Molecular Medicine

Dengue Virus-Danger from Deadly Little Dragon



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Vector (A carrier)

- From the perspective of infectious diseases, vectors are the transmitters of disease-causing organisms that carry the pathogens from one host to another
- Different types of vectors

Invertebrate animals, usually arthropods
Vertebrates can also act as vectors (includes foxes, raccoons, and dogs) Ex:Rabies

- Arthropods account for over 85 percent of all known animal species, and they are the most important disease vectors.
- \succ mosquitoes and ticks are the most notable disease vectors.

Environmental effects of Global changes that drives potential VBD

- Increasing urban populations
- Expanding mosquito breeding due to:
 - Onreliable water supply
 - Traditional water storage practices
 - Poor garbage collection (creates more mosquito breeding places)
 - Changing lifestyles
- Rapid transportation:
 - Movement of infected humans
 - Spread of dengue mosquitos

Other related factors: inadequate health education, limited financial resources, insufficient mosquito control programmes, and resistance of mosquitos to insecticides.



Vector-borne infections differ from other diseases in that one, or sometimes more than one, intermediate host is necessary for the transmission to occur



Vector-Borne

Diseases

Transmission of Vector-Borne Infection

Mode of Transmission

Biological transmission

- Most significant mode of vectorborne disease
- The pathogen multiplies within the vector
- Most protozoa and helminths are transmitted biologically
- The pathogen is transmitted when the arthropod takes a blood meal

Mechanical transmission

- The vector simply carries the parasite in or on its body from one host to another
- Viruses and bacteria are transmitted mechanically



- The word dengue is derived from African word denga: meaning fever with hemorrhage
- Dengue (pronounced den' gee) is a disease caused by any one of four closely related dengue viruses





Epidemiological Trends



Dengue primarily affects the tropical countries

Figure 1 World distribution of the predominant dengue mosquito vector (*Aedes aegypti*) and areas with dengue epidemic activity.



World Health Organization The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement. © WHO 2008. All rights reserved

Data Source: DengueNet, World Health Organization Map Production: Public Health Information and Geographic Information Systems (GIS)

RECENT REPORT IN TAMIL NADU

2,000 CASES IN 2 MONTHS Many dengue cases were reported in parts of Tirunelveli in the past two months (2,000 cases and 29 deaths, as per official figures). (The Hindu, 2012)



First Out break of , DF- 1812, New Delhi- 1967,1970,1982, &1996 DHF-Calcutta between July 1963 & March 1964



The dengue special ward at Tirunelveli Medical College Hospital overflowing. The central team[®] members visited the hospital, where around 100 dengue patients, including 50 children are undergoing treatment.

Photo: A.Shaikmohideen

Characteristic of the Dengue Virus

- 1. It is an arbovirus
- 2. Single-stranded RNA virus (Flaviviridae family)
- 3. Has 4 serotypes (DEN-1, 2, 3, 4)
- 4. Viral genome is 11 kb in length
- 5. Dengue virion are spherical particles approximately 50 nm in diameter.





6. seven structural proteins required for replication of the virus.

7. Infection in human by one serotypes produces life long immunity against re-infection by the same serotype but only short term protection against the others.

8. Subsequent infection with other serotypes may result in a severe illness ie., DHF or DSS

VIRUS



Mosquito vectors in Dengue Infection



Aedes aegypti

They are approximately 5 mm in size:

ا<u>اسا</u> 5 mm



Magnified 5 times

- The most common epidemic vector of dengue in the world is the Aedes aegypti mosquitoes of the stegomyia family.
- Aedes mosquitoes (Tiger mosquito) distinguished by white stripes or scale patterns on its legs and thorax
- All 4 types of virus have been recovered from it
- Important members aedes family:
- A.aegypty, A.polynesiensis and A. albopictus.
- They are most abundant during rainy season.

- > Lives around human habitation
- Lays eggs and produces larvae preferentially in artificial containers
- Lays egg singly, and eggs are cigar shaped.
- > They do not fly over long distance-

<100mts (110yards), this factor facilitates its eradication.

- Dengue transmitted by infected female mosquito
- Primarily a daytime feeder (Early Morning & Late After noon)



1.The virus is inoculated into humans with the mosquito saliva.

2.The virus localizes and replicates in various target organs, for example, local lymph nodes and the liver.

3.The virus is then released from these tissues and spreads through the blood to infect white blood cells and other lymphatic tissues.

4.The virus is then released from these tissues and circulates in the blood.







5. The mosquito ingests blood containing the virus.

6.The virus replicates in the mosquito midgut, the ovaries, nerve tissue and fat body. It then escapes into the body cavity, and later infects the salivary glands.

7. The virus replicates in the salivary glands and when the mosquito bites another human, the cycle continues.

8. Dengue virus may be transmitted sexually from male to female mosquitoes.

Clinical manifestation of Dengue Infection

There are actually four dengue clinical syndromes:

Undifferentiated fever
Classic dengue fever -90%
Dengue hemorrhagic fever, or DHF -7% &
Dengue shock syndrome, or DSS- 3%.

Dengue shock syndrome is actually a severe form of DHF.

Clinical case definition

Clinical Case Definition for Dengue Fever

Classical Dengue fever or **Break bone fever** is an acute febrile viral disease frequently presenting with



The Spectrum of Dengue Haemorrhagic Fever



- 1. Fever, or recent history of acute fever
- 2. Hemorrhagic manifestations
- 3. Low platelet count (100,000/mm3 or less)
- 4. Objective evidence of "leaky capillaries:"

Symptoms – Dangerous form

- Blood vessels are affected
- There is severe oozing into tissues
- Bleeding into all possible parts of body
- Blood clotting mechanism is disrupted
- Blood pressure falls and many end in collapse and death









Hetrologous Ab form Infectious complexs



LABORATORY DIAGNOSIS OF DENGUE INFECTIONS

Virus isolation

- Mosquito cell lines.
- Mosquito inoculation technique.

Serum, Plasma Leucocytes

Serological diagnosis

- Haemagglutination inhibition test.
- ELISA.

Molecular diagnostic methods

RT-PCR.

Prevention and Control of Dengue

1. Elimination of mosquito breeding places

- Cover water containers—Tight covers on water storage containers, will prevent the mosquitos laying their eggs there. If the cover is loose, mosquitos can go in and out.
- Septic tanks and soak-away pits—Cover and seal these, so that dengue mosquitos cannot breed there.
- Removal of rubbish—Garbage articles and other rubbish found around houses can collect rain water. They should be removed or smashed and buried in the ground or burned, where this is permissible.

Health education campaigns

The first step in action against the dengue mosquito is to inform communities about what dengue is and what measures can be taken to combat it.

2. Prevent mosquito bites

People can protect themselves from mosquito bites by using any of the following means—

- Mosquito coils and electric vapour mats—Slow burning mosquito coils or electric vapour mats are effective in the rainy season, just after sunrise and/or in the afternoon hours before sunset, when dengue mosquitos bite.
- Mosquito nets—Nets placed over sleeping places can protect small children and others who may rest during the day. The effectiveness of such nets can be improved by treating them with permethrin (a pyrethroid insecticide). Curtains (cloth or bamboo) can also be treated with insecticide and hung at windows or doorways, to repel or kill mosquitos.
- Repellents—Mosquito repellents can be applied to exposed parts of the body where mosquitos bite. Care should be taken in using repellents on small children and the elderly.
- Screens—Screens on windows and doorways are effective protection against the entry of mosquitos in homes.
- Protection of people sick with dengue—Mosquitos become infected when they bite people who are sick with dengue. Mosquito nets and mosquito coils will effectively prevent mosquitos from biting sick people and help stop the spread of dengue.

Vector Control Methods:

Chemical Control:

Larvicides may be used to kill immature aquatic stages

•Ultra-low volume fumigation against adult mosquitoes

Insecticides (4% malathion & 1% fenitrothion)

Mosquitoes may have resistance to commercial aerosol sprays

•Temephos sand corals (Larvicide) in water tanks kill mosquito larva

BIOLOGICAL CONTROL

- Larvivorous fish such as Gambusia affinis and poecilia reticulate
- Endo toxin producing Bacteria Bacillus Thuringiensis serotype H14 and Bacillus sphaericus.
- Recently, a few countries have also reported success in controlling larvae with mesocyclops (a copepods, small invertebrate crustaceans) that feed on firstand second-stage mosquito larvae.

Current status of Dengue Vaccine

- Recombinant proteins containing B domains of Dengue virus serotype 1-4 were fused to maltose binding protein of *E. coli* and evaluated in mice as a single or tetravalent vaccine
- It may produce specific neutralizing antibodies to all four dengue serotypes
- Significantly greater than Monovalent vaccine

Reference:

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- 2. http://www.cdc.gov/
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- 4. Postgrad Med J 2004;80,588-601

THANKS FOR YOUR ATTENTION!!!!!!!!