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Dengue Fever

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ABSTRACT

Dengue fever is the maximum not unusual place arthropod-borne self-proscribing viral disorder with medical spectrum ranging fromasymptomatic contamination to lifestyles threatening surprise. It is referred to as dengue surprise syndrome. Hemoconcentration andthrombocytopenia are the one-of-a-kind functions of dengue hemorrhagic fever. Supportive fluid substitute therapyand vigilant tracking for the a success control of the condition. Vector manage measures are the maximumcrucial preventive methods. As the outbreaks of Dengue fever growing in India, one country after different getting gaffected, it's miles very important to understand greater approximately this disorder and prevalence, any alternate withinside the viral strain, severityof the disorder pattern, early detection of the virus and early control of the disorder ensuing in correct recovery .Population growth, speedy urbanization, growth in global tour from endemic regions and international warming aregambling a chief position in disorder unfold. Measures ought to be taken to govern the aforementioned reasons to preventdisorder unfold and decrease epidemic flare up.

KEYWORD: Dengue, Flavivirus, Dengue Shock Syndrome, Mac-Elisa

Introduction

Dengue is an infectious ailment resulting from lady mosquito AEDES AEGYPTI. It is a mosquito-borne contamination determined in tropical and sub-tropical areas across the world.[1] Infection with dengue virus consequences in numerous situations like pathological starting from moderate asymptomatic dengue fever to excessive dengue hemorrhagic fever and dengue surprise syndrome that reasons to death.[2]Epidemiology: Dengue has emerge as one of the widestspreadable illnesses globally. In India, outbreak of dengue turned into recorded in 1812. A latest dengue distribution version has anticipated 390 million dengue infections annually, out of which ninety six million instances befell.

A double top hemorrhagic fever epidemic befell in India for the primary time in Calcutta among July 1963 and March 1964. Thus, there's an pressing want of development in surveillance to permit theauthorities to put together correctly for document of outbreak.[3]

Dengue Virus: This virus is likewise referred to as Flavivirus and they may be in round and 40-60 mm in diameter. It is RNA virus this is enveloped includes 3 structural polypeptides are glycosylated and replication in cytoplasm.[4]

Most robust vector having epidemic capacity A. aegypti and different species are Aedes albopictus, stegomyia, A. polnesiensis, A. scutellaris, A. finalaya however in India A. tigris may be very common. Four dengue viruses (sorts 1-4) in the genus flavivirus and own circle of relatives flaviviridae, are the causative agents.

[5] . All 4 subtypes are determined in India. Dengue virions are small debris with lipoprotein envelope and nucleocapsid of unmarried stranded RNA genome with wonderful polarity. There is a near antigenic similarity among the 4 serotypes however the move safety in human beings is at exceptional partial and transient.[6]

Symptoms

Many humans specifically youngsters and teenagers sense no symptoms and symptoms or signs and symptoms all through a slight case of dengue fever. When signs and symptoms do occur, they normally start four to 7 days when you are bitten through an inflamed mosquito.[7]

Dengue fever reasons a excessive fever 104 F and those are following signs and symptoms:

- Headache
- Muscle, bone and joint pain
- Nausea
- Vomiting
- Pain in the back of the eyes
- Swollen glands
- Rash

Most human beings get better inside a week. In a few cases, signs and symptoms get worse and may turn out to be life-threatening.Blood vessels regularly turn out to be harm and leaky and the quantity of clot-forming cells (platelets) to yourbloodstream drops. This can motive a intense shape of dengue fever, known as dengue hemorrhagic fever, intense dengue or dengue surprise syndrome.

Signs and signs and symptoms of dengue hemorrhagic fever or intense dengue a life-threatening emergency include:

- Severe belly pain
- Persistent vomiting
- Bleeding out of your gums or nose
- Blood to your urine, stools or vomit
- Bleeding below the skin, which would possibly appear like bruising
- Difficult or fast breathing
- Cold or clammy skin (surprise)
- Fatigue
- Irritability or restlessness

Diagnosis

Efficient and correct analysis of dengue is of number one significance for scientific care (i.e. early detection of excessive cases, case affirmation and differential analysis with different infectious diseases), surveillance activities, outbreak control, pathogenesis, instructional research, vaccine development, and scientific trials.[8]

A variety of laboratory diagnostic techniques has been advanced to guide affected person control and sickness control. The desire of diagnostic approach relies upon at the cause for which the checking out is done (e.g. scientific analysis, epidemiological survey, vaccine development), the form of laboratory centers and technical understanding available, costs, and the time of pattern collection.[9]

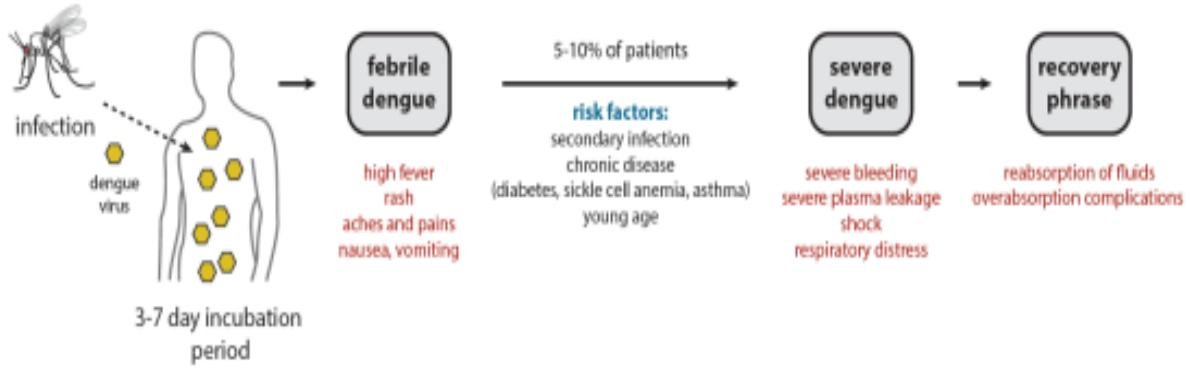
Considerations in The Choice of Diagnostic Methods

Clinical Management

Dengue virus contamination produces a huge spectrum of signs and symptoms, many this is non-specific. Thus, a analysis primarily based totally best on scientific signs and symptoms is unreliable. Early laboratory affirmation of scientific analysis can be treasured due to the fact a few sufferers development over a brief duration from slight to intense sickness and occasionally to death. Early intervention can be life-saving.[10]

Differential Diagnosis

Dengue fever can without difficulty be pressured with non-dengue illnesses, specially in nonepidemic situations.Depending at the geographical foundation of the patient, different etiologies together with non-dengue flavivirusinfections have to be dominated out[11] These consist of yellow fever, Japanese encephalitis, St Louis encephalitis, Zika, and West Nile, alphaviruses (including Sinbis and chikungunya), and different reasons of fever including malaria, leptospirosis, typhoid, Rickettsial diseases (Rickettsia prowazeki, R. mooseri, R. conori, R. rickettsi, Orientia tsutsugamushi, Coxiella burneti, etc.), measles, enteroviruses, influenza and influenza-like illnesses, haemorrhagic fevers (Arenaviridae: Junin, etc.; Filoviridae: Marburg, Ebola; Bunyaviridae: hantaviruses, Crimean-Congo haemorrhagic fever, etc.).



Outbreak Investigations

During outbreaks a few sufferers can be visible imparting with fever without or with rash throughout the extreme contamination stage. a few others can also additionally gift with symptoms and symptoms of plasmaLeakage even as nevertheless others can be found at some stage in the convalescent segment.[12]

One of the priorities in a suspected outbreak is to perceive the causative agent in order that suitable publichealth measures may be taken and physicians may be recommended to provoke suitable acute contamination management.[13] In such cases, the rapidity and specificity of diagnostic assessments is greater essential than take a look at sensitivity. Samples amassed from febrile sufferers might be examined through nucleic acid strategies in a well-ready laboratory or a broader spectrum of laboratories the use of an ELISA-primarily based totally dengue antigen detection kit. Serological assays can be used to decide the volume of outbreaks.[14]

Vaccine trials

Vaccine trials are completed on the way to degree vaccine protection and efficacy in vaccinated persons. The plaque discount and neutralization take a look at (PRNT) and the microneutralization assays are typically used to degree safety correlates.[15]
The assay is primarily based totally at the precept that neutralizing antibodies inactivate the virus in order that it's miles now no longer capable of infect and mirror in goal cells. After a 2d dengue virus infection, high-titre neutralizing antibodies are produced in opposition to as a minimum two, and frequently all 4, dengue viruses in addition to in opposition to non dengue flaviviruses.[16] During the early convalescent level following sequential dengue infections, the highest neutralizing antibody titre is frequently directed in opposition to the primary infecting virus and now no longer the maximum current one.[16]

Current Dengue Diagnostic Methods

Virus isolation

Specimens for virus isolation need to be amassed early withinside the direction of the infection, at some stage in the length of viremia (typically earlier than day 5). Virus can be recovered from serum, plasma and peripheral blood mononuclear cells and tries can be crafted from tissues amassed at (e.g. liver, lung, lymph nodes, thymus, bone marrow). Because dengue virus is heat-labile, specimens waiting for delivery to the laboratory need to be saved in a fridge or packed in moist ice. For garage as much as 24 hours, specimens need to be saved at between +4 °C and +8 °C.[17]

Nucleic acid detection

RNA is heat-labile and consequently specimens for nucleic acid detection should be treated and saved in line with the tactics defined for virus isolation.[18]

RT-PCR

Since the 1990s, numerous opposite transcriptasepolymerase chain response (RT-PCR) assays have beendeveloped. They provide higher sensitivity in comparison to virus isolation with a far greater speedy turnaround time. In situ RT-PCR gives the capacity to stumble on dengue RNA in paraffin-embedded tissues.[19] All nucleic acid detection assays contain 3 simple steps: nucleic acid extraction and purification, amplification of the nucleic acid, and detection and characterization of the amplified product. Extraction and purification of viral RNA from the specimen may be executed through conventional liquid segment separation strategies (e.g. phenol, chloroform) however has been regularly changed through silica-primarily based totally business kits (beads or columns) which can be greater reproducible and faster, mainly considering they may be automatic the use of robotics systems. A mixture of the 4 serotype-precise oligonucleotide primers in a unmarried response tube (onestep multiplex RT-PCR) is an thrilling opportunity tothe nested RT-PCR.[20]

Real-time RT-PCR

The actual-time RT-PCR assay is a one-step assay gadget used to quantitate viral RNA and the use of primer pairs and probes which can be unique to every dengue serotype. The use of a fluorescent probe allows the detection of the response merchandise in actual time, in a specialised PCR machine, with out the want for electrophoresis. Many actual-time RT-PCR assays were advanced using TaqMan or SYBR Green technologies.[21]
The TaqMan actual-time PCR is notably unique because of the collection-unique hybridization of the probe.Nevertheless, primers and probes mentioned in courses might not be capable of hit upon all dengue virusstrains: the sensitivity of the primers and probes relies upon on their homology with the centered gene collection of the unique virus analyzed. The SYBR inexperienced actual-time RTPCR has the gain of simplicity in primer layout and makes use of familiar RT-PCR protocols however is theoretically much less unique.[22]
Real-time RT-PCR assays are both ―singleplex‖ (i.e. detecting handiest one serotype at a time) or ―multiplex‖ (i.e. capable of pick out all 4 serotypes from a unmarried sample). The multiplex assays have the gain that a unmarried response can decide all 4 serotypes with out the cappotential for advent of infection at some stage in manipulation of the sample.[23] However the multiplex actual-time RT-PCR assays, even though faster, are presently much less touchy than nested RT-PCR assays. An gain of this approach is the capacity to decide viral titre in a scientific sample, which can be used to look at thepathogenesis of dengue disease.[24

Isothermal Amplification Methods

The NASBA (nucleic acid sequence-basedamplification) assay is an isothermal RNA particular amplification assay that doesn't require thermal biking instrumentation.[25] The preliminary level is a opposite transcription wherein the single-stranded RNA goal is copied right into a double-stranded DNA

molecule that serves as a template for RNA transcription.[26] Detection of the amplified RNA is finished both by electrochemiluminescence or in real-time with fluorescent-labelled molecular beacon probes. NASBAhas been tailored to dengue virus detection withSensitivity close to that of virus isolation in mobileular cultures and can be a beneficial approach for analyzing dengue infections in area studies.[27]

Detection of Antigens

Detection of dengue antigens in acute-segment serum become uncommon in sufferers with secondary infections due to the fact such sufferers had pre-present virus-IgG antibody immune complexes.[28] New trends in ELISA and dot blot assays directed to the envelop/membrane (E/M) antigen and the non-structural protein 1 (NS1) tested that excessive concentrations of those antigens withinside the shape of immune complexes can be detected in sufferers with each number one and secondary dengue infections as much as nine
days after the onset of illness.[29]

Serological Tests

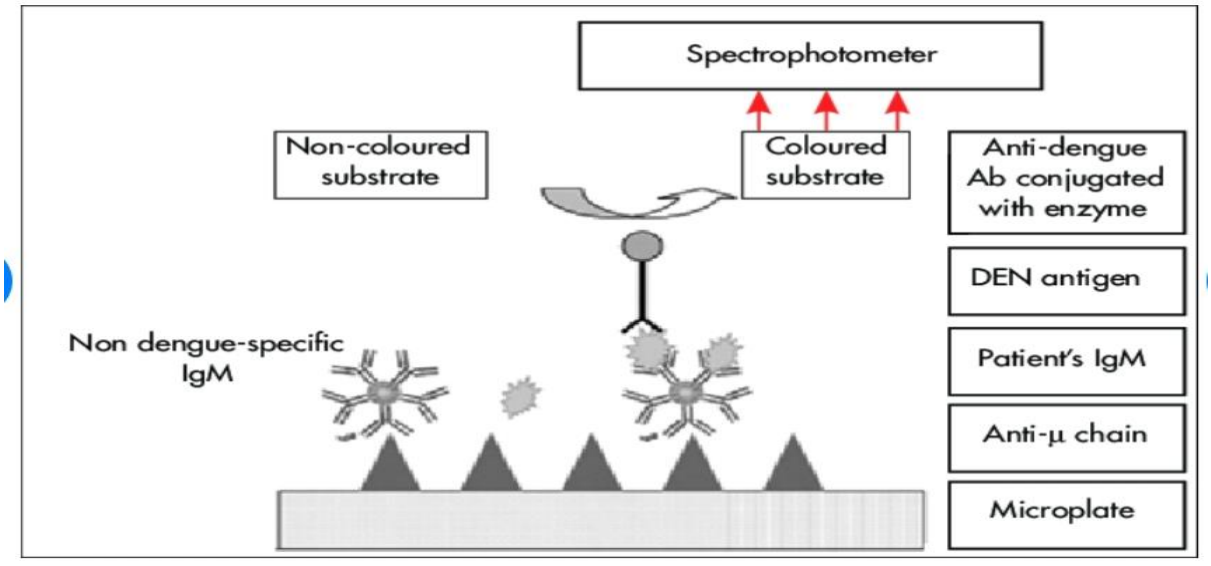
MAC-ELISA

For the IgM antibody-seize enzyme-related immunosorbent assay (MAC-ELISA) overall IgM in sufferers' sera is captured with the aid of using anti-μ chain precise antibodies (precise to human IgM) lined onto a microplate. Dengue-precise antigens, from one to 4 serotypes (DEN-1, -2, -3, and -4), are sure to thecaptured anti-dengue IgM antibodies and are detected with the aid of using monoclonal or polyclonal dengue antibodies without delay or in a roundabout way conjugated with an enzyme with a view to remodel a non-colored substrate into colored products. The optical density is measured with the aid of using spectrophotometer.[30]

IgG ELISA

The IgG ELISA is used for the detection of latest or beyond dengue infections. This assay makes use of the identical antigens because the MAC-ELISA. The use of E/M-unique seize IgG ELISA (GAC) lets in detection of IgG antibodies over a length of 10 months after the infection. IgG antibodies are lifelong as measured via way of means of E/M antigen-covered oblique IgG ELISA, however a fourfold or extra growth in IgG antibodies in acute and convalescent paired sera may be used to file current infections. Test consequences correlate properly with the haemagglutination-inhibition test.[31]
This approach may be used to come across IgG antibodies in serum or plasma and filter-paper saved blood samples and lets in identity of a case as a number one or secondary dengue infection. In general, IgG ELISA lacks specificity in the flavivirus sero complicated groups.

Principle of MAC-ELISA Test



IgM/IgG Ratio

A dengue virus E/M protein-precise IgM/IgG ratio may be used to differentiate number one from secondary dengue virus infections. IgM seize and IgG seize ELISAs are the maximum not unusualplace assays for this purpose.[32] In a few laboratories, dengue contamination is described as number one if the IgM/IgG OD ratio is extra than 1.2 (the use of patient's sera at 1/one hundred dilution) or 1.4 (the use of patient's sera at 1/20 dilutions). The contamination is secondary if the ratio is much less than 1.2 or 1.4. This set of rules has additionally been followed with the aid of using a few business vendors. However, ratios may also range among laboratories, accordingly indicating the want for betterstandardization of check performance.

IgA

Positive detection for serum anti-dengue IgA as measured with the aid of using anti-dengue virus IgA seize ELISA(AAC-ELISA) regularly takes place someday after that for IgM. The IgA titre peaks round day eight after onset of fever and reduces swiftly till it's far undetectable through day 40. No variations in IgA titres have been observed through authors among sufferers with number one or secondary infections. Even aleven though IgA values are normally decrease than IgM, each in serum and saliva, the 2 strategies will be done collectively to assist in deciphering dengue serology.[33] This method isn't used very regularly and calls for extra evaluation.

Haemagglutination-Inhibition Test

The haemagglutination-inhibition (HI) take a look at is primarily based totally at the capacity of dengue antigens to agglutinate purple blood cells (RBC). Anti-dengue antibodies in sera can inhibit this agglutination and the efficiency of this inhibition is measured in an HI take a look at. Serum samples are dealt with with acetone or kaolin to dispose of non-particular inhibitors of haemagglutination, after which adsorbed with gander to dispose of non-particular agglutinins.[34]

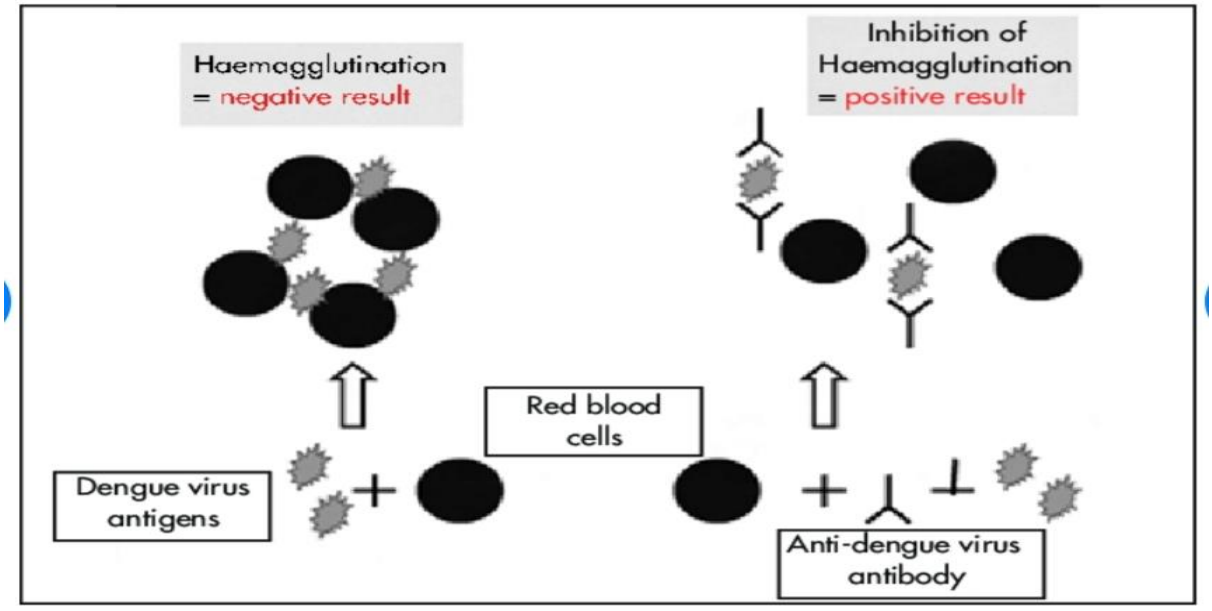


Figure: Haemagglutination-inhibition assay

Haematological Tests

Platelets and haematocrit values are typically measured for the duration of the extreme levels of dengue infection. These need to be achieved cautiously the usage of standardized protocols, reagents and equipment. A drop of the platelet matter underneath a thousand in step with µL can be found in dengue fever however it's miles a consistent function of dengue haemorrhagic fever.[35]

Thrombocytopaenia is normally found withinside the duration among day three and day eight following the onset of illness.Haemoconcentration, as predicted via way of means of an growth in haematocrit of 20% or greater as compared with convalescent values, is suggestive of hypovolaemia because of vascular permeability and plasma leakage.[36]

Treatment

There isn't anyt any precise remedy to be had for dengue virus infections.it's miles critical to exclude different treatable diagnoses. Patients at chance for dengue can collect different illnesses with comparable medical features, including malaria,typhoid fever, and leptospirosis.[37] Symptoms in sufferers with dengue virus infections clear up in 5 to seven days. Supportive remedies are to be had for the precise ailment manifestations of dengue virus infection.[38]

Dengue Fever: Patients with dengue fever need to be advised to preserve their consumption of oral fluid to keep away from dehydration.[39] Fever and myalgias may be controlled as wished with acetaminophen. Aspirin or nonsteroidal antiinflammatory marketers need to commonly be averted due to the chance of bleeding headaches and in kids due to the capability chance of Reye's syndrome.[40] The maximum critical degree to help the affected person with dengue fever is to cautiously compare theaffected person for approaching headaches.

Dengue virus contamination with massive Bleeding:

Gastrointestinal bleeding or menorrhagia in sufferers with DHF, and from time to time in sufferers with dengue fever as well, may be extreme sufficient to require blood transfusion.[41] Factors that make a contribution to bleeding encompass thrombocytopenia because of reduced platelet survival and, in extreme cases, frank disseminated intravascular coagulation. Platelet transfusions are hardly ever given, however can be warranted in sufferers with extreme thrombocytopenia (<10,000/mm3) and lively bleeding.[42]

Dengue Hemorrhagic Fever: Plasma leakage in DHF is crucial to manipulate with competitive intravascularquantity repletion to save you or opposite hypovolemicshock.[43] In moderate cases, specifically whilst medical interest is obtained early, oral rehydration can be sufficient.[44] However, in sufferers with establishedintravascular fluid loss, intravenous fluid management is recommended. Blood transfusion is suitable in sufferers with massive bleeding.[45]

Treatment of Shock: A protocol for intravenous fluid remedy has been evolved through the World Health Organization (WHO) primarily based totally upon medical enjoy in particular in youngsters from Southeast Asia.[46] For sufferers with shock, an preliminary bolus of 5 percentage dextrose in everyday saline or Ringer's lactate (10 to twenty mL according to kg of frame weight) infused swiftly is recommended, observed through non-stop infusion (10 to twenty mL/kg according to hour) till critical symptoms and symptoms and urine output normalize. The infusion rateCan then be regularly decreased till it fits plasma fluid losses.[47]

As a Herbal Treatment

Role of Papaya in Dengue fever

Botanical Name: Carica papaya
Family Name: Caricaceae
Common Name: Papaya, Paw Paw, Kates, Papaw
Part Used: Leaves, Fruits, bark
With the growing wide variety of human beings catching dengue fever, the call for for papaya leaf juice has soared.
Thrombocytopenia is one of the scientific manifestations in dengue fever and contributes to the plasma leakage and haemorrhage withinside the presence of greater vascular permeability.[48] Thrombocytopenia in dengue is taken into consideration to be an immune related, molecular mimicry concerning dengue viral debris and the platelet results in auto-destruction of the platelets with the aid of using immunoglobulin M(IgM) antibodies.[49] Interestingly, C. papaya leaves juice have proven a effective impact on growing platelet remember in healthful mice. C. papaya leaves extract organized in water has been examined in opposition to dengue fever.
After the management of aqueous extract in dengue inflamed patient, the platelet remember accelerated from55x103/µL to 168x103/µL, White blood cells from 3.7x103/µL to 7.7x103/µL and neutrophils from 46%to 78%. Carica papaya leaf juice confirmed a good sized inhibition of haemolysis invitro and will have a capability healing impact on disorder procedures inflicting destabilization of organic membranes may also correctly beautify the survival of platelets.[50] Thus, carica papya may be used to goal dengue fever.

Prevention

The best hazard for dengue virus contamination is in people living in endemic regions and now no longer intravelers.[51] Public fitness efforts in endemic regions: Control of the Aedes aegypti mosquito, which transmits dengue virus, and the improvement of vaccines are capability strategies in stopping dengue virus infections.[52]

Mosquito Control: Mosquito manage is the best technique to the prevention of denguetransmission. Programs focused on the Aedes aegypti mosquito as a way to get rid of city yellow fever withinside the Americas from the Nineteen Forties via Nineteen Seventies have been pretty successful.[53] These packages have been additionally powerful at lowering dengue transmission withinside the vicinity. These packages have been primarily based totally on a "pinnacle down" technique concerning competitive mosquito surveillance and insecticide use. However, loss of interest and investment of those packages withinside the Nineteen Seventies caused re-emergence of A. aegypti all through its former vicinity and the corresponding re-emergence of dengue.[54]Insecticide spraying, in reaction to dengue outbreaks, isn't always fantastically powerful in opposition to A. aegypti mosquitoes, which regularly breed internal houses. Community-primarily based totallyprocedures regarding schooling of the populace in efforts to lessen breeding sites, including discarded tyres and different boxes that gather status water.[55]In one study, a complete network and governmental manipulate strategy, along with the seeding ofwater vessels with Copepods (Fish) that feed on mosquito larvae, became a hit in doing away with A.aegypti and dengue transmission in 32 groups in rural regions of Vietnam.[56]

Vaccination: Infection with dengue gives lengthy-time period safety towards the precise serotype that precipitated the disease, helping the feasibility of a dengue vaccine. However, it gives simplest short-lived immunity to the alternative 3 dengue serotypes.[57] In view of the affiliation of DHF with preceding publicity to dengue viruses and the popularity that each one 4 serotypes are able to inducing DHF it's far the overall consensus withinside the medical and public fitness groups that any candidate vaccine ought to produce defensive immunity towards DEN 1-4. Since waning immunity may additionally boom the hazard for DHF in vaccines, vaccine-caused defensive immunity ought to additionally be lengthy-lived.[58]

Animal research suggest that defensive immunity towards dengue may be mediated through neutralizing antibodies, specifically the ones directed towards the envelope (E) glycoprotein. However, herbal dengue contamination induces low ranges of cross-reactive antibodies which can be detected in neutralization assays, however do now no longer save you contamination with the alternative dengue serotypes.[59]

Tetravalent vaccines that result in immunity towards all 4 serotypes are in development. In a rhesus monkey model, one tetravalent stay attenuated dengue virus vaccine established seroconversion charges of 100, 100, ninety and 70 percentage towards dengue serotypes 1, 2, 3, and 4. In addition, vaccination led to whole safety towards viremia from inoculation with serotype 2; mission with the alternative dengue serotypes established safety in 50 to eighty percentage of animals as compared to controls.[60]

Recommendations for vacationers: Most vacationers from non-endemic nations are at pretty low hazard for DHF due to the fact they lack preceding publicity to dengue viruses.[61] Avoidance of publicity to inflamed A. aegypti mosquitoes is the number one technique to prevention of dengue virus infections in vacationers. These mosquitoes predominantly stay in city regions in and round houses.[62]

There are following a few steps that taken as prevention of dengue virus infection

- Spray mosquito repellant in your pores and skin and clothes.
- Wear lengthy sleeves, lengthy pants, and socks sprayed with mosquito repellant.
- Avoid being outside at sunrise and nightfall while mosquitoes are maximum active.
- Take time to go searching your private home and backyard for mosquito-breeding places, mainly regions where
- there's status water. To keep away from status water round your private home:
- Drain kiddie swimming pools weekly.
- Change water in flower vases, hen baths, and animal watering pans two times a week.
- Get rid of antique tires, buckets, bottles, and cans, or make sure they're empty of water.
- Repair any leaky pipes and outdoor faucets, and flow air conditioner drain hoses frequently.

Conclusion

Though dengue fever is mostly a self-proscribing disorder, loss of right tracking and ok volumesubstitute may also result in deadly outcome. In view of rising outbreaks of dengue fever in numerous states of India, it will become vital for number one care physicians to have an up to date know-how approximately early prognosis and latest control guidelines.

Dengue has advanced as a international life-threatening public fitness concern, affecting round 2.five billion people in extra than a hundred countries. The health practitioner ought to be privy to the numerous scientific manifestations of this circumstance and make sure an early and ok remedy plan. Future guidelines to fight this dreadful disorder goal at techniques of mosquito control, improvement of vaccine, and antiviral drug regimen.

References

1. R. Chen and N. Vasilakis, ―Dengue-Quo Tu et QuoVadis? Viruses‖, 1993; 3(9).
2. B.R. Murphy and S.S. Whitehead, ―Immunereaction to dengue virus and potentialities for avaccine,‖ Annual Review of Immunology, 29.
3. World Health Organiazation, Dengue: Guideline forDiagnosis, Treatment, Prevention, and, Control,WHO, Geneva, 2009.
4. S. Bhatt, P. W. Gething, O. J. Brady et al., ―Thenternational distribution and burden of dengue,‖ Nature,2013; 496: 7446-504–507.
5. O. J. Brady, P. W. Gething, S. Bhatt et al., ―Refiningthe worldwide spatial limits of dengue virus transmissionwith the aid of using evidence-primarily based totally consensus,‖ PLoS Neglected Tropical Diseases, Article ID e1760, 2012; 6(8).
6. G. N. Malavige, S. Fernando, D. J. Fernando, and S.L. Seneviratne, ―Dengue viral infections,‖Postgraduate Medical Journal, 2004; 80: 948-588–601.
7. https://www.mayoclinic.org/diseasesconditions/dengue-fever/symptoms-causes/syc20353078.
8. Vorndam V, Kuno G. Laboratory prognosis ofdengue virus infections. In: Gubler DJ, Kuno G, eds. Dengue and dengue hemorrhagic fever. New York,CAB International, 1997; 313–333.
9. Chanama S et al. Analysis of unique IgM responsesin secondary dengue virus infections: stages andsuperb charges in evaluation with number one infections.Journal of Clinical Virology, 2004; 31: 185–189.
10. Shu PY et al. Comparison of a capturimmunoglobulin M (IgM) and IgG ELISA and nonstructural protein NS1 serotype-unique IgG ELISAfor differentiation of number one and secondary denguevirus infections. Clinical and Diagnostic LaboratoryImmunology, 2003; 10: 622–630.
11. Hunsperger EA et al. Evaluation of commerciallyto be had anti–dengue virus immunoglobulin M tests. Emerging Infectious Diseases (serial online),;March (date cited). Accessible athttp://www.cdc.gov/EID/content/15/3/436.htm.2009.
12. Morens DM et al. Simplified plaque discount neutralization assay for dengue viruses with the aid of using semimicro techniques in BHK-21 cells: evaluation of the BHK suspension check with preferred plaque discount neutralization. Journal of Clinical Microbiology, 1985; 22(2): 250–254.
13. Alvarez M et al. Improved dengue virus plaque formation on BHK21 and LLCMK2 cells: assessment of a few factors. Dengue Bulletin, 2005;29: 1–9.
14. Halstead SB, Rojanasuphot S, Sangkawibha N. Original antigenic sin in dengue. American Journal of Tropical Medicine and Hygiene, 1983, 32: 154–156.
15. Lanciotti RS et al. Rapid detection and typing of dengue viruses from scientific samples with the aid of using using opposite transcriptase-polymerase chain reaction. Journal of Clinical Microbiology, 1992; 30: 545–551.

16. Harris E et al. Typing of dengue viruses in scientific specimens and mosquitoes with the aid of using unmarried tube multiplex opposite transcriptase PCR. Journal of Clinical Microbiology, 1998; 36: 2634–2639.
17. Vaughn DW et al. Dengue viremia titer, antibody reaction sample and virus serotype correlate with sickness severity. Journal of Infectious Diseases, 2000; 181: 2–9.
18. Shu PY, Huang JH. Current advances in dengue prognosis. Clinical and Diagnostic Laboratory Immunology, 2004; 11(4): 642–650.
19. Parida MM et al. Rapid detection and differentiation of denguevirus serotypes with the aid of using a real-time opposite transcription-loop-mediated isothermal amplification assay. Journal of Clinical Microbiology, 2005; 43:2895–2903. (doi: 10.1128/JCM.43.6. 28952903.2005).
20. Vazquez S et al. Serological markers all through dengue three number one and secondary infections. Journal ofClinical Virology, 2005; 33(2): 132–137.
21. Fernandez RJ, Vazquez S. Serological prognosis of dengue with the aid of using an ELISA inhibition method (EIM). Memórias do Instituto Oswaldo Cruz, 1990; 85(three):347–351.
22. Vazquez S, Fernandez R, Llorente C. Usefulness of blood specimens on paper strips for serologic research with inhibition ELISA. Revista do Instituto deMedicina Tropical de São Paulo, 1991; 33(four): 309–311.
23. Vazquez S et al. Kinetics of antibodies in sera, saliva, and urine samples from grownup sufferers with number one or secondary dengue three virus infections. International Journal of Infectious Diseases, 2007;11: 256–262.
24. Nawa M. Immunoglobulin A antibody responses in dengue sufferers: a beneficial marker for serodiagnosis of dengue virus infection. Clinical and Vaccine Immunology, 2005; 12: 1235–1237.
25. Lemmer K et al. External fine manipulate exams in PCR diagnostics of dengue virus infections. Journal of Clinical Virology, 2004; 30:291–296.
26. WHO. Laboratory biosafety manual, third ed. Geneva, World Health Organization, 2004. (ISBN ninety two four 154650 6, WHO/CDS/CSR/LYO/2004.11.
27. http://www.who.int/csr/resources/publications/biosafety/Biosafety7.pdf).
28. Ramos MM et al. Dengue Serosurvey Working Group. Epidemic dengue and dengue hemorrhagic fever on the Texas-Mexico border: consequences of a household-primarily based totally seroepidemiologic survey, December 2005. American Journal of Tropical Medicine and Hygiene, 2008; 78(three): 364--369.
29. Centers for Disease Control and Prevention. Dengue hemorrhagic fever -- U.S.Mexico border, 2005. Morbidity and Mortality Weekly Report, 2007;56(31): 785-789. Erratum in: Morbidity and Mortality Weekly Report, 2007; 56(32): 822.
30. PAHO. Dengue and dengue hemorrhagic fever. Regional Committee decision CD43.R4, followed on the 53rd consultation of the Regional Committee for the Americas, forty third Directing Council. Washington, DC, Pan American Health Organization, 2001(http://www.paho.org/english/hcp/hct/vbd/newgeneration-resolutions.pdf).
31. PAHO. Dengue. Regional Committee decision CD44.R9, followed on the fifty fifth consultation of the Regional Committee for the Americas, forty fourth Directing Council. Washington, DC, Pan American Health Organization, 2003.
32. (http://www.paho.org/english/gov/cd/cd44-r9-e.pdf).
33. PAHO. Grupo de Trabajo sobre Dengue. Estrategia de Gestión Integrada para l. a. prevención y manipulate del dengue en l. a. Región de las Américas. 2.ª versión. Santa Cruz de l. a. Sierra, Bolivia. Pan American Health Organization, (Document OPS/ HDM/CD/440.07, in Spanish), 2003.
34. PAHO. Pan American Health Organization. Prevención y manipulate del dengue en las Américas. Resolución CSP27.R15. 27. a Conferencia Sanitaria Panamericana CSP27. R15 (Esp.) 1--five de octubre de(in Spanish), 2007.
35. Nathan MB, Dayal-Drager R. Recent epidemiological trends, the worldwide method andpublic fitness advances in dengue. Working paper three.1 in: Report of the Scientific Working Groupassembly on Dengue, Geneva, 1–five October 2006.Geneva, World Health Organization, Special Programme for Research and Training in Tropical Diseases, 2007; 29—34. (Document TDR/SWG/07).
36. Kokernot RH, Smithburn KC, Weinbren MP. Neutralising antibodies to arthropodborne viruses inhuman and animals withinside the Union of South Africa. Journal of Immunology, 1956; 77: 313–322.
37. Blackburn NK, Rawal R. Dengue fever imported from India: a file of three cases. South African Medical Journal, 1987; 21: 386–287.
38. Boisier P et al. Dengue 1 epidemic withinside the Grand Comoro Island (Federal Islamic Republic of theComores), March-May 1993. Annales de l. a. Société Belge de Médecine Tropicale, 1993; 74: 217–229.
39. Gubler DJ et al. Dengue three Virus Transmission in Africa. American Journal of Tropical Medicine andHygiene, 1986; 35(6): 1280--1284.
40. Carey DE et al. Dengue virus from febrile sufferers in Nigeria 1964–68. Lancet, 1971; 1: 105–106.
41. Gonzalez JP et al. Dengue in Burkina Faso: seasonal epidemics withinside the city vicinity of Ouagadougu. Bulletin de l. a. Société de pathologie exotique et de ses filiales, 1985; 78: 7–14.
42. Diallo M et al. Amplification of the sylvatic cycle of dengue virus kind 2, Senegal, 1999--2000: entomologic findings and epidemiologic considerations. Emerging Infectious Diseases (serial online), 2003. March (date cited). Accessible at http:// www.cdc.gov/ncidod/EID/vol9no3/02-0219.htm.
43. WHO/EMRO. World Health Organization, Regional Office for the Eastern Mediterranean, Division of Communicable Disease Control, Newsletter, 2005;6: 7–8. (http://www.emro.who.int/pdf/ dcdnewsletter6.pdf).
44. Hyams KC et al. Evaluation of febrile sufferers in Port Sudan, Sudan: isolation of dengue virus.American Journal of Tropical Medicine and Hygiene, 1986; 35: 860– 865.
45. Rodier GR et al. Epidemic dengue 2 withinside the town of Djibouti 1991–1992. Transactions of the RoyalSociety of Tropical Medicine and Hygiene, 1996; 90:237–240.
46. Bushra J. Dengue Virus Serotype three, Karachi, Pakistan. Emerging Infectious Diseases, 2007;13(1).

47. European Centre for Disease Prevention and Control. Dengue worldwide: a top level view of the present day state of affairs and implications for Europe, Eurosurveillance, 2007; 12(25). (http://www.eurosurveillance.org/ViewArticle.aspx? PublicationType=W&Volume=12&Issue=25&OrderNumber=1).
48. WHO. Dengue haemorrhagic fever: diagnosis, treatment, prevention and control, 2d ed. Geneva,World Health Organization, 1997.
49. Guha-Sapir D, Schimmer B. Dengue fever: new paradigms for a converting epidemiology. Emerging Themes in Epidemiology, 2005. (Open get admission to journal, http:// www.ete-online.com/content/2/1/1
50. L. Hermida, L. J. Bernardo, M. Mart´ın et al., ―A recombinant fusion protein containing the domain III of the dengue-2 envelope protein is immunogenic and protecting in nonhuman primates, 2006; 24(16): 3165–3171.
51. J. R. Danko, C. G. Beckett, and K. R. Porter, ―Development of dengue DNA vaccines,‖ Vaccine, 2011; 29(42): 7261–7266.
52. C. G. Beckett, J. Tjaden, T. Burgess et al., ―Evaluation of a prototype dengue-1 DNA vaccine in a Phase 1 scientific trial,‖ Vaccine, 2011; 29(5): 960–968.
53. K. R. Porter, D. Ewing, L. Chen et al., ―Immunogenicity and protecting efficacy of a vaxfectin-adjuvanted tetravalent dengue DNA vaccine,‖ Vaccine, 2012; 30(2): 336–341.
54. K. Raviprakash, T. Luke, J. Doukas et al., ―A dengue DNA vaccine formulated with Vaxfectin® is nicely tolerated, and elicits sturdy neutralizing antibody responses to all 4 dengue serotypes in New Zealand white rabbits,‖ Human Vaccines and Immunotherapeutics, 2012; 8(12): 1764–1768.
55. US Army Medical Research and Materiel Command, Evaluation of the Safety and the Ability of a DNA Vaccine to Protect Against Dengue Disease (TVDV), ClinicalTrials.gov, Bethesda, Md, USA, National Library of Medicine (US), NLM Identifier: NCT01502358, 2000.https://clinicaltrials.gov/ct2/show/ NCT01502358.
56. K. Raviprakash, D. Wang, D. Ewing et al., ―A tetravalent dengue vaccine primarily based totally on a complicated adenovirus vector affords massive safety in rhesus monkeys towards all 4 serotypes of dengue virus,‖ Journal of Virology, 2008; 82(14): 6927–6934.
57. L. J. White, M. M. Parsons, A. C. Whitmore, B. M. Williams, A. de Silva, and R. E. Johnston, ―An immunogenic and protecting alphavirus replicon particle-primarily based totally dengue vaccine overcomes maternal antibody interference in weanling mice,‖ Journal of Virology, 2007; 81(19): 10329–10339.
58. S. Brandler, M. Lucas-Hourani, A. Moris et al., ―Pediatric measles vaccine expressing a dengue antigen induces long lasting serotype-unique neutralizing antibodies to dengue virus,‖ PLoS Neglected Tropical Diseases, 2007; 1(3): article e96.
59. D. H. Holman, D. Wang, K. Raviprakash et al., ―Two complicated, adenovirus-primarily based totally vaccines that collectively result in immune responses to all 4 dengue virus serotypes,‖ Clinical and Vaccine Immunology,2007; 14(2): 182–189.
60. N. U. Raja, D. H. Holman, D. Wang et al., ―Induction of bivalent immuneresponses byex pression of denguevirustype 1andtype 2 antigens from a unmarried complicated adenoviral vector,‖ AmericanJournal of Tropical Medicine and Hygiene, 2007; 76(4): 743– 751.
61. WHO. Dengue hemorrhagic fever: diagnosis, treatment, prevention, and control. second ed. Geneva: World Health Organization, 2002.
62. Nimmannitya, S, Thisyakorn, U, Hemsrichart, V. Dengue haemorrhagic fever with unusual manifestations. Southeast Asian J Trop Med Public Health, 1987; 18: 398.