Letter to the editor: Diagnosis of a single imported dengue case who had travelled to Japan – how serious is it for travellers?

R Ueno1, H Nishiura (nishiura@m.u-tokyo.ac.jp)1
1. Graduate School of Medicine, The University of Tokyo, Tokyo, Japan

To the editor: We enjoyed reading the meticulous clinical report of an imported dengue case in a German traveller returning from Japan [1]. It is, however, unclear what level of risk the 'autochthonous' infection of a single case in Japan represents. By investigating the epidemiological aspects of one imported dengue case, we would like to discuss how serious the implications of autochthonous transmission are for future travellers.

The diagnosed case travelled to Japan in August 2013, during which time the dengue virus infection is believed to have occurred. We would like to estimate how many primary cases there were and how transmissible the dengue virus was.

Let \( I_t \) and \( R_t \) represent the number of primary cases and the effective reproduction number, respectively, at a generation \( t \) (i.e. the mean number of secondary cases generated by a single primary case at generation \( t \)). Supposing there were \( S_t \) susceptible individuals who can be infected with dengue virus, the probability of producing \( I_{t+1} = k \) secondary cases through a single generation interval of dengue (i.e. the time from infection in a primary human case to infection in a secondary human case caused by the primary case through the mosquito vector) is given by [2,3]: (1)

\[
\Pr(I_{t+1} = k; I_t, S_t, R_t) = \left( \frac{S_t}{k} \right) \left[ 1 - \exp \left( - \frac{R_t I_t}{S_t} \right) \right]^k \exp \left( - \frac{R_t I_t}{S_t} \right)^{S_t - k}
\]

If the diagnosed German patient represents all infected cases, \( k = 1 \). However, dengue was not at the forefront of Japanese physicians’ attention before the case report. If there were other undiagnosed cases in the same generation, \( k > 1 \). As can be seen from Equation 1, the reproduction of \( k \) cases in generation \( t+1 \) depends on three unknown epidemiological parameters, i.e. \( I_t, R_t \), and \( S_t \).

The negative loglikelihood of observing \( k \) secondary cases reads as follows: (2)

\[
L(I_t, S_t, R_t; I_{t+1} = k) = \sum_{j=0}^{k} \ln j - \sum_{i=k+1}^{S_t} \ln i - k \ln \left[ 1 - \exp \left( - \frac{R_t I_t}{S_t} \right) \right] + (S_t - k) \frac{R_t I_t}{S_t}
\]

Two limitations of our analysis must be noted. First, an important technical flaw of our exercise is that our
arguments start with a rare event (i.e. diagnosis of a single imported case) and thus our results could have over-interpreted the actual risk of dengue in Japan. The actual risk could be even smaller than what has been calculated here, but we decided to use the biased sample, because the over-interpreted risk would still appear to be far smaller than that in dengue-endemic settings (and this notion should be shared with non-experts). Second, due to data limitation, our exercise only extends to the diagnosed dataset of the reported German case. It is hard to take into account unrecognised transmission events at another time and another geographical location.

Despite these limitations, our crude analysis of this diagnostic event indicates the following: (i) the number of primary cases was probably small; and (ii) even with a certain number of primary cases, a large $I_t$ leads to a small $R_t$, which is substantially below 1. These would not permit dengue virus transmission to continue in the suspected transmission settings in Japan. Of course, demonstrating an autochthonous transmission event is of the utmost importance, because it reflects establishment of a transmission cycle through *Aedes* spp. within Japan. Nevertheless, it should be noted that the diagnosis of an imported case does not directly indicate that the actual risk of infection in Japan is high or that dengue is endemic in that country. Rather, based on the very limited biased data, our exercise indicates that it is very unlikely that dengue is endemic in Japan. Our results and travel history of the diagnosed case are consistent with an exposure near Narita International Airport, where there could be mosquito vectors that have bitten infected travellers from endemic countries. Indeed, there has been a report of ‘airport dengue’ in Australia [4]. A future seroepidemiological survey could help validate the findings from this short note [5].

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**Conflict of interest**

None declared.

**Authors’ contributions**

Ryo Ueno and Hiroshi Nishiura conceived modelling ideas, interpreted the results and revised the manuscript. Hiroshi Nishiura implemented computational analyses and drafted the manuscript.

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**Figure**

Analysis of transmission event data using a chain binomial stochastic model

Panel A. The relationship between the maximum likelihood estimate of the effective reproduction number and the number of primary cases. The number of secondary cases, $k$, has been varied from 1 to 5. The number of susceptible persons has little impact on the results and was fixed at 50. The horizontal dashed line represents the threshold value of the reproduction number, below which the transmission event does not continue through this generation.

Panel B. The simulated negative loglikelihood values as a function of the effective reproduction number and the number of primary cases. The optimal value of the number of primary cases is seen where the negative loglikelihood takes the minimum value. The effective reproduction number, $R_t$, is varied from 0.2 to 0.8. The number of secondary cases, $k$ has been fixed at 1, but $k>1$ does not yield qualitatively different patterns.
References


