

Original Article

Simulation Study of the Effects of Host Availability on Bite Rate of *Aedes albopictus* (Skuse) (Diptera: Culicidae) and Risk of Dengue Outbreaks in Non-Endemic Areas

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SUMMARY: *Aedes albopictus* is an important vector of dengue fever and tends to live in specific area, where it may ambush blood host that it encounters. Thus, host contact frequency may affect the bite rate and risk of disease outbreak, although no studies have examined these parameters. The present study used a simple model to clarify the fundamental relationship between host availability, bite rate, and risk of dengue outbreaks in non-endemic areas. A hypothetical isolated mosquito population was divided into “ambush” and “resting” subpopulations, and human hosts were modeled as visiting the mosquito population at constant intervals. A single infectious human who visited the mosquito population only on a single occasion was responsible for mosquito infections and consequently, secondary infections among humans who subsequently visit the area after the incubation period. The results confirmed that the bite rate per host increased with decreasing host availability. The number of secondary infections among hosts exhibited a unimodal relationship with the frequency of host visits, with a maximum value at host visits every 24 h. Furthermore, when host availability was not very low, the bite rate was a good indicator of the potential risk of dengue outbreaks. Therefore, human-bait-sweep collection data may be useful for monitoring the risk of dengue outbreaks.

INTRODUCTION

A dengue outbreak in Tokyo during 2014 revealed that Japanese citizens are exposed to *Aedes albopictus* at rates that are sufficient to spread the disease (1,2). There is no reason to assume that high exposure to *Ae. albopictus* only occurs in Tokyo. Given the recent increase in the number of imported dengue cases (3,4), it is possible that dengue outbreaks can occur anywhere in Japan or in other temperate areas where *Ae. albopictus* is abundant. Furthermore, *Ae. albopictus* is one of the most common mosquitoes in Japan, where it has adapted well to the urban environment, exhibiting diurnal behavior and aggressively biting humans who are outdoors (5–7).

In general, mosquitoes consume a single blood meal during a gonotrophic cycle, and the female mosquito subsequently focuses on egg development and oviposition. After laying eggs, the female mosquito becomes hungry again. There are 2 distinct host-seeking strategies in mosquitoes: searching and ambush (8). Searching mosquitoes fly long distances to find hosts, whereas ambushing mosquitoes tend to stay in one place and wait for the hosts (8). It is thought that *Ae. albopictus* is an ambush mosquito, as it has a low flight ability (7,9,10).

In this context, low host availability would be expected to lead to an increasing number of ambush mosquitoes, which would increase the number of mosquitoes that actively attack a new host when it appears. Thus, host availability may strongly affect the bite rate per host, and the potential risk of disease transmission. Although several studies have incorporated mosquito population dynamics into disease transmission models (11–14), no studies have considered the effects of host availability of ambush mosquitoes on disease risk.

The present study used a simple model to analyze whether hypothetical human host availability affected the bite rate and the potential risk of disease outbreaks. This approach has 2 important implications for public health. First, it may help to identify mosquito populations at elevated risk in terms of dengue outbreak that should be targeted for priority vector control. Second, it may help us to understand how the data from human-bait-sweep collection of mosquitoes can be used in the context of disease control. Although this collection method is commonly used by Japanese health officers to monitor populations of dengue vectors (15), its epidemiological significance remains unclear.

MATERIALS AND METHODS

The model: This study aimed to evaluate the relationship between human host availability and disease risk using a simple model. The model assumes an isolated mosquito population that is strongly limited by its larval habitat and has a constant emergence rate (e), a constant mortality rate (d), and thus a constant equilibrium population density (e/d). A single human host visits the mosquito population at a constant time

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interval and remains in the area for a short period (< 5 min). During the host visit, a proportion (a) of ambush mosquitoes bite the host and instantly enter a resting stage. Resting mosquitoes become ambush mosquitoes at a constant rate (b) that is equivalent to the reciprocal of the duration of a gonotrophic cycle. Bites only occur during the 12 h of day time on each day. There are no alternative hosts, and mosquitoes do not leave the area. The first human host to visit the area after 12 AM on day 25 is infectious with dengue virus, and no other infectious human host visits the area. Therefore, transmission of the virus from the host to mosquitoes occurs only once. Mosquitoes that bite the infectious human host become infected (exposed) at a probability (c_1). After a fixed incubation period (τ), these exposed mosquitoes become infectious and can infect human host at a probability (c_2) per bite.

The simulation is divided into 5 phases. The formulas for each phase are shown below. In each simulation, a single time step is set to 5 min. During phase A ($t < X$; X is the time when an infectious human host visits the area), the susceptible ambush mosquitoes [$As(t)$] and susceptible resting mosquitoes [$Rs(t)$] at time t are described as:

$$As(t+1) = As(t) + e - aNs(t)As(t) + bRs(t) - dAs(t) \quad (\text{Eq. 1})$$

$$Rs(t+1) = Rs(t) + aNs(t)As(t) - bRs(t) - dRs(t) \quad (\text{Eq. 2})$$

In these formulas, $Ns(t)$ reflects the number of susceptible host visits at time t , and equal to 1 when a host is present and 0 when no host is present. When hosts visit every 5 min, $Ns(t) = 1$ for all time steps in the day-time; when hosts visit every 5 days, a time step with $Ns(t) = 1$ is followed by 1,439 time steps of $Ns(t) = 0$. In phase B ($t = X$), which occurs when a single infectious human host visits the area [$Ni(X) = 1$], some susceptible ambush mosquitoes become exposed resting mosquitoes [$Re(X+1)$]:

$$As(t+1) = As(t) + e - aNi(t)As(t) + bRs(t) - dAs(t) \quad (\text{Eq. 3})$$

$$Rs(t+1) = Rs(t) + a(1 - c_1)Ni(t)As(t) - bRs(t) - dRs(t) \quad (\text{Eq. 4})$$

$$Re(t+1) = ac_1Ni(t)As(t) \quad (\text{Eq. 5})$$

During phase C ($X < t < X + \tau$), which is the extrinsic incubation period of the virus, both susceptible [$As(t)$ and $Rs(t)$] and exposed [$Ae(t)$ and $Re(t)$] mosquitoes coexist, and no new infections occur either among mosquitoes or human hosts:

$$As(t+1) = As(t) + e - aNs(t)As(t) + bRs(t) - dAs(t) \quad (\text{Eq. 6})$$

$$Rs(t+1) = Rs(t) + aNs(t)As(t) - bRs(t) - dRs(t) \quad (\text{Eq. 7})$$

$$Ae(t+1) = Ae(t) - aNs(t)Ae(t) + bRe(t) - dAe(t) \quad (\text{Eq. 8})$$

$$Re(t+1) = Re(t) + aNs(t)Ae(t) - bRe(t) - dRe(t) \quad (\text{Eq. 9})$$

In phase D ($t = X + \tau$), the virus' extrinsic incubation period has completed, and all the exposed mosquitoes become either infectious ambush mosquitoes (Ai) or

infectious resting mosquitoes (Ri):

$$As(t+1) = As(t) + e - aNs(t)As(t) + bRs(t) - dAs(t) \quad (\text{Eq. 10})$$

$$Rs(t+1) = Rs(t) + aNs(t)As(t) - bRs(t) - dRs(t) \quad (\text{Eq. 11})$$

$$Ae(t+1) = 0 \quad (\text{Eq. 12})$$

$$Re(t+1) = 0 \quad (\text{Eq. 13})$$

$$Ai(t+1) = Ae(t) - aNs(t)Ae(t) + bRe(t) - dAe(t) \quad (\text{Eq. 14})$$

$$Ri(t+1) = Re(t) + aNs(t)Ae(t) - bRe(t) - dRe(t) \quad (\text{Eq. 15})$$

During phase E ($X + \tau < t < T_{max}$), the susceptible and infectious mosquitoes coexist in the population:

$$As(t+1) = As(t) + e - aNs(t)As(t) + bRs(t) - dAs(t) \quad (\text{Eq. 16})$$

$$Rs(t+1) = Rs(t) + aNs(t)As(t) - bRs(t) - dRs(t) \quad (\text{Eq. 17})$$

$$Ai(t+1) = Ai(t) - aNs(t)Ai(t) + bRi(t) - dAi(t) \quad (\text{Eq. 18})$$

$$Ri(t+1) = Ri(t) + aNs(t)Ai(t) - bRi(t) - dRi(t) \quad (\text{Eq. 19})$$

The simulation was continued until the 125th day from the beginning ($T_{max} = \text{Day 125}$) because by this day, most ($> 99.9\%$) of the infectious mosquitoes have died even with low mortality rate (0.1/day).

To evaluate the potential risk of dengue outbreaks, the model also calculates the number of secondary infected human hosts. As a single infectious human host only visits the area once in this model, mosquito infections can only occur at phase B. Hosts that visit the area and bitten after the extrinsic incubation period (phase E) become infected at probability of c_2 per bite, and the probability of a human host becoming infected at time t with $aAi(t)$ bites by infectious mosquitoes is:

$$Ih(t) = 1 - (1 - c_2)^{aAi(t)} \quad (\text{Eq. 20})$$

If the host is bitten by one infectious mosquito, $Ih(t)$ is c_2 . If the host is bitten by many ($\gg 1$) infectious mosquitoes, $Ih(t)$ asymptotically approaches 1. This relationship is extended to the decimal values of $aAi(t)$ to calculate the expected number of secondary host infections, which are summed for the all human hosts that visit the area during phase E:

$$Ih_{total} = \sum_{t=X+\tau}^{T_{max}} Ns(t)Ih(t) \quad (\text{Eq. 21})$$

This value is similar to the basic reproductive number (R_0) of vector-borne diseases (16), but differs from it in the following way: the basic reproductive number is defined as the number of the secondary infected hosts caused by the first infectious host until that the host has recovered from the disease, whereas Ih_{total} in the present study counts the number of secondary infected human hosts caused by a single visit of an infectious host to an area with a mosquito population. Thus, this value can be interpreted as a local basic reproductive number. If the value is summed for all mosquito populations that

the infectious host encounters before recovering from the disease, the sum would be equivalent to R_0 . For the present study, Ih_{total} is defined as local R_0 .

To examine the relationship between bite rate per host and the risk of disease outbreaks, the average bite rate per host visit (BR) was calculated as follows.

$$BR = \frac{\sum_{t=Day25}^{T_{max}} a[Ns(t) + Ni(t)][As(t) + Ae(t) + Ai(t)]}{\sum_{t=Day25}^{T_{max}} [Ns(t) + Ni(t)]} \quad (\text{Eq. 22})$$

The parameters that were used in the simulations are as follows: the duration of the gonotrophic cycle (b^{-1}), 3 days (17); probability of virus transmission from host to vector (c_1) and from vector to host (c_2), 0.86 and 0.43, respectively (14); extrinsic incubation period (τ), 9 days (13); daily mortality (d), 0.2 (7). As there is no reasonable assumption that can be used to estimate the bite rate per ambush mosquito (a), it was arbitrarily set to 0.5. As vector density can vary greatly in the field, the emergence rate (e) was altered to provide various population density values ($e/d = 5, 25, 50, 75, 100$, and 150). The effects of the host visit interval (ranging from 5 min to 10 days) on bite rate per host visit and the number of secondary infected hosts (local R_0) were examined for various mosquito population densities. To test the robustness of the latter results, different combinations of bite rate per ambush mosquito ($a = 0.3, 0.5$, and 0.7) and mortality ($d = 0.1, 0.2$, and 0.3) were examined. In each simulation, the parameters for the daily rates (b, d , and e) were multiplied with $0.003472222 (= 1/24/12)$ to convert the time scale from daily basis to 5 min basis.

The simulations were performed using Microsoft Excel (Microsoft, Redmond, WA, USA). The initial proportion of ambush mosquitoes was set to 50%.

RESULTS

Effects of host availability on the proportion of ambush mosquitoes: Fig. 1 shows the proportions of the ambush mosquitoes with different frequencies of host visits. The proportion fluctuated depending on the host visit interval, and tended to increase with increasing host visit interval. The proportion did not depend on mosquito population density (data not shown).

Effects of host availability on bite rate: The average bite rate per host visit increased with the host visit interval for each mosquito population density (Fig. 2). The increase was nearly linear at short visit intervals and then asymptotically approached a constant value that was the total population multiplied by a (0.5 in Fig. 2). The results indicate that, even at a constant mosquito population density, the bite rate per host can vary widely based on host availability.

Effects of host availability on the risk of dengue outbreak: The number of the secondary infected hosts (local R_0) showed a complex relationship with the host visit interval (Fig. 3). The local R_0 increased for intervals that ranged from 5 min to 24 h, and a gradual decline with some small peaks was observed for intervals of > 24 h. The small peak at the host visit interval of 9

days can be explained as follows: as the infectious host visits only once and the extrinsic incubation period was fixed to 9 days, the number of infectious mosquitoes is largest on the 9th day after the infectious host's visit; if another host visits on this day, a large number of infectious mosquitoes would bite and infect the host. To test the robustness of this relationship, simulations were performed for the different combinations of a and d , which revealed a similar trend (Fig. 4). Most of the conditions exhibit a peak of local R_0 at a host visit interval of 24 h, with the exception of a peak value at 12 h for the simulation with $a = 0.3$ and $d = 0.1$.

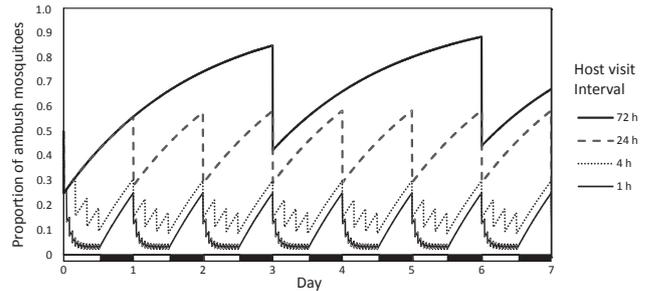


Fig. 1. Changes in the proportion of ambush mosquitoes for different host visit intervals in the first 7 days of simulation. White and black bars under the horizontal axis indicate day and night times, respectively. The initial value of the proportion of ambush mosquitoes was set to 0.5 in each condition. Bite rate per ambush mosquito (a) is 0.5, and mortality (d) is 0.2. The mosquito population density (e/d) is set to 100.

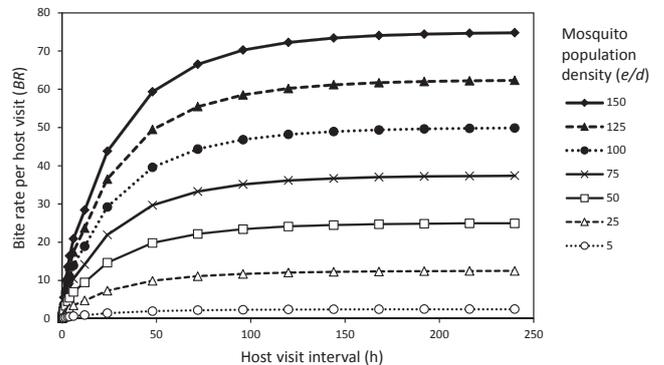


Fig. 2. Relationship between the host visit interval and bite rate per host for different mosquito population densities (e/d). Bite rate per ambush mosquito (a) is 0.5 and mortality (d) is 0.2.

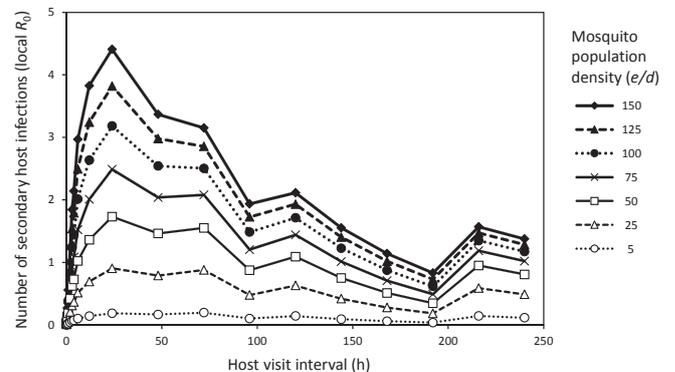


Fig. 3. Relationship between the host visit interval and the number of secondary host infections (local R_0) for different mosquito population densities (e/d). Bite rate per ambush mosquito (a) is 0.5 and mortality (d) is 0.2.

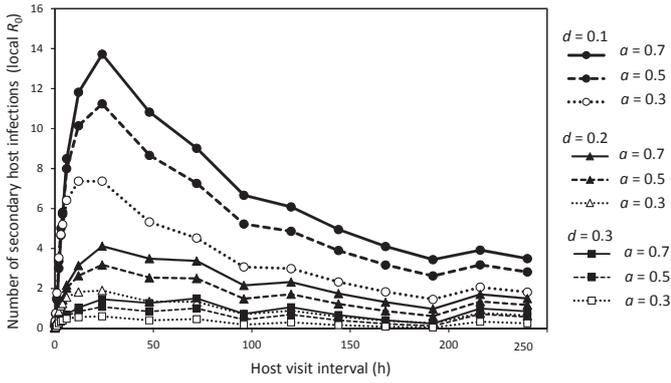


Fig. 4. Relationship between the host visit interval and the number of secondary host infections (local R_0) with different combinations of bite rate per ambush mosquito (a) and mortality (d). The mosquito population density (e/d) is set to 100 for all combinations.

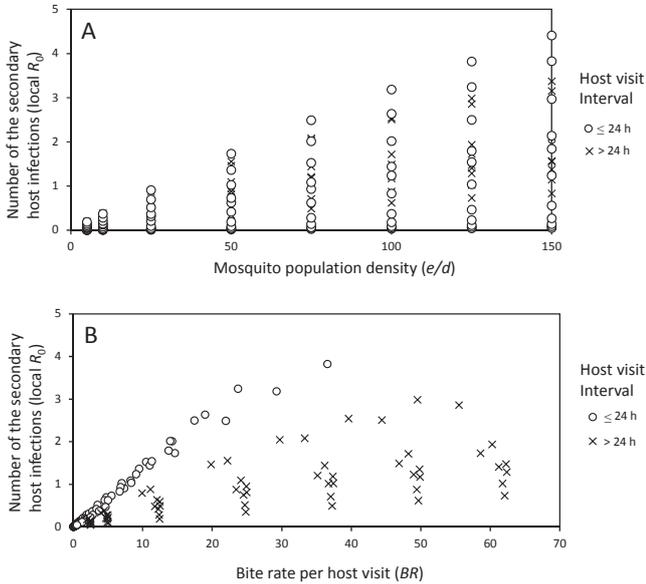


Fig. 5. (A) Relationship between mosquito population density and the number of secondary host infections (local R_0). (B) Relationship between bite rate per host visit and the number of secondary host infections (local R_0).

Table 1. Correlation between biting rate per host visit and secondary host infections (local R_0) with different combinations of 2 parameters

Parameter ¹⁾		Spearman's rank correlation (ρ)
Bite rate per ambush mosquito (a)	Mosquito mortality (d)	
0.3	0.1	0.995
	0.2	0.995
	0.3	0.994
0.5	0.1	0.995
	0.2	0.994
	0.3	0.994
0.7	0.1	0.996
	0.2	0.996
	0.3	0.996

¹⁾: The host visit interval ranged from 5 min to 24 h.

Vector density and bite rate as indicators of outbreak risk: To compare the predictability of disease risk using 2 entomological indicators, local R_0 values (based on different mosquito population densities and host visit intervals) were plotted against mosquito population density (Fig. 5A) and against bite rate per host visit (Fig. 5B). Mosquito population density was significantly, albeit weakly, correlated with local R_0 when the host visit interval was limited to ≤ 24 h (Spearman's rank correlation; $\rho = 0.517$, $P < 0.0001$), and when it was not limited ($\rho = 0.535$, $P < 0.0001$). The bite rate per host visit was more strongly correlated with the local R_0 ($\rho = 0.733$, $P < 0.0001$), especially when the target visit interval was limited to ≤ 24 h ($\rho = 0.994$, $P < 0.0001$). This strong correlation persisted when different combinations of a and d were used (Table 1).

DISCUSSION

The present study's findings indicate that host availability affects the bite rate of the ambush mosquitoes and the number of secondary host infections originating from a single visit by an infectious host. The present study is the first to evaluate the relationship between host availability of ambush mosquitoes and disease risk.

The present study has assumed an isolated mosquito population that was occasionally visited by human hosts. This situation is a simple model of public urban spaces such as parks, cemeteries, and bus stops. It is not surprising that mosquito populations with low host availability would develop high proportions of ambush females that are ready to attack available hosts. However, it is important to note that host availability can vary among different mosquito populations, which may determine the location-specific variations in the risks of dengue outbreaks. The present study revealed that the risk of dengue outbreaks peaked at specific host visit intervals. This unimodal pattern can be explained as follows. Very frequent host visits are associated with a relatively small proportion of ambush mosquitoes, and that the infectious human host is only bitten by a few mosquitoes. When the frequency of host visit is very low, an infectious human host would be bitten by many ambush mosquitoes, although few hosts would visit the area and become infected during the period when the infectious mosquitoes remain abundant. Thus, the number of secondary infected hosts would peak at an intermediate value for host availability. Based on biologically plausible parameters, it appears the host visits of approximately once per day are associated with an elevated risk of spreading the dengue virus. Disease control efforts tend to focus on public places where many people visit frequently (15). However, the present study's finding indicate that relatively infrequent host visits are associated with a greater risk of dengue spread after an infectious human host has visited the mosquito population.

Another important finding is that bite rate per host visit was a good indicator of outbreak risk, even better than population density of the vector mosquito. The human-bait-sweep collection method is often used for monitoring the *Ae. albopictus* population (2,15).

This method has the advantage that it can efficiently collect biting mosquitoes in a short period (8 min per site is recommended; 2,15). A possible disadvantage might be that the data from this sampling method does not reflect the density of whole mosquito population because it does not catch resting mosquitoes. Although the sampling method is practical and convenient, interpretation of the data in the context of disease risks has not been clear. This collection method would be a good proxy of bite rate per host visit in the present study as it collects ambush mosquitoes that actively attack the collector. Therefore, the present study provides theoretical proof that the human-bait-sweep collection method is a good indicator of the site-specific risks of dengue outbreaks. In urban environments, most public areas are likely visited by humans at least once per day. In the present study's results, the bite rate per host visit was strongly correlated with the local R_0 when the host visit interval was ≤ 24 h. Therefore, the bite rate per host, which can be measured by human-bait-sweep collection, could be a useful indicator of disease risk associated with public spaces in most urban public spaces.

There are several potential limitations due to oversimplification of the model. It may be unrealistic that the emergence rate is not affected by host availability. Although it was reported that *Ae. albopictus* populations can be maintained with a relatively low frequency of blood meals (18), very long intervals between host visits may cause low mosquito population density and, hence, low disease risks. However, as mosquitoes do not lay eggs more than once in a gonotrophic cycle (around 3 days), variation in the host visit interval within a few days would not affect mosquito fecundity remarkably. Therefore, the main findings of the present study, the highest disease risk at a host visit interval of 24 h and a high correlation between bite rate per host and disease risk for host visit interval within 24 h, are probably true in real populations.

In addition, with no consideration of dispersing mosquitoes, the fixed time interval of the host visit, and the absence of non-human alternative hosts might be unrealistic in a natural population. The influence of these real-world complexities on disease risks remain as subjects for future studies.

The 2014 outbreak of dengue in Tokyo revealed that outbreaks can occur whenever and wherever the vector mosquitoes are abundant. The present study's findings indicate that a mosquito population with a relatively low host availability has an elevated risk of disease outbreak, and that the risk can be evaluated using bite data from human-bait-sweep collection. This information may be useful for preventing future outbreaks of dengue and other mosquito-borne diseases.

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Conflict of interest None to declare.

REFERENCES

1. Kutsuna S, Kato Y, Moi ML, et al. Autochthonous dengue fever, Tokyo, Japan, 2014. *Emerg Infect Dis.* 2015;21:517-20.
2. Tsuda Y, Maekawa Y, Ogawa K, et al. Biting density and distribution of *Aedes albopictus* during the September 2014 outbreak of dengue fever in Yoyogi Park and the vicinity of Tokyo Metropolis, Japan. *Jpn J Infect Dis.* 2016;69:1-5.
3. Takasaki T. Imported dengue fever/dengue hemorrhagic fever cases in Japan. *Trop Med Health.* 2011;39:Suppl 13-5.
4. Wilder-Smith A, Gubler DJ. Geographic expansion of dengue: the impact of international travel. *Med Clin North Am.* 2008;92:1377-90.
5. Sawabe K, Isawa H, Hoshino K, et al. Host-feeding habits of *Culex pipiens* and *Aedes albopictus* (Diptera: Culicidae) collected at the urban and suburban residential areas of Japan. *J Med Entmol.* 2010;47:442-50.
6. Tamashiro M, Toma T, Mannen K, et al. Bloodmeal identification and feeding habits of mosquitoes (Diptera: Culicidae) collected at five islands in Ryukyu Archipelago, Japan. *Med Entomol Zool.* 2011;62:53-70.
7. Hawley WA. The biology of *Aedes albopictus*. *J Am Mosq Control Assoc Suppl.* 1988;1:1-39.
8. Edman JD. Are mosquitoes gourmet or gourmand? *J Am Mosq Control Assoc.* 1989;5:487-97.
9. Mogi M, Yamamura N. Estimation of the attraction range of a human bait for *Aedes albopictus* (Diptera: Culicidae) adults and its absolute density by a new removal method applicable to populations with immigrants. *Res Popul Ecol.* 1981;23:328-43.
10. Takagi M, Tsuda Y, Wada Y. Temporal and spatial distribution of released *Aedes albopictus* (Diptera: Culicidae) in Nagasaki, Japan. *Jpn J Sanit Zool.* 1995;46:223-8.
11. Focks DA, Daniels E, Haile DG, et al. A simulation model of the epidemiology of urban dengue fever: literature analysis, model development, preliminary validation, and samples of simulation results. *Am J Trop Med Hyg.* 1995;53:489-506.
12. Erickson RA, Presley SM, Allen LJS, et al. A dengue model with a dynamic *Aedes albopictus* vector population. *Ecol Model.* 2010;221:2899-908.
13. Moulay D, Aziz-Alaoui MA, Cadivel M. The chikungunya disease: modeling, vector and transmission global dynamics. *Math Biosci.* 2011;229:50-63.
14. Oki M, Yamamoto T. Simulation of the probable vector density that caused the Nagasaki dengue outbreak vectored by *Aedes albopictus* in 1942. *Epidemiol Infect.* 2013;141:2612-22.
15. National Institute of Infectious Diseases. Guidelines for measures of mosquito-borne diseases including dengue fever and chikungunya fever. Available at < <http://www.mhlw.go.jp/file/06-Seisakujouhou-10900000-Kenkoukyoku/0000163947.pdf>>. Accessed June 26, 2017. Japanese.
16. Anderson RM, May RM. *Infectious Diseases of Humans Dynamics and Control.* Oxford, UK: Oxford University Press; 1991.
17. Delatte H, Gimonneau G, Triboire A, et al. Influence of temperature on immature development, survival, longevity, fecundity, and gonotrophic cycles of *Aedes albopictus*, vector of chikungunya and dengue in the Indian Ocean. *J Med Entmol.* 2009;46:33-41.
18. Tsuda Y, Takagi M, Wada Y. Long-term patterns of laboratory populations of *Aedes albopictus* (Diptera: Culicidae): a comparison between two strains from Japan and Thailand. *Jpn J Sanit Zool.* 1994;45:133-9.