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Biological control of mosquito-borne viral diseases: Prospects and challenges

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ABSTRACT

Diseases caused by arboviruses inflict an enormous drain on world health, and significantly manipulate commercial interests. For instance, dengue and other mosquito-borne viruses unaided are liable for more than a million mortalities on a yearly basis. With the recent emergence and re-emergence of vector borne viral disease, many individuals have been doubtful that established control procedures, such as using pesticides and insect repellants for durable periods will no longer be effective. Moreover, persistent use of insecticide has led to worries of undesirable ecological consequences, and worthy of note is increased resistance of these vectors to insecticides. Consequently, the necessity for a different and novel ecologically friendly biological control strategy has been proposed to balance existing insect control methods.

Keywords: Control, Dengue virus, Health, Insecticide, Mosquito, Viral disease

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INTRODUCTION

Viruses are obligate intracellular parasites, designed through the course of evolution to infect cells, often with great specificity to a particular cell type [1]. Though they exist at the edge of living as particles, they can be spread by vectors to cause infections to humans. Such vectors could be arthropod borne. Vectors include: ticks mosquitoes, lice and fleas. Insect-borne diseases, particularly those transmitted by mosquitoes are among the leading causes of mortality and morbidity in humans [2].

Diseases caused by the bite of mosquitoes results in an estimated 1–2 million deaths per year, taking a dramatic toll on health and socio-economic development in affected areas [3]. Mosquitoes can spread diseases more than every other set of insects and distress millions of individuals throughout the globe. WHO has stated that mosquitoes are “public enemy number one”. Mosquito-borne diseases are established in more than 100 countries within the world, affecting over two million people every year throughout the globe [3]. Dengue fever is the most significant arboviral disease in human beings [4]. Forty percent of the world’s populace in more than 100 countries is endangered of infection and statistics reveal that an estimated of 390 million infection, cases occur yearly [5].

"Today, dengue is categorized the most significant mosquito-borne viral disease on earth. Everywhere the social and economic costs are swaying as stated by the Director General, WHO [6].

Mosquitoes act as vectors for most of the life looming diseases like malaria, yellow fever, dengue fever, chikungunya fever, filariasis, Japanese encephalitis fever, West Nile virus infection, etc. existing in almost all tropical and subtropical countries and many other segments of the world [6]. Anthropogenic dynamics as well as global climate changes have impacted to increase vector mosquito species along with human pathogens comprising of arboviral menaces like dengue, yellow fever, West Nile virus and chikungunya [7].

The annual prevalence and incidence of mosquito-borne viral diseases including dengue fever, yellow fever, West Nile virus and chikungunya virus are increasing due to human travel, rapid development and failures of adequate preventive public health measures [8]. Particularly in Nigeria, infections caused by this virus is often times undiagnosed, underdiagnosed, misdiagnosed as Malaria or referred to as pyrexia of unknown origin, because of the similar symptoms exhibited by both at the onset of the disease. This inconclusive diagnosis is of public health importance since there is a possible spread of the virus from one person to another which may likely result into large epidemics [9].

Dengue viruses (DENV) are predominantly transmitted by the transmissible bite of female *Aedes aegypti* mosquitoes and to a much lesser extent *Aedes albopictus*. No current vaccine or therapy against dengue fever exists (wilder) The global burden of dengue is alarming: nearly half the world's population lives in dengue-predisposed regions, and available control measures are failing to prevent the global increase in the incidence of the disease [10]. New advances are vividly needed if these trends are to be reversed. To prevent proliferation of mosquito-borne viral diseases and to improve quality of environment and public health, mosquito control is vital and is the only obtainable counter-measure.

Before now, the key instrument in mosquito control process is the use of man-made insecticides such as organophosphate and organochlorine compounds. But this has not been very effective due to operational, technical, human, ecological, social and economic factors. In recent years, use of many of the previous artificial insecticides in mosquito regulation programme has been inadequate [11]. There are many factors account for this. These include lack of new insecticides, exploitative costs of synthetic insecticides, worries for environmental nurturing, deleterious effect on human healthiness, and other non-target residents, their non-renewable nature, higher rate of ecological amplification through ecosystem, and escalating insecticide resistance on a global scale [11]. Insecticides are customarily only used for the control of mosquito-borne viral diseases during epidemics, and their efficacy is disputable on. This has instigated researchers to look for new and alternative methods varying from provision of or fostering the approval of effective and visible mosquito management approaches that focus on public enlightenment, surveillance and monitoring, vector source reduction and environment friendly least-harmful larval control-have been advantageous in some cases [11]. However, these approaches often require everyday intervention, and can be costly and arduous to implement. In view of these, the use of environmentally friendly alternatives such as biological control of vectors has become the fundamental focus of the control programme in place of the organic insecticides. To prevent increase of mosquito-borne borne diseases and to develop, quality of environment and public health, mosquito control is key and vital. The purposeful use of environmental enemies to decrease the number of disease causing agents is known as Biological control [12]. It includes methods that have secured approval for controlling irritant arthropods partly due to the emergence and re-emergence of insecticide resistance and also because individuals have become more cognizant about the need to restrain environmental contamination**.** For arthropod-borne viral disease vectors, the hypothetical application of the symbiotic bacteria *Wolbachia pipientis* to the control of mosquito-borne viral disease has recently been proposed and has been added amongst the arsenal of weapons as an effective strategy for regulating and preventing transmission of such diseases [13].

MOSQUITO-BORNE VIRUSES

Viral diseases incriminated by mosquitoes belong to a group of viruses commonly referred to as arboviruses. They can transmit diseases without being affected themselves, i.e, they could serve as natural reservoir's for viruses. Some important viral diseases transmitted by mosquitoes includes, dengue fever, West Nile fever, yellow fever, chikungunya, Japanese encephalitis, St Louis encephalitis, Western equine encephalitis, Eastern equine encephalitis and La Crosse virus [14]. The viral diseases yellow fever, dengue fever and chikungunya are transmitted by *Aedes aegypti* mosquitoes. While the West Nile fever is transmitted by the *Culex* and *Culiseta* species. Others are carried by several different mosquitoes.

Dengue Viruses (Dengue Fever)

Disease caused by a virus of the *Flaviviridae* family (dengue virus; DENV) [15]. It was first described by Benjamin Rush. It is a vector-borne disease and can be transmitted from person to person by the yellow fever mosquito (*Aedes aegypti*) and the Asian tiger mosquito (*Aedes albopictus*) [16]. Other than humans, no known bird or mammal reservoir exists for dengue. A mosquito can become infected with the virus by feeding on a person with the disease, and then the virus must go through an eight to ten day incubation period in the mosquito before it becomes infective. The mosquito will then remain infective for the rest of its life [17].

Symptoms are characterized by sudden onset of high fever, severe headache, backache, and joint pains. The disease is so painful that it is sometimes referred to as "break bone fever." A skin rash may also appear. Infection may be very slight or completely asymptomatic [17]. In some regions, however, a complication called "dengue hemorrhagic fever" and "dengue shock syndrome" may result following subsequent infection with a different serotype causing a high fatality rate, a mechanism to be proposed as the antibody dependent mechanism. Especially amongst children and women [17]. The disease has been raging in Mexico and Central and South America for the last 10 years. It is literally "knocking at the door" with cases frequently occurring along the U.S. -Mexican border.

West Nile Virus

West Nile fever caused by a virus of the *Flaviviridae* family (West Nile virus, WNV). West Nile virus is an enveloped single stranded RNA virus, it is also a vector-borne disease and usually transmitted by bites of infected *Culex* mosquito species. The virus was first isolated in the west Nile district of Uganda in 1937 from a febrile woman and hence the name, West Nile virus. It primarily infects birds and occasionally infects humans and other animals [18].

About 80% of human infection is asymptomatic, and 20% develop mild febrile illness (flu-like illness). Most uncomplicated infections resolve in 3–6 days. Severe clinical cases may result leading to Neurons-invasive disease: there may be signs of encephalitis, meningoencephalitis or meningitis. Approximately 1 in 150 infections results in meningitis or encephalitis [19]. Advanced age is by far the most significant risk factor for severe neurologic disease viremic period can occur up to two weeks prior to symptoms and last up to more than a month from the initiation of the infection person-to-person transmission has not been reported. In rare cases, the virus has been spread by blood transfusions, organ transplants, and transplacental transmission [20].

Yellow Fever Virus

It is also caused by member of the family *Flaviviridae*. It is an acute infectious disease of sudden onset and variable severity caused by a virus transmitted by mosquitoes (*Aedes aegypti*) [19]. Mosquitoes are the primary vectors. Humans and monkeys are affected by the disease. It characterized by fever, jaundice, hemorrhagic manifestations and albuminuria. The incubation period in humans is 3–6 days. Yellow fever virus (YFV) is maintained in nature by mosquito-borne transmission between non-human primates. Yellow fever only occurs in sub-Saharan Africa and tropical South America. Yellow fever exists in two forms the Urban yellow fever and the Jungle yellow fever. The Urban Yellow Fever which usually involves Mosquito-human transmission cycle by the *Aedes aegypti* sp and then Jungle Yellow Fever involving Mosquito-primate transmission cycle with spill over to humans by the Aedes spp. in Africa *Haemagogus*, *Africanus* and *Sabethes* spp in South America [20].

Yellow fever is preventable by a relatively safe effective vaccine known as the 17D strain vaccine which is available. There are some rare but serious complications associated with the vaccine. Rare adverse events following vaccination could lead to death [21]. Doblas et al. (2006) [22] documented a 26-year-old Spanish woman who planned to travel to Africa had contacted yellow fever days after vaccination and died 10 days thereafter. When the genome of the virus was retrieved and sequenced, silent mutations were observed.

Chikungunya Virus

It is an alphavirus. The virus was isolated in 1952 during an outbreak in Tanzania. Characterized by fevers, rigors arthralgias and myalgias. In the local language of Swahili it means 'that which bends up' [23]. The virus is transmitted by *Hematophagous* mosquitoes of the *Aedes* group with secondary transmission by *Mansonia*. The incubation period is short. 2-3 days clinical symptoms includes sudden onset of high fever (>38.5°C) and other (flu-like) symptoms: headache, back pain, myalgia, arthralgia, rash. It is similar to dengue fever and symptoms generally resolve within 7–10 days. No vaccine, therapy or medication is currently available.

Other medically important mosquito-borne viral diseases includes Japanese encephalitis, St Louis encephalitis, Western equine encephalitis, Venezuelan equine encephalitis, Eastern equine encephalitis and La Crosse virus.

CLASSIFICATION OF MOSQUITO-BORNE VIRAL DISEASES

Previously, arboviruses were systematized into one of four clades: A, B, C, and D. Clade A signifies members of the genus *Alphavirus*, Clade B include members of the genus *Flavivirus*, and Clade C continues as the Group C serogroup of the genus *Orthobunyavirus*. Clade D was retitled in the mid 1950s to the Guama group and is presently the Guama serogroup in the genus *Orthobunyavirus* [24]. The leftover of the clades was because the number of clades would ultimately go beyond the length of the alphabet. Since then, the classification of arboviruses into these clades has become extinct. The standard biological classification system has become more preferred for classifying viruses [24].

BIOLOGY OF MOSQUITO VECTORS IN VIRAL DISEASE

Species of mosquitoes vary in their reproducing habitats, biting mode, flight radius and in several other modes [25]. Hence, different methods are needed to control diverse species of mosquitoes. Annual community clean-up campaigns, for instance, are very functional

in reducing populations of Asian tiger mosquitoes that breed majorly in artificial containers. Therefore, it is very necessary and important for mosquito management to know exactly what species of mosquito is found within their region in order to manipulate and create an effective control strategy [25].

DISEASE CYCLES OF SOME MOSQUITO-BORNE VIRUSES

St. Louis Encephalitis

St. Louis encephalitis (SLE) virus spreads naturally in birds. Birds are the natural reservoirs. These viruses are transmitted by *Culex* mosquitoes. Humans become infected only when bitten by an infected mosquito. Humans are actually "dead end" hosts, implying that the virus in human blood at no time reaches a level significant enough to infect a biting female mosquito to continue the infectious cycle. Not all people infected with the virus show and develop clinical disease. However, the virus may produce sudden onset of nausea, fever, vomiting, and severe headache in individuals within 5–7 days after being bitten [25]. Fatality rates range from 2–20% with most mortalities occurring in older subjects. Sporadic outbreaks of St. Louis encephalitis usually happen in mid-summertime to early fall. Since domestic fowls and wild birds are the reservoirs of this virus, municipal areas where large bird populace and abundant *Culex* mosquitoes are found together are major sites for a disease outbreak [25].

In 1957, a major outbreak of St. Louis encephalitis occurred in Mississippi. Many people were infected and many cases resulted in death. The potential risk for this to occur again is imminent. Adequate control measures are needed to implement and manage a good mosquito control practices in those disease risk regions and be prepared to respond promptly to any epidemic [25].

West Nile Virus Encephalitis

This virus is maintained naturally in a way analogous to St. Louis encephalitis, in a bird-mosquito cycle. Numerous *Culex* spp., which includes, the common house mosquitoes, *Culex quinquefasciatus*, *Culex pipiens*, *Culex restuans*, and also *Culex triseratius*, have been implicated and are the primary vectors to individuals [25]. West Nile virus is the most harmful to the elderly or immune-deficient patient. This has also been shown to replicate in the Asian tiger mosquito, *Aedes albopictus* under laboratory atmosphere, the mosquito has also been linked in WNV transmission. In distinction to other mosquito-borne viruses, WNV is a major cause of mortality in birds and horses in the US, especially crows, and blue jays [25]. Monitoring and surveillance efforts to detect the incidence of WNV, and can therefore serve as target for the reporting and testing of those types of dead birds. West Nile virus is asymptomatic and does not cause as serious illness as some other arboviral diseases (e.g., EEE, SLE). Actually, only one out of every 150–200 people exposed to the virus become ill, and less than 10% of individuals who show clinically signs will die. Still, the public's reaction and perception to native reports of WNV cases cause much worry and concern in communities. Local officials are, then obliged by the public to provide mosquito control to "shield" them.

Lacrosse Encephalitis

In divergence to most other mosquito-borne viruses that pose a burden to humans, Lacrosse (LAC) virus cycle is maintained in nature through a small mammal-mosquito cycle. Usually, the mosquito vector is the giant tree-hole mosquito, *Ochlerotatus triseriatus* and the reservoir is the grey squirrel.

In 1967, Mississippi recorded its first established cases of LAC, but was not often diagnosed until eight cases were identified in 2001 in children less than 16 and can cause convulsive disorders in affected wards. Control efforts are obviously different for this disease, because it will focus on plugging tree holes where mosquitoes breed in minute amounts of acidic rainwater. These findings and facts bring extra demands on local officials by parents that control strategies be implemented.

Eastern Equine Encephalitis

Similar to SLE and WNV, birds are the principal hosts and mosquitoes, particularly *Culiseta melanura*, are the vectors from bird to bird. *Culiseta melanura* hardly feeds on humans though. Individuals usually become involved as dead end hosts when bitten by infected salt marsh mosquitoes (*Ochlerotatus sollicitans*), inland floodwater mosquitoes (*Aedes vexans*), *Coquillettidia perturbans*, and a few other species. The disease affects persons irrespective of any age, with infants and young people being the most susceptible. The mortality rate is over 50%, and children surviving the disease often experience hurt from some level of mental retardation or paralysis. Horses are often harshly affected by the disease during epidemics. However, a horse vaccine is accessible.

Dengue

The dengue virus is transmitted from person to person by the bite of an infected yellow fever mosquito (*Aedes aegypti*) and the Asian tiger mosquito (*Aedes albopictus*). Apart from humans, no known bird or mammal reservoir exists for dengue [25]. A mosquito becomes infected with the virus by feeding on a person with the disease, and then the virus must go through an eight to ten day incubation period known as the intrinsic incubation period in the mosquito before it becomes infective. The mosquito then remains infective for the rest of its life [25].

Symptoms are characterized by sudden onset of high fever, severe headache, backache, and joint pains. A skin rash may also appear. Infection may be very mild

or completely asymptomatic. In some areas like Cuba, however, a complication called "dengue hemorrhagic fever" and "dengue shock syndrome" which is mediated by antibody enhancement mechanism can cause a high fatality rate, especially among children [25].

The disease has been raging in Africa, Mexico, Asia and Central and South America for the last 10 years.

MOSQUITO VECTORS OF VIRAL DISEASES

YELLOW FEVER MOSQUITO (*Aedes aegypti*)

Insect Description: This mosquito is dark brown to black with silver-white markings showing:

- White stripes on posterior tarsi
- Silver-white lyre shaped lines on upper sides of thorax
- Short palps with white tips

Breeding Habitat: The species is recovered almost exclusively in colored artificial containers around structures, such as tires, cans, jars, flower pots and gutters. It also breeds in tree holes [25].

Life Cycle: Distinct eggs are laid on the interior surfaces of containers at/or beyond the water mark or periodically on the water surface. The eggs can resist desiccation for several months. Submerged eggs can hatch in two or three days at high altitude temperatures. Under appropriate conditions, larval metamorphosis is completed in 6–10 days. Cool weather extends the development period. The pulpal stage lasts about two days [25]. The life cycle can be ended within 10 days under good conditions or extend to three or more weeks under poor conditions. Breeding rate is lengthier during the winter with eggs remaining latent for several weeks or months.

Biting Behaviors: The vector usually bites during the morning or late afternoon. It prefers human blood meals, biting primarily around the ankles, under sleeves and back of the neck. It swiftly enters houses.

Flight Range: 100 feet to 100 yards.

Important: This mosquito is a potential vector of dengue and urban yellow fever. It is also an important pest species [25].

ASIAN TIGER MOSQUITO (*Aedes albopictus*)

Insect Description: This mosquito is very striking in appearance to the yellow fever mosquito. It is dark brown to black with silver-white stripes that include:

- Silver markings down the middle of the thorax
- White bands on posterior tarsi
- stripped abdomen
- Short palps with white tips

Breeding Habitat: Man-made containers, and especially abandoned tires, are the major breeding sites.

Life Cycle: Not much fact is known about this mosquito. However, its life cycle is probably striking to that of the yellow fever mosquito.

Biting behavior: This is a violent biter, aggressive soon after you disturb a breeding area. Often these mosquitoes land and bite quickly.

Flight Range: Less than a quarter mile.

Seasonal Occurrence: They may be dynamic most of the year. The specie of Asian tiger mosquito introduced into the United States is thought to have originated from the hot Orient and can be more adapted to cold temperatures than the yellow fever mosquito.

Importance: The Asian tiger mosquito may carry the agents of dengue fever, yellow fever, and several encephalitis viruses.

TREE HOLE MOSQUITO (*Ochlerotatus triseriatus*)

Insect Description: This averaged- sized mosquito is brown to black with silver-white markings. Other features include:

- Wide dark brown strip on thorax that becomes larger and broader toward the abdomen
- Abdomen is blue-black with white stripes on the sides
- Second and third pair of legs are yellowish-white at the bottom and dark on the ends
- Proboscis are black with short black palps.

Breeding Habitat: This occurs in man-made containers and tree holes.

Life Cycle: A month is required for complete metamorphosis. Many broods are produced annually from spring to fall. The broods will change into larvae during winter.

Biting Behavior: This species is an aggressive and fierce biter both during the daytime and night.

Flight Range: Minimal

Importance: This pest mosquito is demonstrated to have a value in the laboratory to serve as agents of yellow fever and eastern equine encephalitis. It is considered to be a significant vector of La Cross virus in other parts of the world and United States.

SOUTHERN HOUSE MOSQUITO (*Culex quinquefasciatus*)

Insect Description: This is a brown, medium-sized mosquito with white markings, including:

- Abdominal sections with narrow bands
- Dark unbanded legs having a bronze to metallic blue green imaging
- Dark palps shorter than the proboscis.

Breeding Habitat: Major breeding sites are waters largely and heavily contaminated with organic material such as ditches receiving septic tank overflow, storm-sewer catch basins, poorly drained ditches, and polluted ground water. This mosquito will also breed in man-made containers.

Life Cycle: Eggs are laid in propelling rafts of 50–400, hatching daily or twice in warm temperatures. The water stages are completed in 8–10 days. During cold

weather, several weeks may be necessary for complete development. Generally, reproduction is unceasing throughout the warmer months of the year.

Biting behavior: Feeds on birds, domestic animals, and humans, it quickly enters houses.

Flight Range: These mosquitoes fly only short distances unless large numbers are produced.

Importance: *Culex quinquefasciatus* the main vector of the agent of St. Louis and West Nile encephalitis and a major vector of the dog heartworm.

DARK RICE FIELD MOSQUITO
(*Psorophora columbiae*)

Insect Description: An average to large mosquito that is dark brown to bronze with yellowish white and gray markings including:

- Dark proboscis with large yellow band
- Narrow rings of white scales near the tip of each femur
- Abdominal sections with white to pale yellow markings on the lower segment.

Breeding Habitat: It is found in open freshwater temporary pools and ditches. Very abundant in fallow rice fields; rice fields that have been drained and submerged, and in second cropped rice fields. It can also be found in faintly brackish areas [25].

Life Cycle: Numerous broods are reproduced per season (April to October). Eggs are laid on terrain subject to flooding with regions of low, vegetation being preferred. Eggs that have been dry for 2 or 3 weeks will hatch within minutes upon being submerged. At an average temperature of 79°F, larval stages can be finished in 5 days. The pupal stage lasts 1–2 days. Areas that dry-up and are resubmerged every few days can produce a hatch with each flooding. This mosquito overwinters in the egg stage [25].

Biting Behavior: They are aggressive and fierce biting mosquitoes, attacking either in day or night.

Flight Range: Not less than 10 miles.

Importance: In 1971, this mosquito was supposedly proposed as the vector of Venezuelan equine encephalitis cases in Texas. Western equine encephalitis and California encephalitis viruses have also been derived from dark rice field mosquitoes [25].

BIOLOGICAL CONTROL OF MOSQUITO-BORNE VIRUSES

This involves the conscientious use of ecological enemies to decrease the number of pest organisms [26]. It consists of strategies that have gained wide acceptance for controlling problematic vectors partly due to the re-emergence of insecticide resistance and also because individuals have become more aware about the need to limit environmental degradation [27]. In the case of insect-borne viral disease vectors, biological control has been proven to be a potentially effective method for monitoring and preventing spread of viral diseases such as dengue, West Nile fever and chikungunya, yellow fever, and others. Dengue is an arboviruses spread by species of *Aedes* mosquito. They breed in peridomestic man-made water containers, and their control is the most effective way to decrease the viral transmission.

In 1919, Harry S. Smith proposed biological control, to the current understanding of applied biological control involving basically autecology of insects which has led to integrated vector management principles [28]. The potential and judicious use of a natural enemy to regulate vector abundance has shown quantitative insight into useful principles, i.e. an optimal biological agent concurring to its host tropism, and adaptation to environmental factors. The advancement of vector synanthropism reveal why viral transmission of these mosquito borne diseases can only be decreased by controlling the *Aedes* mosquito vector [29].

SYMBIOTIC BACTERIA AND ADAPTATION IN MOSQUITO GUT

The mosquito gut is a small biome where many bacteria reside. These organisms are vital for mosquito life. Without these symbiotic bacteria, mosquitoes would not be pleased in terms of fecundity/fertility and immune mechanisms [30]. The necessary nutrients provided for the host is very vital for the mosquito life cycle. If the bacteria community is changed inside the mosquito gut, then mosquitoes may produce fewer eggs and the whole populace would be smaller which would help reduce and prevent transmission of these mosquito borne diseases [30].

MECHANISM OF VIRICIDAL PROPERTIES OF BACTERIAL IN MOSQUITO GUT

Aedes and *Culex* species consist the main arthropod vectors for dengue virus, West Nile virus (WNV) and yellow fever virus (YFV) (all *Flaviviridae*), as well as chikungunya (*Togaviridae*). Among main arboviruses vectors, *Aedes albopictus*, *Aedes bromeliae* and members of the *C. pipiens* complex are biologically infected with *Wolbachia endosymbionts* (*Aedes albopictus* harbors *Wolbachia Albopictus* A and *Wolbachia Albopictus* B, and *Culex pipiens, Wolbachia pipiens* whereas *Aedes aegypti* mosquitoes lacks this relationship.

Antiviral effect of *Wolbachia* in different mosquito/arbovirus associations

Wolbachia are obligate intracellular maternally inborn bacteria that have been implicated in diverse arthropod groups including spiders, insects and terrestrial crustaceans, in accumulation to filarial nematodes. It has been projected that >65% of insect species harbor *Wolbachia*, making it one of the most universal intracellular bacteria revealed till date [31]. In

arthropods, *Wolbachia* behave as a reproductive parasite by manipulating the reproductive capability of the host to enhance their vertical transmission.

Previous studies have revealed that the native *Drosophila*/*Wolbachia* interactions, has the ability of homologous *Wolbachia* strains to confer resistance in mosquitoes. This can be is limited by tissue density and distribution. For example, wAlbA and wAlbB did not prevent DENV replication to important levels in *Aedes albopictus* mosquitoes [32], but decreased viral load of the salivary glands and thus may limit spread [33]. Furthermore, the wAlbA and wAlbB infected *Aedes albopictus* cell line Aa23 showed decreased DENV titres compared to *Wolbachia*-cured controls. Consequently, this cell line has a significantly higher *Wolbachia* density than body cell tissues of *Aedes albopictus*, which may elucidate and enunciate its restrictive phenotype [34].

A recent survey of the interaction between CHIKV and wAlbA and wAlbB in *Aedes albopictus* mosquitoes revealed no decrease in viral titres in the manifestation of *Wolbachia* compared to controls. Viral loads in *Wolbachia*-free mosquitoes were extremely different compared to those harboring *Wolbachia*, suggesting some level of symbiosis [33]. Lastly, homologous wPip infections in *Culex quinquefasciatus* resulted in decreased WNV titres and transmission rates [35]. Knowing that *Wolbachia* confers resistance to RNA viruses in *Drosophila* [36], and that these *Wolbachia* strains can be stably introduced and retained in different host mosquitoes [37], multiple studies have shown whether *Wolbachia* trans infection into different mosquito species would result in vectors refractory to infection with important viral pathogens. Further researches have shown that Trans infection of *Aedes aegypti* with the *D. melanogaster w*MelPop-CLA strain of *Wolbachia* deleteriously affects mosquito survival and strongly prevents the replication of DENV when compared to tetracycline-treated (cured of *Wolbachia* infection) control or wild-type mosquitoes, regardless of whether mosquitoes were blood fed or whether the virus was injected intrathoracically [38]. *Wolbachia* also decreased DENV spread to the thorax and head of mosquitoes, and hence possibly transmission [38]. *Aedes aegypti* trans infected with the *Aedes albopictus Wolbachia* strain *w*AlbB also showed increased mosquito permanency upon infection with DENV and reduced viral replication [32].

It is evident that the *Wolbachia*-induced virus refractory phenotype is reliant on the combination of *Wolbachia* strain, virus and host (genetic or other) factors. Understanding these diversities is vital to a successful vector control method. Several mechanisms have been hypothesized to show why *Wolbachia* inhibits arboviral dissemination effectively in some instances but not in others.

PRINCIPLES OF EXTRACTING AND HARNESSING SYMBIOTIC BACTERIA IN VIRAL CONTROL

Symbiotic interactions between *Wolbachia* and insect species could be harnessed for control of mosquito-borne pathogens, by manipulating insect reproduction and interfering with major human pathogens. A reproductive change, cytoplasmic incompatibility (CI) has received much attention for use in applied methods targeting disease vectors. This strategy includes the incompatible insect technique (IIT) and the sterile insect technique (SIT).

The *Wolbachia*-based incompatible insect technique: In this technique, female sterility is artificially continued by recurrent releases of cytoplasmically mismatched males. Since *Wolbachia* is not paternally disseminated, the infection type present in the release specie does not turn out to be established in the field as the size of the field populace reduce due to incompatible mating, the proportion of males of the release strain rises.

Presently, a renewed attention is being directed towards suppression strategies based on the release of sterile insects (SIT) for vector control. The SIT is based on the mass cultivation of a species, with exposure to radiation to induce sterility and release, preferably male-only, against a target population. This interest is driven by the presence of new technologies with the values to provide important improvements in the cost-effectiveness of SIT use, as well as by the recognition of the disadvantages of current vector control principles [39, 40].

The SIT is strain-specific and an ecologically non-polluting approach to insect control that is based on the release of numerous numbers of sterile males that are, however, capable of mating with and inseminating native females. This will lead to a reduction in the reproductive potential of the females and eventually, if males are released in large numbers over a sufficient period of time, to the suppression or local elimination of the pest populace. One advantage of the SIT compared to the use of pesticides is that sterile males may vigorously search for the target females even in regions where the use of chemicals is not visible. However, the main advantage of SIT compared to all other methods is that target insect species cannot develop resistance against irradiation. Studies reveal that the SIT has been successfully used to decrease or to locally eradicate pests and disease vectors such as, the screwworm *Cochliomyia hominovorax Coquel* (Diptera: *Calliphoridae*) in the USA, Mexico and Central America [41] and more lately against dengue in Australia [42], the tsetse fly *Glossina austeni* (Diptera: *Glossinidae*) in the island of Zanzibar [43] and *Anopheles albimanus* in Central America [44].

Although it is more effective to release only males, the SIT can also be successfully used by releasing both sexes, at least for the control of agricultural pests [45].

Table 1: Classification of some medically important mosquito viruses

Group A Alphaviruses	Group B Flaviviruses	Group C Bunyaviruses	Phleboviruses	Coltiviruses
Chikungunya, Venezuelan equine encephalitis	Yellow fever, Dengue, Japanese B encephalitis,West Nile	Crimean-Congo haemorrhagic fever, Hantaviruses	Sandfly Fever, Rift Valley fever	Colorado tick fever
Western equine encephalitis, Eastern equine encephalitis,Ross river fever	Kyasanur Forest disease, Murray Valley	Ossa, Oriboca, Itaqui		

Source: Adetokumbo and Lucas 2010

Nevertheless, there is the major disadvantage of an incompatible insect technique (IIT) method for large scale applications. The inadvertent release of infected females at adequate numbers may result in the replacement of the targeted populace with a population carrying the *Wolbachia* infection of the released mosquitoes if reared females are compatible with the wild males. However, when an IIT program is based on a biCI pattern (i.e., transinfected males released to suppress a target population in which females and males harbor a different and incompatible *Wolbachia* type), this risk is partly reduced [40]. It is also suggested that the local fixation of a population infected by a new *Wolbachia* strain, reciprocally incompatible with the wild bacterial strain, could be advantageous since the newly infected populace would compete with the wild one in an opposed manner. In any case, the consequence of an inadvertent release of infected females needs to be thoroughly monitored and investigated by appropriate semi-field experiments and/or by mathematical templates prior to any field application.

A solution to this setback may be provided by the combination of irradiation with IIT. Application of irradiation at a dose which would sterilize the females without affecting the quality of the released males could ensure that any inadvertent discharge of females will not result in productive crosses and viable offspring [40].

Burt A. [46] tested this idea with *Aedes polynesiensis* and showed that female sterility can be induced by the application of 40 Gy irradiation— a dose that does not affect the male fitness. By combining irradiation with CI, the sterility of released males is due to both *Wolbachia* and irradiation while the female sterility is only due to irradiation. This combined strategy could in principle be applied in any targeted species for which an adequate sexing system is not available. It would also be interesting to test this approach for insect–*Wolbachia* symbiotic associations which do not display complete CI.

MATERIALS AND METHODS

This was an extensive internet search of peer reviewed articles through Google scholar, PubMed, Elsevier, Medscape, Medline, NLM, Bioline, Ajol, Scopus and HINARI on epidemiology, pathogenesis and biological control of mosquito-borne viruses.

PROSPECTS OF *WOLBACHIA* SPP. IN DENGUE, YELLOW FEVER AND WEST NILE VIRUSES CONTROL

The potential use of the symbiotic bacteria *Wolbachia pipientis* to the control of mosquito-borne viral diseases has emerged as an addition to the arsenal of weapons against mosquitoes [47]. It has the advantage of being more ecologically mild than insecticide-based approaches and hypothetically more cost effective. In recent years, there has been a renaissance of interest in *Wolbachia* as a means to control insect-transmitted diseases. *Wolbachia pipientis* is a single group of bacterial strains, closely related to the *Ehrlichia*, *Anaplasma* and *Neorickettsia* genera, all existing members of *Alphaproteobacteria* [48]. This bacterial group is ubiquitous and abundant among insect species and has been linked with the introduction of a number of reproductive changes including male killing, feminization, parthenogenesis and, most commonly, cytoplasmic incompatibility (CI) [48]. *Wolbachia* can shield insects from pathogens and limit their ability to transmit mosquito-borne pathogens [49]. This effect was first observed where naturally *Wolbachia*-infected *Drosophila* was protected against fungal and viral pathogens [50]. Later, it became evident that transferring *Wolbachia* into a novel mosquito host decreased the potential of the mosquito to become infected with and transmit a number of pathogens [50]. The protective phenotype appears to act against a broad variety of pathogens in the context of stable artificial infections, transiently-infected mosquitoes and to some extent in natural infections [51]

The RNA viruses seem particularly susceptible to the protective effect induced by *Wolbachia*. Transfer

of *Wolbachia* into *A. aegypti*, which is naturally uninfected with the symbiont, limited the ability of the mosquito to become infected with dengue, chikungunya, and West Nile and yellow fever viruses [51]. Diverse *Wolbachia* strains from the *w*Mel group, including *w*MelPop from *Drosophila melanogaster* [51], as well as *w*AlbB from *A. albopictus*, appear to interfere with virus development. Pathogen inhibition also occurs in *A. albopictus* mosquitoes infected with *w*Mel, which become resistant to chikungunya and dengue viruses [41]. *Culex quinquefasciatus* mosquitoes cleared of their natural infection displayed higher West Nile virus titers compared to their infected co-specifics [52].

POTENTIAL VALUE ADDED BY THESE APPROACHES

Presently visualized, these diverse genetic strategies to vector control have a number of anticipated characteristics that trigger their continued expansion. And they have been recently used in countries like Australia, India, and Vietnam with about 85% success rates. Key features of these approaches include the following: [53]

- Decrease in transmission rates, not just morbidity and mortality, and thus can make an significant contribution to the ambition of disease abolition and eradication;
- They can be widely used and applied in diverse settings, whether hypo- or holo-endemic, against indoor or outdoor biters, urban or rural daytime or night-time biters, and can target mosquito populace that are not easily accessible;
- They provide a large area control, hence, protection without clear biases relating to a person's wealth, age, education or moral status.
- They should complement other disease control measures, both current (e.g. Organic-based vector control) and measures under advancement (e.g. vaccines);
- They are taxon-precise in their directing, hence reducing ecological threats; and lastly.
- They are relatively simple to deliver and deploy (especially the self-sustaining approaches), with miniature or no change vital in how people behave, and consequently have the potential value to be highly cost-effective when compared to conventional disease control methods (e.g., insecticides against vectors, and drugs and vaccines against pathogens) [54].

POSSIBLE CHALLENGES ASSSOCIATED WITH THE USE OF *WOLBACHIA* IN BIOCONTROL OF VIRAL DISEASES

For successful utility of *Wolbachia* bacteria, these challenges might impede implementation of these biological strategies, these include:

(1) *Wolbachia* infections in the release strain should display high rates of cytoplasmic incompatibility (i.e., egg hatch resulting from incompatible mating little or absent) [55];
(2) The discharge strain should show high rates of maternal heritage, so that infections are naturally passed on to later generations of release strains and release males will constantly harbor incompatible infections;
(3) They require that male mating and release strain fitness should be tried in environmental systems and be comparable to wild type males;
(4) Miniature unwanted hazards or side effects in the biosphere could arise;
(5) Requests for releases should be made public and be met with public acknowledgement before release to avoid problems.
(6) A fundamental yardstick is that only males can be released. If females of the incompatible strain are inadvertently released, there is a risk of the incompatible infection type becoming established and changing the environmental populace [47]

Furthermore, the technological advancement used to generate sterile males (e.g., irradiation and chemo sterilization may result in loss of fitness of the released males [42]. A particular worry with disease vectors is that the inadvertently replaced populace could be a more capable vector than the target population. Therefore, vector competence and the risk of accidental population replacement should be assessed [46].

CONCLUSION

The use of *Wolbachia* if fully explored would decrease the spread of mosquito-borne viral diseases and consequently reducing disease incidence and mortality in the population. Therefore, the possibility of achieving disease eradication and elimination can be envisioned. Though chemical approaches to controlling vector-borne diseases —drugs and insecticides— have been largely useful over the past decades, their harms cannot be over emphasized and neglected as for the environmental pollution and degradation that is acquired as a result of their use. With *Wolbachia* as an alternative approach, millions of lives will be saved.

It has been speculated that mosquitoes, *Wolbachia* or dengue viruses might eventually evolve such that viral transmission is no longer blocked; whether this would be visible in years or decades to come —since it is relatively easy to model the spread of a inheritable factor conferring resistance to endonuclease-based Y drive— these approaches should be tested and experimented.

Combination therapy of using different approaches should be considered to deal with the problem of resistance. Computer- and laboratory-based surveys should be used to provide and give useful information on the potential for resistance to evolve. Such approaches

should be encouraged in Africa and the world at large since it targets at wide source elimination of the vector. The advantages of using *Wolbachia* cannot be ignored.

Finally, Differential diagnostic kits should be available in teaching hospitals to know the true incidence of these diseases as this would enable epidemiologists plan ahead to prevent epidemics.

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Guarantor

The corresponding author is the guarantor of submission.

Conflict of Interest

Authors declare no conflict of interest.

REFERENCES

1. https://www.boundless.com/microbiology/textbooks/boundless-microbiology-textbook/viruses-9/classifying-viruses-119/medical-importance-of-viruses-618-10790/
2. Baba MM, Talle M. The effect of climate on dengue virus infections in Nigeria. New York Science Journal 2011;4(1):28–33.
3. Regional Framework for an integrated Vector Management Strategy for the South-East Asia Region. World Health Organization; 2007. P. 1–13.
4. Gubler DJ. Emerging vector-borne flavivirus diseases: are vaccines the solution? Expert Rev Vaccines 2011 May;10(5):563-5.
5. Guzman MG, Deubel V, Pelegrino JL, et al. Partial nucleotide and amino acid sequences of the envelope and the envelope/nonstructural protein-1 gene junction of four dengue-2 virus strains isolated during the 1981 Cuban epidemic. Am J Trop Med Hyg 1995 Mar;52(3):241–6.
6. Epidemiological data of medically important arboviruses. Margaret Chan. World Health Organization; 2012;55:4–6.
7. Kilpatrick AM. Globalization, land use, and the invasion of West Nile virus. Science 2011 Oct 21;334(6054):323–7.
8. Ayukekbong JA. Dengue Virus in Nigeria: Current Status and Future Perspective. British Journal of Virology 2014:1(3):106–11.
9. Carey DE, Causey OR, Reddy S, Cooke AR. Dengue viruses from febrile patients in Nigeria, 1964-68. Lancet 1971 Jan 16;1(7690):105–6.
10. Stanisic DI, Barry AE, Good MF. Escaping the immune system: How the malaria parasite makes vaccine development a challenge. Trends Parasitol 2013 Dec;29(12):612–22.
11. Brown AW. Insecticide resistance in mosquitoes: a pragmatic review. J Am Mosq Control Assoc 1986 Jun;2(2):123–40.
12. Klasson L, Walker T, Sebaihia M, et al. Genome evolution of Wolbachia strain wPip from the Culex pipiens group. Mol Biol Evol 2008 Sep;25(9):1877-87.
13. Werren JH, Baldo L, Clark ME. Wolbachia: master manipulators of invertebrate biology. Nat Rev Microbiol 2008 Oct;6(10):741–51.
14. Westaway EG, Brinton MA, Gaidamovich SYa, et al. Flaviviridae. Intervirology 1985;24(4):183–92.
15. Tang KF, Ooi EE. Diagnosis of dengue: an update. Expert Rev Anti Infect Ther 2012 Aug;10(8):895–907.
16. NYSDOH Mosquito Borne Illness Surveillance & Response Plan. New York, USA: New York State Department of Health; 2012. p. 1-19.
17. Goddard J. Integrated vector management. Bureau Of General Environmental Services Mississippi State Department of Health. 2003.
18. Carver S, Spafford H, Storey A, Weinstein P. The roles of predators, competitors, and secondary salinization in structuring mosquito (Diptera:

Culicidae) assemblages in ephemeral water bodies of the Wheatbelt of Western Australia. Environ Entomol 2010 Jun;39(3):798-810.
19. Adeniji A. Need for surveillance on dengue virus in Nigeria. 2014.
20. McCall PJ, Lenhart A. Dengue control. Lancet Infect Dis 2008 Jan;8(1):7–9.
21. Endy TP, Anderson KB, Nisalak A, et al. Determinants of inapparent and symptomatic dengue infection in a prospective study of primary school children in Kamphaeng Phet, Thailand. PLoS Negl Trop Dis 2011 Mar 1;5(3):e975.
22. Doblas A, Domingo C, Bae HG, et al. Yellow fever vaccine-associated viscerotropic disease and death in Spain. J Clin Virol 2006 Jun;36(2):156–8.
23. Adetokumbo OL, Herbert MG. Short Textbook on Public health Medicine for the tropics. 4ed. Boca Raton, USA: CRC Press; 2010. p. 175–81.
24. www.blogher.com/ebola
25. Goddard J. Medical Entomology. Bureau of General Environmental services. Mississippi state department of health Jackson Mississippi. 2003.
26. Reyes-Villanueva F, Garza-Hernandez JA, Garcia-Munguia AM, Tamez-Guerra P, Howard AFV, Rodriguez-Perez MA. Dissemination of Metarhizium anisopliae of low and high virulence by mating behavior in Aedes aegypti. Parasites & Vectors 2011;4:171.
27. Marrelli MT, Li C, Rasgon JL, Jacobs-Lorena M. Transgenic malaria-resistant mosquitoes have a fitness advantage when feeding on Plasmodium-infected blood. Proc Natl Acad Sci U S A 2007 Mar 27;104(13):5580–3.
28. Van Driesche R, Hoddle M, Center T. Control of pests and weeds by natural enemies: an introduction to biological control. London, UK: Wiley-Blackwell; 2008.
29. McMeniman CJ, Lane RV, Cass BN, et al. Stable introduction of a life-shortening Wolbachia infection into the mosquito Aedes aegypti. Science 2009 Jan 2;323(5910):141–4.
30. Wiwatanaratanabutr I. WITHDRAWN: Geographic distribution of Wolbachia infection in mosquitoes from Thailand. J Invertebr Pathol 2012 May 23. pii: S0022-2011(12)00116–4.
31. Brelsfoard CL, Dobson SL. Wolbachia-based strategies to control insect pests and disease vectors. AsPac J Mol Biol Biotechnol 2009;17(3):55–63.
32. Min KT, Benzer S. Wolbachia, normally a symbiont of Drosophila, can be virulent, causing degeneration and early death. Proc Natl Acad Sci U S A 1997 Sep 30;94(20):10792–6.
33. Mousson L, Martin E, Zouache K, Madec Y, Mavingui P, Failloux AB. Wolbachia modulates Chikungunya replication in Aedes albopictus. Mol Ecol 2010 May;19(9):1953–64.
34. Glaser RL, Meola MA. The native Wolbachia endosymbionts of Drosophila melanogaster and Culex quinquefasciatus increase host resistance to West Nile virus infection. PLoS One 2010 Aug 5;5(8):e11977.
35. Becnel JJ, Johnson MA. Impact of Edhazardia Aedes (Microsporidia Culicosporidae) on a Semi natural Population of Aedes aegypti (Diptera: Culicidae). Biological Control 2000;18:39–48.
36. Kambris Z, Blagborough AM, Pinto SB, et al. Wolbachia stimulates immune gene expression and inhibits plasmodium development in Anopheles gambiae. PLoS Pathog 2010 Oct 7;6(10):e1001143.
37. Blagrove MS, Arias-Goeta C, Di Genua C, Failloux AB, Sinkins SP. A Wolbachia wMel transinfection in Aedes albopictus is not detrimental to host fitness and inhibits Chikungunya virus. PLoS Negl Trop Dis 2013;7(3):e2152.
38. Favia G, Ricci I, Damiani C, et al. Bacteria of the genus Asaia stably associate with Anopheles stephensi, an Asian malarial mosquito vector. Proc Natl Acad Sci U S A 2007 May 22;104(21):9047–51.
39. Moreira LA, Iturbe-Ormaetxe I, Jeffery JA, et al. A Wolbachia symbiont in Aedes aegypti limits infection with dengue, Chikungunya, and Plasmodium. Cell 2009 Dec 24;139(7):1268–78.
40. Brownstein JS, Hett E, O'Neill SL. The potential of virulent Wolbachia to modulate disease transmission by insects. J Invertebr Pathol 2003 Sep;84(1):24–9.
41. Nolan T, Papathanos P, Windbichler N, et al. Developing transgenic Anopheles mosquitoes for the sterile insect technique. Genetica 2011 Jan;139(1):33–9.
42. Benedict MQ, Levine RS, Hawley WA, Lounibos LP. Spread of the tiger: global risk of invasion by the mosquito Aedes albopictus. Vector Borne Zoonotic Dis 2007 Spring;7(1):76–85.
43. Alphey L. Re-engineering the sterile insect technique. Insect Biochem Mol Biol 2002 Oct;32(10):1243–7.
44. Zabalou S, Apostolaki A, Livadaras I, et al. Incompatible insect technique: incompatible males from a Ceratitis capitata genetic sexing strain. Entomol Exp Appl 2009;132(3):232–40.
45. Bhatt S, Gething PW, Brady OJ, et al. The global distribution and burden of dengue. Nature 2013 Apr 25;496(7446):504–7.
46. Burt A. Heritable strategies for controlling insect vectors of disease. Philos Trans R Soc Lond B Biol Sci 2014 May 12;369(1645):20130432.
47. Sinkins SP. Wolbachia and arbovirus inhibition in mosquitoes. Future Microbiol 2013 Oct;8(10):1249–56.

48. Brelsfoard C, Tsiamis G, Falchetto M, et al. Presence of extensive Wolbachia symbiont insertions discovered in the genome of its host Glossina morsitans morsitans. PLoS Negl Trop Dis 2014 Apr 24;8(4):e2728.
49. Walker T, Johnson PH, Moreira LA, The wMel Wolbachia strain blocks dengue and invades caged Aedes aegypti populations. Nature 2011 Aug 24;476(7361):450–3.
50. Teixeira L, Ferreira A, Ashburner M. The bacterial symbiont Wolbachia induces resistance to RNA viral infections in Drosophila melanogaster. PLoS Biol 2008 Dec 23;6(12):e2.
51. Helinski ME, Parker AG, Knols BG. Radiation biology of mosquitoes. Malar J 2009 Nov 16;8 Suppl 2:S6.
52. Kambris Z, Cook PE, Phuc HK, Sinkins SP. Immune activation by life-shortening Wolbachia and reduced filarial competence in mosquitoes. Science 2009 Oct 2;326(5949):134–6.
53. McGraw EA, Merritt DJ, Droller JN, O'Neill SL. Wolbachia-mediated sperm modification is dependent on the host genotype in Drosophila. Proc Biol Sci 2001 Dec 22;268(1485):2565–70.
54. Schraiber JG, Kaczmarczyk AN, Kwok R, et al. Constraints on the use of lifespan-shortening Wolbachia to control dengue fever. J Theor Biol 2012 Mar 21;297:26–32.
55. Webster DP, Farrar J, Rowland-Jones S. Progress towards a dengue vaccine. Lancet Infect Dis 2009 Nov;9(11):678–87.

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