



Interaction Of *Aedes* Mosquitoes, Gut Symbiotic Bacteria, And Dengue Virus: A Review

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	<p style="text-align: center;">Abstract</p> <p><i>Aedes</i> mosquitoes are vectors for various disease-causing organisms, including Dengue, Chikungunya, Yellow Fever, Zika virus, and other arboviruses. Mosquitoes, including <i>Aedes</i>, inhabit a rich gut microbial community. These gut symbiotic bacteria affect mosquito physiology in different ways. Viral infection regulation strategies depend on controlling vectors through different means, such as chemically, Environmentally, and Biologically. Several recent studies show the use of gut microbial communities to prevent mosquito-borne diseases by controlling the vector. The midgut microbiota differs according to various parameters, including mosquito sex, life stage, and surrounding environmental conditions. This review describes the interaction between the <i>Aedes</i> mosquito, its gut bacteria, and the Dengue virus, highlighting recent advances in research.</p>
<p>CC License CC-BY-NC-SA 4.0</p>	<p>Key words: Mosquito, Midgut bacterial community, <i>Aedes</i>, Arbovirus, Dengue</p>

INTRODUCTION

Mosquitoes are pathologically the largest insect pests, not only in the rate of health problems they create but also in quantity (Service, 1989). Due to their infectivity, they become a major threat to human health (Boutayeb, 2006). They transmit various parasites and viruses that cause diseases, including dengue, Chikungunya, malaria, encephalitis, Zika virus, yellow fever virus, Japanese Encephalitis, and Filariasis.

The origin of the word dengue belongs to the Swahili language term 'Bone Breaking Fever'.

The first suspected case of dengue, transmitted by flying insects known as "water poison," was recorded from the Chin or Jin dynasty (265- 420 AD) (Gubler,1998). Benjamin Rush, in 1779, first identified and named the disease dengue fever (Halstead, 2008). Later, it spread to tropical and subtropical areas in the early 20th century, and dengue fever also began to spread in the US. In the 1990s, the highest number of dengue cases was recorded, in comparison to other mosquito-transmitted pathogens. Dengue hemorrhagic fever (DHF) or dengue shock syndrome (DSS), was first reported in the Philippines in 1954 and then in Southeast Asia (Halstead SB, 1987).

All insects including mosquitoes, harbor different endosymbiotic gut bacteria. These gut bacteria play an important role in affecting the physiology of mosquitoes, including *Aedes*.

AEDES MOSQUITO

Aedes mosquitoes transmit different arboviruses from an infected person to a healthy individual, such as dengue virus, yellow fever virus, chikungunya virus, and Zika virus, making them therapeutically more important. *Ae.albopictus* can transmit approximately 22 different arboviruses (Shroyer, 1986). Different factors have been noticed as the culprits in the proliferation of these arboviral diseases, such as less awareness, cross-border travel, population increase, fast urbanization, etc. (Adams et al, 2009). Previously, most dengue cases were noticed in cities, but nowadays, villages have been seen at an increased pace (Ukey et al., 2010). A comparative study reported that *Ae. albopictus* was distributed approximately equally in villages and cities, whereas *Ae. aegypti* was more prevalent in urban parts than in rural areas (Vijayakumar et al., 2014). This mosquito in tropical and subtropical areas shows endemic behavior and prefers to live near human houses (Carrington et al., 2014). The life cycle of the *Aedes* mosquito is completed in 4 stages, viz. eggs, larva, pupa, and adult. They prefer to breed inside or near human households in small water vessels such as water coolers, buckets, water tubs, flower pots, tires, discarded glasses and cups, plant holes, water vessels for domestic animals and birds, coconut covers, etc (Hawley, 1988).

Different environmental factors can be used to have an idea about the distribution pattern of *Aedes* mosquitoes, such as humidity, temperature, and precipitation (Medley, 2010). Brady and coworkers (2013) reported longer life survival of *Ae.albopictus* compared to *Ae.aegypti*. *Aedes* can withstand a wider range of temperature conditions, which makes it well-suited for different climatic conditions (CDC, 2016). Atieli et al. (2023) investigated the distribution pattern of mosquitoes depending on the wind in Kenya, East Africa. They noticed that at high altitudes, *Culex* was dominating, followed by *Aedes* and *Anopheles* among all windborne migrated mosquitoes.

Ae. albopictus is native to Asia and from here reached Indian and western Pacific ocean countries (Smith, 1956). In the 1980s *Ae.albopictus* reached Brazil, U.S.and European countries (Carvalho et al., 2014). Presently both *Ae. albopictus* and *Ae. aegypti* are distributed in Asia and America (Lambrechts et al., 2011). In the last 4 decades, *Ae.albopictus* had reached every continent excluding Antarctica (Caminade et al., 2012). During the slave trade, *Ae.aegypti* reached from African countries to New World countries and later on to tropical and sub-tropical parts of the world (Brown et al., 2014). Giunti et al. (2023) reviewed the distribution, disease transmission capacity, biological aspects, and invasiveness, of *Ae. atropalus* and *Ae. triseriatus* in European countries. *Ae. aegypti* was also reported as a major transmitter of arboviral infections in a study of the breeding and metamorphosis of larvae from Benin, a sovereign state in West Africa (Aikpon et. al,2019). This work also emphasizes the requirements of establishing the right *Aedes* mosquito surveillance program. There should be full awareness of mosquito-transmitted diseases.

Three species of *Aedes* mosquito have been studied in Tirunelveli, Tamil Nadu, named *Ae. aegypti*, *Ae. albopictus*, and *Ae. vittatus* (Bhat and Krishnamoorthy, 2014). All three species of *Aedes*, for example, *Ae. aegypti*, *Ae. vittatus*, and *Ae. aegypti* were also reported in a study of their breeding habitats from the Ramnathpuram district of Tamil Nadu (Selvan and Jebanesan,2016). *Ae. aegypti* and *Ae. albopictus* in the Central and North East parts of India were also studied (Kalra et. al.,1997).

DENGUE VIRUS

Dengue virus is a single-stranded RNA virus belonging to the Flavivirus genus of the Flaviviridae family. Four different but closely related serotypes of this virus, DENV1, DENV2, DENV3, and DENV4, have been reported to cause dengue in humans. More than 100 tropical and subtropical countries have been noted showing endemism, causing risk for more than 50% of the world's population (Gubler, 2012). Jones et al. (2024) studied travel-related and locally infected Dengue virus-3 (DENV-3) distribution in America. They suggested that many cases are related to patients' travel to dengue-endemic countries. *Ae. aegypti* and *Ae.albopictus* both transmit the dengue virus to humans at the time of blood-sucking and cause dengue disease. This clinically shows Dengue fever (DF) and Dengue shock syndrome (DSS). It has visible symptoms such as fever, myalgia, and arthralgia, but is sometimes confused with another febrile disease. Different complications have been noticed with the progression of dengue disease, such as problems in respiration, thrombocytopenia leading to plasma leakage and internal bleeding, fluid collection, inactivity, or failure of internal organs. Dengue hemorrhagic fever leads to approximately 5 percent of deaths in patients (Beatty et. al., 2011). In the 21st century, dengue as a vector-borne illness is spreading rapidly (Gubler, 2012; Swaminathan & Khanna, 2009).

Frasca et al. (2024) reviewed different aspects of the *culex* and *Aedes*-transmitted dengue and West Nile virus, respectively, including their epidemiological, Entomological, virological, and pathogenic status in

Europe, focusing especially on Italy. They noticed a significant increase in locally acquired dengue infections in Italy in 2023.

All four dengue virus serotypes and different species of *Aedes* mosquitoes are present in India, infecting people. Occasional dengue outbreaks in India prove that this illness is a big health problem due to the country's dense population. The understanding that dengue can reach outside the borders of tropical countries has raised knowledge throughout the world to develop efforts to search for solutions to the problem of public health caused by this illness (Swaminathan and Khanna, 2009). Different factors such as social and economic change, climate change, virus evolution, no successful treatment of the virus, and no anti-dengue vaccine available, are some examples helping to increase dengue (Guzman et.al., 2010).

Aedes mosquitoes infect a healthy person with dengue virus during blood sucking and causes dengue fever (DF), dengue hemorrhagic fever (DHF), and dengue shock syndrome (DSS). The symptoms include myalgia, arthralgia, pyrexia, body rashes, pain in the eyes, vomiting, and swelling of lymph glands. Symptoms in severe conditions of dengue are regular vomiting, high breathing rate, severe pain in the abdomen, weakness, skin turns pale, feeling thirsty, blood from the mouth, nose, stool, and vomit. Raihan et al. (2025) reviewed the latest advancements in the use of bio-detection molecules in electrochemical biosensor systems to diagnose mosquito-transmitted diseases. They described Genosensor, Immunosensor, and Aptasensor approaches for disease diagnosis as point-of-care biosensors.

Currently, dengue fever is the most common disease in tropical and subtropical countries, leading to more suffering and deaths than any other arboviral disease. Dengue fever has spread rapidly in cities and surrounding areas in recent decades (WHO, 2016). More than 96 million people got infected with dengue all over the world, 70% of which alone were reported from Asia in 2010. Whereas approximately 34% of total infections were recorded in India alone (Chakravarti et al., 2012). Approximately 390 million dengue cases are reported worldwide annually (Bhatt et al., 2013), and in 128 countries, approximately 3900 million are under direct threat (WHO, 2016).

The highest number of cases causing medical conditions and deaths, most prevalently in children, have been reported from the countries of Southeast Asia. Dengue cases reported to WHO from 1 January to 30 April 2024 are 7.6 million globally, a 15-fold increase of 505430 in the year 2000 (WHO, 2024). The highest number of dengue cases has been reported from Brazil, 6296795, followed by Argentina, 420867, and Paraguay, 257667 (WHO, 2024).

***Aedes* GUT BACTERIA**

Natural microbial communities inhabit the gut of mosquitoes. Mosquitoes harbor diverse gut bacteria, but one or two taxa are more prevalent. The midgut bacteria in different mosquitoes are highly variable, but a small fraction is common and overlapping. This dissimilar and diverse gut microbiome affects the vectorial capacity of the mosquitoes (Osei-Poku et al., 2012). *Culex*, *Anopheles*, and *Aedes* mosquitoes preferably lay eggs in bacteria-rich aquatic breeding habitats (Lindh et al., 2008). Mosquitoes can feed on natural bacteria during larval breeding in water habitats or adults from flower nectar. It is already known that larvae acquire mid-gut bacteria from their aquatic breeding sites, which are established in adults (Smith et al., 1998). Adult mosquitoes can also feed the bacteria from their habitat during eclosion in water and further transmit it horizontally (Lindh et al., 2008). Still, simultaneously, some are acquired from the surrounding environment, which enhances the rate of immune system activation against plasmodium, dengue virus, and chikungunya virus (Dong et al., 2006). Rodpai et al. (2023) studied the gut microbiota of *Ae. albopictus* and *Ae. aegypti* larvae and adults in Thailand. They revealed a notable change in transstadially transmitted gut bacteria from larvae to adults. High bacterial diversity was noticed in *Ae. aegypti* compared to *Ae. albopictus*. Gut bacteria were found dominant as *Wolbachia* in *Ae. albopictus* male, *Blautia* in *Ae. aegypti*, and *Serratia* in larvae of *Ae. albopictus*.

Different gram-negative bacteria have been detected in the *Anopheles* gut of the family Acetobacteraceae, Enterobacteriaceae, etc (Gendrin Christophides, 2013). Wild-caught mosquitoes have rich bacterial diversity in comparison to laboratory cultures (Rani et al., 2009).

A vector's pathogen transmission capacity can be reduced by modulating the immune system at the genetic level (Beatty, 2000). Presently, gut bacteria are used to control the transmission of pathogens by mosquitoes as a biocontrol strategy. The biocontrol mechanism regulates the mosquito gut's pathogen replication, decreasing the infection rate (Ghosh et al., 2009). Still, there is a research gap in understanding the mechanism of the use of biocontrol strategies in vector regulation (Ferguson et al., 2010).

The correct knowledge of the tri-valent relationship between mosquito-parasite (virus, protozoans) and gut bacteria will make easy and effective application of vector regulation methodologies (Abdul-Ghani et al.,

2012). Understanding gut bacterial communities and their impact on the host is still required. Midgut bacterial communities prevent disease transmission in different ways.

Gut bacteria reduce the multiplication rate of malaria parasites in *Anopheles albimanus*, which decreases the infection rate (Gonzalez-Ceron, 2003). Bacteria of the Enterobacteriaceae family induce reactive oxygen species (ROS) and stop the proliferation of malaria parasites inside *Anopheles gambiae* (Cirimotich et al., 2011b). The gut bacterial communities also show larvicidal activity.

AEDES AND MID-GUT BACTERIA INTERACTION

Insect-gut microbial interactions can be beneficial or destructive. A beneficial or symbiotic association is a close link between the insect host and its gut microorganisms. These two species' associations can be mutualistic, parasitic, or commensal (Moya et al., 2008). The best example of mutualism is between termites and *Triconympha* (a protozoan) (Bayen et al., 2021). Gut microbial communities live as pathogens or are associated in mutualism with *Aedes* (Dillon and Dillon, 2004). Insect guts have been intensely studied due to the uniqueness of their physiological and microbiological features, which enable them to feed on diverse food sources (Serrato-Salas and Gendrin, 2023; Schmidt and Engel, 2021; Martinson and Strand, 2021).

The bark beetle, *Scolytus* spp., and its gut microbial community show commensalism, as the beetle provides food and space to live to the microbes, in contrast microbial community has a neutral effect (Stephen et al., 1993). The relationship between two species in which one gets benefit and the one loses is known as parasitism (Dillon and Dillon, 2004).

Previous exploration of the physiological role played by the microbial community in *Ae. aegypti* depends on the application of an aseptic environment and dietary supplements enriched with different nutritional substances and vitamins (Lang et al., 1972). Lectin group proteins bind to microorganisms and alter the immune response, leading to differences in the gut bacterial establishment in *Culex pipiens pallens* and *Ae. aegypti* (Pang et al., 2016). Coon et al. (2014) reviewed and investigated the relationship between gut microbial richness and pathogenicity in *Aedes*. They demonstrated that differences in gut bacterial diversity affect the vectorial capability of mosquitoes. The correct knowledge of gut bacteria will help in the regulation of mosquito-transmitted pathogens. Bleach and ethanol are used for the sterilization of the outer covering of eggs in recent times in comparison to radiation in older days (Coon et al., 2014, 2016). The larvae showing gnotobiosis are cultured using inoculation of bacterial colony in a glass container having laboratory grade distilled water, aseptic or contamination-free required food, and 1st instar stage larvae (Coon et al., 2014, 2016). Different antibiotics are used to regulate *Ae. aegypti* gut microbiota. Still, a remarkable insecticide resistance has also been detected in some bacteria that negatively impacts the growth and development of earlier-stage larvae (Coon et al., 2016).

Rich gut bacterial diversity enhances the fitness of mosquitoes (Simpson et al., 2015). Martinson and Strand (2021) studied that mosquito development depends on its gut microbiota and diet. The gut microbial community plays an important role in boosting the nutritional and defensive mechanisms of the insect host (Serrato-Salas and Gendrin, 2023). Harrison et al. (2023) revealed that the gut bacteria of *Ae. aegypti* increase the life span, egg production, and pathogen transmission capacity. They noticed that in the absence of gut microbiota, the rate of egg production, metabolism, and vector competence are reduced. Mondal et al. (2023) reviewed the important role of gut bacteria in different insects, including their symbiotic relationship and the development of insecticide resistance.

Mosquito Larvicidal Activity of Midgut Bacteria

Bacillus sphaericus and *Bacillus thuringiensis* serovar *israelensis* (*Bti*) bacteria show larvicidal activity and are popularly used as biocontrol agents against *Anopheles*, *Culex*, and *Aedes*. These bacteria release protein molecules that reduce larval populations by toxic effects on their midgut. These proteins have toxic power and once they enter the larva, they bind to the midgut's cell lining, causing death by damaging the cells with a cytopathic effect. *Bacillus sphaericus* releases a single toxin named the binary toxin (Bin) and has a single type of binding sites on the midgut epithelium, whereas *Bti* releases 4 types of toxins Cry4Aa, CryBa, Cry11Aa, and Cyt1Aa (Ferreira and Filha, 2013). Rique et al. (2024) also studied the larvicidal effect of *Lysinibacillus sphaericus* and *Bacillus thuringiensis* var. *israelensis* (*Bti*) microbes on *Culex quinquefasciatus* and *Ae. aegypti*. Four bacterial species *Serratia marcescens*, *Bacillus subtilis*, *Pseudomonas fluorescens*, and *Streptomyces albus* have shown larvicidal capability against the *Culex pipiens* mosquito (Mansour et al., 2023).

Xenorhabdus and *Photorhabdus* bacterial species have also shown the potential to reduce the populations of *Ae. albopictus* larvae. These bacteria produce some toxic components with larvicidal properties. Fabclavine

and Xencoumacin are the larvicidal compounds released by *Xenorhabdus szentirmaii* and *Xenorhabdus nematophila*, respectively. The above bacteria also lower the rate of *Aedes* egg hatching. These Xenocoumacin and Fabclavine can be produced commercially as bio-larvicide for effective mosquito control (Touray et al., 2024).

Dengue regulation by *Wolbachia* through the development of Cytoplasmic incompatibility

Cytoplasmic incompatibility (CI) is a reproductive incompatibility noticed in many insects. It is developed by the bacteria *Wolbachia*, which prefer to live in the cytoplasm of insect cells and modulate the insect's sperm when fertilizing the eggs of *Wolbachia*-uninfected insects. Due to this, the embryos will not survive. Cytoplasmic incompatibility is unidirectional and bidirectional. It was first studied in *Culex pipiens* mosquitoes (Hertig, 1936).

Trpis et al. (1981) studied cytoplasmic incompatibility in *Ae. polynesiensis* and *Ae. kesseli* mosquitoes are infected by Rickettsia-type microbes. *Wolbachia* has been detected in 15% of insects out of the total analyzed (Werren et al., 1995).

Ae. albopictus has two *Wolbachia* strains, wAlbA and wAlbB, vertically transmitted from females in natural conditions (Gratz, 2004; Sinkins et al., 1995). This bacterium is also present in natural conditions in more than 28% of mosquitoes as examined in Thailand (Kittayapong et al., 2000). Superinfections of more than one strain of *Wolbachia* have been noticed in *Ae. albopictus* (Sinkins et al., 1995; Zhou et al., 1998). Kaur et al. (2024) studied the role of *Wolbachia*-induced cytoplasmic incompatibility in regulating virus transmission by *Ae. aegypti* mosquitoes. Moretti et al. (2018) applied an incompatible insect technique using bidirectional incompatibility to regulate *Ae. albopictus*. Ross et al. (2019) investigated the role of *Wolbachia* transfection in *Ae. aegypti*.

Wolbachia's utilization to develop cytoplasmic incompatibility by transinfection in mosquitoes is an emerging disease-controlling strategy.

Aedes control by Paratransgenesis

The genetic manipulation of the symbiotic gut microbial community of an insect host and its reintroduction to regulate the transmission of disease-causing organisms is known as Paratransgenesis (Wang et al., 2012). This strategy controls vector-transmitted infections by reducing the number of insect vectors after transferring a gene into the gut symbiotic microbe.

Wolbachia is successfully used against the dengue virus, malaria parasite, chikungunya virus, and yellow fever virus (Moreira et al., 2009). Egyirifa & Akorli (2024), investigated two gut bacterial genera, *Asaia* and *Elizabethkingia*, in the control of the *Anopheles gambiae* mosquito by genetically manipulating them using paratransgenesis. Ojha (2025) investigated the role of *Enterobacter* bacteria in the paratransgenic control of *Helicoverpa* insects. Some other microbes, in addition to bacteria, also have paratransgenic capabilities, including fungi and viruses (Ren et al., 2008).

CONCLUSION

It is important to understand the bacterial composition of its native microbiome to enable more effective regulation strategies of virus transmission from *Aedes* to hosts. *Wolbachia*, an endosymbiont, infects and lives naturally in many insect species, including *Aedes* mosquitoes. *Wolbachia* has a negative effect on the replicating dengue virus in the *Ae. aegypti* mosquito. DENV infects different body parts of *Aedes* mosquitoes, including the two crucial for its transmission, the midgut and salivary glands. In *Ae. albopictus*, DENV replication takes place in the midgut, whereas dissemination from the salivary glands. Different gut microbiota, especially *Wolbachia*, regulate pathogens in various ways, such as limiting the vector population through the cytoplasmic incompatibility (CI), weakening the cytoskeleton, and limiting the entry and establishment of arboviruses, including DENV.

Wolbachia strain wAlbB introduction reduces the DENV populations in *Ae. aegypti* by limiting the expression of dystroglycan, a cell adhesion protein, and tubulin.

The transinfection of *Wolbachia* reduces DENV populations by outcompeting them for different nutrients such as lipid, iron, and cholesterol, hindering DENV replication inside *Aedes*. *Wolbachia* downregulates DENV after introduction in *Aedes* mosquitoes by immune priming, activating the immune system in 3 different pathways, as the JAK/STAT pathway, the toll pathway, and the IMD pathway. *Wolbachia* utilizes the available nutrients inside *Aedes* mosquitoes, which reduces the autophagy that reduces DENV replication and establishment. Another alternative way to limit DENV in *Aedes* is the Phenoloxidase cascade activation. The Phenoloxidase cascade produces melanin in *Aedes* mosquitoes, which reduces the pathogen.

Gut symbiotic bacteria are also helpful in synthesizing the nutrients that are deficient in the insect's diet. Paratransgenesis is a novel mosquito control strategy in which different gut bacteria are reintroduced after genetic manipulation.

Notwithstanding the research gaps in understanding the exact mechanism of the *Aedes*-gut bacteria-DENV association at the trophic level, our review aims to elucidate how gut bacteria contribute to dengue control from a perspective. We attempted to understand the tri-trophic relationship between the *Aedes* mosquito, its gut bacteria, and the dengue virus by reviewing the relevant literature. This knowledge of the tripartite relationship will be helpful in efficient DENV management.

Conflicts of Interest:

The authors have no conflict of interest in the publication of this manuscript.

REFERENCES

1. Abdul-Ghani R, Al-Mekhlafi AM, and Alabsi MS (2012) Microbial control of malaria: Biological warfare against the parasite and its vector. *Acta Tropica*, **121**: 71–84.
2. Adams B, and Kapan DD (2009) Man bites mosquito: understanding the contribution of human movement to vector-borne disease dynamics, *PLoS ONE* **4**: e6763.
3. Aikpon R, Klotoe JR, Dramane G, Brettenny M, and Lawani Y (2019) Larval breeding characteristics and distribution of *Aedes* mosquito species in the economic capital of Benin: A public health concern. *International Journal of Entomology Research*, **4**(3): 57–62.
4. Atieli HE, Zhou G, Zhong D, Wang X, Lee M, Yaro AS, Diallo M, Githure J, Kazura J, Lehmann T, and Yan G (2023) Wind-assisted high-altitude dispersal of mosquitoes and other insects in East Africa. *Journal of Medical Entomology*, **60**(4): 698–707.
5. Bayen S, Roy S, Chakraborti D, Mukhopadhyay A, Hazarika L K, Pramanik P, Borchetia S, and Mukherjee S (2021) Mutualistic relation of termites with associated microbes for their harmonious survival. *Symbiosis*, **85**(2): 145–161.
6. Beatty ME, Beutels P, Meltzer MI, Shepard DS, Hombach J, Hutubessy R, Dessis D, Coudeville L, Dervaux B, Wichmann O, Margolis HS, and Kuritsky JN (2011) Health economics of dengue: a systematic literature review and expert panel's assessment. *American Journal of Tropical Medicine and Hygiene*, **84**(3):473-88.
7. Beaty BJ (2000) Genetic manipulation of vectors: A potential novel approach for control of vector-borne diseases. *Proceedings of the National Academy of Sciences of the United States of America*, **97**(19):10295-10297.
8. Bhat MA, and Krishnamoorthy K (2014) Entomological investigation and distribution of *Aedes* mosquitoes in Tirunelveli, Tamil Nadu, India. *International Journal of Current Microbiology and Applied Sciences*, **3**(10):253-259.
9. Boutayeb A (2006) The double burden of communicable and non-communicable diseases in developing countries. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, **100**(3):191-199.
10. Brady OJ, Johansson MA, Guerra CA, Bhatt S, Golding N, Pigott DM, Delatte H, Grech MG, Leishnam PT, Maciel-de-Freitas R, Styer LM, Smith DL, Scott TW, Gething PW, Hay SI (2013) Modelling adult *Aedes aegypti* and *Aedes albopictus* survival at different temperatures in laboratory and field settings. *Parasites and Vectors*, **6**: 351.
11. Brown JE, Evans BR, Zheng W, Obas V, Barrera-Martinez L, Egizi A, Zhao H, Caccone A, Powell JR (2014) Human impacts have shaped historical and recent evolution in *Aedes aegypti*, the dengue and yellow fever mosquito. *Evolution*, **68**(2): 514–525.
12. Caminade C, Medlock JM, Ducheyne E, McIntyre KM, Leach S, Baylis M, Morse AP (2012) Suitability of European climate for the Asian tiger mosquito *Aedes albopictus*: recent trends and future scenarios. *Journal of the Royal Society Interface*, **9**: 2708–2717.
13. Carrington, L. and Simmons, CP (2014) Human to Mosquito Transmission of Dengue Viruses. *Frontiers in Immunology*, **5**: 290.
14. Carvalho RG, Lourenc,o-de-Oliveira R, and Braga IA (2014) Updating the geographical distribution and frequency of *Aedes albopictus* in Brazil with remarks regarding its range in the Americas. *Memorias Do Instituto Oswaldo Cruz*, **109**(6): 787–796.

15. Centers for Disease Control (CDC) (2016) Surveillance and control of *Aedes aegypti* and *Aedes albopictus* in the United State. <http://www.cdc.gov/chikungunya/resources/vector-control.html>; on July 2016.
16. Chakravarti A, Matlani M, Kashyap B, and Kumar A (2012) Awareness of changing trends in epidemiology of Dengue fever is essential for epidemiological surveillance. *Indian Journal of Medical Microbiology*, **30(2)**:222-226.
17. Cirimotich CM, Dong Y, Clayton AM, Sandiford SL, Souza-Neto JA, Mulenga M, Dimopoulos G, 2011. Natural Microbe-Mediated Refractoriness to Plasmodium Infection in *Anopheles gambiae*. *Science* **332**: 855-859.
18. Coon KL, Brown MR, and Strand MR (2016) Gut bacteria differentially affect egg production in the anautogenous mosquito *Aedes aegypti* and facultatively autogenous mosquito *Aedes atropalpus* (Diptera: Culicidae). *Parasites Vectors*, **9**:375.
19. Coon KL, Vogel KJ, Brown MR, and Strand MR (2014) Mosquitoes rely on their gut microbiota for development. *Molecular Ecology*, **23(11)**: 2727–2739.
20. Dillon RJ, and Dillon VM (2004) The gut bacteria of insects: nonpathogenic interactions. *Annual Review of Entomology*, **49**:71-92.
21. Egyirifa RK, and Akorli J (2024) Two promising candidates for paratransgenesis, *Elizabethkingia* and *Asaia*, increase in both sexes of *Anopheles gambiae* mosquitoes after feeding. *Malaria Journal*, **23(1)**: 45.
22. Ferguson HM, Dornhaus A, Beeche A, Borgemeister C, Gottlieb M, Mulla MS, Gimnig JE, Fish D, Killeen GF (2010) Ecology: a prerequisite for malaria elimination and eradication. *PLoS Medicine*, **7(8)**: e1000303.
23. Ferreira LM, and Filha MHNLS (2013) Bacterial larvicides for vector control: mode of action of toxins and implications for resistance. *Biocontrol Science and Technology*, **23:10**: 1137-1168
24. Frasca F, Sorrentino L, Fracella M, D'Auria A, Coratti E, Maddaloni L, Bugani G, Gentile M, Pierangeli A, d'Ettore G, Scagnolari C (2024) An Update on the Entomology, Virology, Pathogenesis, and Epidemiology Status of West Nile and Dengue Viruses in Europe (2018–2023). *Tropical Medicine and Infectious Disease*, **9(7)**: 166.
25. Gendrin M, and Christophides GM (2013) The *Anopheles* Mosquito Microbiota and Their Impact on Pathogen Transmission. In: *Anopheles mosquitoes—New Insights into Malaria Vectors* (Sylvie Manguin. Editor). Publisher: Intech Open
26. Ghosh AK, Devenport M, Jethwaney D, Kalume DE, Pandey A, Anderson VE, Sultan AA, Kumar N, and Jacobs-Lorena M (2009) Malaria parasite invasion of the mosquito salivary gland requires interaction between the Plasmodium TRAP and the *Anopheles* Saglin Proteins. *PLoS Pathogens*, **5**: e1000265.
27. Giunti G, Wilke ABB, Beier JC, and Benelli G, 2023. What do we know about the Invasive Mosquitoes *Aedes atropalpus* and *Aedes triseriatus*? *Current Tropical Medicine Reports*, **10**: 41–46.
28. Gonzalez-Ceron L, Santillan F, Rodriguez MH, Mendez D, Hernandez-Avila JE (2003) Bacteria in midguts of field-collected *Anopheles albimanus* block *Plasmodium vivax* sporogonic development. *Journal of Medical Entomology*, **40(3)**: 371-374.
29. Gratz NG (2004) Critical review of the vector status of *Aedes albopictus*. *Medical and Veterinary Entomology*, **18(3)**: 215-227.
30. Gubler DJ (1998) Dengue and Dengue hemorrhagic fever. *Clinical Microbiology Reviews*, **11**: 480-496.
31. Gubler DJ (2012) The economic burden of dengue. *American Journal of Tropical Medicine and Hygiene*, **86(5)**:743-744.
32. Guzman MG, Halstead SB, Artsob H, Buchy P, Farrar J, Gubler DJ (2010) Dengue: a continuing global threat. *Nature Reviews Microbiology*, **8(12)**:7-16.
33. Halstead SB (2008) Tropical Medicine: Science and Practice. In: Dengue, (Halstead SB. International Vaccine Institute, Korea. Editor) Publisher. Imperial College Press. **182**: pp.1-28.
34. Harrison RE, Yang X, Eum JH, Martinson VG, Dou X, Valzania L, Wang Y, Boyd BM, Brown MR, Strand MR (2023) The mosquito *Aedes aegypti* requires a gut microbiota for normal fecundity, longevity, and vector competence. *Communications Biology*, **6(1)**: 1154.
35. Hawley WA (1988) The biology of *Aedes albopictus*. *Journal of the American Mosquito Control Association (Suppl)*, **1**: 1-39.
36. Hertig M (1936) The Rickettsia, *Wolbachia pipientis* (gen. et sp.n) and associated inclusions of the mosquito, *Culex pipiens*. *Parasitology*, **28(4)**:453-486.
37. Jones FK, Morrison AM, Santiago GA, Rysava K, Zimler RA, Heberlein LA, Kopp E, Saunders KE, Baudin S, Rico E, Mejía-Echeverri Á, Taylor-Salmon E, Hill V, Breban MI, Vogels CBF, Grubaugh ND, Paul LM, Michael SF, Johansson MA, Adams LE, Munoz-Jordan J, Paz-Bailey G, Stanek DR (2024)

- Introduction and Spread of Dengue Virus 3, Florida, USA, May 2022-April 2023. *Emerging Infectious Diseases*, **30(2)**:376-379.
38. Kaur R, Meier CJ, McGraw EA, Hillyer JF, and Bordenstein SR (2024) The mechanism of cytoplasmic incompatibility is conserved in *Wolbachia*-infected *Aedes aegypti* mosquitoes deployed for arbovirus control. *PLOS Biology*, **22(3)**: e3002573.
 39. Kittayapong P, Baisley KJ, Baimai V, and O'Neill SL (2000) Distribution and diversity of *Wolbachia* infections in Southeast Asian mosquitoes (Diptera: Culicidae). *Journal Of Medical Entomology*, **37**: 340–345.
 40. Lambrechts L, Paaijmans KP, Fansiri T, Carrington LB, and Kramer LD, (2011) Impact of daily temperature fluctuations on dengue virus transmission by *Aedes aegypti*. *Proceedings of the National Academy of Sciences of the United States of America*, **108**: 7460–7465.
 41. Lang CA, Basch KJ, and Storey RS (1972) Growth, composition and longevity of the axenic mosquito. *The Journal of Nutrition*, **102**: 1057–1066.
 42. Mansour T., Wafaa H. Radwan, Menna Mansour, Mohamed Gomaa, Farouk Farouk, Mohamed Shep, Ahmed G. Soliman, Basma T. Abd Elhalim, Mohamed M. K. El Senosy, Ashraf Bakry, Naglaa M. Ebeed, Neima K. Alsenosy, Hesham Elhariry, Ahmed Galal, Salwa M. El Sayed, Eslam Adly, and Samah H. Abu Hussien, 2023. Larvicidal potential, toxicological assessment, and molecular docking studies of four Egyptian bacterial strains against *Culex pipiens* L. (Diptera: Culicidae). *Scientific Reports*, **13**:17230
 43. Martinson VG, and Strand MR (2021) Diet–microbiota interactions alter mosquito development. *Frontiers in Microbiology*, **12**:650743.
 44. Medley KA (2010) Niche shifts during the global invasion of the Asian tiger mosquito, *Aedes albopictus* Skuse (Culicidae), revealed by reciprocal distribution models. *Global Ecology and Biogeography*, **19**: 122–133.
 45. Mondal S, Somani J, Roy S, Babu A, and Pandey AK (2023) Insect microbial symbionts: ecology, interactions, and biological significance. *Microorganisms*, **11(11)**: 2665.
 46. Moreira LA, Iturbe-Ormaetxe I, Jeffery JA, Lu G, Pyke AT, Hedges LM, Rocha BC, Hall-Mendelin S, Day A, Riegler M, Hugo LE, Johnson KN, Kay BH, McGraw E A, Van Den Hurk, AF, Ryan PA, and O'Neill SL (2009) A *Wolbachia* Symbiont in *Aedes aegypti* limits infection with dengue, Chikungunya, and Plasmodium. *Cell*, **139(7)**: 1268–1278.
 47. Moretti R, Marzo GA, Lampazzi E, and Calvitti M (2018) Cytoplasmic incompatibility management to support Incompatible Insect Technique against *Aedes albopictus*. *Parasites and Vectors*, **11(S2)**:649.
 48. Moya A, Peretó J, Gil R, Latorre A (2008) Learning how to live together: Genomic insights into prokaryote-animal symbioses. *Nature Reviews Genetics*, **9**: 218–229.
 49. NL Kalra, SM Kaul, and RM Rastogi (1997) Prevalence of *Aedes aegypti* and *Aedes albopictus*– Vectors of Dengue and Dengue hemorrhagic fever in North, North-East and Central India. *Dengue Bulletin – Vol 21*.
 50. Ojha A (2025) Paratransgenesis: The dynamics of engineered *Enterobacter* symbionts and Cry1Ac-producing *Enterobacter* for biocontrol of *Helicoverpa* insect pests in crop production. *BioRxiv: the preprint server for biology*.1-21
 51. Osei-Poku J, Mbogo CM, Palmer WJ, Jiggins FM (2012) Deep sequencing reveals extensive variation in the gut microbiota of wild mosquitoes from Kenya. *Molecular ecology*, **21(20)**:5138-50.
 52. Pang Xiaojing, Xiaoping Xiao, Yang Liu, Rudian Zhang, Jianying Liu, Qiyong Liu, Penghua Wang, and Gong Cheng (2016) Mosquito C-type lectins maintain gut microbiome homeostasis. *Nature Microbiology*, **1**: 16023
 53. Prothero RW (1989) Urbanization: A Hot-Bed Of Vector-Borne Diseases. In: Demography and vector-borne disease (Service MW, 1989. Editor), CRC Press.17-35
 54. Raihan MF, Septiani NLW, Gumilar G, Manurung RV, Jenie SNA, Nuruddin A, and Yulianto B (2025) Developing point-of-care diagnosis using electrochemical biosensor: Mosquito-borne disease. *Sensors and Actuators Reports*, **9**: 100261.
 55. Rani A, Sharma A, Rajagopal R, Adak T, and Bhatnagar RK (2009) Bacterial diversity analysis of larvae and adult midgut microflora using culture-dependent and culture-independent methods in lab-reared and field-collected *Anopheles stephensi*-an Asian malarial vector. *BMC Microbiology*, **9(1)**: 96.
 56. Ren X, Hoiczyk E, and Rasgon JL (2008) Viral paratransgenesis in the malaria vector *Anopheles gambiae*. *PLoS Pathogens*, **4(8)**: e1000135.
 57. Rique HL, Menezes HSG, Melo-Santos MAV, and Silva-Filha MHNL (2024) Evaluation of a long-lasting microbial larvicide against *Culex quinquefasciatus*, and *Aedes aegypti* under laboratory and a semi-field trial. *Parasites and Vectors*, **17(1)**: 391.

58. Rodpai R, Boonroumkaew P, Sadaow L, Sanpool O, Janwan P, Thanchomnang T, Intapan PM, Maleewong W (2023) Microbiome composition and microbial community structure in mosquito vectors *Aedes aegypti* and *Aedes albopictus* in Northeastern Thailand, a dengue-endemic area. *Insects*, **14**(2):184.
59. Ross PA, Ritchie SA, Axford JK, and Hoffmann AA (2019) Loss of cytoplasmic incompatibility in *Wolbachia*-infected *Aedes aegypti* under field conditions. *PLoS Neglected. Tropical Disease*, **13**: e0007357
60. Selvan PS, and Jebanesan A (2016) Studies on potential breeding habitats of dengue and Chikungunya vector mosquitoes in Ramanathapuram district, Tamil Nadu, India. *Indian Journal of Natural Products and Resources*, **7**(3): 234- 239.
61. Serrato-Salas J, and Gendrin M (2023) Involvement of microbiota in insect physiology: focus on B vitamins. *mBio*, **14**(1): e02225-22.
62. Shroyer DA (1986) *Aedes albopictus* and arboviruses: a concise review of the literature. *Journal of the American Mosquito Control Association*, **2**: 424-428.
63. Simpson SJ, Clissold FJ, Lihoreau M, Ponton F, Wilder SM, Raubenheimer D (2015) Recent advances in the integrative nutrition of arthropods. *Annual Review of Entomology*, **60**: 293–311.
64. Sinkins SP, Braig HR, and O'Neill SL (1995) *Wolbachia* superinfections and the expression of cytoplasmic incompatibility. *Proceedings of the Royal Society B: Biological Sciences*, **261**:325–330.
65. Smith CE (1956) The history of dengue in tropical Asia and its probable relationship to the mosquito *Aedes aegypti*. *American Journal of Tropical Medicine and Hygiene*, **59** (10): 243-251.
66. Smith TW, Walker ED, and Kaufman MG (1998) Bacterial density and survey of cultivable heterotrophs in the surface water of a freshwater marsh habitat of *Anopheles quadrimaculatus* larvae (Diptera: Culicidae). *Journal of the American Mosquito Control Association*, **14**(1):72-77.
67. Stephen FM, Berisford CW, Dahlsten DL, Fenn P, and Moser JC (1993) Invertebrate and microbial associates. In: Beetle-Pathogen Interactions in Conifer Forests; (Schowalter, T.D., Filip, G.R., Eds.); Academic Press: San Diego, CA, USA, 129–153.
68. Swaminathan S and Khanna N (2009) Dengue: recent advances in biology and current status of translational research. *Current Molecular Medicine*. **9**: 52-173.
69. Touray Mustapha, Derya Ulug, Sebnem Hazal Gulsen, Harun Cimen, Canan Hazir, Helge B. Bodee, Selcuk Hazira (2024) Natural products from *Xenorhabdus* and *Photorhabdus* show promise as biolarvicides against *Aedes albopictus*. *Pest Management Science*, **80**: 4231–4242
70. Trpis M, Perrone JB, Reissig M, and Parker KL (1981) Control of cytoplasmic incompatibility in the *Aedes scutellaris* complex Incompatible crosses become compatible by treatment of larvae with heat or antibiotics. *Journal of Heredity*, (72):313-317
71. Ukey PM, Bondade SA, Paunipagar PV, Powar RM, and Akulwar SL (2010) Study of seroprevalence of dengue fever in central India. *Indian Journal of Community Medicine*, **35**(4): 517-519
72. Vijayakumar K, Kumar TKS, Nujum ZT, Umarul F, and Kuriakose A (2014) A study on container breeding mosquitoes with special references to *Aedes (Stegomyia) aegypti* and *Aedes albopictus* in Thiruvanthapuram district. *Journal of Vector-Borne Diseases*, **5**: 27-32.
73. Wang S, Ghosh AK, Bongio N, Stebbings KA, Lampe DJ, Jacobs Lorena M (2012) Fighting malaria with engineered symbiotic bacteria from vector mosquitoes. *Proceedings of the National Academy of Sciences of the United States of America*, **109**:12734-12739.
74. Werren JH, Windsor DM, and Guo LR (1995) Distribution of *Wolbachia* among neotropical arthropods. *Proceedings of the Royal Society of London. Series B: Biological Sciences*, **262**: 197 – 204.
75. WHO (2016) Chikungunya fever Fact sheet. http://www.searo.who.int/entity/emerging_diseases/topics/Chikungunya/en/. (Accessed on December 2016)
76. WHO (2024) Dengue-Global Situation/30 May 2024/<https://www.who.int/emergencies/disease-outbreak-news/item/2024-DON518>
77. Zhou W, Rousset F, and O'Neill SL (1998) Phylogeny and PCR-based classification of *Wolbachia* strains using wsp gene sequences. *Proceedings of the Royal Society of London. Series B: Biological Sciences*, **265**: 509 - 515.

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