Dengue – An overview of determinants, distribution, clinical presentation and prevention

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Dengue is a mosquito borne viral disease caused by 4 closely related viruses: DENV 1, DENV 2, DENV 3 and DENV 4. All 4 virus serotypes cause human disease.

Dengue range from self-limited Dengue Fever (DF) to more severe Dengue Haemorrhagic Fever (DHF) and to life threatening Dengue Shock Syndrome (DSS). Of all infected people 75% will remain asymptomatic, while the rest will have symptomatic disease. From these majority will have the simple dengue fever, and only 1-2% will develop into DHF or DSS.

Infection with one serotype will provide lifelong immunity, but does not protect against the other serotypes. Subsequent infection with other serotypes puts the individual at greater risk of developing the severe form of Dengue if not diagnosed and treated in time.
Dengue is spread widely throughout the tropics and sub tropics. It is an endemic disease, occurring throughout the year, usually when rainfall is optimal for breeding. The other factors that influence the spread are, local spatial variations of rainfall, temperature, relative humidity, degree of urbanization and quality of vector control services in those areas.

Dengue was first reported in Sri Lanka in early 1960s, but it was not until the late 1980s that dengue haemorrhagic fever the more severe form became endemic. Since year 2000, the magnitude of dengue epidemics have increased and dengue viruses have started to spread from urban to semi-urban and rural settings.

Dengue is a vector borne disease, an intermediate host carrying the virus from one person to another. The virus is transmitted by the female mosquito of *Aedes aegypti* and *Aedes albopictus*. These vectors are found throughout the world, and in Sri Lanka the main vector is *Aedes aegypti*. This mosquito also transmits chikungunya, yellow fever and Zika infection.
Dengue should be suspected when a high fever (>38°C/104°F) is accompanied by 2 of the following symptoms: severe headache, pain behind the eyes, muscle and joint pains, nausea, vomiting, or rash. Symptoms usually last for 2–7 days, after an incubation period of 4–10 days following the bite from an infected mosquito. Some patients may also present with sore throat, and diarrhoea with the above main symptoms.
As it is a viral disease there is no medication for dengue or effective vaccine at present. Therefore the main method to control or prevent the transmission of dengue virus is to combat vector mosquitoes through integrated vector control methods.

History

All four dengue viruses (DENV1-4) originated in monkeys several years back. They independently jumped to humans in Africa or Southeast Asia between 100 to 800 years ago. Dengue remained a relatively minor, geographically restricted disease until the middle of the 20th century.
The first record of a case of probable dengue fever is in a Chinese medical encyclopaedia from the Jin Dynasty (265–420 AD), which referred to a "water poison" associated with flying insects. The first recognized

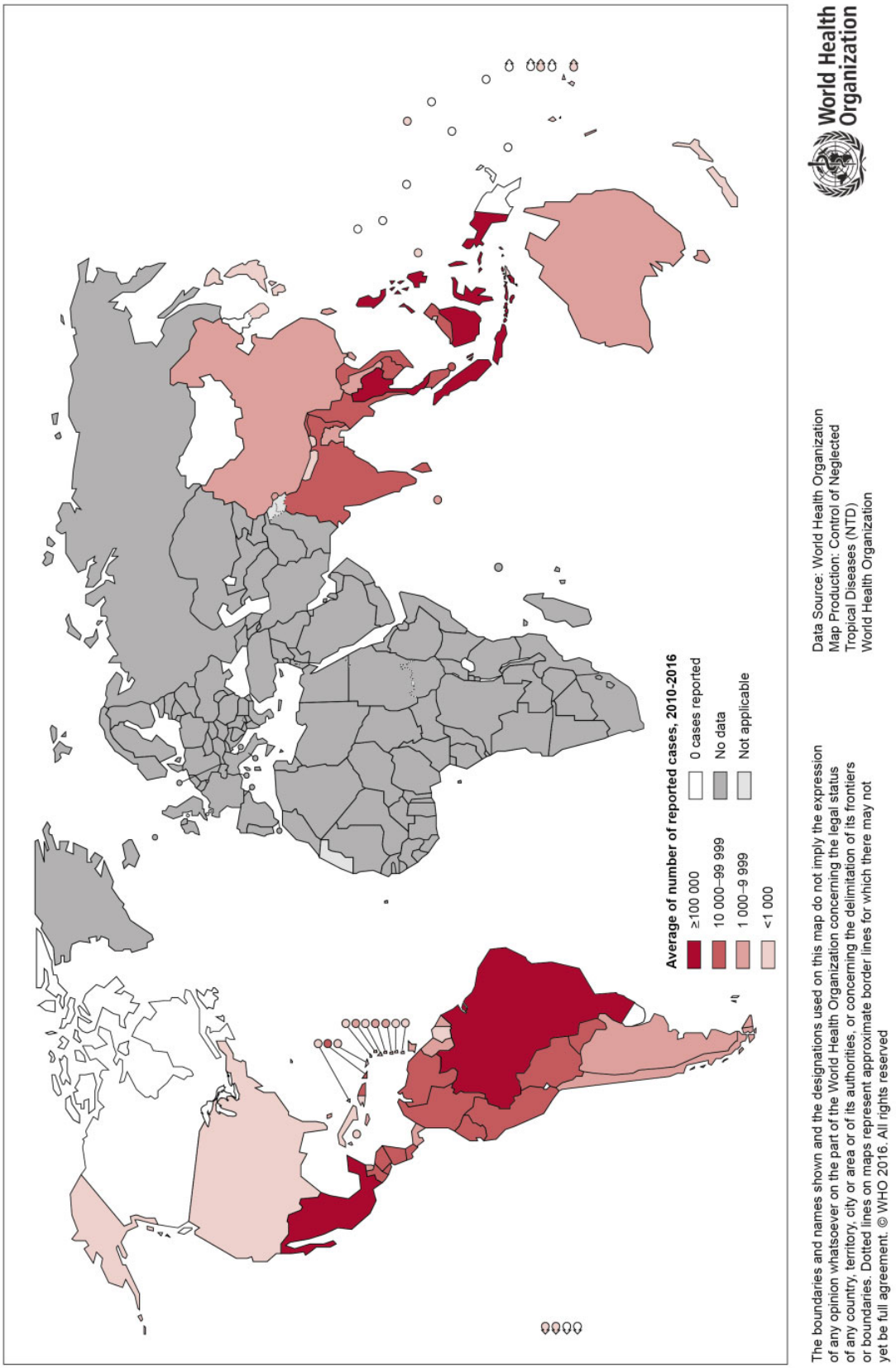


Fig 1 : Distribution of Dengue, worldwide, 2016

Dengue epidemics occurred almost simultaneously in Asia, Africa, and North America in the 1780s, shortly after the identification and naming of the disease in 1779. The first confirmed case was reported in 1779 by Benjamin Rush, who coined the term "break bone fever" because of the symptoms of myalgia (muscle pain) and arthralgia (joint pain).
The viral aetiology and the transmission by mosquitoes were discovered in the 20th century. Population movements during the World War II spread the disease globally. The first epidemic of dengue haemorrhagic fever (DHF) was described in Southeast Asia, Manila in 1953, after which, outbreaks of dengue fever became more common. In the 1950s, 9 countries reported dengue outbreaks. Epidemic dengue has become more frequent since the 1980s. By late 1990s, dengue was the most important mosquito-borne disease affecting humans after malaria, with around 40 million cases of dengue fever and several hundred thousand cases of dengue haemorrhagic fever each year.

Global situation of dengue

Before 1970, only nine countries had experienced severe dengue epidemics. At present, the disease is endemic in more than 100 countries in Africa, America, Eastern Mediterranean, South-East Asia and Western Pacific regions, with America, South-East Asia and Western Pacific regions being the most seriously affected (Fig.1).

According to the World Health Organization (WHO) a recent (2013) study estimates that, 390 million dengue infections occur every year (95% CI 284–528 million) world-wide, out of which 96 million (67–136 million) are with clinical manifestation (with any severity of disease, DF,DHF and DSS). Another (2012) study, on the prevalence of dengue, estimates that 3.9 billion people in 128 countries are at risk of infection with dengue viruses.

The year 2016 was characterized by large scale dengue outbreaks worldwide. The American region reported more than 2.38 million cases in 2016, where Brazil alone contributed slightly less than 1.5 million cases, approximately 3 times higher than in 2014. 1032 dengue deaths were also reported in this region. The Western Pacific Region reported more than 375 000 suspected cases of dengue in 2016, of which the Philippines reported

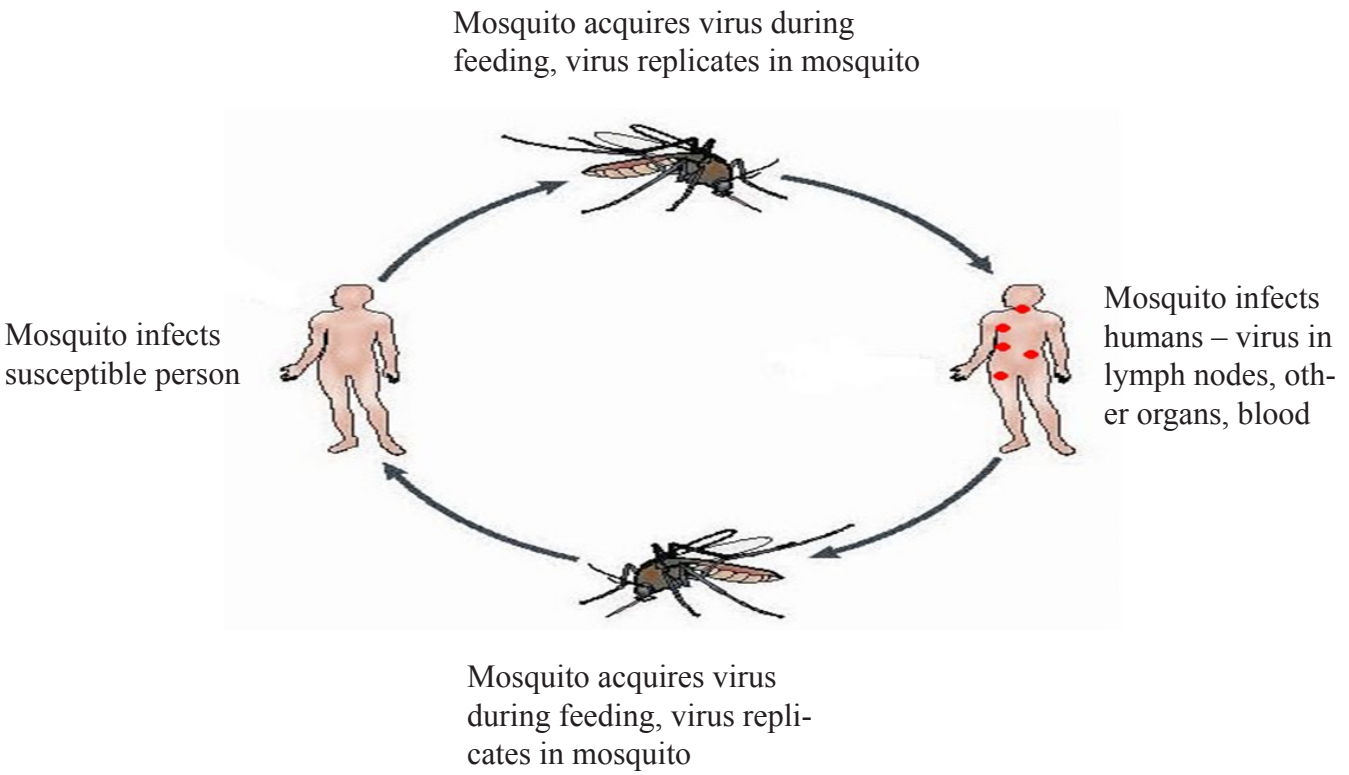


Fig 2 : Transmission of Dengue by mosquitoes

Fig 3 : Image of *Aedes aegypti*

Fig 4 : Image of *Aedes albopictus*

176 411 and Malaysia 100 028 cases, representing a similar burden to the previous year for both countries. The Solomon Islands declared an outbreak with more than 7000 suspected cases. In the African Region, Burkina Faso reported a localized outbreak of dengue with 1061 probable cases.

The map published by the WHO, indicates the distribution of dengue worldwide in year 2016.

Sri Lanka situation

In Sri Lanka serologically confirmed first dengue case was detected in 1962 in the Western Province. The First epidemic in Sri Lanka was reported during 1965-68 with 51 cases

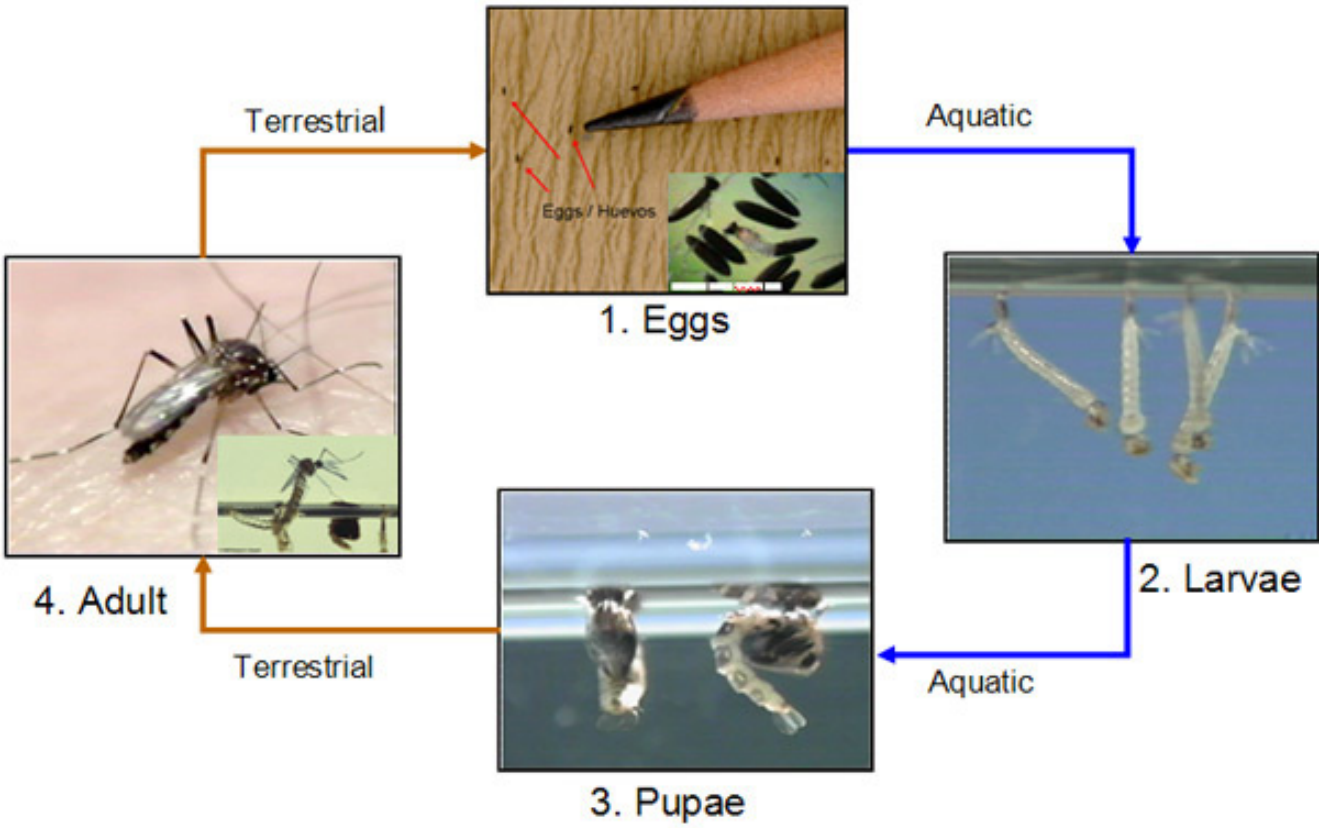


Fig 5 : Life cycle of *Aedes* mosquito

and 15 deaths with a case fatality rate (measure of the severity of a disease and is defined as the proportion of reported cases of a specified disease which are fatal within a specified time) of 30%.

In 1990 resurgence of disease occurred with 440 cases and 11 deaths with a case fatality rate (CFR) of 2%. Since the year 2000, a dramatic increase of cases with over 5000 per year in respect of both DF and DHF has been experienced in Sri Lanka. Reporting of cases has gradually increased yearly, but reducing the CFR to less than 1% from 2004. The year 2017 is exceptional for dengue in Sri Lanka, facing a huge outbreak which exceeded 100 000 cases in the first six months of the year and almost 150 000 cases to date with significant number of deaths. This is the highst ever in the history of this disease.

Disease transmission

The disease is transmitted by the female mosquito of *Aedes aegypti* and *Aedes albopictus*. In Sri Lanka the main vector is *Aedes aegypti*.

For transmission to occur, the mosquito must have a blood meal from a symptomatic person in the first few days (day 0 to 5) when a large amount of virus is in the human blood. But some people who never had significant symptoms, still can infect the mosquitoes. Once the virus enters the mosquito in the blood meal, it will take 8-12 days of incubation before it is transmitted to another person.
Symptoms of infection appear after 4-7 days of incubation period and lasts for 3-10 days.

As the mosquito has a life span of 2 weeks to one month the virus will remain in the mosquito once infected for a period which may be days or a few weeks. The infected mosquito can transmit the virus to several people during of its life span (Fig.2).

There is evidence for viral transmission from a pregnant mother to her foetus, if she got infected during her late pregnancy.

Aedes aegypti

Aedes aegypti, the principal mosquito vector of dengue viruses is well adapted to transmit Dengue virus among human beings (Fig.3). This mosquito is closely associated with humans and their dwellings and is adapted to breed near human habitations It also breeds

Fig 6 : Pictures of common mosquito breeding sites

year round and therefore is able to transmit the disease throughout the year. They prefer human blood meal (Anthrophophilic), and take multiple blood meals (Multiple feeder) for satire. It is identified as a day biter as it is active during the day time (6.00 am to 10.00 am in the morning and 4.00 pm to 6.00 pm in the evening)

inundates the eggs as a result of rains. In the following days, the larvae (picture 2- figure 5) will feed on microorganisms and particulate organic matter. They shed their skins three times to be able to grow from first to fourth stages. When the larva has acquired enough energy and size in the fourth stage, metamorphosis is

mosquitoes. There is a great variety of man-made containers on backyards or patios that collect rain water or that are filled with water by people where dengue vectors thrive.

The common breeding habitats (Fig.6);

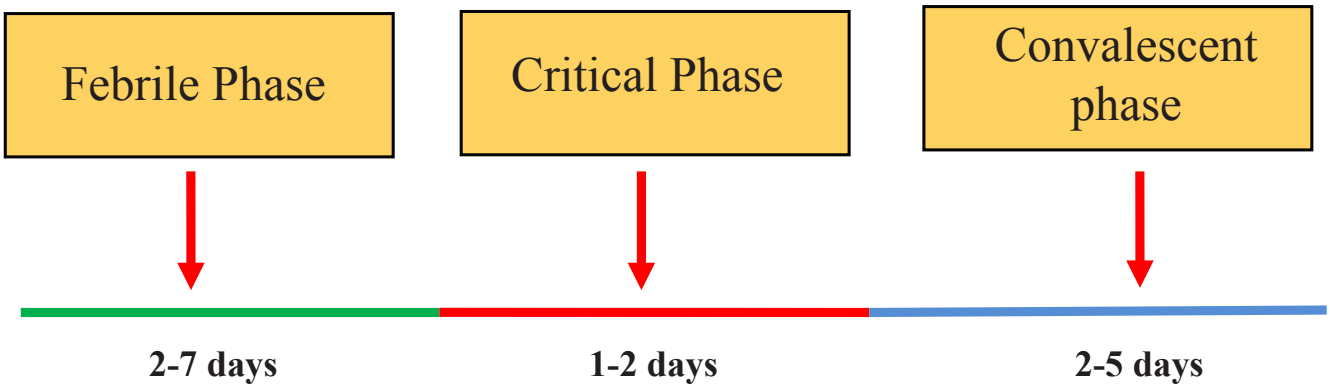


Fig 7 : The clinical course of DHF

Aedes albopictus

Another important mosquito vector of dengue is *Aedes albopictus* which is less adapted to transmit dengue virus, and prefer multiple animal blood meals (Fig.4). It goes into diapause (a period during which growth or development is suspended and physiological activity is diminished, as in certain insects in response to adverse environmental conditions) when cold. It is also a day biter which breeds near human habitation.

Life cycle of the *Aedes*

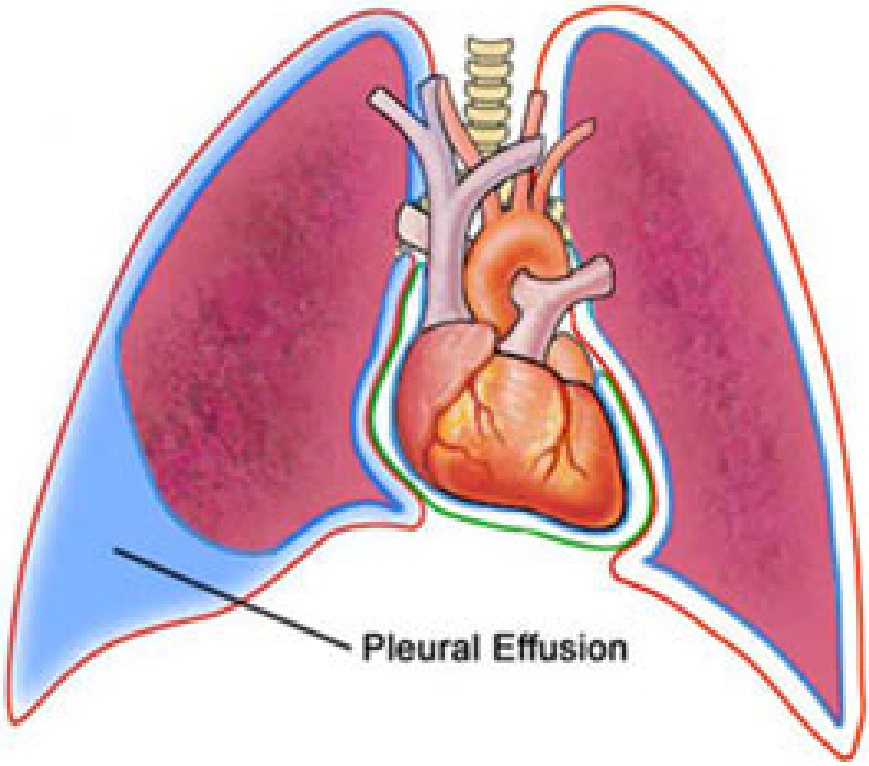
Aedes mosquitoes have a short life-cycle with changes in shape, function, and habitat. It has two phases, terrestrial (eggs, adults) and aquatic (larvae, pupae). Female mosquitoes lay their eggs on the inner, wet walls of containers with water. Larvae hatch when water

triggered, changing the larva into a pupa (picture 3- figure 5). Pupae do not feed; they just change in form until the body of the adult, flying mosquito is formed. Then the newly formed adult emerges from water after breaking the pupa skin (picture 4- figure 5). The entire life cycle lasts 7-10 days at room temperature, depending on the level of feeding.

There is a very important adaptation of dengue vectors; their eggs can withstand desiccation for several months (6 to 12). This allows even if all larvae, pupae, and adults were eliminated at some point in time, repopulation will occur as soon as the eggs in the containers are flooded with water. Female mosquitoes can lay 100 to 200 eggs during their lifetime. Aquatic habitats are containers in which eggs develop into adult

- Disposed items
- Uncovered tyres
- Concrete slabs
- Non usable commodes and cisterns
- Refrigerator and air conditioner trays
- Roof gutters Ponds and bird baths
- Blocked flower pots and plates
- Construction sites
- Blocked drains and manholes
- Covering polythene
- Water tanks and water collecting containers
- Plants collecting rain water eg. Bromelia
- Tree holes

Aedes mosquitoes are highly sensitive to environmental conditions. Temperature, precipitation and humidity are critical for mosquito survival, reproduction, and development, and can influence mosquito



Fluid leak to the lung cavity known as pleural effusion

Fluid leak to the abdominal cavity known as ascites

presence
in

Fig 8 : Plasma leakage during the Critical Phase

abundance.

Clinical features and treatment

People who suffer from dengue fever have no risk of death as it is a self-limiting condition, but rarely some of them develop Dengue Haemorrhagic Fever (DHF) or Dengue Shock Syndrome (DSS). Patients present with fever (>38 oC) with 2 or more of the other symptoms; headache, myalgia (muscle pain), arthralgia (joint pain), purpuric rash, bleeding (eg. gum bleeding), nausea and vomiting need to be suspected as DF.

Severe dengue (DHF) is a potentially deadly complication due to plasma leaking, fluid accumulation, respiratory distress, severe bleeding, or organ impairment. Warning signs occur 3–7 days after the first symptoms in conjunction with a decrease in temperature (below 38°C/100°F) and include, severe abdominal pain, persistent vomiting, rapid breathing, bleeding gums, fatigue, restlessness and blood in vomit. The next 24–48 hours of the critical stage can be lethal; proper medical care is needed to avoid complications and risk of death, DHF and DSS.

It is difficult to identify DF vs DHF in the first 2-3 days as both are clinically very similar. Loss of appetite, Defervescence (afebrile state but sick), Haemodynamic changes (low blood pressures, rapid pulse rate, reduce urine output or no urine output for last 4-6 hours) and laboratory findings (mentioned below) are the mainstay to detect DHF.

If a clinical diagnosis is made early, a health care provider can

effectively treat DHF using fluid replacement therapy. Adequate management of DHF requires hospitalization.

The clinical course of DHF can be demonstrated as below (Fig.7);

Critical Phase

• The critical phase is also known as the leakage phase starting with onset of plasma leakage (often after the 3rd day of fever, with settling of fever)
• Plasma leakage is due to increased capillary permeability. Plasma leakage is transient and usually lasts 24-48 hours.
• Plasma leakage occurs selectively in lungs and abdomen.
• However some patients may enter the critical phase while having high fever.

During this phase there may be significant fluid accumulation in the chest and abdominal cavity due to increased capillary permeability and leakage (Fig.8). This leads to depletion of fluid from the circulation and decreased blood supply to vital organs.

The main laboratory findings noted are leucopenia (White Blood Cell count less than 5000), Thrombocytopenia (low platelets or platelet count less than 100 000) in Full Blood Count (FBC). Thrombocytopenia can be seen 50% in DF and 100% in DHF.
Because dengue is caused by a virus, there is no specific medicine or antibiotic to treat it, the only treatment is to treat the symptoms. For typical dengue, the treatment is purely concerned with relief of the symptoms (symptomatic). Rest and fluid intake for adequate hydration is very important.
The mainstay of treatment is timely supportive therapy to tackle shock due to haemoconcentration and bleeding. Close monitoring of vital signs (pulse rate, blood pressure, and capillary refilling time) in the critical period (between day 2 to day 7 of fever) is vital. Increased oral fluid intake is recommended to prevent dehydration. Supplementation with intravenous fluids may be necessary to prevent dehydration and significant concentration of the blood if the patient is unable to maintain oral intake. The presence of bleeding may require red blood cell transfusion.

What to DO and What NOT to DO if you suspect Dengue Fever
What to DO

• Take only recommended dose of PARACETAMOL and hot water sponging to control fever

• Adequate fluids along with the patient's normal diet (Water, Milk, Fruit juices,
Kanji, ORS)
• The patient should take complete rest
• Immediately consult a qualified doctor or go to the nearest hospital if any of the following manifestations are present;

• No clinical improvement or worsening of the situation
• Persistent vomiting with blood,
• Severe abdominal pain
• Lethargy and/or restlessness, sudden behavioral change
• Black stools
• Giddiness
• Pale, cold clammy hands and feet
• Less/no urine output for 4-6 hours
• Bleeding from the nose or gums
• If a baby crying constantly
• Difficulty in breathing

What NOT to DO

• Taking pain relieving drugs : Aspirin, Diclofenac Sodium, Ibuprofen, Mefenamic acid and Steroids (NSAIDs)
• Resorting to unsolicited treatment methods
• Engaging in vigorous exercise and attending tution
• Do not wait until warning signs appear

Prevention and control

To avoid dengue it is important to break the link between virus, human and mosquito.

This is done through integrated vector control measures (IVM) aiming at both immature and adult stages of *Aedes* mosquito. IVM strategy incorporates the following environmental, biological/bio chemical methods, chemical methods, and law enforcement.

A. Environmental management
- Preventing mosquitoes from accessing egg-laying habitats by:
• Environmental modification (source reduction) – long lasting physical translation of vector breeding habitats to eliminate and/ or prevent mosquito breeding
eg. Disposal of solid waste properly and removing artificial man-made habitats

• Environmental manipulation (source reduction) – temporary changes in vector breeding habitats to prevent or to reduce breeding
eg. Covering, emptying and cleaning of domestic water storage containers on a weekly basis

• Personal protection (changes to human habitation or behaviour) – action to reduce human vector contact
eg. Using personal household protection such as window screens, long- sleeved clothes, insecticide treated materials (mosquito nets), coils and vaporizers, skin applicable repellents

B. Biological/ bio-chemical methods
• Biological – vector control agents parasitize and/or compete with the target vector species
eg. Larvivorous fish- guppy, nalahandaya, dandi, Bti
• Bio-chemical – interfere with the development of vector species
eg. Insect growth regulators (IGR)

C. Chemical methods - Applying appropriate insecticides for larval and adult mosquito control
• Chemical larviciding - applying insecticides to water storage outdoor containers
eg. Temephos
• Adult vector control - applying insecticides as space spraying
eg. Fogging

D. Intersectoral collaboration with Health education - improving community participation and mobilization for sustained vector control

E. Law enforcement – Taking legal action (spot fine, court case) against those who deliberately keep breeding places with larvae even after repeated notifying.

Active monitoring and surveillance of vectors should be carried out to determine effectiveness of control interventions.

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