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Dengue Vector Control in Malaysia: A Review for Current and Alternative Strategies

(Kawalan Vektor Denggi di Malaysia: Semakan Kajian Semasa dan Strategi Alternatif)

SONG-QUAN ONG*

ABSTRACT

Dengue is a major issue in Malaysia as the dramatic emerge of infection. Yet an effective vaccine or medicine is not yet available, although many attempts are undergoing. Dengue vector control is still considered the most effective way for controlling and preventing the transmission of dengue virus. Nonetheless, as the conventional approaches are less successful in managing the dengue transmission, it is time to review the current applied and other available approaches. Current dengue vector relied greatly on the chemical approach as space treatment either thermal or ULV fogging, however, the approach seem like under the expectation. Beside space treatment, new control methods for example biological control (bacterium Bacillus thuringiensis, *predatory mosquito* Toxorhynchites*) and attractive trap were carried out at certain location of Malaysia. Moreover, new emerged approaches such as mass release of genetic modification or artificially* Wolbachia *infected male dengue vector for the objective of generating sterile offspring when mate with wild population is urge to be tested in Malaysia, although concerns have to be taken before the actual mass release. In conclusion, control of dengue vector shall not consist exclusively for a single approach, neither genetic modification of artificially* Wolbachia *infected technique, nor the conventional insecticidal treatment. It should, however, comprise of the environment management as the fundamental approach, a well-planned integrated control program and a good cooperation among the organization.*

Keywords: Aedes; dengue control; dengue vector; Malaysia; strategies

ABSTRAK

Denggi merupakan isu yang penting di Malaysia disebabkan oleh kemunculan jangkitan yang dramatik. Namun, vaksin atau perubatan yang berkesan masih belum diperoleh walaupun banyak cubaan sedang dijalankan. Kawalan vektor denggi masih dianggap sebagai cara yang paling berkesan untuk mengawal dan mencegah penyebaran virus denggi. Namun begitu, cara kawalan konvensional kurang berjaya dalam pencegahan denggi; ia merupakan masa untuk mengkaji kaedah sedia ada dan cara lain yang berpotensi. Kini, kawalan vektor denggi sangat bergantung kepada kawalan kimia iaitu rawatan ruang sama ada terma atau ULV fogging, walau bagaimanapun, kaedah ini adalah di bawah jangkaan. Selain rawatan ruang, kaedah kawalan seperti kawalan biologi (bakteria Bacillus thuringiensis, *nyamuk pemangsa* Toxorhynchites*) dan perangkap telah dijalankan di lokasi tertentu di Malaysia. Selain itu, kaedah baru yang muncul seperti pelepasan populasi pengubahsuaian genetik ataupun infeksi* Wolbachia *pada vektor denggi jantan dengan objektif untuk menghasilkan anak yang disteril apabila disenyawakan dengan populasi liar telah dicadangkan di Malaysia, walaupun pengawasan perlu diberi perhatian sebelum pelepasan yang sebenar. Kesimpulannya, kawalan vektor denggi tidak hanya terdiri daripada pendekatan tunggal atau teknik modifikasi genetik infeksi buatan* Wolbachia, *ataupun rawatan racun serangga konvensional. Ia sepatutnya terdiri daripada pengurusan alam sekitar untuk vektor denggi sebagai kaedah asas, program kawalan yang pelbagai dan dirancang dengan baik serta kerjasama yang baik antara organisasi.*

Kata kunci: Aedes; kawalan denggi; Malaysia; strategi; vektor denggi

INTRODUCTION

Dengue fever (DF) and dengue hemorrhagic fever (DHF) are always a major health concern in Malaysia. The incidences have a dramatic increase in recent years, from 2012 to 2013 (21900 to 43346 cases) and until 16 weeks of the year 2015, there were more than 32000 cases have been reported (CPRC 2015), almost three folds compared to the year 2014.

The infection of dengue is due to the dengue virus, which consists of 5 serotypes (DENV-1 to 5) with the filth serotype, DENV-5 was newly identified and announced in 2013 (Normile 2013). Among these serotypes, four of the serotypes virus (DENV-1 to 4) could be isolated from the infected people in Malaysia at any time; this indicates hyper-endemic of dengue epidemic in the country (Cheah et al. 2014). At present, there is yet a specific antiviral drugs for dengue treatment (Simmons et al. 2012), although dengue vaccine development is underway, but the vaccine introduction is complicated (WHO 2000) due to several concerns such as the high risk of severe disease through antibody-dependent enhancement (Webster et al. 2009) and the threats of the new serotype, DENV-5 (Normile 2013). Consequently, control on the two well urban-adapted vector mosquitoes, the primary vector, *Aedes aegypti* and the secondary vector, *Aedes albopictus* still play the main role to reduce or prevent the viral transmission. Both mosquitoes are an effective viral vector due to their preferences to breed on artificial and household container, which existed abundantly in the urbanized community area. Nonetheless, the rapid rise of dengue cases has generated considerable attention on the effectiveness of the control strategies in Malaysia. Thus, this review was aimed to provide overview information of vector control approaches for the public health and vector control practitioners in combating the vector in order to manage the dengue fever in Malaysia.

FACTORS ASSOCIATED TO THE EMERGING EPIDEMIC IN MALAYSIA

The dengue cases have increased globally and the reasons for the sudden emergence of the vector-borne disease might be complicated, but several factors such as population growth, urbanization, global warming and globalization were attributed to an epidemiological condition that favors viral transmission by both the mosquito vector, *Ae. aegypti* and *Ae. albopictus* (Gubler 2011; Kumarasamy 2006; Natasha et al. 2013; Patz & Reisen 2001; Reiter 2011; Wilder & Gubler 2008).

Among these factors, global warming and urbanization might be the key factors for the striking increase of dengue cases in Malaysia. Global warming or climate changes alter much of insect life cycles and temperature is known to affect the *Aedes* life cycles the most, as demonstrated by Mohammed and Chadee (2011), who reared the *Ae. aegypti* at higher temperature (34-35ºC) showed significant greater pupation than lower temperature (24-25ºC). Additionally, increase in temperature may result in higher survival and migration of vectors into previously non-endemic geographic areas (Hales et al. 2002). Banu et al. (2011) observed that temperature increases over the last four decades corresponded with the increased risk of dengue outbreaks in the Southwest Pacific region. Some studies in Singapore have also showed a strong association of climate change with the increase in dengue transmission due to higher temperatures, humidity and precipitation associated with changes in climate (Hii et al. 2009).

Climate change may not be the only factor that caused sudden rise of dengue cases in Malaysia, the rapid urbanization could contribute to the rise as well. Urbanization in Malaysia has resulted in a great increase of human population density and vector breeding sites in the urban area. The factor for the great urbanization may due to the population growth and the settlement of the people (local from rural to urban area and foreigner). As suggested by Gubler (2011), urbanization and globalization have contributed greatly in the global dengue transmission and geographical expansion. The most significant influence for urbanization could be the increase of breeding habitats for the vector mosquitoes. The vector, *Ae. aegypti* exhibited good breeding behavior on artificial container such as plastic container, flower pots, septic tank, basin, jar, roof gutter, refrigerator water collector tray and some rare location like gap spaces present on the plastic paint container and toilet flushing tank (Abu Hassan 2014), this explained how well the adaptation is of the mosquito to the human living. Additionally, population growth increases the housing construction site and lots of places at the site might consist of neglected rain water accumulation, these provided good breeding environment for both *Ae. aegypti* and *Ae. albopictus*. This was supported by the study of Abu Hassan (2005), which *Aedes* larval survey has been conducted on several potential breeding sites in Penang, Malaysia and construction site consists of significantly great larval density.

CURRENT VECTOR CONTROL

Strategy for dengue prevention and control in Malaysia were focused on five elements listed in Table 1 (Guzman 2010; WHO 2006; Zahari 2001) and currently in Malaysia, there was no alternative but vector control in order to reduce or prevent the dengue virus transmission (Kumarasamy 2006; WHO 2000).

Both larva and adult of mosquitoes are control under the vector control program of Malaysia. For larva control, the strategies that have been conducted were environment management, source reduction, use of larvicides such as temephos (Abate), house inspection and enforcement of Destruction of Disease-Bearing Insect Act 1975; while for adult control, fogging will be carried out based on the

TABLE 1. The strategies for dengue prevention and control in Malaysia as recommended by WHO (2006)

1. Vector control, based on the principles of integrated vector management
2. Active disease surveillance based on a comprehensive health information system
3. Emergency preparedness
4. Capacity building and training
5. Vector control research

viral cases reported (Kumarasamy 2006; Tham 2000). All the fogging activities were employed by the trained practitioners of Ministry of Health, Ministry of House and the local government.

HOUSE INSPECTION

House and premise inspection was carried out mainly for surveillance of *Aedes* potential breeding site, to inspect the owner for a regular clean up to reduce the breeding site for the mosquito (Tham 2000). However, as mentioned by Guzman (2010) and Tham (2000), the delivery and the coverage for many issue encountered houses were ineffective or insufficient. The poor coverage and ineffective inspection might be because of the problem of man-power and the ability of the mosquitoes to breed in small and hidden area. The insufficient man-power should be resolved by the support of the community, especially the owner of the premises. Nevertheless, Destruction of Disease-Bearing Insect Act 1975 is enforced to the owner of the premise when *Aedes* larva was found within their premises.

INSECTICIDAL TREATMENT

Larvicidal treatment consist of temephos (Abate) the most, this was due to its low toxicity to human; it was even applied in the drinking water. Larviciding is largely depended on the community themselves. Unfortunately, most household did not apply the larvicides regularly (Lee 2005) and lead to incorrect of dosage. The majority adulticidal treatment is space treatment, either thermal or ULV fogging. Fogging was mainly conducted by the trained health practitioners after the viral cases have been reported. In Malaysia, the insecticides that applied in fogging consist of numerous formulation and active ingredients; some of the common applied products are detailed in Table 2.

Malaysia dengue vector control program relied heavily on these chemical controls and therefore challenges were often raised when the dengue cases fail to manage. The imperfection of the chemical control approaches might be due to several factors; generally they were the technical problem of the fogger (for example droplet size), treatment timing, circumference factors (for example wind direction) and insecticide effectiveness/resistance.

HEALTH PUBLIC EDUCATION

Beside the vector control, health education has been conducted by the Malaysia government in order to gain support and cooperation for the vector control. The education composed of advertisements on media (television, radio, press, poster & leaflet), campaign and seminar talk.

THE PUBLICITY

In the country, there were lots of advertisements and campaigns related to dengue. The contents include basic understanding about the diseases, the ways for prevention and some syndromes for the infection. Nevertheless, the impact of the advertisement and campaigns is still unclear and hard to be measured even though lots of affords have put on this approach for educating the public. One of the challenges that was faced by the advertisement and campaign was be the ignorance of public to the disease, therefore, alternatives such as more creative advertisement that raised out sympathetic response have to be investigate, plus, other publicity like 'No Dengue Competitions' may be introduced among the area to encourage the involvement of the public in combating the diseases. Although awareness from the public was crucial in managing the dengue, nonetheless, methods for vector control were the focused in this review.

ALTERNATIVES VECTOR CONTROL IN MALAYSIA

There are some alternatives to vector control in Malaysia, they were either freshly tested in field stages or already applied in certain locations of Malaysia. These methods are presented in Table 3.

BACILLUS THURINGIENSIS H-14

Microbial is always a crucial tool in the biological control of dengue vector. Both *Ae. aegypti* and *Ae. albopictus* are highly susceptible to the microbes *Bacillus thuringiensis* H-14 in Malaysia (Lee 2005). The aerobic, gram positive, endospore- and crystal-forming bacterium that belong to Bacillaceae family were infecting the mosquito larvae. When bacteria were ingested by mosquito larvae,

TABLE 2. Selected insecticides products that applied as space treatment in Malaysia

Product name	Active ingredient(s)
Malathion	Malathion
Sumithion	Fenitrothion
Bayetex	Fenthion
Resigen	s-bioallethrin + permethrin + piperonyl butoxide
Pesguard	d-tetramethrin+ cyphenothrin
Gokilat	Cyphenothrin
Actellic	Primiphos-methyl
Abate	Temephos

TABLE 3. Alternatives vector control in Malaysia

	Places	Organization
Bacillus thuringiensis H-14	Klang (Lee et al. 1997)	Institute of Medical Research (IMR)
Toxorhynchites mosquito	Subang Jaya (Teoh 2014)	Subang Jaya Municipal Council (MPSJ)
Attractant trap	Penang Island (Tan 2014)	City Council of Penang Island
Genetic modified (GM) mosquito	Pahang (third phase field-trial, Lee & Nazni 2012)	IMU, Oxitec®

the crystals were activated in the naturally alkaline environment of the larval mid-gut. This cause the proteolytic enzymes that existed in the mid-gut of larval to break down the endotoxin of the crystallized bacteria, as the result, a polypeptide toxin fraction was released by the bacteria and triggers the killing mechanism (Lee 2005). The polypeptide fraction reacted with the cell of the mid-gut and causing swollen, lysis and slough into the lumen of the gut consequently, causing death to the infected larvae (WHO 1997).

Numerous experiments have established the efficacy and persistency of *B. thuringiensis* H-14 for the control of *Ae. aegyptii*. Foo and Yap (1982) showed that efficacy of *B. thuringiensis* H-14 for used against 4 species of mosquitoes in Malaysia; it was found that the bacterium was highly effective in controlling *Ae. aegypti*. Additionally, Lee et al. (1986) demonstrated the great persistency of *B. thuringiensis* H-14 was not affected for up to 2 months even though the bacteria contained water was removed. Additionally, a comparison testing among other insecticide formulation (pirimiphos–methyl, s-bioallethrin, permethrin+piperonyl butoxide, s-bioallethrin+permethrin+piperonyl butoxide and alphacypermethrin) to a commercial product of *B. thuringiensis* H-14 (Vectobac) has showed that 95-100% mortality was achieved to the *Aedes* larval after 7 days of fogging. In controlling of *Ae. albopictus*, a semi-field trial was conducted by Lee and Cheong (1987) for evaluating 2 formulations of *B. thuringiensis* H-14, a dosage of 1and 2 mg/L were found to prevent the mosquito from breeding for 5 and 6 weeks, respectively.

In Malaysia, *B. thuringiensis* H-14 often applied simultaneously as adulticide and larvicide (Lee 2005; Yap et al. 2002). As the bacterium is available in commercial product such as Vectabac and Mosbac®, therefore the biological agent is able to integrate with other commercial chemical formulation for example malathion in ULV formulation in the *Aedes* control program of Malaysia (Seleena et al. 1996). The control for both adult and larval stages of *Ae. aegypti* also reported by Yap et al. (2002), which the ULV fogging of a mixture of *B. thuringiensis* H-14 and Aqua Resigen and Pesguard PS102 was highly effective in controlling larva and adult *Aedes* mosquito. Nevertheless, trials that have been conducted in Klang area showed that various ratio of the mixture of chemical and *B. thuringiensis* H-14 has to take consideration when applied in ULV machines (Lee et al. 1997). Moreover, in a study of mixture of *B. thuringiensis* H-14 with different formulation of insecticides, malathion, primiphos-methyl 50EC and Aqua-Resigen has found that *B. thuringiensis* H-14 was most compatible to the malathion in terms of the persistency to larva of *Aedes* (Seleena et al. 1999).

However, Ali et al. (1995) have demonstrated that *Ae. albopictus* is capable of developing resistance to *B. thuringiensis* H-14 and this indicate the application of *B. thuringiensis* H-14 might not be sustainable for a long-term control program because of its potential in developing resistance. Furthermore to the problem of resistance, it was found that although *B. thuringiensis* H-14 has great persistency against both *Ae. aegypti* and *Ae. albopictus,* the toxic proteins were weak and insufficient to form residues to kill the mosquitoes (Orduz et al. 1995). Thereafter, other attempts such as discovering other strain of the bacteria or extracting the toxin were on the way to overcome the defects.

TOXORHYNCHITES MOSQUITO

Traditional insecticides have been reported ineffective against the dengue vector in Malaysia (Lee 2003). The ineffectiveness might be due to the resistance of both *Ae. aegypti* and *Ae. albopictus* to the conventional applied insecticides. The resistance of malathion, permethrin and temephos have been reported by Lee (2003) as these insecticides were often used in the dengue vector control program. Moreover, depending on the application method and climatic factors, only 10% of conventionally applied insecticides may reach their target in sufficient time and quantities (Kenawy 1998). Therefore, other approaches including the way to reach the target of vector were urged for reviewed.

One of the alternatives to the traditional used insecticides and application (thermal and ULV fogging) is using the predator of *Aedes* mosquito, *Toxorhynchites* sp. mosquito. In Malaysia, *Toxorhynchites* sp. was found to be present in the natural breeding site of *Ae. aegypti* and *Ae. albopictus* (Nyamah et al. 2011). The predator was ideal as a biological control for the dengue vector due to its natural ability in seeking the breeding site of the vector, which were difficult for trace artificially (Collins & Blackwell 2000). Additionally, the female *Toxorhynchites* sp. do not blood feed and therefore not suitable to act as a vector of disease.

In fact, Subang Jaya Municipal Council (MPSJ), Malaysia has attempted the release of *Toxorhynchites spin* into the area since 2010. The result was promising as the dengue cases and the hotspot area of the Subang Jaya has reduced significantly (Teoh 2014).

Nonetheless, some disadvantages of *Toxorhynchites* sp. would be its complexity of life cycle and feeding behavior, in which the oviposition of the predatory mosquito is often affected by the abiotic factor such as type of container (Mohamad and Zuharah 2014), and also the semiochemicals, particularly pheromones that existed specifically in dosage at the breeding site of *Aedes* mosquito. The performance of *Toxorhynchites* sp. is not consistent as the mosquitoes do not all oviposit into *Ae. aegypti* infested containers in urban environments (Collins & Blackwell 2000; Rawlins et al. 1991). Moreover, the levels of control would be affected by introducing different stages of *Toxorhynchites* sp. (Collins & Blackwell 2000; Gerberg & Visser 1978; Jones 1993), which larvae introduction was more effective than adult stage of *Toxorhynchites* sp. Although the application of *Toxorhynchites* sp. as biological control to the dengue vector was not capable to many occasion, nevertheless, the predatory mosquitoes was believed to provide a long-term control when large enough population had been established (Focks 1982). In addition, *Toxorhynchites* sp. also not capable to integrate with other conventional control method such as inseciticidal treatment as the insecticides will kill both predator and prey of mosquitoes (Collins & Blackwell 2000).

Attractant Trap

Most research of vector control in recent years has focused on sustainable control method. A sustainable control method should be compromised among 3E; environment, economic and effective. Attractant trap has attracted considerable attention as a tool for sustainable control for the dengue vector. Traditionally, the approach consists of an attractant to lure the mosquito and a killing component, either physical or chemical. In fact, attractant trap is considered rare in the mosquito control program in Malaysia although few attempts have demonstrated the attractiveness and effectiveness of ovitrap for *Ae. aegypti* (Nazni et al. 2009; Ong & Zairi 2015). The unfavorable consideration might due to the complexity of the attractant components, passive killing mechanism and took relatively long-time for a desired result.

Nonetheless, some area of Malaysia has proposed the application of attractant trap, for example City Council of Penang Island has proposed an application of a commercial attractant trap, Mosquito Magnet® (Tan 2014). In some other countries, the commercial product has proved attracted good number of *Ae. albopictus* in several researches which loaded with various of tested attractant such as dry ice, octanol and its originally propane converted to carbon dioxide (Hoel et al. 2009; Laban 2010; Qualls & Mullen 2007; Xue 2008), although the addition of octanol has found to significantly enhanced the performance of the trap (Xue 2008).

Nonetheless, some concerns have to be considered before the large scare introduction into the market. First is the target dengue vector been attracted was only *Ae. albopictus* (Laban 2010; Xue 2008), which is the secondary vector of dengue; however, the effect of the Mosquito Magnet® towards the primary vector, *Ae. aegypti* is still unclear. This was supported by the research of Xue (2008) that a field evaluation to the type of mosquito been attracted to the trap, it is found that significant higher number of *Ae. albopictus* were caught but relatively low number of *Ae. aegypti* was trapped.

The appropriateness of this attractant trap in an urbanized area especially a city area has to pay considerable attention. As most of the researches were conducted at the back yard and garden (Hoel et al. 2009; Qualls & Mullen 2007; Xue 2008), where the areas consist of less competitiveness between the human odor and the artificially generated semochemicals. Furthermore the relatively high cost of the product also required to compare with some other approaches as the trap is limited to control the adult mosquito but not including the immature stages.

Nevertheless, some of the attempts on both immature and adult stages of dengue vector were performed in Malaysia (Nazni et al. 2015; Ong et al. 2015; Zairi et al. 2015). Nazni et al. (2009) studied the oviposition behavior of *Ae. albopictus* for combining the temephos or Bti in ovitraps and both were effectively control the mosquito. Ong and Zairi (2015) extracted caproic acid from the eggs of *Ae. aegypti* and found that it was good candidate as an attractant in trap due to its significant attractive egg laying effect.

Although attractant trap such as ovitrap was originally developed as surveillance tool for dengue cases (WHO 1995), however as suggested by Zeichner and Peric (1999), attractant trap could also play an important role in an integrated control program for dengue vector and it might act as a surveillance tool to indicate the control threshold.

Other Potential Vector Control

Genetic Modified (GM) Mosquito

New proposed methods such as genetic modification of dengue vector control is greatly needed in dengue control program as continue outbreaks occurred in the country. Actually, genetically modified vector is not new in the pest control exercise as the attemps has proven effective in controlling some of the pest for example fruit fly and some Lepidoptera (Rose 2009). At the beginning of the invention, the technology for the genetic modification of vector used Sterile Insect Technique (SIT), which was radiation mediated sterilization towards the vector insect, then mass rearing and release of a large population of male insects for suppressing the wild population (Lee & Nazni 2012; Wilke & Marrelli 2012). Nevertheless, there were several concerns to the SIT especially on the random radiation mediated mutation on the male insect which may not bring any killing effect on the wild female insect (Wilke & Marrelli 2012).

In Malaysia, attempts on genetic modified (GM) mosquito was using the advance version of SIT, known as release of insects carrying a dominant lethal (RIDL), which work on similar operation but provides several improvements (Lee & Nazni 2012). The RIDL method consists of two different type of strategies in eliminating the dengue vector by spreading. For the first one, the males were microinjected and carrying a female-acting transgene that could result in disability of flight, which resulted as flightless strategy. Thereafter, when the GM males released and mate with wild type females, consequently the females offspring were flightless and unable to mate or seek for their host (Fu et al. 2010). On the other strategy, the GM males consist of a late-acting lethality transgene that could result in elimination of the offspring when the males were released in the open field and mate with the wild-type female (Phuc et al. 2007). In Malaysia, microinjection of late-acting lethality transgene was preferred in the investigation of GM *Ae. aegypti* program (Lee & Nazni 2012).

There were mainly two advantages of the RIDL method that make it suitable for community application; the GM mosquito is short-lived and the release of male's mosquito will not cause any nuisance biting (Elizabeth & Scott 2013). According to Lacroix et al. (2012), RIDL was the most advanced genetic modification technique to the implementation. In Malaysia, the technique was mostly tribute to the cooperation of Institution of Medical Research (IMR), UK-based biotech company-Oxitec® and Malaysian government. As the transgenic males of strain OX513A from Oxitec was released in a forested area in Pahang, Malaysia as the third phase trial (Lacroix et al. 2012), community waited for the publication of the studies that able to explain the ability of transgenic males in reducing the wild-type population.

In order to make a mass release to the community area of Malaysia, a clear guideline for regulatory of genetically modified *Ae. aegpyti* has been conducted by the IMR and Oxitec. These include 30-day public consultation process that involved newspaper advertisements, public forums and surveys (Elizabeth & Scott 2013). Nevertheless, beforehand of large population been introduced to the community of Malaysia, there are still several issues have to take into consideration.

The concerns of the effects of tetracycline to the killing mechanisms of RIDL method were always raised by other GM mosquito critics. This is because the RIDL method is based on a molecular technology that composed of a gene encoding the tetracycline transactivator (tTA) protein under the control of the tetracycline-responsive element (tRE). In a condition without tetracycline, tTA instead binds to tRE, thereby inducing a positive feedback loop that accumulates production of tTA, which is a toxin when accumulated (Gabrieli et al. 2014). Nevertheless, rearing the transgenic mosquito in the present of tetracycline in laboratory has found that the killing mechanism has been inhibited by the tetracycline (Susan 2008; Wise de Valdez et al. 2011), it was found that the antibiotic-tetracycline is commonly existed in our domestic meat-type such as chicken and pork and although less field trial has been conducted for further declaration, but the defeat has to take into consideration before mass release.

The transparency and accuracy of the research methods and data has also been questioned since the trials use data that was not published or reviewed (Reeves et al. 2012). These including the open-field release of GM mosquito on Grand Cayman, in the Cayman Islands, which bio-safety regulation is weak while in Malaysia, relied heavily on the unpublished experiment, such as semi-trial and predation toxicity experiment, which both stated to refer to release documents (NBBM 2010; Reeves et al. 2010). All those uncertainties have attracted controversy either locally or internationally.

Economic might be to the major issue when the genetic modification (GM) of mosquito proposed to the community. The cost for the synthesis of GM *Ae. aegypti* and the post-maintenance could burn a hole in taxpayers' pocket. The high cost for the strategy was mainly due to the large population of GM *Ae. aegypti* that has be generated and released, as the wild population is less fit to the GM *Ae. aegypti* (an estimation of 10:1 ratio of GM to wild type was needed to establish desired traits; Christophides et al. 2006). This phenomenon also demonstrated by Harris et al. (2011) in the field performance for the open-field releases of OX513A *Ae. aegypti* on Grand Cayman in which the study suggested that the released males showed reductions in mating competitiveness relative to wild males, but this can be solved by releasing greater numbers of GM *Ae. aegypti*. The release of the GM mosquito has to continue until certain positive result were obtained.

After all, the RIDL strategy was still known as the most advanced with respect to implementation, as the technology is currently being trialed by Oxitec in Brazil, India and Malaysia. The approach was claimed to be promising in long-term vector combats and of course, the scientific and public community is observing for further validated publication that demonstrated for proving its capacity in controlling the dengue vector.

BACTERIUM *WOLBACHIA PIPIENTIS*

Wolbachia pipientis has attracted great concerns for a number of years in the pest control. The *Wolbachia* is an endosymbiotic bacterium that can be found in up to 65% of all insects, some arachnids, crustaceans and filarial nematodes (Hilgenboecker et al. 2008). Hedges et al. (2008) and Teixeira et al. (2008) have first reported the success for using *Wolbachia* in control of vinegar flies, *Drosophila melanogaster*, which sex manipulation, parthenogenesis, male killing and sperm–egg incompatibility have been observed in the *Wolbachia*-infected arthropods.

The bacterium has numerous studies recently for its potential in the control of *Aedes* mosquito (McMeniman

& O'Neill 2010; McMeniman et al. 2009; Rances et al. 2012). In fact, the idea of releasing *Wolbachia*-infected mosquito was originally from Laven (1967) in a program for eradicates the population of *Culex pipiens* through cytoplasmic incompatability by releasing artificially *Wolbachia*-infected *Cx. pipiens*. Cytoplasmic incompatibility (CI) is a phenomenon where the embryo failed to develop at the early stages. The infection can be unidirectional and bidirectional. Unidirectional infection occurred when a *Wolbachia*-infected male mated with an uninfected female, then the action of CI occurred; in contrast, when two *Wolbachia*- infected adults mate, the egg of the infected female might rescues *Wolbachia*-mediated changes to the sperm and allows the offspring to develop normally (Scott 2014; Teixeira et al. 2008). These come to the idea of bidirectional infection, or called bidirectional incompatibility, which is a strategy that mating pairs of males and females that were infected with different *Wolbachia* strains (Scott 2014). At this time, the eggs from the female may not be able to rescue the *Wolbachia*-induced changes in the sperm of the male. The consequence is an incompatibility in the embryo such that few or no offspring survive, despite the fact that both parents carry *Wolbachia*.

The strategy of using *Wolbachia* in dengue control program was similar to the RIDL method with release of a large population of artificially infected-males mosquito. The males was infected by a lab strain *Wolbachia* bacterium using microinjection and allowed then released and mated with either uninfected females or infected females and trigger either unidirectional or bidirectional incompatibility, respectively.

Nonetheless, the concerns might be similar to the genetic modification of mosquito, which public consultancy and transparency of the research data is crucial if the method is proposed in Malaysia.

Conclusion

As suggested by WHO, no other alternative but dengue vector control in preventing the diseases by 2050. There is no any magic bullet for the dengue vector control, neither genetic modification/artificially *Wolbachia*-infected of dengue vector nor chemical approaches. This was suggested the management of environment should be the fundamental approach for other control methods as the breeding sites is available; the vector can manage to breed. The existed control approaches are considered effective as long as integrating multiples compatible strategies. Unfortunately, as the economic and politic obstacles fall, dengue vector control in Malaysia is considered slow-reacted. For economic problems, more funds should be provided to the research; moreover, small funding might be provided by the government for some school, communities and non-government organization to initiate some dengue prevention activities. On the other hand, although the assessment of data for controlling vector restricted by the Data Protection Act, however, health issue never should be influenced by the factor of political, as cooperative and data sharing shall be assessed by both government and opposition parties, for fighting the disease together.

Future strategies should consist of a fast reacted anti-dengue team, either under government or not, for designing the control program, tracking the dengue cases and communicate with the residents from the hot spot area. In addition, review and update to all the health practitioners should be carried out for renewing the knowledge of control. After all, the success in control the dengue's vector is near.

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Vector Control Research Unit
Universiti Sains Malaysia
11800 Pulau Pinang
Malaysia

KDU University College Penang
Jalan Anson, George Town
10400 George Town, Pulau Pinang
Malaysia

*Corresponding author; email: songguan26@gmail.com

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