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Dengue and chikungunya seroprevalence in Gabonese infants prior to major outbreaks in 2007 and 2010: A sero-epidemiological study

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Summary *Background:* Apart from outbreak reports, little is known about the endemicity of dengue and chikungunya virus in African countries. We investigated serum samples collected in Gabon before major outbreaks in 2007 and 2010 in order to identify pre-outbreak-circulation of both viruses.
Methods: Serum samples from Gabonese infants (162) were analyzed at 3, 9, 15 and 30 months of age by commercial ELISA for dengue and chikungunya IgG-antibodies. If samples were positive medical records of participants were analyzed for symptoms concordant with dengue and chikungunya infections during the time period of assumed seroconversion.
Results: IgG-antibodies against dengue were found in 12.3%, and IgG-antibodies against chikungunya in 0.6% of infants tested. Using the four measuring time points, we estimated corresponding incidences of 51/1.000 person-years and 2.5/1.000 person-years, respectively. Symptoms in positive-tested infants were mostly non-specific.
Conclusion: Seropositivity suggests that both viruses circulated before the well-noticed outbreaks. Clinical diagnosis of dengue and chikungunya is difficult especially in infants,

Abbreviations: DENV, dengue virus; CHIKV, chikungunya virus; ELISA, Enzyme-Linked Immunosorbent Assay; IgG, immunoglobulin G; IgM, immunoglobulin M; EDTA, ethylene-diamine-tetra-acetic acid; IPTi, Intermittent Preventive Treatment in Infants study; GmbH, company with limited liability; Rt-PCR, quantitative reverse transcription–polymerase chain reaction.

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underscoring the need for accurate and reliable diagnostic tests as well as awareness of medical personnel.
Clinical trials registration: NCT00167843.

1. Introduction

On a global scale, dengue and chikungunya rank high amongst the recently most successful emerging arboviruses [1,2]. In parts of Southeast Asia and the Americas, dengue virus (DENV) is highly endemic. However, little is known about the overall endemicity in Africa, where outbreaks frequently occur. *Aedes* spp. (with *Aedes aegypti* as the principal vector) are firmly established throughout sub-Saharan Africa, and DENV circulates at various levels of endemicity, bearing the potential for causing large outbreaks [3—5]. Exported cases of DENV in travelers from Africa to Europe and elsewhere were reported [6].

Since the first isolation of chikungunya virus (CHIKV) in Tanzania in 1952, major epidemics occur cyclically mainly in Asia and Africa, with inter-epidemic periods of 7—20 years. A massive outbreak in Kenya in 2004 and epidemics in the Indian Ocean region raised public and medical awareness for CHIKV [7]. There were two large outbreaks in Gabon in 2007 and 2010 of DENV and CHIKV, with DENV-CHIKV co-infections reported in humans and mosquitoes [8—11]. However, little is known about circulation of these viruses in the pre-outbreak era. In the present study, we assessed seropositivity for anti-CHIKV and anti-DENV IgG antibodies before the abovementioned outbreaks in young Gabonese children at different consecutive ages, in order to assess previously ongoing transmission in the country.

2. Material and methods

2.1. Sero-epidemiological survey

Venous blood samples were collected from 162 infants participating in the Intermittent Preventive Treatment in Infants study (IPTi) in Lambaréné, Gabon (Clinical trials registration: NCT00167843; see Section 2.2) [12,13] and stored at −80 °C. Selection criteria for the sero-epidemiological survey presented here were a complete blood collection on all 4 study visits at 3 (M 3), 9 (M 9), 15 (M 15) and 30 (M 30) months of age (Fig. 1). Only infants were included in the analysis that were recruited in the first 12 months of the IPTi trial to keep a time gap to the outbreaks of chikungunya and dengue in 2007.

To avoid recording of seropositivity due to maternal antibodies in the first months of life, all M 30 blood samples were tested first by a screening ELISA. In case of seropositivity, analysis was continued with samples from the next-earlier time point, and so on. Time from birth to the midpoint between time intervals of being seronegative and becoming seropositive was taken as proxy time point of infection. At birth other information such as the use of bed nets and vaccination status was recorded and re-assessed at each time point of blood draws. Statistical analysis was performed with R 2.14.2 (www.r-project.org).

2.2. Intermittent Preventive Treatment in Infants study (IPTi) in Lambaréné, Gabon

The IPTi study was a randomized, placebo-controlled, double-blind trial to reduce anemia and malaria by prophylactic administration of sulfadoxine/pyrimethamine or placebo to infants at the age of 3, 9, 15 month of age. Infants were followed up to the age of 30 months [12,13]. The study was conducted from December 2002 to April 2007. Recruitment at birth of 1189 infants at two Lambaréné hospitals took place between December 2002 and February 2005. Informed consent was obtained from primary caretakers before study related procedures were performed.

2.2.1. Evaluation of health status and adverse events in the IPTi study

To monitor health status of participating infants and to count adverse events, anemia and malaria cases, infants were actively followed up (and visited at home) once per month. Primary caretakers were encouraged to present the infant participating in the IPTi study in case of illness at the study center for medical examination and treatment free of charge. Additional examinations at the study center were performed for study drug administration at the age of 3, 9, 15 months. Study drug administration and study related blood sampling (at months 3, 9 and 15) was performed when there were no signs of acute illness. In case of acute illness, study drug related procedures were postponed. In case of malaria infants were treated according to the IPTi study protocol [12]. An additional final examination took place at the age of 30 months. On each visit, the health status of study participants was assessed and reported illnesses were recorded.

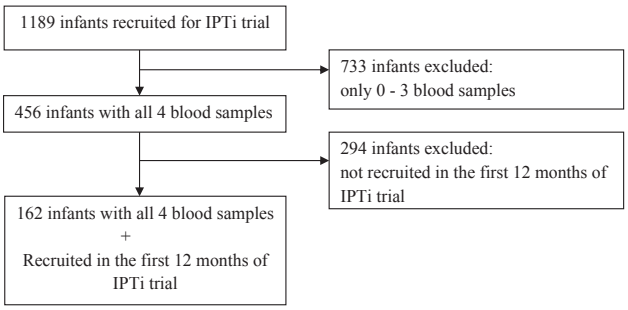

Figure 1 Study flow chart.