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Dengue epidemic: Homoeopathic approach

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Abstract
Global incidence of Dengue has noticeably increased worldwide in recent years. Dengue is a mosquito-borne viral infection, commonly found in tropical and sub-tropical climates worldwide. Dengue virus is responsible for the disease to commence in 4 different types (serotypes). Severe Dengue is serious leading cause of serious illness and death in various Asian and Latin American countries. Dengue is an acute viral infection with potential fatal complications so early detection of disease progression with severe dengue and proper medical care helps in lowering fatality rates of severe dengue. Homoeopathy has long success record in treatment of Epidemics and is recognized for secondary level prevention of dengue fever during outbreaks.

Keywords: Dengue, dengue fever, dengue shock syndrome, dengue haemorrhagic fever, homoeopathy

Introduction
As per WHO, Dengue has rapid spread in all regions in recent years which is a mosquito-borne disease. Dengue virus commonly spread through female mosquitoes mainly of Aedes aegypti and to a lesser extent, Aedes albopictus. Every year, an average estimate of 100-400 million infections of Dengue virus is seen [1]. Dengue causes a wide spectrum of disease ranging from sub-clinical disease to severe flu-like symptoms. Severe dengue has a higher risk of death when it is not managed timely. Dengue is endemic in south-east Asia, India, Africa and America [4]. Asia continues to bear the burden of high dengue cases and South-east Asia, the tropical and warmer part of Asia, reported higher cases, mortality and morbidity rates of dengue annually [7].

Dengue fever was first referred as “water poison” associated with flying insects in a Chinese medical encyclopedia in 992 from the Jin Dynasty (265-420 AD). The term ‘Dengue’ is Spanish attempt at the swahii phrase “ki denga pepo” which means ‘cramp like seizure caused by an evil spirit’. It emerged during a Caribean outbreak in 1827-1828. The first clinically recognized dengue epidemics occurred almost simultaneously in Asia, Africa, and North America in the 1780s. The first clinical case reported dates from 1789 of 1780 epidemic in Philadelphia is by Benjamin Rush, who coined the term “break bone fever” because of the symptoms of myalgia and arthralgia. The term dengue fever came into general use only after 1828. The first epidemic of clinical dengue-like illness was recorded in Madras (now Chennai) in 1780 and the first virologically proved epidemic of DF in India occurred in Calcutta and Eastern Coast of India in 1963-1964 [18, 19, 20]. Since then, India faced many outbreaks of Dengue Epidemic; the latest being in 2020. In 2021, dengue continues to affect Brazil, Cook Islands, Colombia, Fiji, Kenya, Paraguay, Peru and Reunion Island.

The COVID-19 pandemic is placing immense pressure on health care and management systems worldwide. WHO has emphasized the importance of sustaining efforts to prevent, detect and treat vector-borne diseases such as dengue and other arboviral diseases during this crucial period, as case numbers increase in several countries, exposing urban populations at highest risk for both diseases. The combined impact of COVID-19 and dengue epidemics can potentially result in devastating consequences for the populations at risk. The post-Zika outbreak period (after 2016) saw a decline of cases of dengue and the exact factors leading to this fall are still unknown [1].

With the rising incidence of dengue and dengue hemorrhagic fever, some homoeopathic practitioners and associations have approached the Central Council for Research in Homoeopathy (CCRH) for providing guidelines for treatment and prevention of dengue. The Council has prepared the guidelines from various guidelines issued by different authorities (such as World Health Organization, National Vector Borne Disease Control Program, etc.) and from` the experiences of senior homoeopathic practitioners.

Epidemiology

Almost half of the world's population i.e., about 4 billion people, live in areas with risk of Dengue. Dengue is often a leading cause of illness in areas with risk. Each year, up to 400 million people get infected with dengue. Approximately 100 million people get sick from infection, and 40,000 die from severe dengue [6].

One modelling estimate indicates 390 million dengue virus infections per year (95% credible interval 284–528 million), of which 96 million (67–136 million) manifest clinically (with any severity of disease) [21]. Another study on the prevalence of dengue estimates that 3.9 billion people are at risk of infection with dengue viruses. Despite a risk of infection existing in 129 countries [22], 70% of the actual burden is in Asia [21].

The number of dengue cases reported to WHO increased over 8 fold over the last two decades, from 505,430 cases in 2000, to over 2.4 million in 2010, and 5.2 million in 2019. Reported deaths between the year 2000 and 2015 increased from 960 to 4032 [1].

Etiology

Dengue is caused by any four of serotypes DENV-1, DENV-2, DENV-3, DENV-4 of single stranded RNA (ss RNA) viruses of the genus Flavivirus [8]. Dengue virus is spread by *Aedes* mosquitoes, and the most common vectors are *Aedes aegypti*, followed by *Aedes albopictus*, *Aedes polynesiensis*, and *Aedes sutellaris* [9].

Pathophysiology

Part of the *Flavivirus* family, the dengue virus is a 50 nm virion with three structural and seven nonstructural proteins, a lipid envelope, and a 10.7 kb capped positive sense single strand of ribonucleic acid. Infections are asymptomatic in up to 75% of infected humans. A spectrum of disease, from self-limiting dengue fever to hemorrhage and shock, may be seen. A fraction of infections (0.5% - 5%) progress to severe dengue. Without proper treatment, fatality rates may exceed 20%. These occur primarily in children. The typical incubation period for the disease is 4 to 7 days, but it can last from 3 to 10 days. Symptoms more than two weeks after exposure are unlikely to be due to dengue fever.

The exact course of events following the dermal injection of dengue virus by a mosquito bite is unclear. Skin macrophages and dendritic cells appear to be the first targets. It is thought that the infected cells then move to the lymph nodes and spread through the lymphatic system to other organs. Viremia may be present for 24 to 48 hours before the onset of symptoms. A complex interaction of host and viral factors then occurs and determines whether the infection will be asymptomatic, typical, or severe. Severe dengue fever with increased micro-vascular permeability and shock syndrome is thought to be associated with infection due to a second dengue virus serotype and the patient's immune response. However, cases of severe dengue do occur in the setting of infection by only a single serotype. Worsening micro-vascular permeability often transpires even as viral titers fall.

Classification

The WHO classifies Dengue Fever into 2 groups [2, 3].

1. Uncomplicated.
2. Severe.

The four serotypes of dengue viruses are all transmitted by the mosquito Aedes aegypti, which is also a vector for yellow fever. The incubation period is of 4-7 days. After that, sudden onset of fever, frontal headache, retroorbital pain, back pain, severe myalgia (break-bone fever), adenopathy, palatal vesicles and sclera injection [5].

- The illness usually lasts for a week and maculopapular rash often appears near the time of defervescence (usually day3-5).
- A second infection with a different dengue serotype can lead to severe dengue (previously called dengue haemorrhagic fever) [5].

Severe dengue: Previous infection with a heterologous dengue virus serotype may elicit non-protective antibodies and exacerbate disease if there is re-infection. Dengue can manifest with a wide spectrum of clinical presentations, ranging from a mild non-specific febrile syndrome to severe symptoms, including plasma leakage [10].

- In mild cases, lethargy, thrombocytopenia, hemoconcentration occur within 2-5 days.
- In severe cases, frank shock occurs with cyanosis, hepatomegaly, ascites, pleural effusion and GI bleeding. The period of shock lasts for 1-2 days.
- The risk decreases considerably after age 12.
- Severe Dengue is more common in females and more common if dengue virus 1 as opposed to dengue virus 4- precedes infection with dengue virus 2 [5].

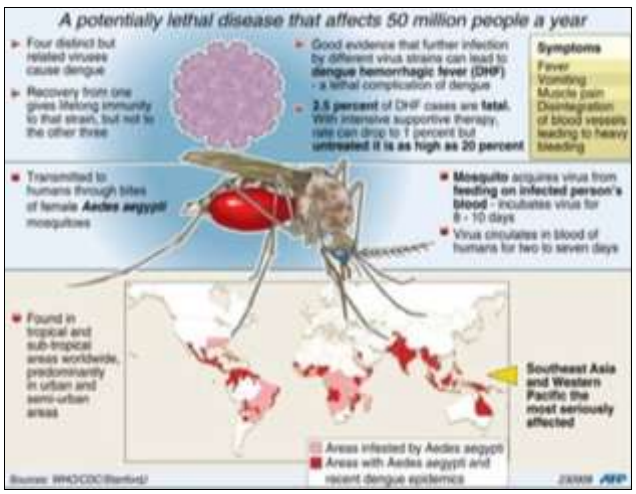

Fig 1: Dengue fever

Severe manifestations

Dengue haemorrhagic fever and dengue shock syndrome

Viral Haemorrhagic Fever syndrome is constellation of findings based on vascular instability and decreased vascular integrity. All these severe manifestations occasionally complicate infection: Circulatory failure, features of capillary leak syndrome and disseminated intravascular coagulation (DIC) with haemorrhagic complications such as petechiae, ecchymoses, epistaxis, Gastro-intestinal bleeding and multi-organ failure [4].

Other complications

1. Encephalitis
2. Hepatitis
3. Myocarditis
4. Liver injury
5. Cardiomyopathy
6. Pneumonia
7. Orchitis
8. Oophoritis
9. Seizures
10. Encephalopathy

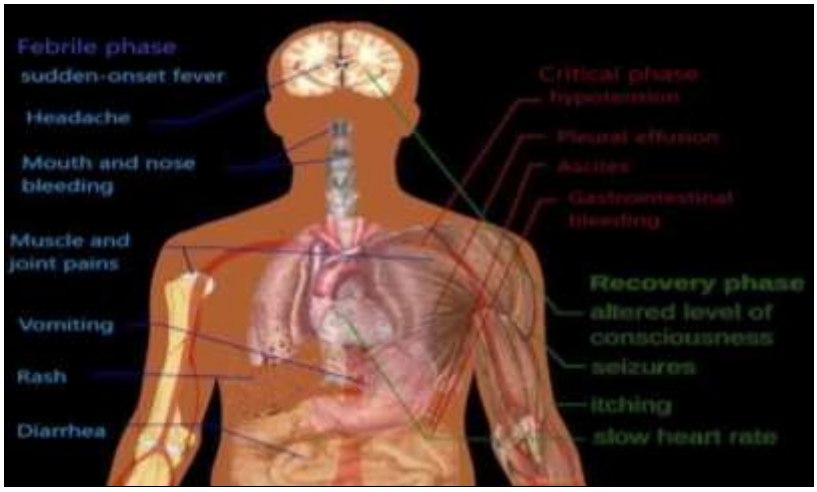

Fig 2: Dengue hemorrhagic fever and dengue shock syndrome viral hemorrhagic fever syndrome is a group of findings based on vascular instability and decreased vascular integrity.

Diagnosis

Diagnosis is made by IgM ELISA or paired serologic tests during recovery or by antigen-detection ELISA or paired serologic tests during recovery or antigen-detection ELISA or RT-PCR during the acute phase.

- Virus is easily isolated from blood during the acute phase by inoculation of mosquitoes or mosquito cell culture.
- Leucopenia, Thrombocytopenia and increased serum aminotransferase levels may be documented.
- No laboratory tests can predict the progression to severe disease.
- In epidemic situation, for every patient reporting with fever, platelet count and hematocrit estimation is recommended, unless some other cause for the fever is identified.

Prevention/management

1. Personal prophylactic measures

- Not allowing the water to settle in the surrounding areas.
- Mosquito repellents or mosquito nets should be used.
- Full body covering can also helps in protecting ourselves.
- Use mosquito repellent creams, liquids, coils, mats, etc.
- Use bed nets for sleeping infants and young children to prevent mosquito bite

2. Environmental management & source reduction methods

- Identify & eliminate mosquito breeding sources
- Prevent collection of waters on roof tops, porticos and sunshades.
- Properly cover stored water
- Frequently change water in water pots, flower vases, water coolers, etc.
- Waste must be disposed properly and should not be allowed to collect

3. Biological & Chemical control for control of mosquitoes breeding

- Use larvivorous fishes in ornamental tanks, fountains, etc.
- Use biocides or chemical larvicides for control of mosquitoes breeding
- Aerosol space spray

4. Health education

Impart knowledge to common people regarding measures to reduce vector breeding and safeguards for preventing mosquito bites.

As mentioned in the guidelines of CCRH, the approach towards patients suffering from dengue/suspected to be suffering from dengue involves detailed history taking and examination, which includes details of onset & nature of fever/illness and assessment for warning signs (hemorrhage from any orifice, hypotension, persistent vomiting, inability to tolerate oral fluids). Conditions, in which, dengue is likely to be more severe must also be identified.

Examination includes assessment of hydration and hemodynamic status (pulse, systolic and diastolic blood pressure), checking for tachypnoea, pleural effusion, examination of rash and bleeding manifestations, assessment of abdominal tenderness, ascites and

hepatomegaly. Appropriate investigations are advised for diagnosis and assessment of disease severity. Individual characterizing symptoms specially physical and mental generals should be recorded for the selection of appropriate Homoeopathic regimen.

Follow up of the patients requires strict monitoring for temperature pattern, volume of fluid intake and losses, urine output (volume and frequency) and appearance of warning signs. The investigations for hematocrit and platelet counts are important to assess the progress of each case.

Medicines most frequently indicated in cases of classical dengue fever are *Aconitum napellus, Arsenic album, Bryonia alba, Chamomilla, Eupatorium perfoliatum, Ferrum phosphoricum, Gelsemium, Ipecacuanha, Natrum muriaticum, Nux vomica, Pulsatilla and Rhus toxicodendron* which are prescribed on the basis of symptom similarity.

Differential diagnosis

- The clinical diagnosis of dengue can be challenging as many other illnesses can present similarly early in the disease course. Other considerations should include malaria, influenza, Zika, chikungunya, measles, and yellow fever. Obtain a detailed history of immunizations, travel, and exposures.
- Rapid laboratory identification of dengue fever includes NS1 antigen detection and serologic tests. Serologic tests are only useful after several days of infection and may be associated with false positives due to other *flavivirus* infections, such as yellow fever or Zika virus.

Vaccine for dengue virus

Dengue vaccines have been under development since the 1940s, but a tetravalent vaccine which simultaneously provides long-term protection against all DV serotypes is round the corner [23].

A tetravalent antigen was designed by splicing the EDIIIs of DV-1, DV-2, DV-3 and DV-4 using flexible pentaglycyl linkers. A synthetic gene encoding this tetravalent antigen was expressed in *Pichia pastoris* and purified to near homogeneity. This tetravalent antigen when injected into inbred BALB/c mice, elicited neutralizing antibodies specific to each of the four DVs in plaque reduction neutralization tests[24]. Efforts are underway to present the tetravalent antigen on a chimeric VLP platform.

Homoeopathic point of view

Homoeopathy depends upon the similia similibus curanter i.e., law of similars. According to the said principle, the curative power of medicines depends upon ability to produce symptoms similar to disease but in higher strength. Homoeopathy is effective in treatment and prophylaxis of acute infectious diseases.

As per the principles of Homoeopathy, a genus epidemicus can be identified for the sporadic and epidemic situations. The process of the selection of Genus Epidemicus is specialized and involves following steps:

- The Totality of Symptoms related to the current Epidemic is formulated by in depth study of all the signs and symptoms of minimum 20-30 cases preferably from different regions to cover the complete spectrum of diseases in the community.
- The TOS to be thoroughly studied and following appropriate repertorization process, a group of medicines are to be identified. These medicines are required to be given to these cases on the basis of individualization. The medicine, which is most frequently indicated and has potential of providing the quick and favourable response to the patient, shall be the Genus Epidemicus.
- Drugs commonly found indicated as Genus Epidemicus in the past are *Eupatorium perfoliatum*, Rhustoxicodendron, Bryonia alba. One of these in 30 or 200 potency can be safely taken twice daily for three days as prophylactic. Further research in this area is being undertaken.

***Eupatorium perfoliatum*:** Named "bone-set" because on account of the severe aching as if bones were broken that occurred in an epidemic of intermittent fever this was the remedy that cured or set the bones. The epidemic was called break bone fever[11]. Great prostration is felt, partly because of pains and partly of lassitude that naturally accompanies 'la grippe'[12]. Chill spreads from back, Thirst before chill[13]. It is often indicated in the warmer climates for fevers, yellow fever, bilious fever, break-bone fever and intermittent fever. The time for administration is at the close of the paroxysm [14]. Bruised feeling as if broken, all over the body; adapted to worn-out constitutions, especially from inebriety [15]. Cachexia from old chronic, bilious intermittents; marked periodicity [16]. Thirst or nausea, then violent shaking chill; begins in small of back [17].

***Aconitum napellus*:** The Aconite Restlessness is oftenest found in a high grade of synochal or inflammatory fevers [11]. Aconite by Hering - Heat, with thirst; hard, full and frequent pulse, anxious impatience, inappeasable, beside himself, tossing about with agony. Burning thirst for large quantities of cold water; Hahnemann says "whenever Aconite is chosen homeopathically, you must, above all, observe the moral symptoms and be careful that it closely resembles them; the anguish of mind and body; the restlessness; the disquiet not to be allayed" [15]. Sudden, violently acute, painful effects; Terror, Anxiety, Agonizing Fear, Fear of death; beside himself, frantic from intensity of the pain [17].

***Gelsemium sempervirens*:** *Gelsemium* is useful in remittent fever in children. The fever is never of that active or violent, but of a milder form. Complete relaxation and prostration of the whole muscular system with almost or quite entire motor paralysis [11]. Useful in the treatment of Intermittents; suffers from nervous chills running from the sacrum to the nape of neck; Chill throughout stage of chill and profuse urination [12]. Chill ascends [13]. Tongue begins to coat, nausea comes on, ending in vomiting of bile and instead of there being an intermission a continued fever extends from one paroxysm to another [14].

RHUS toxicodendron: Lameness and stiffness and pain on first moving after rest or on getting up in the morning, relieved by continued motion [11]. Any continuous exertion to mid or body exhausts the Rhus patient. The prominent projections of bones become sore to touch especially cheek bones. It has cured many cases of intermittent fever, often remittent and continued fevers and low form of Typhoid fever. Pains are tearing, aching, bruised often with numbness and paralytic weakness of the limbs [14].

***Belladonna*:** Guernsey says this medicine is particularly applicable and in fact takes the lead over all others in cases in which quickness or suddenness of either sensation or motion is predominant. Rush of blood to the head and face[15]. 'Starting and jumping' or 'twitching in sleep' or 'on going to sleep' is characteristic [11]. With the heat, there is loquacity and drowsiness [13]. Eyes wild, pupils dilated; pulse full and bounding, globular like buckshot striking the finger, mucous membrane of mouth dry; stool tardy and urine suppressed [15]. A high feverish state with comparative absence of toxaemia. No thirst with fever. Burning, pungent, steaming, heat [16].

***Carica papaya*:** Useful in increasing platelet count. Many other remedies such as bryonia, arsenicum album, cantharis, cinchona, ipecac, nux-vomica, RHUS-v also helpful in the management of dengue with symptom-similarity.

Although many medicines were present in the literature, Eupatorium perf is indicated most frequently in the treatment of Dengue Fever.

Based on observations and facts seen in prior studies with *Eupatorium perfoliatum* and earlier outbreaks, Council has announced *Eupatorium perfoliatum 30 as preventive medicine* for outbreak of Dengue Epidemic.

Conclusion

The prognosis for untreated Dengue is abysmal but with supportive care, most patients can survive, albeit with residual multi-system organ damage. The care is supportive with fluid, blood transfusion for hemorrhage. Dengue disease continues to involve newer areas, newer populations and is increasing in magnitude, epidemic after epidemic. Every aspect of dengue viral infection continues to be a challenge but can be controlled with active participation of the community. Need is to organize health education programmes about dengue disease to increase community knowledge and sensitize the community to participate in integrated vector control programmes. The Homoeopathic Treatment is holistic and is based on individualization. The selection of the homoeopathic medicines depends upon the individual response to the infection, severity of the disease and clinical manifestation of the case. Homoeopathy has a potential to reduce the intensity of fever, headache, bodyache, weakness, loss of appetite, nausea and other associated symptoms and also reduce the probability of developing shock, haemorrhage and other complications.

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