Human movement can explain heterogeneous propagation of dengue fever in Cambodia

Magali Teurlai[1], Rekol Huy[2], Bernard Cazelles[3,4], Raphaël Duboz[5], Christophe Baehr[6,7] & Sirenda Vong[1]

[1]Epidemiology and Public Health Unit, Institut Pasteur du Cambodge, Phnom Penh, Cambodia
[2]National Dengue Control Program, National Centre for Parasitology, Entomology and Malaria Control, Ministry of Health, Phnom Penh, Cambodia
[3]CNRS UMR 7625, Ecole Normale Supérieure, Paris, France
[4]IRD UR GEODES, Bondy, France
[5]CIRAD UPR Agirs, Montpellier, France
[6] Météo France, CNRM, Toulouse, France
[7] CNRS, GAME URA 1357, Toulouse, France

INSTITUT PASTEUR DU CAMBODGE

FONDATION PIERRE LEDOUX Jeunesse Internationale

Université Paul Sabatier TOULOUSE III

1. Introduction

Dengue fever is the most important arboviral disease worldwide and a major public health problem in tropical and subtropical areas. It is endemic in Cambodia where it causes high hospitalisation and mortality rates among children. In the absence of a vaccine, control is limited to vector control measures. Understanding the forces driving spatial spread is essential in low income countries to aid better allocation of resources, and control measures implementation. In this study, we analyse dengue fever national surveillance data to characterize its spatio-temporal pattern of propagation in Cambodia from 2002 to 2008.

2. Material and methods

The data

Cambodia National surveillance recorded 109,332 dengue cases during 2002-2008. Cases were declared on a clinical basis. We calculated dengue weekly incidence rates in each of the 183 districts. Population data were interpolated linearly using two national censuses. Assuming that dengue epidemic patterns would be highly stochastic in low populated areas, we discarded the 48 districts with less than 20 people per km² from the analysis.

Temporal analysis

We used wavelet analysis (Torrence, 1998) to filter incidence rates in the 0.8-1.2 year periodic band. This spectral technique also allowed us to extract the phase of this annual component of incidence and to calculate time lags between annual epidemics in different districts (Figure 1).

Spatial analysis

The study of dengue incidence maps revealed two geographic areas seminal in the propagation of dengue fever: the national road between Phnom Penh and Siem Reap and the Mekong river (see Fig. 2a). To reveal spatial heterogeneity, we performed, each year, an analysis of covariance:

$\mathbf{Y} = \beta_0 + \beta_1 \mathbf{X_1} + \beta_2 \mathbf{X_2} + \beta_3 \mathbf{X_1} * \mathbf{X_2} + \varepsilon$, with Y the annual mean of temporal lag time series relative to the district #306, X_1 the corresponding distance separating districts centres, and X_2 the geographic area "Mekong" or "National Road" (Fig. 2a). Separate regressions were then performed in each geographic area to evaluate the speed of propagation of the annual epidemic.

3. Results

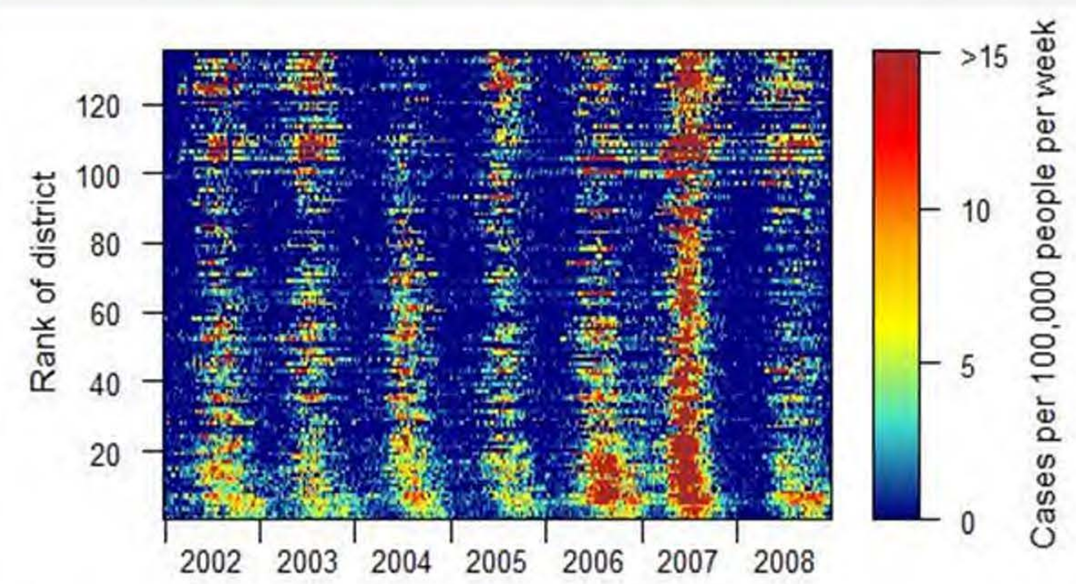

Figure 1: Apparent dengue haemorrhagic fever weekly incidence rates in each of the 135 districts where population density is higher than 20 people per km^2 in Cambodia. Districts are ranked by increasing distance to Phnom Penh from bottom to top.

Dengue is hyper-endemic in Cambodia. It presents with a strong seasonal pattern, the epidemics starting in April, peaking in July and ending in November. Spatial study of dengue incidence rates reveals that epidemics are not synchronous over the country, peaking at different times of the year in different districts. Surprisingly, Phnom Penh does not seem to be the starting point of the national annual epidemic (Fig.1). This is contrary to the common thought that big urban centres act as a reservoir and spread the disease.

The analysis of the phase of the annual component of incidence in a space-time domain reveals an heterogeneous pattern of propagation (Fig. 2): along the National road linking Phnom Penh to Siem Reap, annual epidemics are highly synchronous (Fig. 2c) whereas along the Mekong River, a travelling wave emanates from two rural areas and travel slowly towards Phnom Penh (Fig. 2b). Fig. 2 shows that this pattern is repeating year after year, with the national epidemic starting in the same few rural areas every year (district #306 for example).

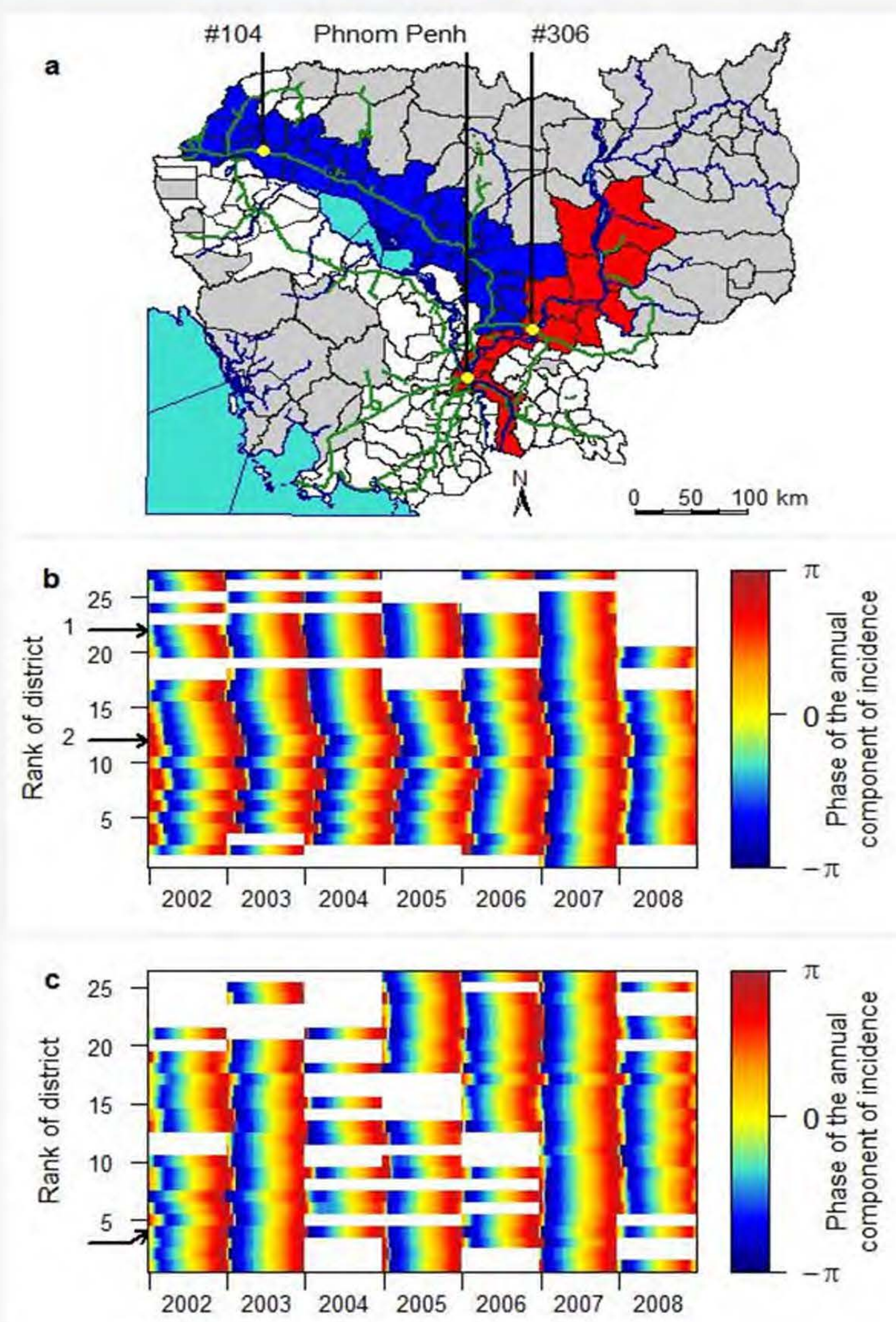

Figure 2: Phase of the weekly incidence rates computed in the 0.8-1.2 periodic band in two geographic areas. **a,** Map of the two geographic areas chosen. Grey districts have less than 20 people per km². **b,** Phase of districts along the Mekong River (red in Fig. 2a), presented from the most southerly to the most northerly from bottom to top. **c,** Phase of districts along the National Road 6 (blue in Fig. 2a), presented from West to East from bottom to top. The arrows indicate districts: 1, #306; 2, Phnom Penh (Fig. 2b) and #104 (Fig. 2c).

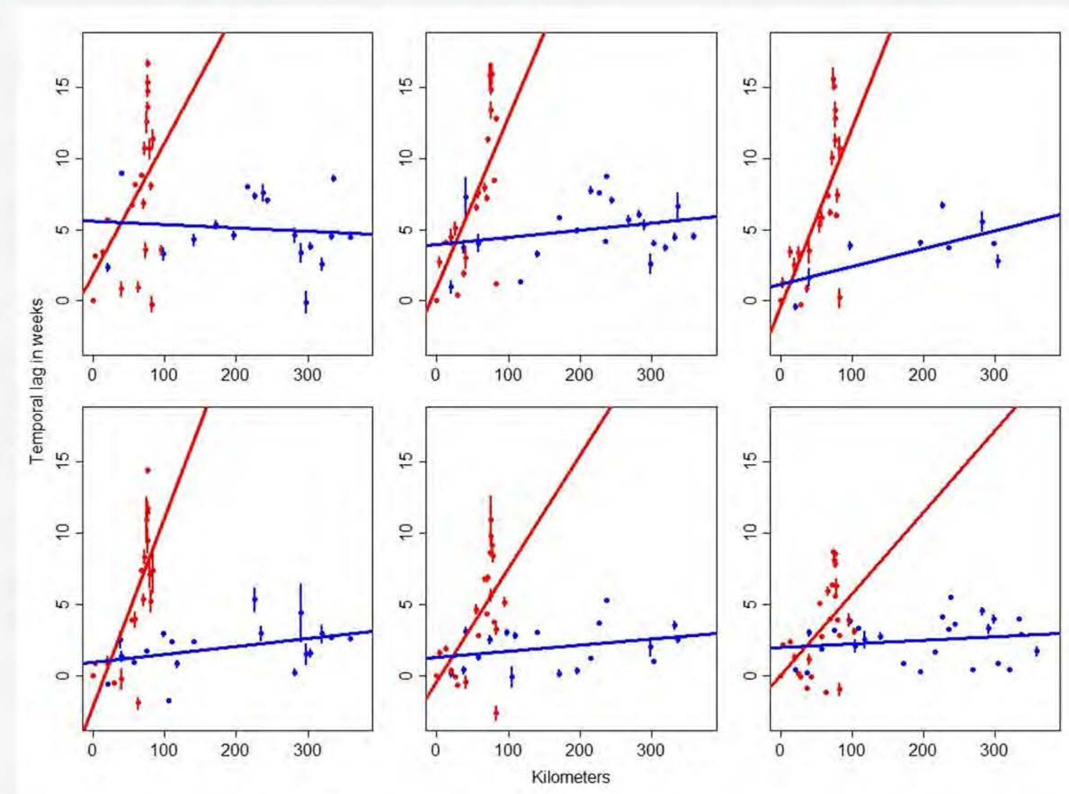

Figure 3 Linear regressions between the mean annual temporal lag of the annual epidemic in each district and the distance, relative to the district surrounding Kampong Cham (#306) from 2002 (**a**) to 2007 (**f**). Colours represent the geographic localisation of each district, according to Fig. 2a. The number of districts included in the analysis changes every year, according to whether an epidemic occurred in the district (Table1). Error bars represent the 95% C.I. associated with the mean. Normality and homoscedasticity of residuals was confirmed using the Shapiro-Wilks and the Bartlett tests respectively (alpha level

The results of the ANCOVA confirmed the heterogeneity of propagation within the country: each year, the speed of propagation of the epidemic, as estimated by the inverse of the regression slope in Fig. 3, was significantly higher along the national road than along the Mekong River (mean annual speed of 11 km per week).

In 2007, there has been a major epidemic characterised by a four fold increase in dengue incidence, a higher synchronisation of the epidemics over the country (Fig. 2b), and an acceleration of the speed of propagation along the Mekong River (Fig.

4. Discussion

Propagation is heterogeneous according to the type of road: first empirical proof of the role of human movement in the propagation of dengue.

Starting point in rural areas.

2007 : serotype 2 replacing serotype 3

Implications for operational purposes : treat starting points in priority.

Limits of the study: surveillance biases, but wavelet technique very robust.

References: **Cazelles B.**, Chavez M., McMichael A., Hales S. (2005). Nonstationary Influence of El Niño on the Synchronous Dengue Epidemics in Thailand. *Plos Medecine* 2 (**4**) 313-318.

Cummings D., Irizarry R., Huang N., Endy T., Nisalak A., Ungchusak K., Burke D. (2004). Travelling waves in the occurrence of dengue haemorragic fever in Thailand. *Nature* (**427**) 344-347.

Grenfell B., Bjørnstad O., Kappey J. (2001). Travelling waves and spatial hierarchies in measles epidemics. *Nature* (**414**) 716-723.

Torrence C., Compo G (1998). A Practical Guide to Wavelet Analysis. *Bulletin of the American Meteorological Society* (**79**) 61-78.

Acknowledgments: I would like to thank the Pasteur Institute of Cambodia (IPC) for welcoming me, Anne Conan for database cleaning and all the technical discussions, the « Fondation Ledoux Jeunesse Internationale » for financial support, the Pasteur Institute International Network for plane tickets, and all the IPC epidemiology unit for useful exchanges.