Rift Valley fever in Mayotte : from surveillance to genome detection

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Introduction

Rift valley fever virus (RVFV) usually causes large explosive epidemics in animals and human illness and circulates in many African countries as well as in the Arabian Peninsula. The medical and veterinary importance of this mosquito-borne virus was again highlighted at the end of 2006 and early 2007, when a large epidemic-epizootic occurred in East Africa and Madagascar, during two successive rainy seasons. More recently, South Africa and Mauritania were severely affected. This wide dissemination potential emphasizes that RVF constitutes a threat for the whole African continent and beyond, both for human and animal health. In July 2007, recent RVF infection was detected in Mayotte in a 12 year old boy with a severe neuroinvasive illness. This patient had recently arrived from Grande Comore, Union of the Comoros where RVF circulation had been confirmed.

Given the proximity of Comoros and Mayotte, the RVF situation was assessed in Mayotte among human beings and in susceptible ruminants, from April 2008 onwards. Serum samples from seven human cases of dengue-like syndromes were detected with the presence of anti-RVFV IgM or RVFV RNA. Here we report on one hand the isolations and the full sequence analysis of two RVF viral isolates from these human sera and on the other hand RVF animal seroprevalence evaluated with a series of four surveys. A first preliminary survey targeted illegally introduced goats and cattle living in the northern part of Mayotte, where most illegal imports are thought to occur owing to the proximity with the Comoros island of Anjouan (Figure 1). To capture a broader view of the situation, a second island-wide serological survey in ruminants was carried out in 2007-2008. To increase knowledge on the history of the virus in the island, a four-year (2004-2007) retrospective survey in ruminants was implemented. Finally, to assess whether the virus was still circulating in 2008, a longitudinal study was implemented on goat farms.
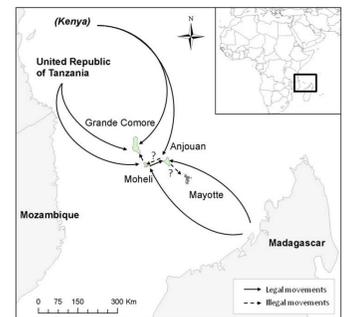

Figure 1: Potential legal and illegal movements of animals around the Comoros and Mayotte

Material & Methods

RVF prevalence in domestic animals

104 June 2007 to May 2008 **301**

ELISA

Competitive ID-Screen RVF ELISA (ID-Vet, Grabels, France)

Cross-sectional and retrospective study

130 animals (bovine) for each of the following years : Year 2004, 2005, 2006 and 2007

Human genome detection and sequencing

Seven patients were admitted to the hospital for severe dengue-like syndromes : two patients were found RVF seropositive (IgM and IgG) and the 5 others were RVF specific RT-PCR positive.

RVFV isolates were obtained on VeroE6 cells from the serum of two hospitalized patients (sera collected respectively on 21/02/2008 and 20/03/2008) and sequenced using the Big Dye Terminator v1.1 cycle sequencing kit (Applied Biosystems).

Maximum likelihood and the Bayesian inference methods for phylogenetic reconstruction were used. The best models of nucleotide substitution for each data set were selected from the uncorrected and corrected Akaike Information Criterion, the Hannan and Quinn performance-based decision theory and Bayesian Information Criterion of Jmodeltest version 0.1 and Treefinder version October 2008. Comparison of the maximum likelihood method implemented by the TreeFinder program with others was performed on the S, M and L segments using the neighbour joining and maximum parsimony methods from Mega5 software and the Bayesian approach using MrBayes v3.0B4 for phylogenetic reconstruction with random starting trees and run for 2,000,000 generations, sampling the Markov chains at intervals of 100 generations. Branch support values were obtained using non parametric bootstrapping with 1000 resampling for PhyML and Treefinder and the posterior probabilities for the Bayesian approach estimated on 10,000 samples (sample frequency set to every 100th generation using the Markov Chain Monte Carlo sampling). Topologies of the maximum likelihood and Bayesian trees obtained for the different segments were compared.

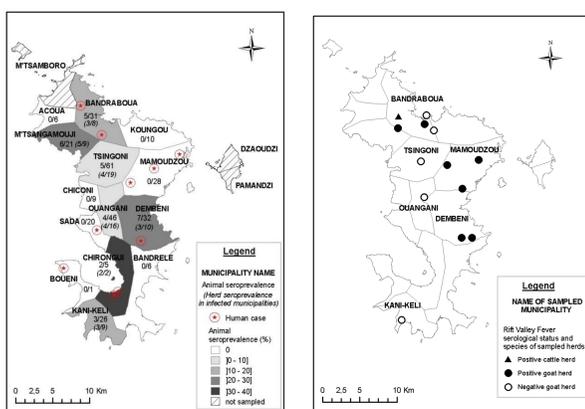## Results

RVF prevalence in domestic animals

Figure 2: Rift Valley fever in Mayotte. a. human cases and animal and herd seroprevalences, b. status of herds sampled for the longitudinal serological study

A total of 301 bovine sera sampled from June 2007 to May 2008 in 104 different farms and 17 different districts located all over the island were analysed for RVFV exposure by competitive IgG ELISA for the specific detection of RVF antibodies. Thirty two sera were found positive in 9 different districts. The overall apparent RVF seroprevalence was 10.6% (95% CI 7-14) supported by the high specificity of the ELISA test. The thirty two positive sera were distributed all over the island (Figure 2)

Phylogenetic relationships

The complete genome sequences performed on 2 human RVF isolates from Mayotte referenced as 2008/00099 and 2008/00101 (Deposited in GenBank/EMBL under accession numbers HE687302-HE687307) are embedded within the larger 2006-2007 East African clade, specifically within the lineage previously termed Kenya-1 (Figure 3)
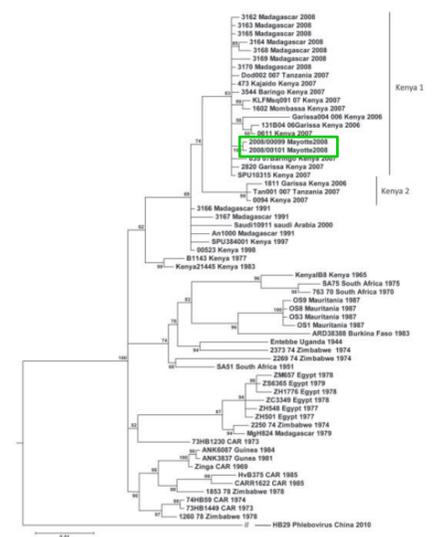

Figure 3: Fifty-two complete sequences of RVF S segments aligned and analysed by either ML techniques with 1,000 replicate bootstrap values or the Bayesian approach.

Cross-sectional and retrospective study

Year	Seroprevalence (%)	Nb Pos/Total Nb
2004	22.66	29/130
2005	3	4/130
2006	12.31	16/130
2007	30.95	39/126

The serological animal surveys carried out in Mayotte revealed medium to high percentages of RVF seroprevalence distributed all over the island. Results of the 4-year study show that the virus was already present in 2004. Following a low level of seroprevalence in 2005, the increase of seroprevalence in 2006 and 2007 suggests that the virus had re-circulated or that a new introduction had occurred.
It is unclear why a relatively important circulation of RVF in Mayotte with seroprevalence rising to 22% did not result in detectable clinical cases in animals while RVF was diagnosed in human patient sera with brain disorders. This may be due to the density of susceptible animals in the island being sufficient for virus circulation but too low for supporting epidemic abortion and mortality waves. This study, coupled with the epidemics in East-Africa illustrates the risk of introduction to Mayotte or other Comoros islands of infectious agents from the African mainland. Entomological studies need to be continued to identify all potential vector species on the island and to better understand the ecological and climatic factors which favor RVFV dissemination. The role of wildlife should also be investigated.

Acknowledgements