A Review on: Dengue

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Summary

Dengue is a disease of many tropic and subtropics regions that can occur epidemically; caused by dengue virus, a member of the family "Flaviviridae". Dengue fever, also called dengue, is a potentially serious disease caused by a virus. There are four types of dengue virus that can cause illness in humans. Dengue viruses are transmitted between humans by the bite of an infected Aedes mosquito. Dengue is rare in the U.S., but is common and a serious public health threat in warm sub-tropical and tropical areas of the world. These include areas of Central and South America, Africa, Southeast Asia, China, India, the Middle East, Australia, the Caribbean and the South and Central Pacific. Dengue fever is most common in urban areas and outbreaks occur commonly during the rainy season when mosquitoes breed heavily in standing water. The incidence of dengue fever is on the rise worldwide, and in some areas of Asia, complications of the disease are a leading cause of serious illness and death in children. Treatment of acute dengue is supportive, using either oral or intravenous rehydration for mild or moderate disease, and intravenous fluids and blood transfusions for more severe cases. The rate of infection has increased dramatically over the last 50 years, with around 50–100 million people being infected yearly.

Keywords: Dengue, Dengue Fever, Hemorrhagic.

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Introduction

Dengue is "A disease of many tropic and subtropic regions that can occur epidemically; caused by dengue virus, a member of the family Flaviviridae".

Dengue fever, also called dengue, is a potentially serious disease caused by a virus. There are four types of dengue virus that can cause illness in humans. Dengue viruses are transmitted between humans by the bite of an infected Aedes mosquito. Dengue is rare in the U.S., but is common and a serious public health threat in warm sub-tropical and tropical areas of the world. These include areas of Central and South America, Africa, Southeast Asia, China, India, the Middle East, Australia, the Caribbean and the South and Central Pacific. Dengue fever is most common in urban areas and outbreaks occur commonly during the rainy season when mosquitoes breed heavily in standing water. The incidence of dengue fever is on the rise worldwide, and in some areas of Asia, complications of the disease are a leading cause of serious illness and death in children. Mosquitoes pick up a dengue virus when they bite a human who is already infected with the virus. The mosquito then carries it in its own blood and spreads it when it bites other humans. After a dengue virus enters the human bloodstream, it spreads throughout the body. Symptoms appear in about eight to ten days after a bite from an infected mosquito. Symptoms are flu-like and can include high fever, nausea, vomiting, body aches, and headache. Most people can recover from dengue fever, but some cases can progress into a life-threatening complication called dengue hemorrhagic fever. Symptoms of this disease include severe, uncontrolled hemorrhage and shock. For more information on symptoms, refer to symptoms of dengue fever. Making a diagnosis of dengue fever begins with taking a thorough personal and family medical history, including symptoms, and completing a physical examination. Recent travel to sub-tropical or tropical areas of the world is an important clue that may increase the suspicion of a diagnosis of dengue fever.

Dengue is usually transmitted by the mosquito *Aedes aegypti*, and rarely *Aedes albopictus*. The virus exists in four different types, and an infection with one type usually gives lifelong immunity to that type,but only short-term immunity to the others. There is currently no available vaccine, but measures to reduce the habitat and the number of mosquitoes, and limiting exposure to bites, are used to decrease the incidence of dengue. Treatment of acute dengue is supportive, using either oral or intravenous rehydration for mild or moderate disease, and intravenous fluids and blood transfusions for more severe cases. The rate of infection has increased dramatically over the last 50 years, with around 50–100 million people being infected yearly.

A global disease, dengue is currently endemic in more than 110 countries. Early descriptions of the condition date from 1779, and its viral cause and the transmission were elucidated in the early 20th century. Dengue has become a worldwide problem since the Second World War.

Types

Dengue fever is sub-typed as,

1. Classical

2. Haemorrhagic.

In the Classical type of fever, the patient displays all the typical symptoms, but the mortality rate is very low. The Haemorrhagic fever or 'Shock Syndrome' is the severe variety, which could be fatal. The patient suffers from high fever, bleeds from the nose, ears, gums and the skin and enters a state of shock due to blood loss. Most often death becomes inevitable and occurs within 24 hours, especially among children. This type of fever is fatal in 5% of those affected.

All four dengue virus (Den 1, 2, 3 and 4) infections may be asymptomatic or may lead to undifferentiated fever, dengue fever (DF), or dengue haemorrhagic fever (DHF) with plasma leakage that may lead to hypovolemic shock, dengue shock syndrome (DSS).

Manifestation of dengue virus infections:

> **Asymptomatic**
> **Symptomatic**

> **Undifferentiated Fever**
> - Dengue Fever
> - Without haemorrhage
> - With unusual haemorrhage
> - Dengue Haemorrhagic
> - No shock
> - DSS

According to the World Health Organization (WHO):

- ✓ Approximately 2.5 billion people, or two-fifths of the world's population, are now at risk from dengue.

- ✓ The disease is now endemic in over 100 countries.

- ✓ Dengue hemorrhagic fever is a leading cause of serious illness and death among children in some Asian countries.

- ✓ In 2007, there were over 890,000 reported cases of dengue in the Americas, of which 26,000 cases were DHF.

- ✓ Dengue infection rates among people who have not been previously exposed to the virus are commonly 40% to 50% during epidemics, but may sometimes reach 80% to 90%.

- ✓ Approximately half-a-million people with DHF are hospitalized each year, of whom many are children. About 2.5% of these patients die.

- ✓ DHF fatality reads may exceed 20% if untreated. If there is access to medical care with health care professionals trained in treating DHF, the death rate may be less than 1%.

Etiology
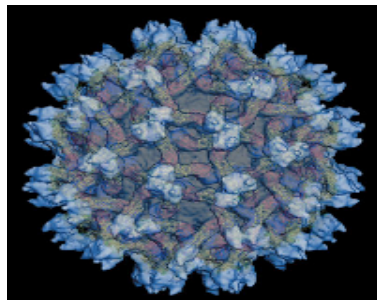
Etiologic agents

The Arenaviridae include the viruses responsible for Lassa fever and Argentine, Bolivian, Brazilian and Venezuelan hemorrhagic fevers.

The Bunyaviridae include the members of the Hantavirus genus that cause hemorrhagic fever with renal syndrome (HFRS), the Crimean-Congo hemorrhagic fever (CCHF) virus from the Nairovirus genus, and the Rift Valley fever (RVF) virus from the Phlebovirus genus.

The Filoviridae include Ebola and Marburg viruses.

Finally, the Flaviviridae include dengue, yellow fever, and two viruses in the tick-borne encephalitis group that cause VHF: Omsk hemorrhagic fever virus and Kyasanur Forest disease virus.

The most recently recognized virus capable of causing hemorrhagic fever is Lujo virus, a new member of the are naviruses described in 2009 and found in South Africa.

Pathophysiology

Dengue infection is caused by 1 of 4 related, but antigenically distinct, viral serotypes: dengue virus 1 (DENV-1), dengue virus 2 (DENV-2), dengue virus 3 (DENV-3), and dengue virus 4 (DENV-4). Genetic studies of sylvatic strains suggest that the 4 viruses evolved from a common ancestor in primate populations approximately 1000 years ago and that all 4 viruses separately emerged into a human urban transmission cycle 500 years ago in either Asia or Africa. Albert Sabin speciated these viruses in 1944. Each serotype is known to have several different genotypes.

Infection with one dengue serotype confers lifelong homotypic immunity and a very brief period of partial heterotypic immunity, but each individual can eventually be infected by all 4 serotypes. Several serotypes can be in circulation during an epidemic.

Dengue viruses are transmitted by the bite of an infected Aedes (subgenus Stegomyia) mosquito. Globally, A aegypti is the predominant highly efficient mosquito vector for dengue infection, but A albopictus and other Aedes species can also transmit dengue with varying degrees of efficiency.

Aedes mosquito species have adapted well to human habitation, often breeding around dwellings in small amounts of stagnant water found in old tires or other small containers discarded by humans. Female Aedes mosquitoes are daytime feeders. They inflict an innocuous bite and are easily disturbed during a blood meal, causing them to move on to finish a meal on another individual, making them efficient vectors. Entire families who develop infection within a 24- to 36-hour period, presumably from the bites of a single infected vector, are not unusual.

Humans serve as the primary reservoir for dengue; however, certain nonhuman primates in Africa and Asia also serve as hosts but do not develop dengue hemorrhagic fever. Mosquitoes

acquire the virus when they feed on a carrier of the virus. The mosquito can transmit dengue if it immediately bites another host. In addition, transmission occurs after 8-12 days of viral replication in the mosquito's salivary glands (extrinsic incubation period). The mosquito remains infected for the remainder of its 15- to 65-day lifespan. Vertical transmission of dengue virus in mosquitoes has been documented. The eggs of Aedes mosquitoes withstand long periods of desiccation, reportedly as long as 1 year, but are killed by temperatures of less than 10°C.

Once inoculated into a human host, dengue has an incubation period of 3-14 days (average 4-7 d) while viral replication takes place in target dendritic cells. Infection of target cells, primarily those of the reticuloendothelial system, such as dendritic cells, hepatocytes, and endothelial cells, result in the production of immune mediators that serve to shape the quantity, type, and duration of cellular and humoral immune response to both the initial and subsequent virus infections. Following incubation, a 5- to 7-day acute febrile illness ensues. Recovery is usually complete by 7-10 days.

Dengue hemorrhagic fever or dengue shock syndrome usually develops around the third to seventh day of illness, approximately at the time of defervescence. The major pathophysiological abnormalities caused by dengue hemorrhagic fever and dengue shock syndrome include the rapid onset of plasma leakage, altered hemostasis, and damage to the liver, resulting in severe fluid losses and bleeding. Plasma leakage is caused by increased capillary permeability and may manifest as hemoconcentration, as well as pleural effusion and ascites. Bleeding is caused by capillary fragility and thrombocytopenia and may manifest in various forms, ranging from petechial skin hemorrhages to life-threatening gastrointestinal bleeding. Liver damage manifests as increases in levels of alanine aminotransferase and aspartate aminotransferase, low albumin levels, and deranged coagulation parameters (PT, PTT).

In persons with fatal dengue hepatitis, infection was demonstrated in more than 90% of hepatocytes and Kupffer cells with minimal cytokine response (tumor necrosis factor [TNF]–alpha, interleukin [IL]–2). This is similar to that seen with fatal yellow fever and Ebola infections. Most patients who develop dengue hemorrhagic fever or dengue shock syndrome have had prior infection with one or more dengue serotypes. In individuals with low levels of neutralizing antibodies, nonneutralizing antibodies to one dengue serotype, when bound by macrophage and monocyte Fc receptors, have been proposed to result in increased viral entry and replication and increased cytokine production and complement activation. This phenomenon is called antibody-dependent enhancement.

Signs and Symptoms

Classic dengue fever is characterized by
Fever:
▶ Sudden and abrupt onset
▶ May go up to 39.5-41.4°C
▶ Lasts for about 1-7 days, then fades away for 1-2 days
▶ It soon recurs with secondary rashes which is usually not as severe as before
Headaches:
Fever is usually accompanied by headache in front portion of head or behind the eyes
Muscular (Myalgia) or bone pain:
▶Occurs after onset of fever
▶ Affects legs, joints, and lumbar spine
▶ Usually the pain gets severe after its onset
▶ The pain may last for several weeks even after the fever has subsided
▶ Pain is usually absent in DHF/DSS
Other symptoms:
▶ Nausea and vomiting
▶ Loss of appetite
▶ Increased sensation to touch
▶ Change in taste sensation

Rash -Red and white patchy rashes:
The illness is clinically indistinguishable from Influenza, Measles or Rubella. Initial stages of the disease resembles symptoms of dengue fever. However fever subsidies after 2 to 7 days followed by signs and symptoms of Restlessness Signs of circulatory failure Bleeding or hemorrhagic manifestations including:
✓ Skin bleeds that appear as blotchy red patches called - Petechiae
✓ Bleeding from Nose or Epistaxis
✓ Bleeding from gums
✓ Bleeding from Stomach - appearing as blood in the vomit
✓ Decrease in the blood platelet count (Thrombocytopenia).

Symptoms of
Dengue fever
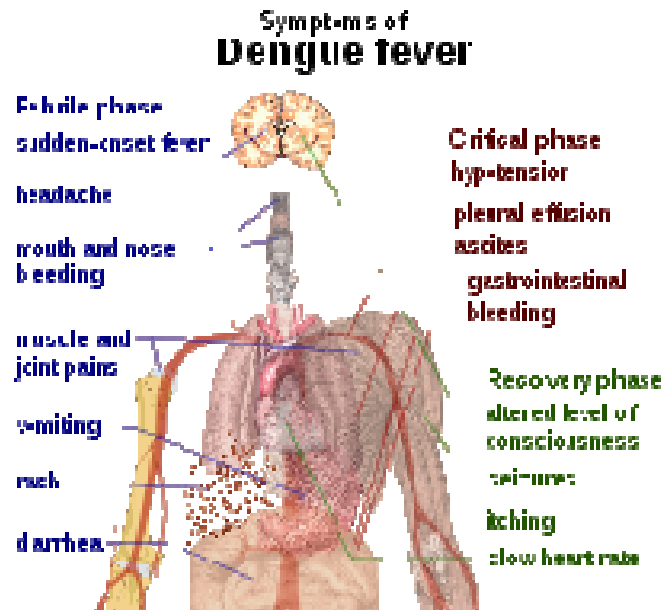
As there are different severities of dengue fever, the symptoms can vary.

Mild Dengue Fever –

Symptoms can appear up to seven days after the mosquito carrying the virus bites, and usually disappear after a week. This form of the disease hardly ever results in serious or fatal complications. The symptoms of mild dengue fever are:

- ✓ Aching muscles and joints

- ✓ Body rash that can disappear and then reappear

- ✓ High fever

- ✓ Intense headache

- ✓ Pain behind the eyes

- ✓ Vomiting and feeling nauseous

Dengue hemorrhagic fever (DHF) –

Symptoms during onset may be mild, but gradually worsen after a number of days. DHF can result in death if not treated in time. Mild dengue fever symptoms may occur in DHF, as well as the ones listed below:

- ✓ Bleeding from your mouth/gums

- ✓ Nosebleeds

- ✓ Clammy skin

- ✓ Considerably damaged lymph and blood vessels

- ✓ Internal bleeding, which can result in black vomit and feces (stools)

- ✓ Lower number of platelets in blood - these are the cells that help clot your blood

- ✓ Sensitive stomach

- ✓ Small blood spots under your skin

- ✓ Weak pulse

Dengue shock syndrome –

This is the worst form of dengue which can also result in death, again mild dengue fever symptoms may appear, but others likely to appear are:

- ✓ Intense stomach pain

- ✓ Disorientation

- ✓ Sudden hypotension (fast drop in blood pressure)

- ✓ Heavy bleeding

- ✓ Regular vomiting

- ✓ Blood vessels leaking fluid

- ✓ Death

Symptoms may be milder in children than in adults. The acute phase of illness can last for 1 week followed by a 1 to 2 week period of recovery period that is characterized by weakness, malaise and loss of appetite.

Causes of Dengue Fever

Dengue fever virus (DENV) is an RNA virus of the family Flaviviridae; genus Flavivirus. Other members of the same family include yellow fever virus, West Nile virus, St. Louis encephalitis virus, Japanese encephalitis virus, tick-borne encephalitis virus, Kyasanur forest disease virus, and Omsk hemorrhagic fever virus. Most are transmitted by arthropods (mosquitoes or ticks), and are therefore also referred to as arboviruses

(arthropod-borne viruses). The dengue virus genome (genetic material) contains of about 11,000 nucleotide bases, which code for the three different types of protein molecules that form the virus particle (C, prM and E) and seven other types of protein molecules (NS1, NS2a, NS2b, NS3, NS4a, NS4b, NS5) that are only found in infected host cells and are required for replication of the virus. There are four strains of the virus, which are called serotypes, and these are referred to as DENV-1, DENV-2, DENV-3 and DENV-4. All four serotypes can cause the full spectrum of disease. Infection with one serotype is believed to produce lifelong immunity to it but only short term protection against the others.

The severe complications on secondary infection seem to occur particularly if someone previously exposed to serotype DENV-1 then contracts serotype DENV-2 or serotype DENV-3, or if someone previously exposed to type DENV-3 then acquires DENV-2.

Diagnosis:

The diagnosis of dengue is typically made clinically, on the basis of reported symptoms and physical examination; this applies especially in endemic areas.[1] Early disease can however be difficult to differentiate from other viral infections.[4] A probable diagnosis is based on the findings of fever plus two of the following: nausea and vomiting, rash, generalized pains, low white blood cell count, positive tourniquet test, or any warning sign (see table) in someone who lives in an endemic area.[19] Warning signs typically occur before the onset of severe dengue.[7] The tourniquet test, which is particularly useful in settings where no laboratory investigations are readily available, involves the application of a blood pressure cuff for five minutes, followed by the counting of any petechial hemorrhages; a higher number makes a diagnosis of dengue more likely.[7] It may be difficult to distinguish dengue fever and chikungunya, a similar viral infection that shares many symptoms and occurs in similar parts of the world to dengue.[6] Often, investigations are performed to exclude other conditions that cause similar symptoms, such as malaria, leptospirosis, typhoid fever, and meningococcal disease.

The earliest change detectable on laboratory investigations is a low white blood cell count, which may then be followed by low platelets and metabolic acidosis.[4] Plasma leakage may result in hemoconcentration (as indicated by a rising hematocrit) and hypoalbuminemia.[4] Pleural effusions or ascites may be detected on clinical examination when large,[4] but the demonstration of fluid on ultrasound may assist in the early identification of dengue shock syndrome. The use of ultrasound is limited by lack of availability in many settings.

Here's how to diagnose dengue:

Observe the first symptoms of dengue. Facial flushing occurs in about half the cases and is a specific indicator of dengue. This is often accompanied by chills and a mottling of the skin. A fever usually begins on the third day and lasts five to seven days, sometimes reaching 104 degrees.

Obtain blood cell counts. A low white blood cell count is a common finding at the end of the feverish phase of dengue and is often accompanied by a reduced lymphocyte count. Monitor the

hematocrit and platelet count every day. A 20 percent rise in the hematocrit and a platelet count less than 100,000 are early warning signs of a progression to dengue hemorrhagic fever.

Run a metabolic panel. A low sodium level is the most common electrolyte imbalance. Patients in shock will also have elevated blood urea nitrogen and metabolic acidosis.

Confirm a diagnosis of dengue with serologic testing and polymerase chain reaction (PCR), if possible. This is important because the symptoms of dengue fever are nonspecific. The antibody titer of immunoglobulin M is most commonly measured with an enzyme-linked immunosorbent assay (ELISA.). A fourfold increase in antibody titers is considered confirmatory.

Use other tests to obtain antibody titers. These include a complement fixation, neutralization test, hemaggluination (HI) and an ELISA of immunoglobulin G.

Laboratory Diagnosis of Dengue Fevers

Confirmed diagnosis of dengue infection requires lab tests:

1. Platelet count:

Any fever not settling down after three or four days should invite further tests like a blood count, a routine urine and chest x-ray. In countries like India one should also keep in mind malaria and do test to rule out the infection. Dengue fever is usually charcterised by lowering of platelets in the blood. It is due to the lack of platelets that the person is more prone to bleeding episodes. The platelets plug the bleeding points and their lack can lead to bleeding. Thrombocytopenia or platelets less than 100 000 cells per mm^3 may be seen in dengue. The platelet count may need to be repeated everyday if they show a lowering trend. If these keep going down it is best to hospitalise the patient for further treatment. In severe cases platelet transfusion may be required.

2. Hematocrit Test:

Hemorrhagic dengue fever leads to leakage from blood vessels and this can lead to increased vascular permeability. This is manifested by one or more of the following - Increase by more than 20% in average hematocrit for age and sex.

3. Detecting specific antibodies:
Serologic diagnosis requires collection of serum within 6 days after onset of symptoms. The serum is tested for detecting specific anti-dengue antibodies by Enzyme-linked Immunosorbent assay (ELISA). Increase of a fourfold concentration of IgG or IgM antibody titers to one or more of the dengue virus antigens in serum sample is diagnostic of dengue fever.

4. Isolation of the virus:
Isolation of virus requires collection of serum sample from patients within 5 days after appearance of symptoms. To do the isolation of virus a 'Polymerase Chain Reaction (PCR)' is done. This detects the viral genomic sequence from Serum samples. (9)

Prevention

Prevention of Dengue Fever is easy, cheap and better. What is required are some simple measures for -

> ➢ Preventing breeding of Aedes mosquitoes
> ➢ Protection from Aedes mosquitoes' bites.

There are currently no approved vaccines for the dengue virus. Prevention thus depends on control of and protection from the bites of the mosquito that transmits it.

The World Health Organization recommends a Integrated Vector Control program consisting of five elements:

- Advocacy, social mobilization and legislation to ensure that public health bodies and communities are strengthened.
- Collaboration between the health and other sectors (public and private).
- An integrated approach to disease control to maximize use of resources.
- Evidence-based decisions making to ensure any interventions are targeted appropriately.
- Capacity-building to ensure an adequate response to the local situation.

The primary method of controlling A.aegypti is by eliminating its habitats. This may be done by emptying containers of water or by adding insecticides or biological control agents to these areas. Reducing open collections of water through environmental modification is the preferred method of control, given the concerns of negative health effect from insecticides and greater logistical difficulties with control agents. People may prevent mosquito bites by wearing clothing that fully covers the skin and/or the application of insect repellent (DEET being the most effective). A number of novel methods have been used to reduce mosquito numbers with some success including the placement of the fish Poecilia reticulata or copepods in standing water to eat the mosquito larva.

There are ongoing programs working on a dengue vaccine to cover all four serotypes. One of the concerns is that a vaccine may increase the risk of severe disease through antibody-dependent enhancement. The ideal vaccine is safe, effective after one or two injections, covers all serotypes, does not contribute to ADE, is easily transported and stored, and is both affordable and cost-effective. A number of vaccines are currently undergoing testing. It is hoped that the first products will be commercially available by 2015.

The best way to prevent dengue fever is to take special precautions to avoid contact with mosquitoes. Several dengue vaccines are being developed, but none is likely to be licensed by the U.S. Food and Drug Administration in the next few years. (8)

When outdoors in an area where dengue fever has been found,

➢ Use a mosquito repellant containing DEET.

➢ Dress in protective clothing—long-sleeved shirts, long pants, socks, and shoes.

➢ Because Aedes mosquitoes usually bite during the day, be sure to use precautions especially during early morning hours before daybreak and in the late afternoon before dark.

Other precautions include

• Keep unscreened windows and doors closed.

• Keep window and door screens repaired.

• Get rid of areas where mosquitoes breed, such as standing water in flower pots or discarded tires.

For protection against mosquitoes –

1. Mosquitoes breed only in water sources such as stagnant water in drains and ditches, room air coolers, broken bottles, old discarded tyres, containers and similar sources.

✓ Don't allow water to remain stagnant in and around your house. Fill the ditches. Clean the blocked drains. Empty the room air coolers and flower vases completely atleast once in seven days and let them dry. Dispose off old containers, tins and tyres etc. properly.

✓ Keep the water tanks and water containers tightly covered so that the mosquitoes cannot enter them and start breeding.

✓ Wherever it is not possible to completely drain the water off from room cooler, water tanks etc., it is advised to put about two tablespoons (30 ml.) of petrol or kerosene oil into them for each 100 litres of water. This will prevent mosquito breeding. Repeat it every week.

✓ You can also put some types of small fish (Gambusia, Lebister) which eat mosquito larvae into these water collections. These fish can be obtained from the local administrative bodies (e.g., Malaria Officer's office in the area).
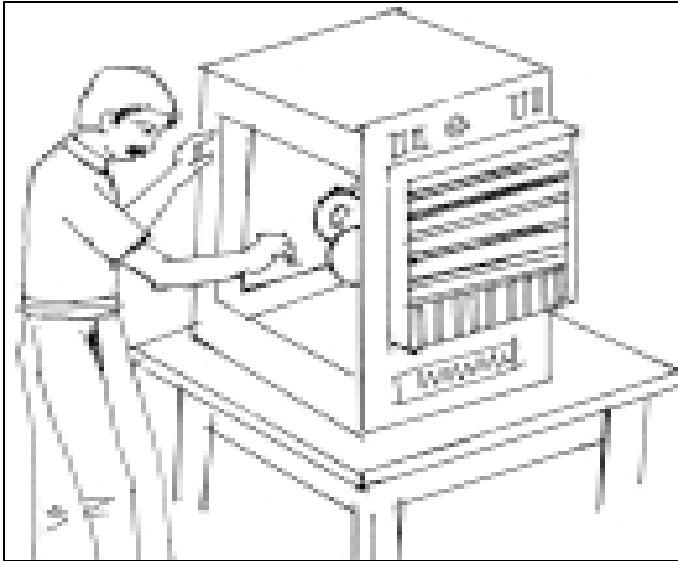
✓ Wherever possible, practicable and affordable, prevent entry of mosquitoes into the house by keeping wire mesh on windows and doors.

✓ Use mosquito repellent sprays, creams, coils, mats or liquids to drive away/ kill the mosquitoes. Use of googal smoke is a good indigenous method for getting rid of mosquitoes.

✓ Wear clothes which cover the body as much as possible. This is more relevant in case of children. Nickers and T-shirts are better avoided during the season of Malaria and Dengue fever, i.e., from July to October.

✓ Don't turn away spray workers whenever they come to spray your house. It is in your own interest to get the house sprayed.

✓ Use insecticidal sprays in all areas within the house atleast once a week. Don't forget to spray behind the photo-frames, curtains, calendars corners of house, stores.

✓ Keep the surroundings of your house clean. Don't litter garbage. Don't allow wild herbs etc. to grow around your house (atleast in a radius of about 100 metres around your house). They act as hiding and resting places for mosquitoes
.

✓ Do inform and take help from your local health centre, panchayat or municipality in case you notice abnormal density of mosquitoes or too many cases of fever are occurring in your area.
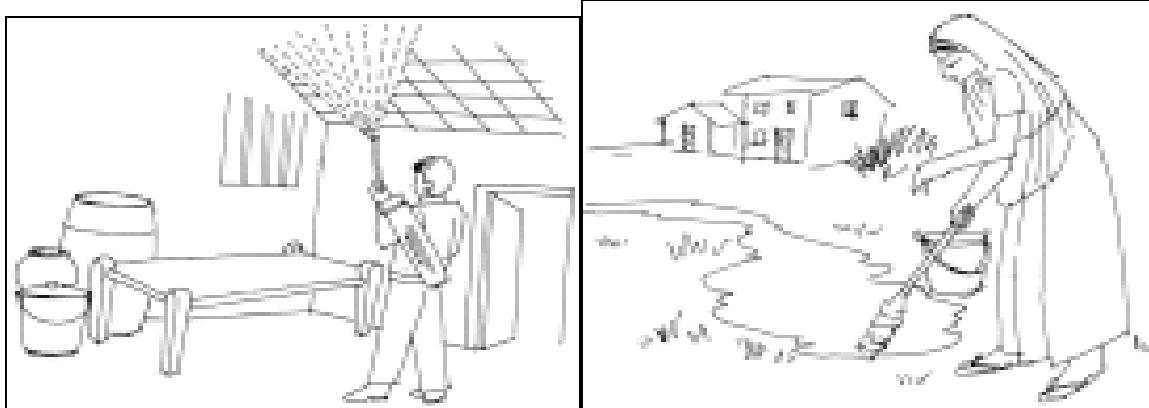
It is good to remember that Aedes mosquitoes bite even during daytime and hence you should take precautions against their bite during day time also. If fencing of the doors and windows is not possible due to any reason, spray the entire house daily with pyrethrum solution.

Dengue fever occurs most frequently in India in the months of July to October because this season provides very suitable conditions for breeding of mosquitoes. Hence all these preventive steps must be taken during the season.
Lastly, it is advisable to always keep the patient of Dengue fever under a mosquito net in the first 5-6 days of the illness so that mosquitoes don't have an access to him/her. This will help in reduction in spread of Dengue fever to other persons in the Community. (10)
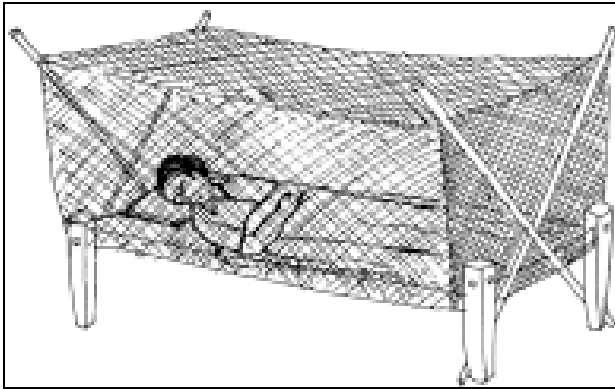
Treatment

There are no specific anti-viral tablets or injections that can kill the virus. However a lot of supportive care and treatment can go a long way to save a patient suffering from dengue fever.

Fever is treated by anti-pyretics, like paracetamol. Pain in the bone should be treated by analgesics or pain killing tablets. In case of Dengue Hemorrhagic Fever or Dengue Shock Syndrome hospitalization is a must. The mortality rate in the absence of hospitalization can be as high as 50%. With proper treatment the mortality comes down to 3%. More supportive treatment, like intravenous fluid replacement is required to prevent shock in these patients. Vaccines are being developed against all 4 serotypes and they will definitely be the most effective way to prevent the disease. Prevention of mosquito breeding has by and large failed in most endemic countries. Patients are prone to dehydration hence they should drink plenty of fluids. If necessary a few days of intra-venous fluids can be administered in the form of normal saline or dextrose saline. In some cases, oxygen is helpful. Steroids are not known to help.

If it is classical (simple) Dengue Fever, the patient can be managed at home. As it is a self-limiting disease, the treatment is purely supportive and symptomatic e.g. –

- Keep the fever low by giving paracetamol tablet or syrup as per health worker's advise.
- Avoid giving Aspirin or Dispirin tablets to the patient
- If fever is more than 102°F, carry out hydrotherapy to bring down the temperature.
- Give plenty of fluids water, shikanji etc. to the patient.
- Continue normal feeding. In fever, the body, infact, requires more food.
- Allow the patient to rest. If any of the symptoms indicative of DHF or DSS develop, rush the patient to the nearest hospital at the earliest where appropriate investigations will be carried out and necessary treatment instituted, e.g., transfusion of fluids or platelets (a kind of blood cells which become low in DHF and DSS). Please remember that every patient does not require blood platelet transfusion.(11)

Intravenous fluids if used are usually only needed for one or two days. Fluids are titrated to a urinary output of 0.5–1 mL/kg/hr, stable vital signs and normalization of hematocrit. Procedures that increase bleeding risk such as nasogastric tubes, intramuscular injections and arterial punctures are avoided. Acetaminophen may be used for fever and discomfort while NSAIDs such as ibuprofen or aspirin are avoided due to an increased bleeding risk. The need for blood transfusions is based on the presence of unstable vital signs and a decreasing haematocrit rather than the usual haematocrit of less than 30% used in sepsis. Packed red blood cells or whole blood are recommended, while platelets and fresh frozen plasma are usually not.

During the recovery phase intravenous fluids are discontinued to prevent a state of fluid overload. If fluid overload occurs and vital signs are stable, stopping further fluid may be all that is needed. If a person is outside of the critical phase, the loop diuretic furosemide may be used to eliminate excess fluid from the circulation.

Though specific treatment's of dengue fever is not yet, evolved, there are several antiviral vaccines and antiviral drugs were prepared to prevent the peoples from dengue virus infection.

Dengue vaccines:

Live attenuated vaccines (LAVs) can induce durable humoral and cellular immune responses since they most closely mimic a natural infection. Several parameters are crucial for LAVs:

- The viruses must be sufficiently attenuated and viral replication reduced so that viraemia is low and symptoms of illness are minimal.
- Transmission of the viruses by mosquitoes is reduced or eliminated.
- The viruses should replicate well in cell culture and be sufficiently immunogenic to provide long-lasting immunity in humans, so that low doses can be used.
- A balanced immune response to all four dengue viruses must be elicited.
- The genetic basis for attenuation must be known and must be stable.

Several live attenuated vaccines are in advanced stages of development. One is a chimeric tetravalent vaccine in which the structural genes (prM and E) of each of the

four dengue viruses were inserted individually to replace those of yellow fever virus

in the backbone of the yellow fever 17D vaccine. Thus, the nonstructural genes of

Yellow fever are provided to allow replication of the chimeric virus, and attenuation is imparted by the yellow fever portion of the chimera. Monovalent vaccines, as well as tetravalent mixtures of all four viruses, have been given to human volunteers of varying ages in phase 1 and phase 2 trials in both non-endemic and endemic regions. At least two doses were required to achieve high rates of tetravalent neutralizing antibodies, and somewhat higher seroconversion rates were observed in subjects with pre-existing immunity to yellow fever.

Dengue antiviral drugs

It is very difficult task to evolve the antiviral drug on dengue. Still there are very few significant and efficient drugs evolved on dengue. Many of scientist's were give description about the targets on which the anti viral drugs should be act, they are listed as bellow:

- Dengue virus structural proteins as potential drug targets.
- Dengue virus nonstructural proteins as potential drug targets.
- Dengue virus ns3 protease as a potential drug target.
- Others drugs.

Conclusion

Dengue has been considered as the most dreadful disease and mortal. It is caused by the Aedes Agypti mosquito. Dengue and chikenguniya more or less caused by same similar viruses. Severe pain, severe internal bleeding are the various symptoms. Decrease in platelate count leading for the fatal and death.

Dengue is caused by the negligence of enviormental hygienic, stored water/ retention of sewage. Severe garbage will lead for the genesis of life ated Mosquito's. Man should live in life healthy without diseases.

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