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## Lessons learned from previous dengue outbreaks

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## PEER REVIEW

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## Comments

This is a review on important tropical infection. The reviewed issue is interesting and rarely available in the literature. This work can be referencing piece of work for general practitioner. The summarization and recommendation are interesting and suggested, and they support the concept that dengue is the disease should not to be neglected in the present day.

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## ABSTRACT

Dengue is an important tropical infection caused by an arbovirus dengue. As a mosquito borne infection, this disease is widely spread in several tropical endemic countries. Millions of world populations are at risk for this arboviral infection. Each year, thousands of dengue infections are reported and there are several death cases. Each year, the outbreaks of dengue emerge in several countries and this implies the global importance of this infection. Fighting with dengue outbreak is important in public health. In this specific chapter, the author discussed lessons learned from previous dengue outbreaks.

## KEYWORDS

Vector, Outbreak, Lesson

## 1. Introduction

Dengue infection is an important mosquito borne infection. An arbovirus, namely, dengue virus is the causative agent. This disease is highly endemic in several tropical countries especially for those in Southeast Asia and South Asia. Dengue infection is considered as an important blood infection. The infection starts from getting mosquito bite. The known mosquito vector is *Aedes* spp. The transmission of dengue virus into the bitten human occurs and this leads to further development of dengue. Pathophysiologically, dengue virus mainly attacks the blood system<sup>[1]</sup>. The infection causes major problem on blood platelets. The pathoimmunological process is described as the main cause of bleeding complication in

dengue<sup>[1]</sup>.

The main clinical presentations of this infection include acute febrile illness, thrombocytopenia and hemoconcentration<sup>[1]</sup>. Patients infected with dengue usually developed high fever that cannot be relieved by simple acetaminophen intake<sup>[1]</sup>. Patients can develop many hemorrhagic manifestations in the course of disease. Bleeding can be seen at several sites such as skin bleeding (petechiae), gastrointestinal bleeding, *etc.* The severity of dengue can be from simple acute febrile illness to severe shock (dengue shock syndrome)<sup>[1]</sup>. Clinically, dengue is considered as a viral disease that requires good supportive and symptomatic management<sup>[1]</sup>. The fluid replacement therapy corresponding to the hemorrhagic complication of dengue is the main therapeutic concept<sup>[1]</sup>.

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Following up of the hemodynamic fluctuation that is an important problem in dengue is required.

In each year, dengue infections occur in several countries around the world, not only tropical but also non-tropical countries. Due to the good transportation and globalization in present day, new emerging dengue in setting where it has never existed is reported. It is accepted that dengue is one of the most problematic mosquito borne infections. Dengue is one of the leading public health threats in the world.

It should be noted that there are several outbreaks of dengue in each year. The possible reasons for many outbreaks are: a) dengue is caused by virus, of which there is no specific antiviral drug; b) dengue virus can be simply carried by mosquito and the infective dosage required for human infection is low; c) dengue can be transmitted by mosquito vector, which is very hard to control; d) increased mosquito vector is presently existed due to the climate change; e) dengue virus can be well maintained in the tropical climate where the endemic area is; f) dengue is the disease existed in city where there are many people taking risk to get infection; g) dengue is highly endemic in developing countries where the poor live and there is no good sanitation system; h) diagnosis of infection can be easily overlooked and under-diagnosis of infective case can be cause of uncontrolled consecutive transmission; i) some dengue patients are not well treated and left within the community to increase the risk of disease spreading.

## 2. Mosquito vector, vector control and outbreak of dengue

As already mentioned, dengue is a mosquito borne infection. This means that the mosquito vector is required for transmission of disease[2]. Hence, it is important to describe the nature of vector and how to control the vector.

The important nature of mosquito vector of dengue, *Aedes* spp., includes: a) the vector is mosquito that has its habitat in city; b) the vector has high rate of breeding; c) the vector can maintain its life cycle in the left water reservoir within the house; d) the vector can well survive in the tropical climate; e) the vector resists to the insecticide; f) the vector bite at daytime[2].

Focusing on the described nature of dengue vector, the focus on vector control should be: a) how to avoid mosquito bite; b) how to cut the life cycle of mosquito vector; c) how to get rid of mosquito vector[1,2]. As a mosquito borne disease, it is very difficult to have a successful control. There are several common methods for vector control of dengue including use of bed net, insecticide, mosquito coil and repellent and abate sand[1,2]. However, these methods are usually unsuccessful and the result is persistent high infection rate in many developing countries. Outbreak of dengue is strongly related to the unsuccessful mosquito control. In addition to unsuccessful mosquito control, the other reasons that contribute to the unsuccessful reducing numbers of dengue outbreaks around the world include: a) dengue exists in poor developing countries with many low educated populations; b) the under-diagnosis, delayed-diagnosis and mis-

diagnosis (with other similar tropical infection that share common clinical presentations) exists; c) there is no dengue vaccine; d) there is no dengue chemoprophylaxis; e) there is no protective immunity to dengue after getting a dengue infection; f) there are many serotypes of dengue and many continuous mutations of dengue virus.

## 3. Dengue outbreak in world history: past to present

Dengue has been known for hundred years (it was first known at 1780's). Historically, there are many well-documented dengue outbreaks (Table 1)[3].

**Table 1**

Well-documented dengue outbreaks in world history.

Outbreaks	Brief details
China (Jin dynasty , 265–420 AD)	There was a record on an outbreak of disease that was related to mosquito and believed to be dengue.
Global pandemic (17's century)	There was a worldwide pandemic of a disease which was firstly named as dengue.
Greece (1927)	This was well-documented dengue in the Mediterranean. The dengue type 1 was believed to be the causative agent[4].
The Philippines (1953)	This was an outbreak of severe dengue infection with many death cases.

Interestingly, there are still many outbreaks of dengue at present despite many advances in medicine. Within the past year (2012–2013), there were many interesting reports of dengue outbreaks such as: a) Madani *et al.* reported the outbreak of dengue virus type 3 in Yemen[5]; b) Hassan *et al.* reported the outbreak of dengue in Pakistan[6]; c) Yang *et al.* reported the outbreak of dengue in China[7]; d) CDC reported the outbreak of dengue in U.S. Virgin islands[8]. The interesting observations on the dengue outbreak at present include: a) outbreak can be due to any type of dengue; b) new emerging outbreak in new setting; c) migration of disease to non-endemic non-tropical areas; d) use of new surveillance tool such as molecular diagnostic tool for outbreak survey.

## 4. Natural history of dengue outbreak

### 4.1. Mosquito vector breeding site: the starting point of dengue outbreak

There are many outbreaks of dengue in each year. An interesting concern is on the primary foci or starting points of those outbreaks. The breeding site of mosquito vectors are usually forgotten in dealing with dengue outbreak. According to a report from Brazil, the interrelationship between vector breeding sites and indices of infestation of buildings in adjacent areas was accessed[9]. Although there is no conclusion, concept on the relationship between breeding site and consequence of high infestation levels in nearby area is raised[9]. However, not only the site but also related meteorological parameters on vector breeding should be considered. In a report from Malaysia, rainfall,

temperature and humidity were proved related to breeding of mosquito vectors<sup>[10]</sup>. Those meteorological parameters were also proved to be useful for setting a predictive model for forecasting possible outbreak<sup>[10]</sup>. Egg and larva survey along with the meteorological parameters monitoring could be a good preventive method for dengue outbreaks<sup>[10,11]</sup>.

#### 4.2. People attacked by dengue

Basically, people living in urban areas are the common group attacked by dengue. Almost all outbreaks occur in the urban areas. The ratio of vector larvae (pupae) to population density is proposed as an important determinant for the outbreak<sup>[12]</sup>. Nevertheless, there are also other factors that determine the susceptibility of people at risk. Human immunity plays an important role in determining the infection. Genetic factor controlling the immunity should be mentioned<sup>[13]</sup>. Difference of outbreak occurrence among the Blacks and Whites might be explained by this fact<sup>[13]</sup>. Nevertheless, the invasion by new viral serotype usually causes the problem<sup>[14]</sup>. The existence of new dengue serotype in population with low immunity can lead to the problematic dengue outbreak<sup>[14]</sup>.

Another important concern should be the new emerging dengue outbreaks in non-endemic area. The expansion of dengue in epidemic area is of concern in global public health. Several factors are proposed for this observation. Focusing on epidemiological mechanisms in the transmission of dengue in temperate regions, Kuno raised increasing tendency of indoor activity of mosquito vector and massive human movement associated with unpredictable political development as two factors to be concerned<sup>[15]</sup>.

#### 4.3. Clinical presentation and mortality

Normally, patients in dengue outbreak usually present the classical symptoms, acute febrile illness with hemorrhagic complication. However, some outbreaks present uncommon clinical presentations and this might be problematic in diagnoses<sup>[1]</sup>. The severity of infection varies in different outbreak. The mortality rates in different outbreaks are usually different. The medical facilities and skill of local practitioner seems to be the important determinants for outcome of cases management. For example, the recent report on an outbreak in Puerto Rico showed the death rate equal to 0.38% while another report on an outbreak in Sudan showed the death rate equal to 3.8%<sup>[16,17]</sup>.

### 5. What we learn from dengue outbreaks?

#### 5.1. Pre-outbreak stage

In each outbreak, the root cause analysis of the problem should be done. In general, the outbreak is usually due to unsuccessful control of mosquito vector and lack of early diagnosis of the case, good disease control process and good surveillance system. The use of vector monitoring is a classical tool but it is usually not effective. To find an innovative tool for the surveillance and control of dengue

is very important. A recent international attempt to set a study, namely, Dengue Tools becomes the hope for dengue outbreak prediction and control<sup>[18]</sup>.

#### 5.2. Outbreak stage

To solve the problem of delayed diagnosis of outbreak is a challenging query. Training local medical personnel and good on-site diagnostic facilities might be the answer. Some point of care tools are proposed to serve early diagnosis to fight dengue outbreak. However, many reports showed unacceptability of those tools. For example, very diagnostic property of the rapid test was observed during outbreak in Nepal<sup>[19]</sup>. In the real situation, when an outbreak occurs, the control of disease is usually unsuccessful. When an outbreak occurs, the preparedness of other nearby countries is required. The system to control the imported cases is required. According to a recent report from Taiwan, the use of airport fever screening system seems to be effective<sup>[20]</sup>.

#### 5.3. Post outbreak stage

After a resolution of an outbreak, the important thing is to re-evaluate of the situation. It is important to find the root cause of the problem and the pitfall. Nevertheless, these activities are usually forgotten and not routinely performed. It should be note that the lessons learned from different outbreaks are usually different.

### 6. Conclusion

Here are the key learning points that we can see: a) dengue is still an important infection, whose endemicity has been expanded to many new areas; b) outbreak of dengue has been observed for centuries and it is still the present global public health threat; c) vector control seems to be important for control of dengue, however, it is usually unsuccessful; d) diagnosis of dengue might be delayed or missed and this can be the cause of outbreak; e) the management of dengue outbreak must cover pre-outbreak, outbreak and post-outbreak periods.

#### Conflict of interest statement

We declare that we have no conflict of interest.

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#### Comments

##### Background

This is a review on important tropical infection. The reviewed issue is interesting and rarely available in literature. In fact, dengue has become a worldwide public health problem. The outbreak of dengue increases and is usually a public health threat. According to WHO, dengue is the major disease to be controlled and researches for management is required. The present literature review is of a high interest for practitioner since the specific review dealing with outbreak is extremely limited. Readers can

get useful information for adapting to use in their routine clinical practice in tropical medicine.

### Research frontiers

This is an interesting paper in tropical medicine. As already noted, dengue is a tropical disease under surveillance and is suggested by WHO to be a disease to be focused and should not be neglected. Studies are being performed in order to determine the pathophysiology and management of dengue. Nevertheless, the topic that should not be less dealt is the prevention. To succeed in disease management, update data is needed. Due to the changing disease in each outbreak, the summarization on the knowledge dealing with disease as presented in this paper is highly required.

### Related reports

The data about dengue might be presented in many publications, however, most are not on the outbreak. And paper on the outbreak is usually the outbreak report, not dealing with summation and recommendation as the present work. Responding to the question whether other reports are related to this research, it should be said that there is relationship but there is no good summarizing review as this paper. Conclusively, work like this review is not much available. This review has its high originality.

### Innovations & breakthroughs

This is a review paper on limited known topic. Hence, although it is a review paper, it retains its high originality. Data regarding dengue outbreak is usually scattering and the systematic review with additional synthesized idea to form the final recommendations seems to be a very useful piece of work.

### Applications

As already noted, this work can be useful for tropical doctors who practice in tropical region and have a possibility and chance to deal with dengue. In addition, this work can be reference paper for epidemiologist and can also be further useful basic information in preventive medicine.

### Peer review

This is a review on important tropical infection. The reviewed issue is interesting and rarely available in literature. This work can be reference work for general practitioner. The summarization and recommendation are interesting and suggested, and they support the concept that dengue is the disease should not to be neglected in present day.

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