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A Review on Dengue and Treatments.

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Review Article

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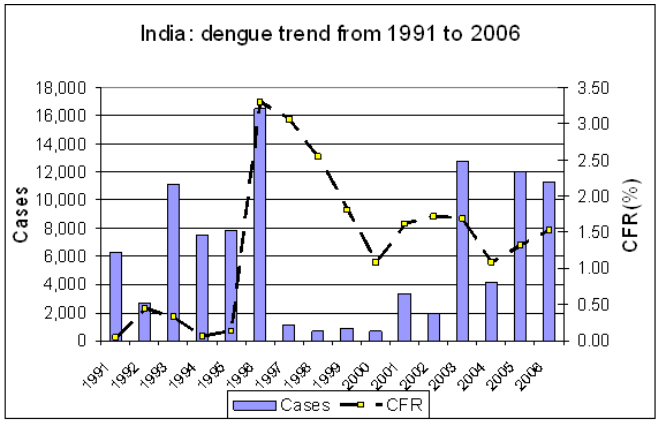
ABSTRACT

Dengue fever and dengue hemorrhagic fever (DHF) are acute febrile diseases, found in the tropics, with a geographical spread similar to malaria.Caused by one of four closely related virus serotypes of the genus Flavivirus, family Flaviviridae, each serotype is sufficiently different that there is no cross-protection and epidemics caused by multiple serotypes (hyperendemicity) can occur. It is transmitted to humans by the mosquito. The incidence of dengue has grown dramatically around the world in recent decades. Over 2.5 billion people – over 40% of the world's population – are now at risk from dengue. WHO currently estimates there may be 50–100 million dengue infections worldwide every year.The rapidly expanding global footprint of Dengue is a public health challenge with an economic burden that is currently unmet by licensed vaccines,specific therapeutic agents or vector control strategies. This review highlights current understanding of dengue, including its clinical manifestations, pathogenesis, diagnostic tests, its management & prevention.

INTRODUCTION

Dengue is a viral infection transmitted by the bite of an infected female Aedes mosquito. There are four different viruses that can cause dengue fever, all of which spread by a certain type of mosquito. Because it is caused by one of four serotypes of virus, it is possible to get dengue fever multiple times.

Statistics



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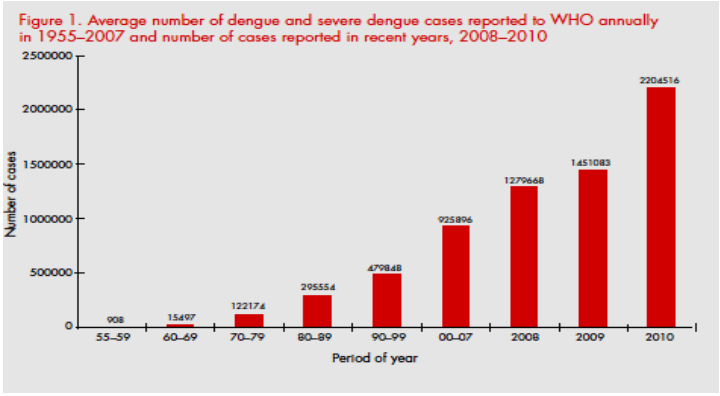
However, an attack of dengue produces immunity for a lifetime to that particular serotype to which the patient was exposed. Dengue can vary from mild to severe; the more severe forms include dengue shock syndrome and dengue hemorrhagic fever (DHF). Dengue can affect anyone but tends to be more severe in people with compromised immune systems. The incidence of dengue has increased 30-fold over the last 50 years. Up to 50-100 million infections are now estimated to occur annually in over 100 endemic countries, putting almost half of the world's population at risk. The inadequate awareness as well as increased global incidence has leaded us to write this article [1,2].

Incidence of Dengue in India [3]:

Dengue fever has been reported from India over a long time, but dengue haemorrhagic fever was first reported in 1963 from Calcutta city. Since then several outbreaks of dengue fever was reported from India with a major epidemic of dengue haemorrhagic fever that occurred in Delhi in 1996 and also cases have been reported from the neighboring states of Haryana, Punjab, Rajasthan, Utter Pradesh and two southern and western states. The case fatality has been above 1% for the last 10 years. After 1996,once again dengue fever outbreak was observed in the 2003,2005 and 2006 but they were less intense than the former one.



Seasonal trends of dengue in India [3]:

The trend data from India shows that cases generally start to increase from august onwards, which is post monsoon season. It is observed that breeding of Aedes mosquitoes however begins in June itself.

Incidence of Dengue over the Globe[4, 42]

During the 19th century, dengue was considered a sporadic disease that caused epidemics at long intervals, a reflection of the slow pace of transport and limited travel at that time. In 2012, dengue ranks as the most important mosquito borne viral disease in the world.

Outbreaks exert a huge burden on populations, health systems and economies in most tropical countries of the world. The emergence and spread of all four dengue viruses ("serotypes") from Asia to the Americas, Africa andthe Eastern Mediterranean regions represent a global pandemic threat. Although the full global burden of the disease is still uncertain, the patterns are alarming for both human health and the economy.

During the past five decades, the incidence of dengue has increased 30-fold.

Anatomy of Aedesaegypti [5,6,7]

The Aedesaegypti is a day biting mosquito. Mosquito is small in comparison to other species, usually between three to four millimeters in length discounting leg length. It is totally black apart from white 'spots' on the body and head regions and white rings on the legs. The thorax is decorated with a white 'Lyre' shape of which the 'chords' are two dull yellow lines. Its wings are translucent and bordered with scales.

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Facts about the mosquito [5,6]

- Only the female Aedes mosquito bites as it needs the protein in blood to develop its eggs.
- The mosquito becomes infective approximately 7 days after it has bitten a person carrying the virus. This is the extrinsic incubation period, during which time the virus replicates in the mosquito and reaches the salivary glands.
- Peak biting is at dawn and dusk. This species is most active for approximately two hours after sunrise and several hours before sunset. The average lifespan of an Aedes mosquito in nature is 2 weeks.
- The A. aegypti is adapted to breed around human dwellings and prefers to lay its eggs in clean water free of other organisms. Artificial or natural water containers (water storage containers, flower pots, old tires, etc.) that are within or close to places where humans live are ideally larval habitats for the A. aegypti.The mosquito can lay eggs about 3 times in its lifetime, and about 100 eggs are produced each time.
- The eggs can lie dormant in dry conditions for up to about 9 months, after which they can hatch if exposed to favorable conditions, i.e. water and food.
- Under optimal conditions, the egg of an Aedes mosquito can hatch into a larva in less than a day. The larva then takes about four days to develop in a pupa, from which an adult mosquito will emerge after two days. Three days after the mosquito has bitten a person and taken in blood, it will lay eggs, and the cycle begins again.

Transmission of dengue virus [31,32,33,34,35,36]

Virology

Dengue virus (DENV) is a positive-strand RNA virus of the family Flaviviridae, genus Flavivirus. It exists as four closely related but antigenically distinct serotypes (DENV-1, -2, -3, and -4), all of which have Aedesaegypti mosquitoes as their primary vector, with A. albopictus as a secondary vector.

The virion comprises a spherical particle, 40–50 nm in diameter, with a lipopolysaccharide envelope. The positive single-strand RNA genome, which is approximately 11 kb in length, has a single open reading frame that encodes three structural proteins — the capsid (C), membrane (M) and envelope (E) glycoproteins — and seven non-structural proteins (NS1, NS2A, NS2B, NS3, NS4A, NS4B and NS5). Important biological properties of dengue viruses, including receptor binding, haemagglutination of erythrocytes and the induction of neutralizing antibodies and the protective immune response, are associated with the E glycoprotein.

Vector:

The various serotypes of the dengue virus are transmitted to humans through the bites of infected Aedesmosquitoes, principally Aedisaegypti. This mosquito is a tropical and subtropical species widely distributed around the world, mostly between latitudes 35 °N and 35 °S. The immature stages are found in water-filled habitats, mostly in artificial containers closely associated with human dwellings and often indoors. Studies suggest that most female A. aegypti may spend their lifetime in or around the houses where they emerge as adults. This means that people, rather than mosquitoes, rapidly move the virus within and between communities. Dengue outbreaks have also been attributed to Aedesalbopictus, Aedespolynesiensis and several species of the Aedesscutellaris complex. Each of these species has a particular ecology, behaviour and geographical distribution. In recent decades Aedesalbopictus has spread from Asia to Africa, the Americas and Europe, notably aided by the international trade in used tyres in which eggs are deposited when they contain rainwater. The eggs can remain viable for many months in the absence of water.

Transmission :

Though vertical transmission of the virus has been reported , mosquitoes mainly acquire DENV by feeding on the blood of an infected human. DENV first infects and replicates in the mosquito midgut epithelium. It subsequently spreads through the hemolymph to replicate in other organs such as the fat body and trachea, finally infecting the salivary gland at approximately 10–14 days post-bloodmeal. Once in the saliva, DENV can be inoculated into a human host when the mosquito acquires a blood meal, thus spreading the disease.

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The mosquito vectors, principally Aedesaegypti, become infected when they feed on humans during the usual five-day period of viraemia. The virus passes from the mosquito intestinal tract to the salivary glands after an extrinsic incubation period, a process that takes approximately 10 days and is most rapid at high ambient temperatures. Mosquito bites after the extrinsic incubation period result in infection, which might be promoted by mosquito salivary proteins.

The transmission area of this disease continues to expand due to many direct and indirect factors linked to urban sprawl, increased travel and global warming.

Pathophysiology of dengue infection [14,15,16,17,18,19,20]:

Dengue infection is a systemic and dynamic disease. It has a wide clinical spectrum that includes both severe and non-severe clinical manifestations. After the incubation period, the illness begins abruptly and is followed by the three phases – febrile, critical and recovery.For a disease that is complex in its manifestations, management is relatively simple, inexpensive and very effective in saving lives so long as correct and timely interventions are instituted. The key is early recognition and understanding of the clinical problems during the different phases of the disease, leading to a rational approach to case management and a good clinical outcome.

Febrile phase

Patients typically develop high-grade fever suddenly. This acute febrile phase usually lasts 2–7 days and is often accompanied by facial flushing, skin erythema, generalized body ache, myalgia, arthralgia and headache. Some patients may have sore throat, injected pharynx and conjunctival injection. Anorexia, nausea and vomiting are common. It can be difficult to distinguish dengue clinically from non-dengue febrile diseases in the early febrile phase. A positive tourniquet test in this phase increases the probability of dengue.

Mild haemorrhagic manifestations like petechiae and mucosal membrane bleeding (e.g. nose and gums) may be seen. Massive vaginal bleeding (in women of childbearing age) and gastrointestinal bleeding may occur during this phase but is not common. The liver is often enlarged and tender after a few days of fever. The earliest abnormality in the full blood count is a progressive decrease in total white cell count, which should alert the physician to a high probability of dengue.

Critical phase

Around the time of defervescence, when the temperature drops to 37.5–38°C or less and remains below this level, usually on days 3–7 of illness, an increase in capillary permeability in parallel with increasing haematocrit levels may occur . This marks the beginning of the critical phase. The period of clinically significant plasma leakage usually lasts 24–48 hours.

Progressive leukopenia followed by a rapid decrease in platelet count usually precedes plasma leakage. Pleural effusion and ascites may be clinically detectable depending on the degree of plasma leakage and the volume of fluid therapy. Hence chest x-ray and abdominal ultrasound can be useful tools for diagnosis. The degree of increase above the baseline haematocrit often reflects the severity of plasma leakage.

Shock occurs when a critical volume of plasma is lost through leakage. It is often preceded by warning signs. The body temperature may be subnormal when shock occurs. With prolonged shock, the consequent organ hypoperfusion results in progressive organ impairment, metabolic acidosis and disseminated intravascular coagulation. This in turn leads to severe haemorrhage causing the haematocrit to decrease in severe shock. Instead of the leukopenia usually seen during this phase of dengue, the total white cell count may increase in patients with severe bleeding. In addition, severe organ impairment such as severe hepatitis, encephalitis or myocarditis and/or severe bleeding may also develop without obvious plasma leakage or shock .

Recovery phase

If the patient survives the 24–48 hour critical phase, a gradual reabsorption of extravascular compartment fluid takes place in the following 48–72 hours. General well-being improves, appetite returns, gastrointestinal symptoms abate, haemodynamic status stabilizes and diuresis ensues. Some may

experience generalized pruritus. Bradycardia and electrocardiographic changes are common during this stage.

The haematocrit stabilizes or may be lower due to the dilutional effect of reabsorbed fluid. White blood cell count usually starts to rise soon after defervescence but the recovery of platelet count is typically later than that of white blood cell count.

Respiratory distress from massive pleural effusion and ascites will occur at any time if excessive intravenous fluids have been administered. During the critical and/or recovery phases, excessive fluid therapy is associated with pulmonary oedema or congestive heart failure.

Severe dengue

Severe dengue is defined by one or more of the following: (i) plasma leakage that may lead to shock (dengue shock) and/or fluid accumulation, with or without respiratory distress, and/or (ii) severe bleeding, and/or (iii) severe organ impairment.

As dengue vascular permeability progresses, hypovolaemia worsens and results in shock. It usually takes place around defervescence, usually on day 4 or 5 (range days 3–7) of illness, preceded by the warning signs. During the initial stage of shock, the compensatory mechanism which maintains a normal systolic blood pressure also produces tachycardia and peripheral vasoconstriction with reduced skin perfusion, resulting in cold extremities and delayed capillary refill time. Uniquely, the diastolic pressure rises towards the systolic pressure and the pulse pressure narrows as the peripheral vascular resistance increases. Prolonged hypotensive shock and hypoxia may lead to multi-organ failure and an extremely difficult clinical course.

The patient is considered to have shock if the pulse pressure (i.e. the difference between the systolic and diastolic pressures) is ≤ 20 mm Hg in children or he/she has signs of poor capillary perfusion (cold extremities, delayed capillary refill, or rapid pulse rate). In adults, the pulse pressure of ≤ 20 mm Hg may indicate a more severe shock. Hypotension is usually associated with prolonged shock which is often complicated by major bleeding.

Major bleeding, associated with profound shock in combination with thrombocytopaenia, hypoxia and acidosis, can lead to multiple organ failure and advanced disseminated intravascular coagulation. Massive bleeding may occur without prolonged shock in instances when acetylsalicylic acid (aspirin), ibuprofen or corticosteroids have been taken.

Unusual manifestations, including acute liver failure and encephalopathy, may be present, even in the absence of severe plasma leakage or shock. Cardiomyopathy and encephalitis are also reported in a few dengue cases. However, most deaths from dengue occur in patients with profound shock, particularly if the situation is complicated by fluid overload.

Severe dengue should be considered if the patient is from an area of dengue risk presenting with fever of 2–7 days plus any of the following features:

- There is evidence of plasma leakage, such as:
  High or progressively rising haematocrit;
  Pleural effusions or ascites
  circulatory compromise or shock (tachycardia, cold and clammy extremities, capillary refill time greater than three seconds, weak or undetectable pulse, narrow pulse pressure or, in late shock, unrecordable blood pressure).
- There is significant bleeding.
- There is an altered level of consciousness (lethargy or restlessness, coma, convulsions).
- There is severe gastrointestinal involvement (persistent vomiting, increasing or intense abdominal pain, jaundice).
- There is severe organ impairment (acute liver failure, acute renal failure, encephalopathy or encephalitis, or other unusual manifestations, cardiomyopathy) or other unusual manifestations.

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Diagnosis [41] :

Confirmed diagnosis of dengue infection requires lab tests:

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.Dengue fever is usually charcterised by lowering of platelets in the blood. 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.

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.

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.

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.

Prognosis

Careful clinical examination and history-taking supplemented by newer rapid diagnostic tests may lead to early etiological diagnosis. For severe dengue, early recognition of vascular permeability followed by rapid physiological replacement of fluids is life-saving. Prognosis of patients depends upon optimum management, an outcome that requires preparation via organization, training, and use of evidence-based practice guidelines. Prognosis is determined by an ill-understood combination of viral, immunological, and host factors, all of which begin with the sudden onset of high fever. There are no early signs that make it possible to predict severe outcomes, which only appear late and are accompanied by defervescence. It is critical that physicians who monitor dengue illnesses stay alert to the onset of the unique syndrome: dengue vasculopathy (dengue hemorrhagic fever [DHF]/dengue shock syndrome [DSS]). With the onset of this syndrome, prognosis rests squarely in the hands and prepared mind of the physician.

Treatment of Dengue Fever[22,23,24,25,26]:

Given that dengue is an infection, treatment can be performed using the simple concept of 'getting rid of the pathogen and limiting the complications'. In general, the use of supportive and symptomatic treatment is widely used for dengue treatment, aiming to limit the complications of the infection. The application of fluid therapy has become key in dengue management and this is applied based on the severity of disease. In simple dengue, oral fluid replacement is sufficient and there is no need for hospitalization. In severe cases of dengue infection, fluid replacement should be carefully used and must be performed under close observation in a hospital. Parenteral, intravenous fluid replacement by either colloids or crystalloids should be considered in order to prevent shock. The basic recommendation for intravenous fluid-replacement therapy is administration of 0.9% normal saline solution at a rate of 20 ml/kg/h in the first 2 h, followed by 10 ml/kg/h for 6 h, then the rate can be adjusted according to the status of the patient in the following 16 h. Water and electrolyte status should be maintained during treatment to avoid under and over administration of fluid. It is noted that a progressive rise in hematocrit with a progressive reduction of platelet count implies a high risk for developing shock so monitoring hematocrit and platelet count should be done for at least 1 day after the discontinuation of intravenous fluid administration to prevent possible fluid intoxication in the convalescent phase due to fluid redistribution.

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The preferable new treatment for dengue would be an antiviral drug. At present, a specific antiviral drug is not available; however, there have been a lot of attempts to discover one. In phytomedicine, several sulfated polysaccharides extracted from seaweeds have been studied and high antiviral activity against dengue virus has been observed.In modern medicine, ribavirin, glycyrrhizin and 6-azauridine are reported to have cytostatic and inhibitory effects on the dengue virus. 'NITD008' is an adenosine analog is another promising drug currently being studied. .

Alternative Treatment For Dengue [27,37] :

Ayurvedic Treatment

Several Ayurvedic herbs have been shown to be effective in treatment of dengue fever.

They include:

Amaltas: Amaltas is the root of the cassia tree. It is used as a tonic for reducing fever in dengue infection.
Chirayata: Chirayata is very effective for reduction of fevers. It is useful for treating convulsions that occur with fever in dengue.
Datura: Datura leaves are effective in reducing the fever in dengue infection. It helps to reduce the seriousness of fever in dengue infection.
Hara dhania: Coriander leaves taken as a tonic can reduce fever in dengue.
Hermal: PowederedHermal seeds taken either as an infusion or as a decoction can help to treat intermittent and recurrent fevers in dengue.
Kanghi: An infusion of kanghi can help to reduce fever in dengue.
Giloy or Amrita:It is an anti-inflammatory (that reduces inflammation) and antipyretic (that reduce fever) herb . This herb, which has been used in AyurvedicRasayanas since centuries, is very helpful in building up the immune system and the body's defense against infecting organisms. In a scientific study conducted using human WBC (white blood corpuscles), the Ayurvedic herb helps in enhancing the killing ability of macrophages (the resistant cells which are responsible for fighting foreign bodies as well as microorganisms).
Some other herbs that are effective in the treatment of fever in dengue include methi, punarnava, rojmari, tulsi leaves.

Homeopathic Treatment for Dengue[28,45,46,47] :

Since ages, homeopathic treatment has successfully treaded into realms where allopathic medications have failed to provide convincing cures. Homeopathy has also been increasingly favoured by today's generation because it is free from side effects and negative repercussions. Homeopathic doctors have come up with a particular formulation which has been reasonably successful in combating dengue fever. The formulation reads as cRHUS TOX. / EUPATORIUM PERF. / LEDUM PALUSTRE. / GELSEMIUM. / 5CH.

cRHUS TOX- RhusTox is from Poison Ivy. Rhustox is the remedy in Backache, Body aches during flu, Lumbago, Rheumatism, Sprains.
EUPATORIUM PERF –*Eupatorium perfoliatum*,a common perennial plant relieves pain in limbs and muscles that accompanies some forms of febrile disease, like malaria and influenza. Eupatorium acts principally upon the gastro-hepatic organs and bronchial mucous membrane.
Ledum Palustre - It is used for muscle and joint pain (rheumatism), cough, bronchitis, cold, cough, and chest and lung ailments. It is also used to stimulate milk flow, cause sweating, increase urine flow to relieve water retention, and loosen phlegm. Some women use marsh tea to cause an abortion.

Diet For Dengue Patient [29]

There is no recommendation regarding diet during dengue fever and after dengue fever. Like with any other febrile illness, eat foods which can be easily digested.

- Patient's diet can include boiled vegetables, rice gruel, porridge, soup, toast, apples, bananas and tea.
- Drink plenty of fluids such as oral rehydration solution, fresh juice, soups, and coconut water. This will help to prevent dehydration due to vomiting and high fever. Avoid fried foods and foods with oil, spices and salt.

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- One can use lemon juice or certain herbs to enhance the flavour of their food. According to some experts of Ayurveda, tea made with fever reducing herbs such as ginger and cardamom is helpful.
- Ayurveda recommends having the juice or the extract of two fresh crushed papaya leaves. Take this juice daily. It is considered a good home remedy for the treatment of dengue fever.

Centres for Treatment of Dengue:

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Recent Advances in the treatment of dengue [30,38,40,8,9,10,11,12,13]:

Mobile app does a dengue check

Now mobile phone could be the first diagnosis tool to find out whether the fever isdengue or not. A new mobile application developed for Android phones helps in mapping the disease based on real time reporting.

Dr Saji Salam, an NRI doctor in his mid-40s and currently based in the US, has developed the mobile application on dengue. The app not only provides a guide on the symptoms and causes of the disease but also maps dengue as it spreads its tentacles across the world. To get started with, firstly download the dengue app on Android smart phone. Next, feed the patient must feed his current body temperature using its fever meter. Based on the severity of your the, the app will guide the patient to go for a physician consultation and blood sample test.

Home cure for dengue death sting

The juice of the humble papaya leaf has been seen to arrest the destruction of platelets that has been the cause for so many deaths. Ayurveda researchers have found that enzymes in the papaya leaf can fight a host of viral infections, not just dengue, and can help regenerate platelets and white blood cells. Papaya has always been known to be good for the digestive system. The enzymes in papaya leaf, chymopapain and papain, help revive platelet count.The juice has to be prepared from fresh papaya leaves. Devein the leaves and grind the green, pulpy part into a paste. The paste is very bitter and probably has to mix it with fruit juice. Doctors recommend 20-25 ml (about four to five teaspoons), twice a day, for at least a week to get the best results. It is reported that several dengue patients have had a remarkable platelet recovery after taking papaya leaf juice.

Vaccine development

As a result of the failure of vector control, the continuing spread and increasing intensity of dengue has renewed interest and investment in dengue vaccine development, making a safe, effective and affordable tetravalent dengue vaccine a global public health priority. Dengue vaccine development has been in progress for several decades, however the complex pathology of the illness, the need to control four virus serotypes simultaneously and insufficient investment by vaccine developers have hampered progress.

The observation that DHF/DSS is associated with DENV secondary infection poses a special challenge to the development of a dengue vaccine, leading to a requirement that such vaccines should induce a robust immune response against the four serotypes in naive as well as previously immune individuals. Animal models are only partially useful for vaccine evaluation. The poor understanding of the mechanisms involved in inducing protective immunity against dengue infection poses additional challenges. Finally, cases of DHF/DSS have recently been documented 20 or more years after primary dengue infection, which adds a new dimension to the problem[44]. The ideal dengue vaccine should be free of important reactogenicity, induce life-long protection against infection with any of the four DENV serotypes and be affordable. Vaccine candidates should be evaluated in population-based efficacy trials in several at-risk populations in different geographical settings including Asia and the Americas, which experience different patterns of dengue transmission intensity and dengue virus circulation.

DENVax[44]

In 2011, Inviragen completed a Phase 1 clinical study of DENVax, which had been conducted in collaboration with PECET (Program for the Study and Control of Tropical Diseases) in Colombia, South America. Currently, DENVax is being investigated in an additional Phase 1b clinical study in the U.S. and a Phase 2 clinical study in the U.S. (Puerto Rico), Colombia, Singapore and Thailand.DENVax is a tetravalent (four-component) combination vaccine containing the original attenuated DEN-2 PDK-53 vaccine and each of the chimeric vaccines (DEN-2/1, DEN-2/3 and DEN-2/4). In DENVax, all four of the components contain the same, identical safety mutations. Thus, the safety of DENVax can be assured by sensitive genetic tests throughout its manufacture. In addition, the possibility of generating a pathogenic strain by recombinantion between the vaccines is eliminated. These are distinct advantages over competitive dengue vaccine technologies.

DENVax generated antibody responses that could neutralize all four dengue viruses in animal models. Preclinical data demonstrate that this tetravalent DEN vaccine candidate is safe and immunogenic in mice and non-human primates.

With its global partners, Inviragen is preparing DENVax for human clinical trials. A safe, affordable and effective vaccine that can neutralize all four dengue viruses will have tremendous impact on global health.

Vaccine developed by Sanofi Pastuer[48,49] :

Sanofi (SAN)'s experimental dengue vaccine succeeded in a study in reducing the mosquito-borne disease, moving the company closer to introducing the first inoculation against dengue.Sanofi Pasteur has been working on a dengue vaccine for more than 20 years. The two, pivotal Phase III efficacy studies

involve more than 31,000 volunteers from Asia (Indonesia, Malaysia, the Philippines, Thailand and Vietnam) and Latin America (Brazil, Columbia, Honduras, Mexico and Puerto Rico). The Phase III evaluations provide pivotal data on efficacy, safety, and immunogenicity of the vaccine candidate in a broad population and different epidemiological environments and assess the potential impact of the vaccine on the disease burden.

Results from 10,275 children showed a 56 percent reduction of dengue-disease cases. The initial safety data from the late-stage study are consistent with previous trials.. Sanofi didn't disclose how well the vaccine protected against each of dengue's four strains. Sanofi's study was conducted in Indonesia, Malaysia, the Philippines, Thailand and Vietnam between 2011 and 2013 on children and adolescents from ages 2 to 14.The participants received either three injections of the vaccine or a placebo at six-month intervals.

Mid-stage trials of the vaccine had yielded mixed results, providing good protection against three of the four viruses that cause the disease in a trial among 4,000 children in Thailand last year. Yet it was ineffective against type 2, the dominant dengue strain in Thailand at the time of the trial.It was stated that results from a second late-stage efficacy trial conducted in Latin America will be unveiled in the third quarter.

CONCLUSION

Dengue is emerging as aglobal treat and is pressing public health priority in many countries. The government and the pharmaceutical industries have been taking initiative to develop new strategies to improve the diagnosis and treatment of dengue. The challenge here lies in how effectively the strategies developed are put into use. There also an obligatory need to globalize awareness and precautionary measures among the masses in order to control the incidence. Combined efforts of the health care industries, governing bodies and efforts at individual level would help us to tackle the prevalence of dengue.

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