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Chapter 7

Vector Control in Chikungunya and Other Arboviruses

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Additional information is available at the end of the chapter

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Abstract

Mosquito vectors are solely responsible for transmitting diseases, such as malaria, yellow fever, chikungunya, dengue, Japanese encephalitis, lymphatic filariasis and zika virus. Mosquito borne diseases are a leading killer of people and animals in developing countries. The resurgence of diseases and the economic impact caused has brought mosquito control to the forefront. There are 3 mosquitos' genera which are vectors of these diseases, viz. Anopheles, Aedes and Culex, among these the day biting mosquito *Ae. aegypti* and *Ae. albopictus* has become important vectors to two important disease namely Dengue and Zika virus. These diseases have alone been responsible for bringing about morbidity in the large population around the world. *Cx. quinquefasciatus* is a vector of Chikungunya, which is a viral affection. It's widely spared distribution across various countries. Malaria caused by *An. stephensi* and *An. arabiensis* still affects large population in developing world. For control of emerging and reemerging mosquito borne diseases, a sound integrated approach towards comprehensive control is the need of hour which could produce sustained effect. The reemergence of mosquito borne diseases like Zika, DHF and CHIKV coupled with the problem of insecticide resistance has both posed a danger as well as a challenge towards mosquito control. In future novel technologies especially Wolbachia based mosquito control, pesticide nanoemulsions, identification of novel bioactive molecules, and novel bacterial pathogens are the key to success of vector control.

Keywords: Mosquito vector, Zika, Wolbachia, Chikungunya, Biological control

1. Introduction

Vector-borne diseases are medically and economically important to the well being of humans and domesticated animals. In the past these diseases were considered to affect the humans living in tropical environment, but today with these diseases have a cosmopolitan distribution virtually encompassing the entire continent including temperate countries [1]. Vector borne diseases have a major impact on the economic well being of human population. A recent WHO

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report estimates the economic loss due to vector borne diseases worldwide is to the tune of more than 2.5 billion people in over 100 countries are at risk of contracting dengue alone [30].

There are several parasites transmitted by mosquitoes and other insects. The most common transmitters being mosquitoes, which are vectors of several diseases like malaria, zika, dengue, filariasis, chikungunya, Japanese encephalitis, and yellow fever. Three mosquito genera, viz. Anopheles, Aedes and Culex are primarily the vectors which transmit these diseases. Among these diseases Chikungunya is an arthropod-borne virus transmitted mainly by *Aedes* species mosquitoes. Only the female are infective since they need blood meals for egg formation. Chikungunya virus (CHIKV) is an alphavirus from the *Togaviridae* family, which is transmitted by Aedes mosquitoes, and causes epidemic tropical and subtropical countries [28].

CHIKV is a positive-sense, single-stranded RNA virus of about 11.8 kb. There are three main genotypes, West African, Central/East African (C/EA), and Asian, the names reflecting the initial geo-graphic restriction of each type. Since CHIKV was first isolated in Tanzania in 1952 [23], the disease was mainly confined to localized outbreaks in Asia and Africa, sometimes with hundreds of thousands of cases [6]. In 2005, a C/EA strain of CHIKV, which likely originated in coastal Kenya, spread to islands of the Indian Ocean and India [19]. Since then, CHIKV spread worldwide to cause large out breaks in Southeast and East Asia, as well as many imported cases in travelers returning to non-endemic regions in Europe and North America. This global epidemic affecting millions was unprecedented in its scale and was likely driven by several factors. These include the increased volume of travellers, the widening geographic distribution of the mosquito vectors and the adaptation of the epidemic strain to *Aedes albopictus* [26]. The susceptibility of mosquitoes in non-endemic regions such as Australia [27] and North America [21], and the occurrence of autochthonous outbreaks in Italy [22] and France [10], have shown that CHIKV can no longer be considered as a problem of tropical countries. A recent work has also pointed that CHIKV may be present in severe forms, particularly neurological, which may be fatal [15]. It is also increasingly recognized that there is a significant burden of long-term morbidity due to chronic arthralgia [25]. Chikungunya is currently considered as a real threat in these European and American countries, which are colonized by *Aedes* species mosquitoes [2].

There has been little progress in finding cure for the disease. Chikungunya fever is currently symptomatically treated with antipyretics and non-steroidal anti-inflammatory drugs. There will be a continued search for new antiviral candidates with a clearly defined mechanism of viral inhibition in cell-based systems and significant activity in animal models. Considering the global threat this disease poses the immediate disease control measures solely lies in controlling mosquito population.

Dick, Kitchen and Haddow (1952) reported the first isolations of Zika virus from the blood of a sentinel rhesus monkey and from a pool of *Aedes africanus* mosquitoes in Zika forest, Uganda. Virus surveillance elsewhere has yielded more Zika virus isolations from other species of mosquitoes (Lee, 1969). Zika virus (ZIKV), a little known arbovirus, has gained prominence when it caused a large scale epidemic in the Pacific Island in 2007 [9]. It is a member of the genus *Flavivirus* of the Family Flaviviridae. The virus is a positive single stranded RNA virus with a 10,794 nucleotide genome that is closely related to the Spondweni virus [7]. It was first

isolated from a febrile sentinel monkey in Uganda in 1947, but human ZIKV infection was first reported in 1964. The virus causes dengue-like syndromes such as rash, fever, arthralgia, headache and periorbital pain [24].

Zika is a tropical disease transmitted by day biting mosquito *Aedes aegypti* and like CHIKV was a largely neglected disease, until its high epidemic potential was demonstrated in pacific island of YAP in 2007 [9]. Currently this virus has made its presence in Central and South American countries in 2015 and in Feburary 2016 WHO declared Zika infections as public health emergency [32]. Like many vector-borne diseases, the absence of vaccines and specific treatment against ZIKV means prevention and control relies heavily on vector control measure which is needed in order to develop and implement sound mosquito control program.

2. Integrated vector control

Vector control remains the primary defense against diseases like malaria, dengue fever, Chikungunya, zika viral infections etc. The success of vector control relies on the assumption that vector density is related to disease transmission. Vector control and disease prevention strategies are essentially divided into larval and adult mosquito control

1. Removal of stagnant water/ Treatment with biocide oils to prevent egg

   The best method of mosquito is preventing the development of the eggs into adult mosquitoes, by reducing the source of breeding.

2. Insectides-Treated Bed Nets (ITNs)

   The insecticides that are used for treating bed nets kill mosquitoes, as well as other insects. Only pyrethriods insecticides are approved for use on ITNs, these insecticides have been shown to pose very low health risk to humans and other mammals.

3. Personal production creams/sprays

   These type insecticides used as repellent for some human personal production creams for control of mosquitoes against biting.

4. Biological control

   Potential biological control agents such as fungi, *Bacillus thuringiensis*, nematodes, parasites and kill larval mosquitoes, but they are not efficient for mosquito control and are not widely used, likewise mosquito fish have largely been in effective except few studies.

Mosquito control strategies for *Aedes aegypti*, requires special attention as it has ability to breed in polluted water in addition to fresh water. Further this mosquito bites during day as well as night. *Ae. aegypti* and *Ae. albopictus* also called as tiger mosquitoes are highly dangerous in their spectral capacity of spreading dengue fever, DHF, zika and to a certain extent chikungunya diseases among people across the world. These mosquitoes have adapted themselves to be closely associated with human habitation. These mosquitoes breed in polluted as well as

freshwater. They can bite at day as well as night. Their breeding sites, including overhead tanks, water in ditches, unused tyres, container harboring water, and polluted sewage water.

The control of Aedes mosquitoes can be done by removing/cleaning waste water, emptying unused water, keeping neighbor's wood are free of open source water bodies and treatment of open water bodies with chemical/biolarvicides, various personal protection steps can be undertaken like use of skin ointment/repellent, covering your bodies with cloth during day time, use of ITNs bed nets during sleeping, households, mosquito coils and other smoke repellents can reduce biting efficacy, similarly windows, household treatment etc., reduce infection

In several countries public awareness programme are conducted by different government agencies involved in mosquito control. In addition, children in schools can be educated about the ways of controlling breeding of mosquito. These community based programme can be successful in large scale eradiation of mosquito breeding sites.

Natural biological control of mosquitoes essentially targets the larval stages. Several predatory insects nymphs like of dragonflies are like Toxorhynchites each larvae and pupa. In addition like *G. affinis, G. holbrooki*, *Guppy*, and molly, found in normal/natural stress fishes, lakes are efficient in mosquito control. These are known to be very important organisms in paddy ecosystem and other water intensive crops. In addition other non-specific predators like tadpoles and other aquatic predations can help in biological control of mosquitoes.

Chemical pesticides are used by state and local government agencies to control of public health nuisance/pests dangerous to human health. Chemical pesticides are used as a last resort, to do source reduction of mosquitoes populations or when biological control flexible biological control is not feasible, may require larvicidal treatment to prevent the emergence of adult mosquitoes [20]. Use of larvicides is less controversial than use of adulticides, although use of larvicides may lead to public concern about their effects on untargeted beneficial aquatic arthropods and vertebrates.

Effective adult mosquito control with insecticides requires small droplets that drift through areas where mosquitoes are flying. The droplets that impinge on mosquitoes provide the contact activity necessary to kill them. Adulticide applications, particularly aerial applications and thermal fogging, are quite visible and contribute to public apprehension. Ground Ultra Low Volume (ULV) application may be less alarming than aerial application but is not effective over large or inaccessible areas. This technology is being developed and needs validation under different conditions with different mosquito species before it can be universally used.

Several chemical insecticides have been used in mosquito control, primary they fall into 3 broad categories viz. carbamates, organophosphate and synthetic pyrethriods, those chemical insecticides are the most powerful tool available for control of mosquito. They are highly effective for vector control and a reliable alternative for emergency action when insect pest populations exceed the economic threshold [17]. Despite the hazards of conventional insecticides, some use is unavoidable. However, careful chemical choice and application can reduce ecological damage. An array of chemicals has been developed for the killing purpose of insects. These enter the insect body either by penetrating the cuticles or dermal entry, by inhalation into the tracheal system, or by oral ingestion into the digestive system.

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Chemical insecticide may be synthetic or natural products. Natural plant derived products, usually called botanical insecticides, include: alkaloids, including nicotine from tobacco, rotenone and other rotenoids from roots of legumes, pyrethroids from flowers of *Tanacetum cinerariifolium*, neem extracts from *Azadirachta indica*. The other major classes of insecticide are synthetic carbamates (carbaryl, aldicarb, methiocarb, methomyl etc), organophosphates (e.g. chlorpyrifos, dichlorvos, malathion, dimethoate and phorate) and organochlorine (aldrin, DDT, dieldrin and endosulfan etc.). Organochlorine are stable chemicals and persistent in the environment, have a low solubility in water and moderate solubility in organic solvents and accumulate in mammalian fat body. The use of this chemical is banned in many countries and they are unsuitable for use in Integrated Pest Management (IPM). Organophosphate are being less environmentally damaging and non-persistent, are suitable for IPM [11]. Most synthetic insecticides are broad spectrum in action and act on insect nervous system. Owing to its high insecticidal activity, low mammalian toxicity and high photostability pyrethroid insecticides are considered as most successful chemical classes of insecticide [4].

Today, world economy is integrated, which has led to transnational flow of goods, people, knowledge, as well as flow of pests, pathogens and vectors across geographical range where natural control is not available. Such kind of emerging infection diseases have become resurgent like zika viral infection in South America and North America, Ebola in Africa and Dengue, in India. What we thought as diseases we controlled are given becoming a threat to people across the world today.

3. *Wolbachia* in the vector control

A new approach to dengue control has recently been proposed that targets mosquito longevity rather than abundance, through the introduction of a life-shortening strain of the bacterium *Wolbachia pipientis* into *Ae. aegypti* populations [5]. α- proteobacteria is best endosymbiotic bacteria species present in insects and nematodes [13]. They infect diverse several arthropods, this is known to affect reproduction and produce nutrients, provide production against pathogens [12, 14]. Wolbachia is an intracellular inherited bacterium, predicted to naturally infect more than 60% of all insect species worldwide [13] that is able to invade host populations through either the induction of a number of reproductive parasitism traits [18] or by positively influencing host fitness [3].

Wolbachia is cytoplasmically inherited, so, infected females usually give rise to females. CI occurs when infected male mates with normal female. In reserve case the offspring are female multiple wolbachia stains may be present in one insect.

Wolbachia is known reproduce parasite when produces cytoplasmic incompatibility, sex ratio distorters, parthenogenesis [29]. They can also enhance reproduce fitness [8]. Mosquito control CI incompatible mates, in *Ae. aegypti* which in naturally uninfected with wolbachia. Wolbachia infected cell lines developed by embryonic microinjection [16], cathartic produces based vector control strategy have been tested in several regions of the world. The release of Wolbachia infected males is an approach that may suppress/reduce natural mosquito population.

4. Future perspective

Vector control strategy essentially needs to encompass 4 broad strategies 1. Spreading and effective way to contain diseases outbreak. 2. Adult mosquito repellant 3. Larval control in aquatic systems 4. Personal protection gear and tools.

Environmental management is a community based approach to eradicate mosquito breeding sites in their locality. To a large extent this exercise can reduce the mosquito population and is rather an effective strategy in urban and sub-urban areas. This approach has its limitations in villages due to the presence of large open water bodies for irrigation and irrigation systems, also environment such as paddy agroecosystem is a rich reservoir of water and is an ideal breeding ground for mosquitoes natural control by entomophagous predators and predatory fishes contain mosquito population to a large extent.

Adult mosquito management using mosquito repellants, in the form of mosquito coils, mats and liquid vaporizers are still in existence; however these are not a permanent solution to adult mosquitoes as they quickly develop resistance to these insecticides in few years. Use of entomopathogenic nematodes, fungus for adult control has limited success. However a new method/ approach of recombinant genetic transformation of Wolbachia in *Aedes* and *Anopheles* genera has been shown to be a promising method for disrupting mosquito –viral interaction thus can be a substantially reduce the disease progression. Personal protection creams like DEET, and other herbal products are still the better choice for person safety, ITNs have been very successful in the control of *Culex* and *Anopheles* borne diseases, however this is rather ineffective against day biting behavior of *Aedes* genera. Sterile male insect technique has met with only limited success and transgenic mosquitoes carrying dominant lethal genes is another method which is still in its infancy. Research needs to address the dynamics of inheritance of these lethal genes and it should also address the sexual selection of transgenic mosquitos' males to others in order to fully analyse its potential in mosquito control. The recent reemergence of mosquito borne diseases like Zika, DHF and CHIKV coupled with the problem of insecticide resistance has both posed a danger as well as a challenge towards mosquito control. In future novel technologies especially Wolbachia based mosquito control, nano emulsions, identification of novel bioactive molecules, and novel bacterial pathogens are the key to success of vector control.

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