

Although the patient in the scenario is haemodynamically stable and there are no warning signs present, he should be admitted until he is out of the critical phase as he has social circumstances that are likely to prevent him from seeking timely healthcare if and when complications develop.

Management: specific principles (click to expand)

Management of fever

- Paracetamol
  - Dose: 10 mg/kg per dose, not more than 3 g/day in adults
  - It is to be used cautiously in the critical phase of illness and in patients with elevated liver enzymes
- Tepid sponging: This is defined as sponging the body with lukewarm water (temperature around 32°C) to bring down fever
- Drugs to be avoided are non-steroidal anti-inflammatory drugs (NSAIDS) including aspirin, ibuprofen, and diclofenac
  - Rationale:
    - Increased risk of gastritis with NSAIDS and subsequent gastrointestinal bleeding
- Intramuscular (IM) injections should be avoided as there is risk of haematoma formation at the site of injection

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Dengue: a guide to diagnosis and management

When to discharge?

All of the following prerequisites must be fulfilled:

Clinical

1. Improvement in wellbeing, appetite, haemodynamic status, urine output
2. Absence of respiratory distress
3. Absence of fever for 48 hours without antipyretics

Laboratory

1. Increasing trend of platelet count (Indian guidelines specify a cut off of 50 000/mm^3 prior to discharge)
2. Stable haematocrit without the need of intravenous fluids

Indications of referral to specialist centres [13]

Patients with severe dengue who have received an initial fluid bolus but have:

- Persistent bleeding
- Persistent hypotension
- Oliguria
- Altered sensorium
- Rapidly falling haematocrit
- Other end organ failure: myocarditis, ARDS, liver failure.

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Dengue: a guide to diagnosis and management

Role of complementary and alternative medicine in dengue fever

- Complementary and alternative medicine has been used in the management of dengue fever [19]
- Preparations that have been used include [19 (https://app.elucidat.com/projects/build_view_wrapper/57c6abfeefa15/57c6bd223210e#)]:
  - Isotonic drinks
  - Crab soup
  - Papaya leaf extract
  - Papaya seeds
  - Giloy
- Of these, papaya extract has been most commonly used and is even available in tablet formulations. The postulated mechanism of papaya extract in dengue is an increase in platelet counts caused by its membrane stabilising properties

Giloy has also been commercially available in India and is said to be effective in increasing the platelet count in dengue; however, no scientific evidence exists to justify this claim.

Current evidence

Current evidence suggests that although papaya leaves may have beneficial effects in dengue by increasing the platelet count, there is not sufficient scientific evidence to suggest a routine therapeutic role of this intervention and more randomised clinical trials are needed to confirm its efficacy.[21]

Common myths in management

- Other treatment modalities like vitamin C, folic acid, and steroids have been tried in dengue infection. However, there is no robust scientific evidence to advocate their use [16]
- Most patients with dengue need only outpatient care. Only patients who are sick require hospitalisation. It is imperative for the media to play its part in spreading awareness about this disease so that people understand when a hospital visit is really necessary so that undue pressure is not put on limited health resources
  - Platelet clumps may be spuriously interpreted as thrombocytopaenia in automated counters; hence, manual platelet count is the gold standard

Dengue: a guide to diagnosis and management

Prevention

Prevention is largely centred on vector control and interruption of transmission of infection from man to mosquito and vice versa. There has been rapid advancement in the field of dengue vaccines.

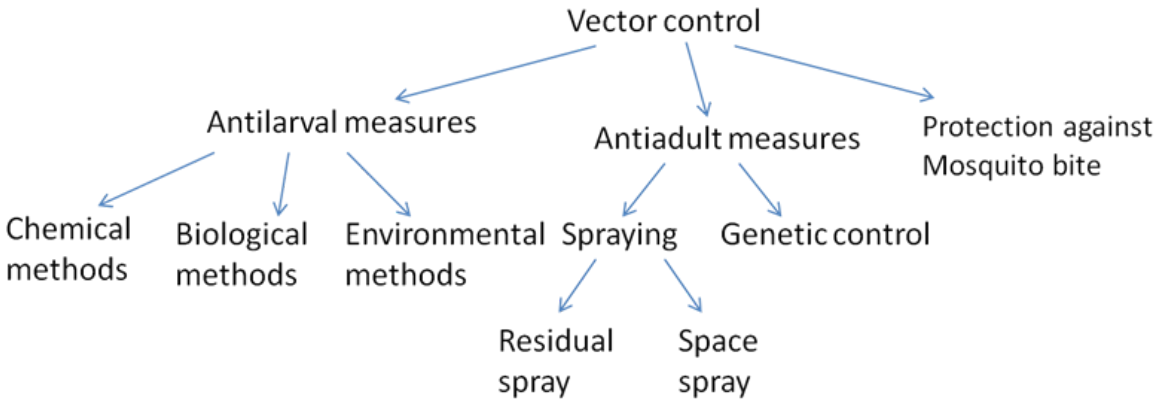

Figure 8: Strategies of vector control for prevention of dengue

Anti-larval measures

- Chemical
  - Mineral oils: applied once a week to potential breeding places; kerosene oil, diesel oil and other forms of crude oil are commonly used
  - Paris green: stomach poison, kills larvae at the surface predominantly
  - Synthetic insecticides (eg temephos and fenthion): organochlorines (eg DDT) are generally avoided in view of their long residual effect and high resistance rates

Biological

- Larvivorous fishes (eg, *Gambusia*, *Lebister*, *Pecilia*)
- Biolarvicides (eg, *Bacillus thuringiensis H14*, *Bacillus sphericus*). **Note**: Biological methods have proven efficacy only when used as adjuncts to other standard methods

Environmental (called source reduction methods)

- Filling, levelling, and drainage of breeding places most commonly empty water coolers, car tires and rain water puddles
- Intermittent irrigation
- Increasing salinity of water. **Note**: The environment should be cleaned of potential breeding places like open tins, pots, and empty bottles. A dry day should be observed once a week in which air coolers/air conditioners should be cleaned and thoroughly scrubbed

Anti-adult measures

- Spraying
  - Residual spray (spraying inside shelters)
  - Since *Aedes* has a shorter flight range compared to other mosquitoes, residual spraying is of paramount importance in dengue
- Space spray (fogging): spraying outside shelters, in open air
- Genetically modified mosquitoes [22]: introduction of *Wolbachia*, which is an obligate intracellular bacterium, results in *A. aegypti* that are partially resistant to infection with dengue
- Sterile male technique: a large number of sterile male *Aedes* mosquitoes is released into the environment
- Genetic editing: CRISPR-Cas9 gene editing technology, which induces female embryos to develop male internal and external genitalia, essentially converting all females to males or killing all females

Protection against mosquito bites

- Use of light coloured full sleeve clothing
- Use of long lasting insecticidal nets and insecticidal treated bed nets
- Mosquito repellant creams containing diethyl toluamide are effective. Mosquito coils are not recommended in view of indoor air pollution

Dengue vaccine

CYD-TDV, the most promising dengue vaccine, has been licensed recently. Five more dengue vaccines are in clinical development, with two of them expected to begin phase III trials soon.[23]

CYD-TDV was licensed in Mexico in December 2015 for individuals in the age group 9 to 45 years living in dengue endemic areas. It is a tetravalent recombinant live dengue vaccine given in three doses at 0, 6, 12 months.

WHO's recommendations related to CYD-TDV [24]

The WHO Strategic Advisory Group of Experts (SAGE) on immunization held a meeting in April 2016 and recommended consideration of the CYD-TDV vaccine in high endemic settings.

Potential drawbacks of the CYD-TDV vaccine [25]

- Low efficacy against dengue serotype 2 (35 to 50%)
- Lower efficacy for recipients seronegative for dengue at baseline
- Increased risk of hospitalisation in children less than 9 years of age (more so, in the 2 to 5 years age group). The benefits in this age group are also uncertain, necessitating the need for more data

Continue (%7B%7Bnext.url%7D%7D)

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Final assessment

Question 1

What is the most common site of bleed during the febrile phase of dengue infection?

- Skin
- Nose
- Venipuncture sites
- Upper gastrointestinal tract

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Question 2

A 25 year old female presented to the medical outpatients with complaints of fever for two days associated with a generalised maculopapular rash. On evaluation her platelet count was 50 000/mm^3 and NS1 antigen was positive. She was sent home after counselling since there were no warning signs. Three days later she came back for a follow up visit when she was noted to have hepatomegaly and bilateral pleural effusion.

Which of the following is the next best step in management?

- ○ Other diagnosis should be considered
- ○ An urgent haematocrit should be ordered and she should be hospitalised
- ○ Blood transfusion is indicated urgently
- ○ She should be sent home after counselling since there are no warning signs

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Question 3

A 55 year old male patient presented with history of fever for three days followed by sudden onset of paraplegia, altered sensorium, and shock. At presentation the patient had hypotension with a collapsed inferior vena cava and complete paraplegia with altered sensorium. There has been a recent outbreak of dengue fever in his area and he has a platelet count of 25 000/mm^3 with a haematocrit of 48%.

What is the most likely diagnosis?

- ○ Guillain–Barre syndrome
- ○ Multiple sclerosis
- ○ Acute disseminated encephalomyelitis
- ○ Bickerstaff encephalitis

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Question 4

A 30 year old female who is twelve weeks pregnant comes to you with fever for two days along with nasal congestion, throat pain, and nausea without any rash. She has mild thrombocytopaenia of 100 000/mm^3 and dengue IgM ELISA is positive. On further history she tells you that she had dengue two months back from which she had recovered spontaneously and had recently travelled to Brazil on a vacation.

What congenital anomaly will you counsel her for in this situation?

- Zika virus associated microcephaly
- Zika virus associated congenital heart disease
- Dengue virus associated limb defects
- Dengue virus associated thrombocytopaenia

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Question 5

A 12 year old male presents with history of fever for three days and one episode of haematemesis. He is haemodynamically stable. NS1 antigen is positive. His platelet count is 50 000/mm^3 and haemoglobin is stable at 14 g/dl. Coagulation profile is normal.

What decision would you take regarding transfusion in this patient?

- Packed red blood cells (PRBC) transfusion is indicated
- Platelets should be transfused
- Fresh frozen plasma (FFP) should be transfused
- No transfusion indicated

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Question 6

Which statement is correct about CYD-TDV?

- It has been approved by WHO for use worldwide
- It is primarily indicated in children less than 9 years of age in whom the mortality is higher
- Complete course consists of three doses given subcutaneously

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Question 7

Which is the most appropriate fluid to be used for resuscitation in patients with dengue shock syndrome?

- 25% dextrose
- 0.9% saline
- 5 % dextrose
- 0.45% saline

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Question 8

A 14 year old male came to the emergency room. He had a with fever for three days which was high grade, with chills and rigors along with generalised malaise and headache. He was found to have thrombocytopaenia, an elevated haematocrit, and NS1 antigen was positive. His liver enzymes were elevated with SGOT- 800 IU/l and SGPT-1200 IU/l. He had no bleeding manifestations and was haemodynamically stable. He was treated with intravenous fluids and supportive measures following which he improved. However, his liver enzymes remained persistently elevated and peaked at the fourth day after admission reaching 1500/2600 respectively. He also had persistent nausea and vomiting although his abdomen ultrasound was normal.

What is the most likely explanation?

- ○ Dengue-associated transaminitis
- ○ Viral hepatitis without dengue fever
- ○ Co-infection of viral hepatitis and dengue fever
- ○ Drug-induced liver injury

Submit