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DENGUE: A GLOBAL HEALTH CHALLENGE - CURRENT VIEWS ON PATHOGENESIS, DIAGNOSIS, TREATMENT AND PREVENTION

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ABSTRACT

Background: Dengue is a global threat expanding its geographic reach and spreading to a growing world population. Up to 3 billion people are at risk. Dengue virus infection can be asymptomatic or sparse, but can also cause dengue hemorrhagic fever and dengue shock syndrome.
Aim: The purpose of this article is to highlight the challenges of effective treatment, multi-pronged prevention and safe immunoprophylaxis of dengue virus.
Methods: A review of scientific articles published on PubMed and Google Scholar from 2020 to 2025.
Results: Due to the number and complexity of dengue serotypes, as well as the antibody-dependent amplification mechanism characteristic of this virus, creating a universal, effective and safe vaccine is a difficult task. It is all the more important because of the lack of specific treatment, which is so necessary in the case of a severe course of the disease in the form of hemorrhagic fever or shock syndrome. It is also necessary to control vectors through chemical, biological and environmental methods.
Conclusion: Dengue is now a serious global public health threat that requires urgent action. Key areas for further research and development include a better understanding of pathogenesis, especially in the context of symptomatic DENV infections, and increased work on a variety of treatment and control options, as well as the development of a universal, safe and effective vaccine. The ultimate goal is to reduce the threat of the disease worldwide.

KEYWORDS

Dengue, Dengue Virus, Dengue Fever, Dengue Vaccines, Tropical Disease

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Introduction

Dengue is an infectious tropical disease caused by the dengue virus (DENV). It is a member of the *Flaviviridae* family, along with yellow fever virus (YFV), Zika virus (ZIKV) and Japanese encephalitis virus (JEV), among others.[1][2] Four antigenically distinct serotypes of dengue virus have been identified, and within each serotype, different genotypes can be distinguished. Each serotype may elicit a different immune response due to its effect on different target cells, and thus may result in a different course and severity of the disease.[3] Furthermore, reinfection with a different dengue virus serotype may elicit a more rapid immune response than the original infection due to immunoglobulin-dependent amplification.[4] Infection may be asymptomatic or symptomatic. We can divide the course of the disease, based on the severity of symptoms, into three categories: dengue fever (DF), dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS).[1] There are nearly 400 million infections each year, including more than 100 million symptomatic infections, but approx. 90% of these are characterized by a mild, self-limiting course, and severe cases of hemorrhage and shock are fortunately relatively rare.[5] The vector of infection is mainly mosquitoes of the *Aedes aegypti* species and, less frequently, *Aedes albopictus*, while their spread to previously unoccupied areas of the world is a consequence of, among other things.global warming, among other factors.[3][5] It is a disease that occurs mainly in tropical and subtropical areas with a predominance of infections in Latin America, especially in Brazil and Mexico, and in Southeast Asia, especially in Thailand and Indonesia, but also in Central Africa and Australia.[6] There are two vaccines on the world pharmaceutical market used as dengue immunoprophylaxis - Qdenga and Dengvaxia, which will be discussed in more detail later in this article.[5]

Aim

The purpose of this article is to present the current state of knowledge about dengue virus infection - epidemiology, symptoms, methods of diagnosis, treatment and prevention, and challenges associated with the disease, as well as to systematize knowledge about immunization and its effectiveness against dengue fever.

Methodology

Review of scientific articles, guidelines from scientific societies and epidemiological reports published between 2020 and 2025. Searches were conducted in PubMed and Google Scholar, using the search terms: "dengue", "dengue virus", "dengue fever", "dengue hemorrhagic fever", "dengue shock syndrome", "dengue vaccines", "Qdenga", "Dengvaxia". Meta-analyses and case reports were preferred.

Results

Dengue virus and its vectors

Dengue virus belongs to the *Flaviviridae* family, along with yellow fever virus (YFV), Zika virus (ZIKV) and Japanese encephalitis virus (JEV), among others.[1][2] It has a single-stranded RNA genome of 11 kb in length. At the early stage of the virus' replication, its particles attach to mammalian cell receptors (including C-SIGN/L-SIGN, heparan sulfate, dopamine receptor, mannose receptor) and then enter their interior by protein-clathrin-dependent endocytosis. Once inside the cell, the dengue virus fuses with the endosomal membrane and is then released into the cytoplasm. When the virus particle splits, its genome is released. After replication, fully grown viruses escape from the cell and are free to infect subsequent cells.[7] Four antigenically distinct serotypes of dengue virus have been identified, and within each serotype, different genotypes can be distinguished. Based on antigenic differences, serotypes DENV1, DENV2, DENV3 and DENV4 were found to have 65% genomic similarity, with the exception being serotype DENV-5, discovered in Malaysia. It is noteworthy that this serotype, despite the case of its detection in humans (Malaysia, 2013), is found almost exclusively in non-human primates because, unlike the first four serotypes, it is subject to the forest transmission cycle.[1][3]

The vector of infection is mainly mosquitoes of the species *Aedes aegypti* (responsible for global transmission of DENV) and, less frequently, *Aedes albopictus*, and their spread to previously unoccupied areas of the world is a consequence of global warming, the expansion of trade or international travel.[1][8]

Aedes aegypti mosquitoes are native to Africa, but have been imported to other continents. They are endophilic, meaning they prefer shaded, moist and warm habitats, such as buildings in urban areas in tropical and subtropical zones. They breed in containers filled with water, such as car tires or rain barrels. Males feed on fruit juices, while females feed on the blood of humans and monkeys. In addition to dengue, they also transmit yellow fever.[9]

In contrast, mosquitoes of the species *Aedes albopictus* (tiger mosquitoes), originally from Southeast Asia, are able to survive in lower temperatures and have even reached the southern reaches of Scandinavia. Tiger mosquitoes are exophilic, their habitat is in open areas, and adults reproduce similarly to Egyptian mosquitoes - in containers of water. Females feed on human blood, as well as animal blood - mammals, reptiles, amphibians and birds. They feed in the early morning and late afternoon. In Europe, stable populations of them have been identified in Albania, Italy, France, Greece or Spain, among others. *Aedes albopictus* mosquitoes are vectors not only of dengue, but also of Japanese encephalitis, yellow fever, West Nile fever and chikungunya. [9][10]

Epidemiology

Dengue was first reported several hundred years ago. According to World Health Organization estimates, there are nearly 400 million infections each year, including about 100 million symptomatic infections, but about 90% of these are characterized by a mild, self-limiting course, while cases of dengue hemorrhagic fever and shock syndrome affect approx. 500,000 people, causing more than 35,000 deaths per year.[3][5] This most common arboviral disease in the world occurs mainly in tropical and subtropical areas with a predominance of infections in Latin America, especially Brazil and Mexico, and in Southeast Asia, especially Thailand and Indonesia, but also in Central Africa and Australia.[11]

The area of exposure is much larger, covering more than 100 countries and two-fifths of the world's population - about 2.5-3 billion people. Due to the increasing prevalence of international travel and global trade, as well as the increasing population in areas affected by the Egyptian and tiger mosquito (especially in Africa, India and Southeast Asia), we can expect the exposed population to increase. Climate change is also

not insignificant, resulting in an increase in average air temperature in countries far from the equator, which in turn increases the geographic feeding area of *Aedes* species mosquitoes. This will result in an increase in the population at risk of infection with dengue and other arboviral diseases.[12]

Course and clinical manifestations

Due to the presence of four serotypes of dengue virus and their effects on different target cells, we can expect a varied immune response and thus a variable course, clinical manifestations and severity of the disease.[3] Moreover, reinfection with a different dengue virus serotype can elicit a more rapid immune response than the primary infection due to antibody-dependent amplification.[4] A fairly common observation, especially in hyperendemic regions, is simultaneous infection with several dengue virus serotypes. This is associated with the mosquito carrying more than one serotype or with multiple bites by mosquitoes infected with different serotypes.[13]

Infection can be asymptomatic or symptomatic. We can divide the course of the disease, based on the severity of symptoms, into three categories:

- dengue fever (DF),
- dengue hemorrhagic fever (DHF),
- dengue shock syndrome (DSS).[14]

Dengue fever (DF) usually lasts between 2 and 7 days, and its symptoms are:

- fever
- severe headache (often extra-orbital)
- severe muscle and joint pain
- nausea
- rash/brooding

Dengue hemorrhagic fever (DHF) appears after 3-5 days of fever,and its symptoms are:

- thrombocytopenia with a platelet count <100,000/µl
- bleeding, pleural effusion
- abdominal pain
- vomiting
- sudden drop in body temperature

Dengue shock syndrome (DSS), also after 3-5 days of fever. Symptoms are:

- temperature up to 38 °C
- hypotension
- further drop in platelet count leading to plasma leakage and subsequent shock
- critical bleeding
- organ damage
- cardiopulmonary failure[15][16]

Diabetes, hypertension, cardiovascular disease, and sickle cell anemia increase the risk of severe dengue. Pregnant women with dengue are also at higher risk of complications.[15]

Studies indicate that in addition to systemic effects, dengue can also cause serious neurological complications such as encephalopathy or encephalitis, as well as ophthalmic complications such as optic nerve edema and inflammation, retinal hemorrhages and visual disturbances.[19]

Diagnostics

Because dengue virus infection has similar symptoms to other febrile diseases (including other hemorrhagic fevers), the diagnosis must be further confirmed by laboratory tests. Typically, laboratory diagnostics use tests aimed at detecting dengue, mainly RT-PCR.[15] RDT tests of dengue IgM and IgG immunoglobulin and nonstructural protein 1 are widely used in the diagnosis of dengue virus in Asia.[17] Using this combined method, false positives caused by other viruses in the Flaviviridae group can be almost eliminated, and the sensitivity of dengue detection reaches nearly 100%. Even rapid cassette tests are used for this.[15] Regarding the diagnosis of the different stages of the disease, it was found that elevated levels of C-reactive protein, aspartate aminotransferase, interleukin-8, and hypoalbuminemia were clearly associated with dengue hemorrhagic fever, while elevated levels of vascular cell adhesion protein 1, syndecan-1, aspartate aminotransferase, and C-reactive protein were strongly associated with severe dengue.[18] In the past, when dengue was suspected, the WHO recommended performing a tourniquet test - inflating a blood pressure cuff, waiting 2 minutes, and then counting the number of petechiae in the ulnar fossa. When there are more than 10 per square inch (about 6.5 square centimeters), then we can suspect dengue.[11][20]

Treatment

Currently, there is no approved antiviral drug to treat dengue. However, several potentially effective drugs are currently being tested on humans and are in various phases of clinical trials. Interestingly, substances of natural origin, e.g., flavonoids from plant sources (quercetin, rutin, oroxylin A), mangiferin or curcumin, have been proven to have activity against the dengue virus.[21][22] In addition, some drugs approved for the treatment of other diseases, such as chloroquine, prednisolone and ribavirin, are also being tested for potential activity against the dengue virus, but studies to date have not shown sufficient efficacy.[23] Due to the lack of an official drug against dengue, mainly symptomatic treatment - antipyretic, analgesic and intravenous fluid therapy to maintain adequate intravascular volume - is used, and bed rest is recommended for the most common - lightest forms.[15] The lack of specific and effective treatment prompts the use of prophylaxis to prevent the disease, especially immunization.[24]

Prevention

The use of multi-pronged prevention appears to be the most effective method against many diseases, including dengue. Preventive measures can be taken at the individual level - immunization - as well as at the societal level - reducing the risk of bites through vector control. We can divide these controls into chemical, biological and environmental.[25]

Chemical control involves the use of chemical solutions, usually in the form of sprays, to repel (repellents) or kill mosquitoes and chemically destroy their breeding sites. Pyrethroids are used outdoors, while insecticides are used indoors and outdoors for residual spraying.[26] In homes, insecticide-treated mosquito nets and even whole house nets, also treated with mosquitocidal chemicals, can be used.[27][28]

Biological control involves introducing biological agents - fish, crustaceans and bacteria - into the mosquito's living and reproductive environment. These agents include larval fish, cyclopod copepods and the bacteria *Bacillus thuringiensis israelensis*. [25][29] Biological control methods may also include modifying the genetic material of vectors, thus preventing them from transmitting dengue virus. Prominent among such measures are the sterilization of insects, the use of genetically modified mosquitoes carrying a dominant lethal gene, or the introduction of Wolbachia bacteria. [25][30]

Environmental control methods include reducing breeding sites by installing efficient water and sewage systems, emptying or destroying containers/tubs/barrels that are incidental reservoirs of rainwater, and appropriate waste management.[31][32]

Vaccine

The number and complexity of dengue virus serotypes (DENV1-4), as well as the role of antibody-dependent amplification in severe dengue, pose difficulties in developing a universal, effective and safe dengue vaccine.[33] The biggest challenge is the complex immune interactions between the four antigenically different dengue virus serotypes [34][35]. These interactions lead to unbalanced vaccine performance, which can increase the risk of antibody-dependent potentiation. There are currently two dengue vaccines on the pharmaceutical market - TAK-003 (Qdenga) and the currently withdrawn CYD-TDV (Dengvaxia), but neither has been widely deployed. Each is aimed at a slightly different target group due to the mechanism of action and the specificity of the body's immune response to first and subsequent contact with different serotypes of DENV.[36] Both vaccines are quadrivalent, live and attenuated, but differ in the backbone of the genome. There are studies of a third vaccine, also quadrivalent, live and attenuated, TV003/005, which has undergone phase III clinical trials in Brazil, but the results have not yet been published.[35]

Dengvaxia (CYD-TDV), developed by Sanofi Pasteur, was the first licensed dengue vaccine. This quadrivalent, live attenuated vaccine contains the 17D yellow fever core. Phase III studies showed that the efficacy of Dengvaxia varied by age, serostatus of the vaccinated person and serotype of the virus. At the population level, the vaccine had clear overall benefits, but in seronegative individuals, it increased the risk of severe dengue at the time of exposure. As a result, the WHO recommended screening before vaccination. This was to result in the vaccination of only those seropositive for dengue virus. For commercial reasons, the company decided to stop further production of this vaccine and withdraw it from the market.[37]

Qdenga (TAK-003), developed by Takeda, is based on a weakened backbone of the DENV2 virus.[38] Proteins from the DENV1, DENV3 and DENV4 serotypes were inserted into the backbone. As a result, compared to the Dengvaxia vaccine, Qdenga contains more non-structural proteins, which is an advantage. Qdenga effectively stimulates the production of neutralizing antibodies against DENV2, and to a lesser extent also acts on DENV1, DENV3 and DENV4.[39] Numerous studies have been conducted on Qdenga and no

serious safety risks have been identified. TAK-003 was well tolerated by people between the ages of 4 and 60, regardless of their age, gender or previous exposure to DENV. In pivotal studies conducted in countries where dengue is endemic, the vaccine's efficacy over 5 years against laboratory-confirmed dengue was 61%, and its effectiveness in preventing dengue-related hospitalizations was as high as 84%.[40] Significantly, Qdenga showed efficacy against all four serotypes in people who had previous contact with the virus (seropositive), while in people who had no previous contact with the virus (seronegative), efficacy was observed only for serotypes DENV1 and DENV2. In seronegative subjects, no efficacy was observed against DENV3 and DENV4. Modeling suggests that the Qdenga vaccine could provide significant benefits at the population level. Its beneficial public health impact will be greatest in regions where a high percentage of the population is already seropositive and where DENV2 serotype is predominantly circulating.[41]

Available data from clinical trials indicate that the benefits of this vaccine far outweigh the potential risks. However, it is important to keep in mind that, as with many other vaccines, it provides only partial protection. This means that vaccinated individuals - both seropositive and seronegative - can still contract the disease. Such "breakthrough" infections can range from mild to severe. In regions where dengue is spreading at a low to moderate rate, the World Health Organization does not recommend introducing the TAK-003 vaccine into universal vaccination programs. This recommendation is based on the need for even more data on its efficacy and safety profile in people who have never been infected with dengue virus before, especially in the context of protection against DENV3 and DENV4 serotypes.[36]

As for travelers, they are an important link in the global spread of dengue virus while exposing themselves to infection. However, the World Health Organization's efforts and recommendations for the Qdenga vaccine focus primarily on its use in populations living in endemic areas, rather than among travelers.[42] Currently, there is no comprehensive evaluation of the benefit/risk ratio for administering dengue vaccines to travelers. The WHO does, however, recognize the benefits of vaccinating seropositive travelers going to areas of high disease endemicity. However, for seronegative travelers, the benefits are noticeably less.[36] Given that a large proportion of travelers are seronegative, the overall efficacy of the Qdenga vaccine in this group is noticeably lower compared to endemic populations with high seropositivity rates. This means that the vaccination strategy for travelers requires further research and analysis.[43][44]

Discussion

Dengue is a huge challenge for communities around the world. Due to expanding international travel, global trade and global warming, regions not previously affected should stop thinking that the problem does not affect them, as they are likely to face new health challenges over the next decade. Due to dengue's expanding geographic range and consequently expanding population area, governments and organizations should spare no effort or money for research on the virus, disease forms, drugs, vaccines and vector control.

The main goal should be to develop an effective quadrivalent vaccine that is safe regardless of the serological status of the vaccinated. This would reduce severe and symptomatic cases of the disease.

In addition, research should continue on an effective drug to combat dengue virus infection and reduce the severe course of the disease and its unpredictable complications. Given the proven efficacy of some substances, it is worth focusing efforts on further research.

Moreover, the spread of vectors i.e. Egyptian and tiger mosquitoes should be controlled through chemical, biological and environmental methods. Governments and local governments in endemic countries can play a major role here, through the development of efficient water and sewage networks and proper waste management.

Conclusions

This article presents an up-to-date review of data on dengue virus infection, including: characteristics of the virus, epidemiology of clinical manifestations, current treatment methods, ways to prevent dengue, and a review of available vaccines. It stresses that it is essential to better understand the pathogenesis of DENV infections, explore a variety of treatment and control strategies, and make efforts to develop a universal, effective and safe vaccine. Today, dengue is already a global public health threat that requires safe vaccines, improved vector control methods and effective drugs to reduce the threat of the disease.

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REFERENCES

1. Khan, M. B., Yang, Z. S., Lin, C. Y., et al. (2023). Dengue overview: An updated systemic review. Journal of Infection and Public Health, 16(10), 1625–1642. https://doi.org/10.1016/j.jiph.2023.08.001
2. Barnard, T. R., Abram, Q. H., Lin, Q. F., Wang, A. B., & Sagan, S. M. (2021). Molecular determinants of flavivirus virion assembly. Trends in Biochemical Sciences, 46(5), 378–390. https://doi.org/10.1016/j.tibs.2020.12.007
3. Parveen, S., Riaz, Z., Saeed, S., et al. (2023). Dengue hemorrhagic fever: A growing global menace. Journal of Water and Health, 21(11), 1632–1650. https://doi.org/10.2166/wh.2023.114
4. Bosch, I., Reddy, A., de Puig, H., et al. (2020). Serotype-specific detection of dengue viruses in a nonstructural protein 1-based enzyme-linked immunosorbent assay validated with a multi-national cohort. PLoS Neglected Tropical Diseases, 14(6), e0008203. https://doi.org/10.1371/journal.pntd.0008203
5. Witte, P., Venturini, S., Meyer, H., Zeller, A., & Christ, M. (2024). Dengue fever—Diagnosis, risk stratification, and treatment. Deutsches Ärzteblatt International, 121(23), 773–778. https://doi.org/10.3238/arztebl.m2024.0175
6. Kularatne, S. A., & Dalugama, C. (2022). Dengue infection: Global importance, immunopathology and management. Clinical Medicine (London), 22(1), 9–13. https://doi.org/10.7861/clinmed.2021-0791
7. Sinha, S., Singh, K., Ravi Kumar, Y. S., et al. (2024). Dengue virus pathogenesis and host molecular machineries. Journal of Biomedical Science, 31(1), 43. https://doi.org/10.1186/s12929-024-01030-9
8. Facchinelli, L., Badolo, A., & McCall, P. J. (2023). Biology and behavior of Aedes aegypti in the human environment: Opportunities for vector control of arbovirus transmission. Viruses, 15(3), 636. https://doi.org/10.3390/v15030636
9. Roy, S. K., & Bhattacharjee, S. (2021). Dengue virus: Epidemiology, biology, and disease aetiology. Canadian Journal of Microbiology, 67(10), 687–702. https://doi.org/10.1139/cjm-2020-0572
10. Nie, P., & Feng, J. (2023). Niche and range shifts of Aedes aegypti and Ae. albopictus suggest that the latecomer shows a greater invasiveness. Insects, 14(10), 810. https://doi.org/10.3390/insects14100810
11. Pajor, M. J., Long, B., & Liang, S. Y. (2024). Dengue: A focused review for the emergency clinician. American Journal of Emergency Medicine, 82, 82–87. https://doi.org/10.1016/j.ajem.2024.05.022
12. Sirisena, P. D. N. N., Mahilkar, S., Sharma, C., Jain, J., & Sunil, S. (2021). Concurrent dengue infections: Epidemiology and clinical implications. Indian Journal of Medical Research, 154(5), 669–679. https://doi.org/10.4103/ijmr.IJMR_1219_18
13. Andrade, E. H. P., Figueiredo, L. B., Vilela, A. P. P., et al. (2016). Spatial-temporal co-circulation of dengue virus 1, 2, 3, and 4 associated with coinfection cases in a hyperendemic area of Brazil: A 4-week survey. American Journal of Tropical Medicine and Hygiene, 94(5), 1080–1084. https://doi.org/10.4269/ajtmh.15-0892
14. Kok, B. H., Lim, H. T., Lim, C. P., Lai, N. S., Leow, C. Y., & Leow, C. H. (2023). Dengue virus infection: A review of pathogenesis, vaccines, diagnosis and therapy. Virus Research, 324, 199018. https://doi.org/10.1016/j.virusres.2022.199018
15. Wang, W. H., Urbina, A. N., Chang, M. R., et al. (2020). Dengue hemorrhagic fever: A systemic literature review of current perspectives on pathogenesis, prevention and control. Journal of Microbiology, Immunology and Infection, 53(6), 963–978. https://doi.org/10.1016/j.jmii.2020.03.007
16. Ly, H. (2024). Dengue fever in the Americas. Virulence, 15(1), 2375551. https://doi.org/10.1080/21505594.2024.2375551
17. Dubot-Pérès, A., Vongsouvath, M., Phimolsarnnousith, V., Ashley, E. A., & Newton, P. N. (2021). Dengue diagnostic test use to identify Aedes-borne disease hotspots. Lancet Planetary Health, 5(8), e503. https://doi.org/10.1016/S2542-5196(21)00174-1

18. Moallemi, S., Lloyd, A. R., & Rodrigo, C. (2023). Early biomarkers for prediction of severe manifestations of dengue fever: A systematic review and a meta-analysis. Scientific Reports, 13(1), 17485. https://doi.org/10.1038/s41598-023-44559-9
19. Trivedi, S., & Chakravarty, A. (2022). Neurological complications of dengue fever. Current Neurology and Neuroscience Reports, 22(8), 515–529. https://doi.org/10.1007/s11910-022-01213-7
20. Paraná, V. C., Feitosa, C. A., da Silva, G. C. S., Gois, L. L., & Santos, L. A. (2024). Risk factors associated with severe dengue in Latin America: A systematic review and meta-analysis. Tropical Medicine & International Health, 29(3), 173–191. https://doi.org/10.1111/tmi.13968
21. Kalaimathi, K., Rani, J. M. J., Vijayakumar, S., et al. (2022). Anti-dengue potential of mangiferin: Intricate network of dengue to human genes. Revista Brasileira de Farmacognosia, 32(3), 410–420. https://doi.org/10.1007/s43450-022-00258-6
22. Ratanakomol, T., Roytrakul, S., Wikan, N., & Smith, D. R. (2022). Oroxylin A shows limited antiviral activity toward dengue virus. BMC Research Notes, 15(1), 154. https://doi.org/10.1186/s13104-022-06040-0
23. Tayal, A., Kabra, S. K., & Lodha, R. (2023). Management of dengue: An updated review. Indian Journal of Pediatrics, 90(2), 168–177. https://doi.org/10.1007/s12098-022-04394-8
24. Araiza-Garaygordobil, D., García-Martínez, C. E., Burgos, L. M., et al. (2021). Dengue and the heart. Cardiovascular Journal of Africa, 32(5), 276–283. https://doi.org/10.5830/CVJA-2021-033
25. Ogunlade, S. T., Meehan, M. T., Adekunle, A. I., & McBryde, E. S. (2023). A systematic review of mathematical models of dengue transmission and vector control: 2010–2020. Viruses, 15(1), 254. https://doi.org/10.3390/v15010254
26. Durrance-Bagale, A., Hoe, N., Lai, J., Liew, J. W. K., Clapham, H., & Howard, N. (2024). Dengue vector control in high-income, urban settings: A scoping review of approaches and methods. PLoS Neglected Tropical Diseases, 18(4), e0012081. https://doi.org/10.1371/journal.pntd.0012081
27. Killeen, G. F. (2020). Control of malaria vectors and management of insecticide resistance through universal coverage with next-generation insecticide-treated nets. The Lancet, 395(10233), 1394–1400. https://doi.org/10.1016/S0140-6736(20)30745-5
28. Okumu, F. (2020). The fabric of life: What if mosquito nets were durable and widely available but insecticide-free? Malaria Journal, 19(1), 260. https://doi.org/10.1186/s12936-020-03321-6
29. Bohari, R., Jin Hin, C., Matusop, A., et al. (2020). Wide area spray of bacterial larvicide, Bacillus thuringiensis israelensis strain AM65-52, integrated in the national vector control program impacts dengue transmission in an urban township in Sibu district, Sarawak, Malaysia. PLoS ONE, 15(4), e0230910. https://doi.org/10.1371/journal.pone.0230910
30. Ogunlade, S. T., Meehan, M. T., Adekunle, A. I., Rojas, D. P., Adegboye, O. A., & McBryde, E. S. (2021). Aedes-borne arboviral infections, controls and Wolbachia-based strategies. Vaccines (Basel), 9(1), 32. https://doi.org/10.3390/vaccines9010032
31. Sim, S., Ng, L. C., Lindsay, S. W., & Wilson, A. L. (2020). A greener vision for vector control: The example of the Singapore dengue control program. PLoS Neglected Tropical Diseases, 14(8), e0008428. https://doi.org/10.1371/journal.pntd.0008428
32. Jones, R. T., Ant, T. H., Cameron, M. M., & Logan, J. G. (2021). Novel control strategies for mosquito-borne diseases. Philosophical Transactions of the Royal Society B: Biological Sciences, 376(1818), 20190802. https://doi.org/10.1098/rstb.2019.0802
33. Shukla, R., Ramasamy, V., Shanmugam, R. K., Ahuja, R., & Khanna, N. (2020). Antibody-dependent enhancement: A challenge for developing a safe dengue vaccine. Frontiers in Cellular and Infection Microbiology, 10, 572681. https://doi.org/10.3389/fcimb.2020.572681
34. Izmirly, A. M., Alturki, S. O., Connors, J., & Haddad, E. K. (2020). Challenges in dengue vaccine development: Pre-existing infections and cross-reactivity. Frontiers in Immunology, 11, 1055. https://doi.org/10.3389/fimmu.2020.01055
35. Waggoner, J. J., Katzelnick, L. C., Burger-Calderon, R., et al. (2021). Antibody-dependent enhancement of severe disease is mediated by serum viral load in pediatric dengue virus infections. Journal of Infectious Diseases, 221(11), 1846–1854. https://doi.org/10.1093/infdis/jiz618
36. Wilder-Smith, A., Cherian, T., & Hombach, J. (2025). Dengue vaccine development and deployment into routine immunization. Vaccines (Basel), 13(5), 483. https://doi.org/10.3390/vaccines13050483
37. Wilder-Smith, A., Hombach, J., Ferguson, N., et al. (2019). Deliberations of the Strategic Advisory Group of Experts on Immunization on the use of CYD-TDV dengue vaccine. The Lancet Infectious Diseases, 19(1), e31–e38. https://doi.org/10.1016/S1473-3099(18)30494-8
38. Rivera, L., Biswal, S., Sáez-Llorens, X., et al. (2022). Three-year efficacy and safety of Takeda's dengue vaccine candidate (TAK-003). Clinical Infectious Diseases, 75(1), 107–117. https://doi.org/10.1093/cid/ciab864
39. White, L. J., Young, E. F., Stoops, M. J., et al. (2021). Defining levels of dengue virus serotype-specific neutralizing antibodies induced by a live attenuated tetravalent dengue vaccine (TAK-003). PLoS Neglected Tropical Diseases, 15(3), e0009258. https://doi.org/10.1371/journal.pntd.0009258

40. López-Medina, E., Biswal, S., Sáez-Llorens, X., et al. (2022). Efficacy of a dengue vaccine candidate (TAK-003) in healthy children and adolescents 2 years after vaccination. Journal of Infectious Diseases, 225(9), 1521–1532. https://doi.org/10.1093/infdis/jiaa761
41. Daniels, B. C., Ferguson, N., & Dorigatti, I. (2024, August 11). Efficacy, public health impact and optimal use of the Takeda dengue vaccine. medRxiv. https://doi.org/10.1101/2024.08.10.24311393
42. Freedman, D. O. (2023). A new dengue vaccine (TAK-003) now WHO recommended in endemic areas; What about travellers? Journal of Travel Medicine, 30(7), taad132. https://doi.org/10.1093/jtm/taad132
43. Köpke, C., Rothe, C., Zeder, A., et al. (2025). First clinical experiences with the tetravalent live vaccine against dengue (Qdenga®) in travellers: A multicentric TravVacNet study in Germany. Journal of Travel Medicine, 32(2), taaf004. https://doi.org/10.1093/jtm/taaf004
44. Angelin, M., Sjölin, J., Kahn, F., et al. (2023). Qdenga®—A promising dengue fever vaccine; Can it be recommended to non-immune travelers? Travel Medicine and Infectious Disease, 54, 102598. https://doi.org/10.1016/j.tmaid.2023.102598