



# Rift Valley Fever

## An emerging mosquito born virus

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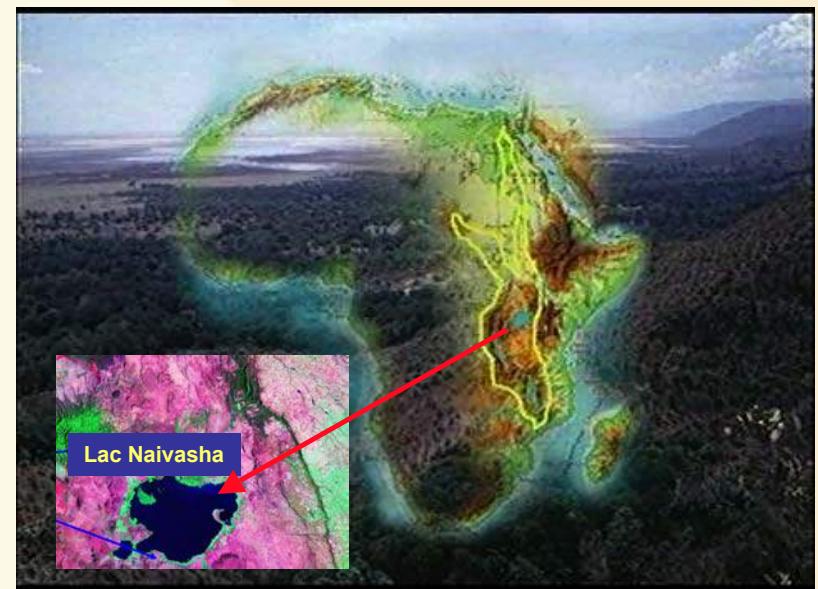


MediLabSecure regional meeting\_ RVF \_Tunisia 4 July 2017\_MDIALLO



## History

- 1912-1913, clinical description, Naivasha Lake, Kenya
- 1930, First evidence of RVF outbreak in Kenyan
- 1930, First isolation of the virus in Kenya (Daubney *et al.*, )
- **Person in close contact with animal mostly infected (direct contamination)**
  - farmer, herdsmen, slaughterhouses, the butchers are persons at risk
- **Suspicion of transmission by mosquito bite**
  - The disease was associated with particular ecological environment
  - Animal at high altitude not affect (i.e. disease under control when animals are setting at altitude)

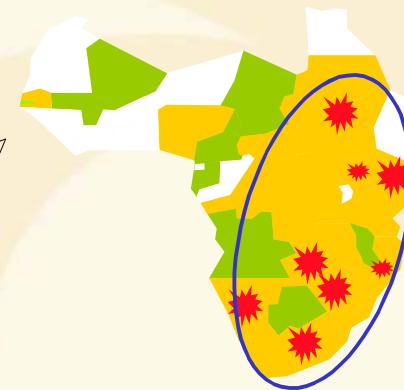




1912 -1930



1930-1951



1951-1976



1977-2015

- **Until 1976 Outbreak recorded limited in the Eastern and Southern part of Africa**

- 1977: First outbreak in North Africa Egypt (600 human death)
- 1987: First Outbreak, West Africa Mauritania (220 death)
- 1990 : First outbreak in Madagascar Island
- 2000: First outbreak out of African continent (Saudia, Yemen)



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# Transmission cycles East Africa



Amplification Cycle

*Aedes spp*  
*Culex spp*  
*Mansonia*



Epidemic/epizootic cycle



Infected mosquitoes  
after heavy rain

*Ae. mcintoshi (EA)*



Enzootic Cycle  
(temporary Ponds  
i.e **Dambos** in Kenya)

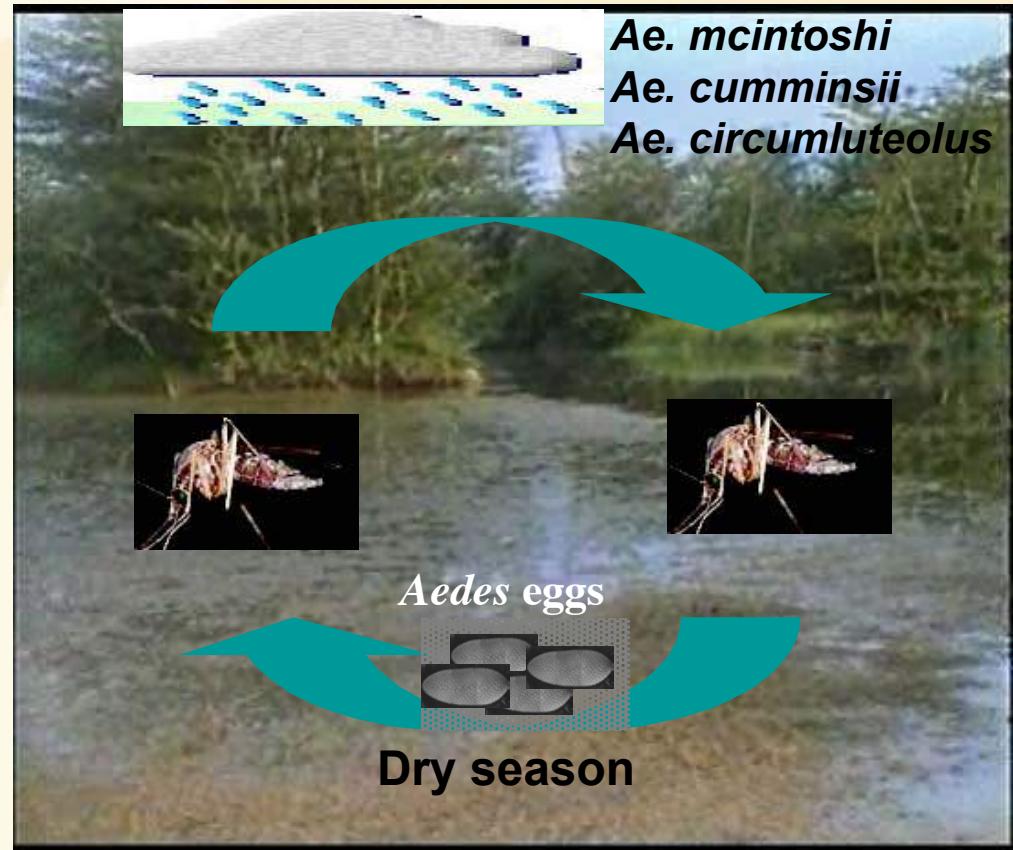




# Transmission cycle East Africa

## The enzootic cycle

- Maintenance of the virus in **Aedes** mosquito eggs during inter-epizootic periods (*Ae. mcintoshi*)
- Emergence following heavy rainfall à



Epidemic/epizootic cycle



# Transmission cycle

*East Africa*



## Observations supporting the existence of an enzootic cycle

- Periodicity of the virus circulation (long period of silence)
- Any reservoir identified during that period
- Evidence of vertical transmission by *Ae. mcintoshi* (ex. *lineatopennis*) collected from ponds artificially flooded during the dry season
- The disease emergence took place concurrently, in areas distant from several hundreds of kms



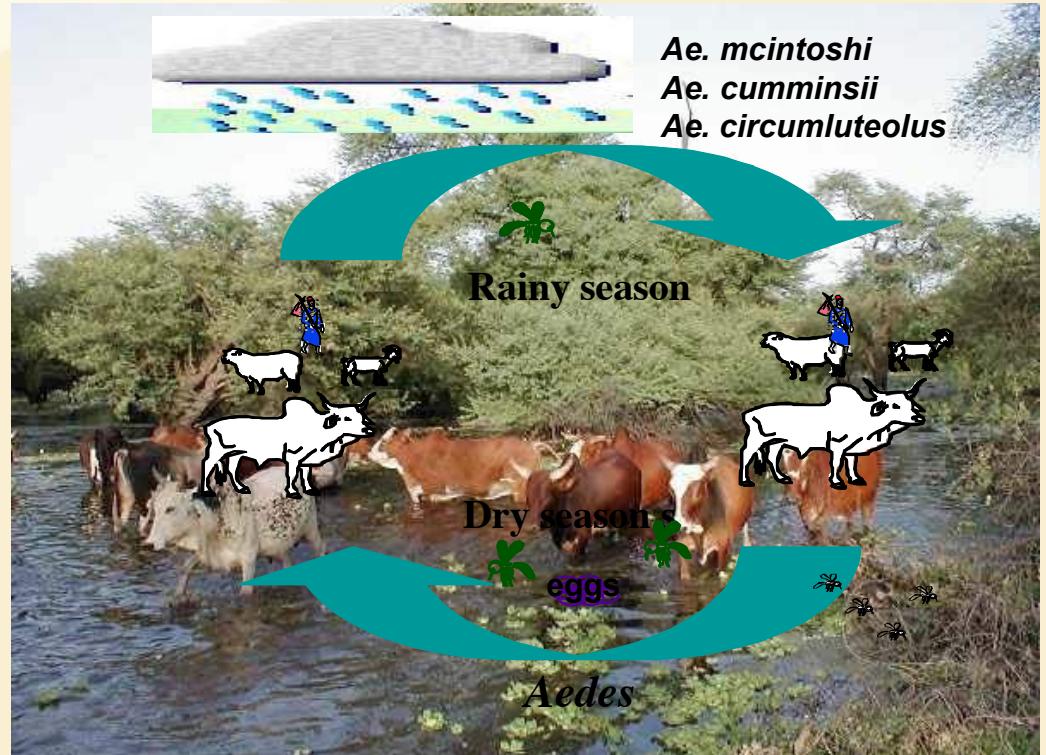
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# Transmission cycle East Africa

## The Amplification cycle

- High mosquito density
- Involvement vector other than Aedes
- Concentration of animal
- Increasing density of animals susceptible to the virus



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## Epidemic/epizootic transmission

- Transmission by mosquitoes (*Aedes*, *Culex*...)
- Other mode of contamination to human
  - Direct contact, with tissues and blood of infected animal
  - Aerosol



Epidemy/epizooty /  
Domestic environment

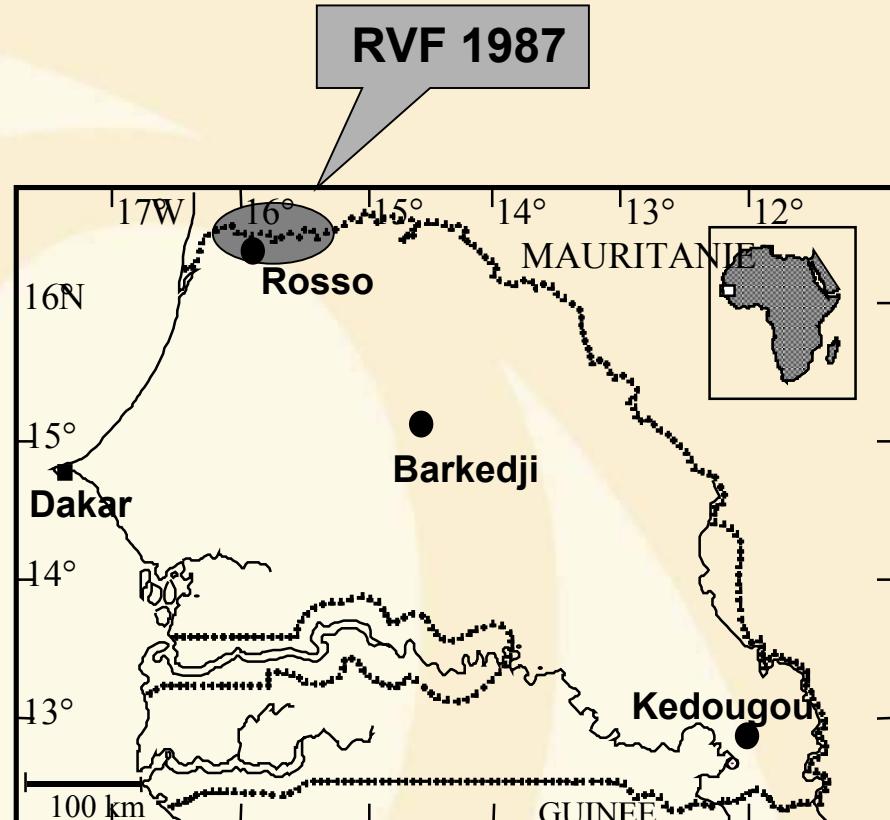


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# Transmission cycle West Africa - Senegal

- Programme set up in Barkedji
- Barkedji selected based on east Africa transmission cycle
  - Sylvo-pastoral zone,
  - network of temporary ponds exist



The main mosquito species looked for was ***Aedes mcintoshi***





# Mosquito sampling



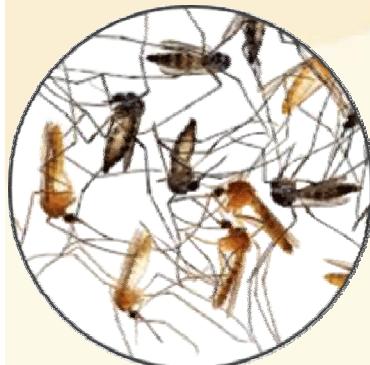
*CDC Light Trap/Animal Bait trap*



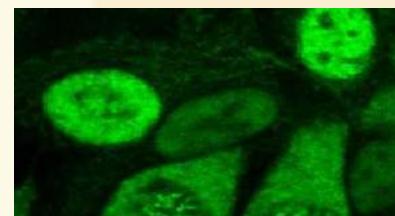
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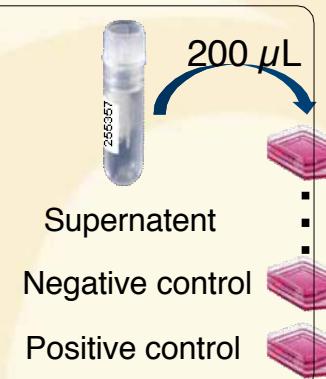
# Virus detection



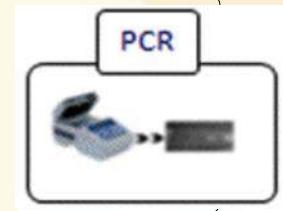
**Trituration  
&  
Centrifugation**



etc.



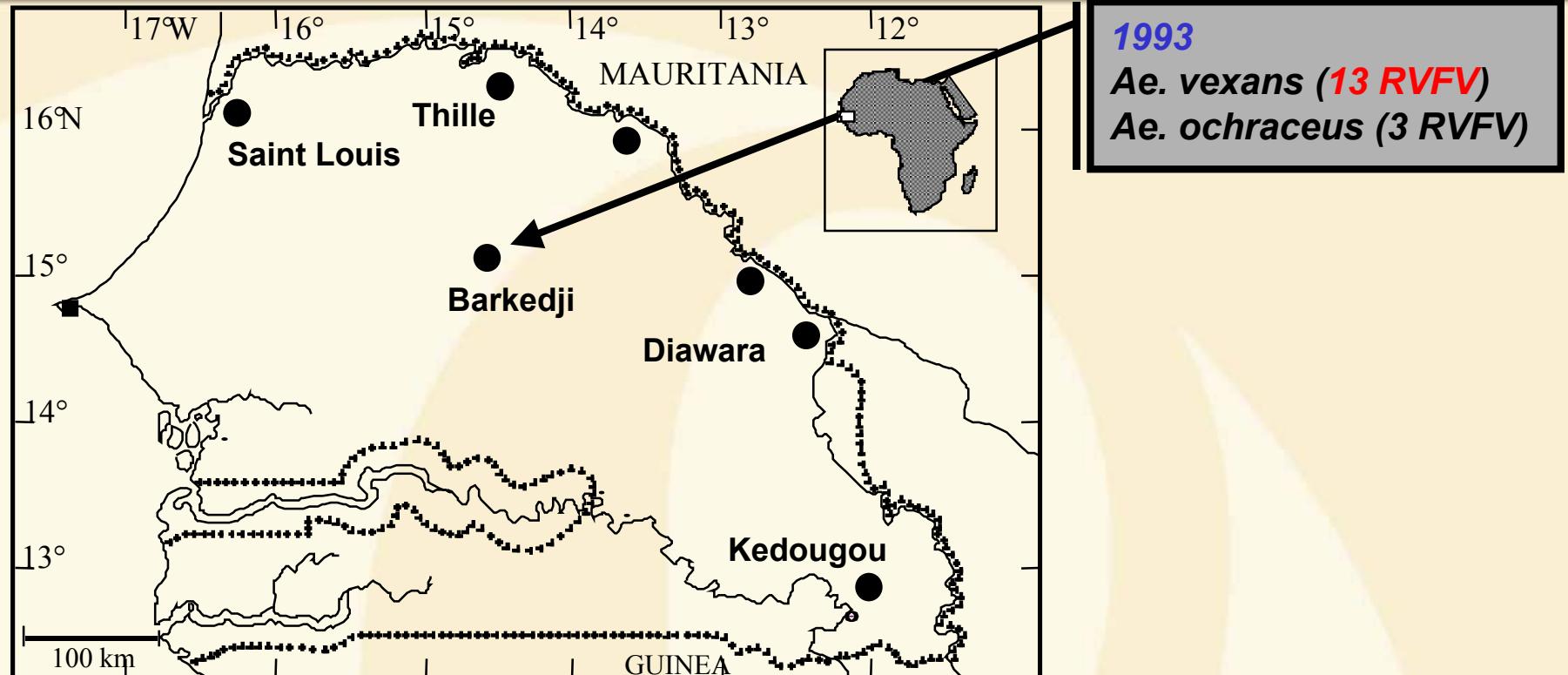
RT – PCR



**Real time or  
Conventional**



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- *Ae. mcintoshi* the East african vector rare in the study area
- *Ae. vexans* and *Ae. ochraceus* were first found infected.



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# Transmission cycle West Africa



**Probable Vectors**  
*Aedes vexans*  
*Aedes ochraceus*

**Transmission cycle likely similar to the East Africa cycle except for vectors**

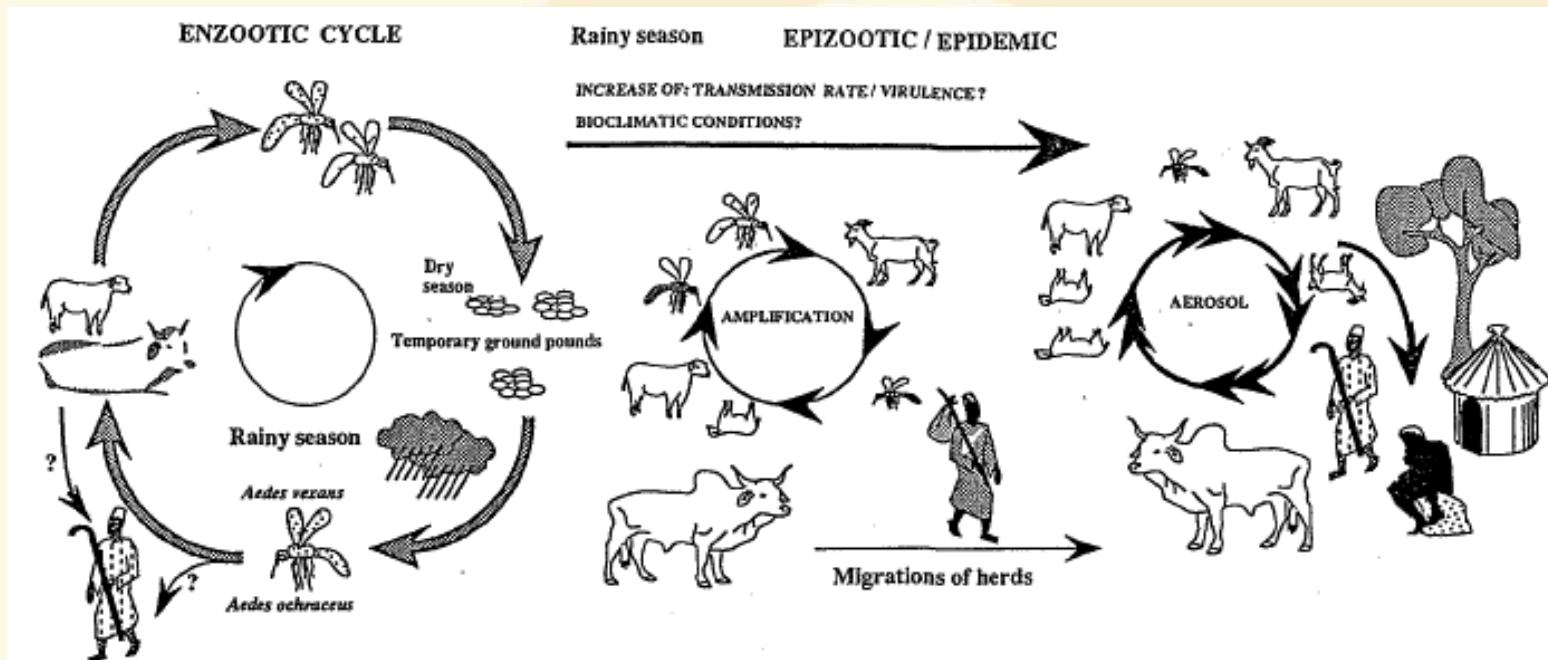
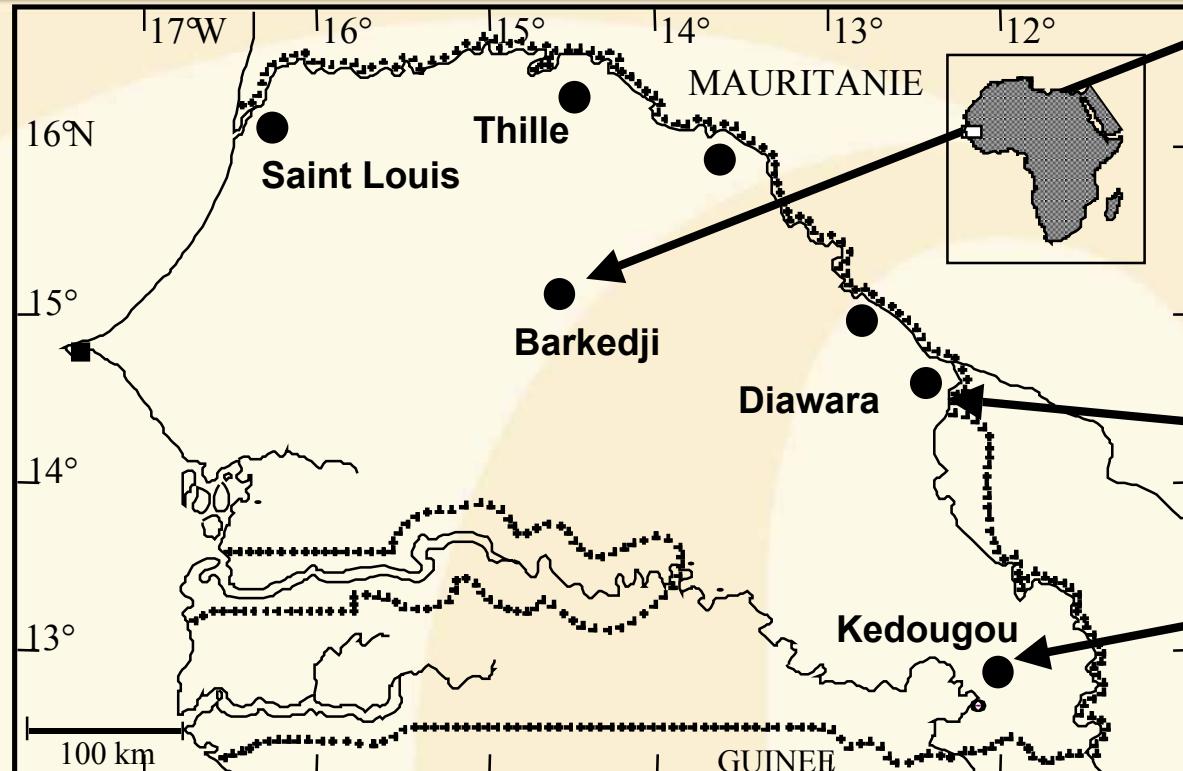


FIGURE 3. Possible cycles of Rift Valley fever in Sahelian western Africa with an enzootic virus maintenance around temporary ground pools involving *Aedes vexans* and *Ae. ochraceus* primarily vectors and epizootic/epidemic amplifications involving various mosquito species, movements of animals, and direct transmission (aerosol, contact with abortion products).

Zeller et al., 1997 AJTMH



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1993 ; 2002 ; 2003  
*Ae. vexans* (50 RVFV)  
*Ae. ochraceus* (3 RVFV)  
*Ae. fowleri* (1 RVFV)  
*Cx. poicilipes* (32 RVFV)  
*Ma. africana* (2 RVFV)  
*Ma. uniformis* (1 RVFV)

1998  
*Cx. poicilipes* (36 RVFV)

1974 ; 1983  
*Ae. dalzieli* (4 RVFV)

- *Ae. mcintoshi* the East african vector rare in the study area
- 7 mosquito species found naturally infected by RVFV
- First isolation of RVFV from *Cx. poicilipes*
- *Ae. vexans* and *Cx. poicilipes* as main vector because of their abundance





# Transmission cycle West Africa



## Probable Vectors

*Aedes vexans*

*Aedes ochraceus*

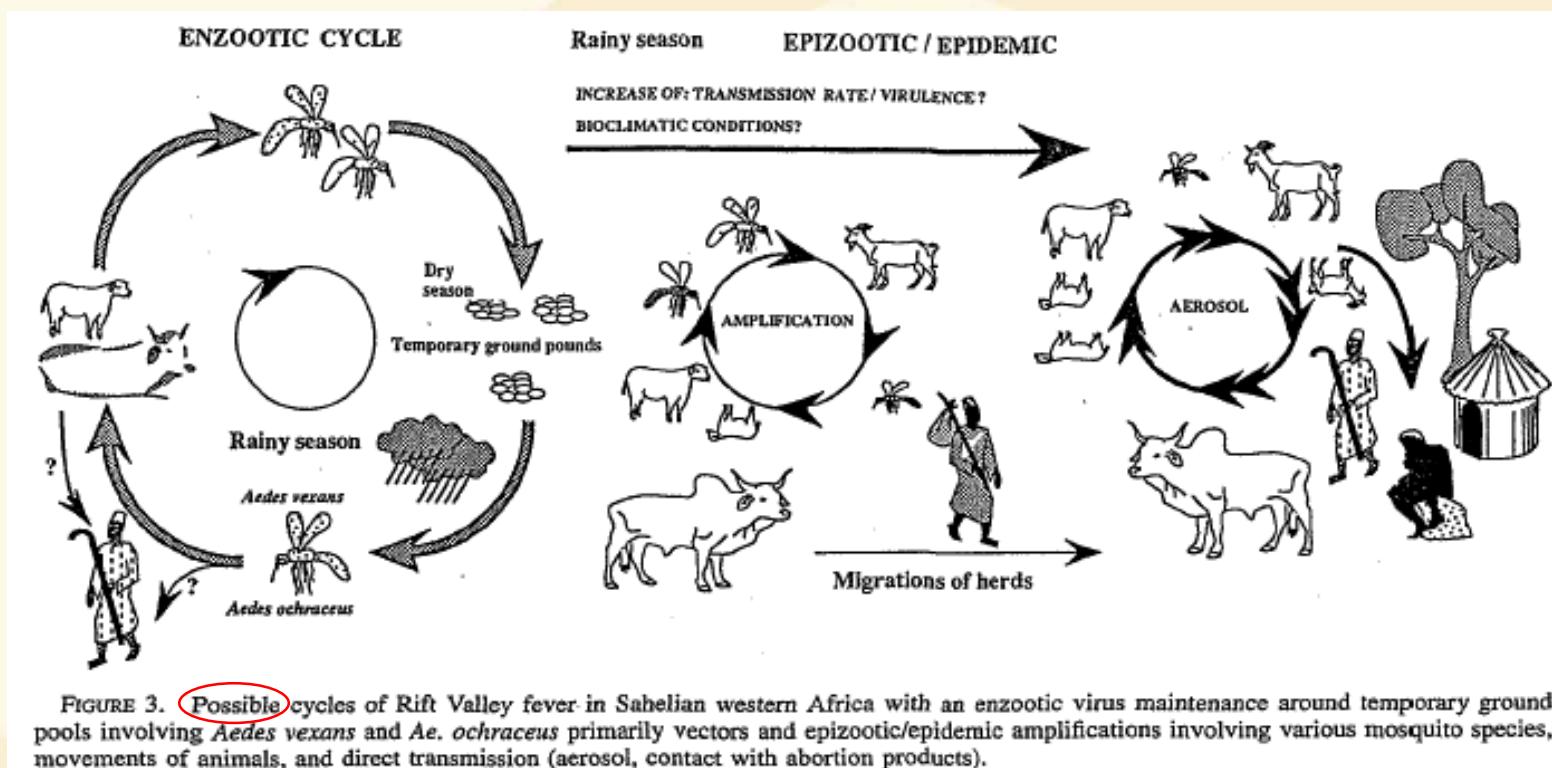
*Ae. fowleri*

*Ae. dalzielii*

*Ma. uniformis*

*Ma. africana*

*Culex poicilipes*



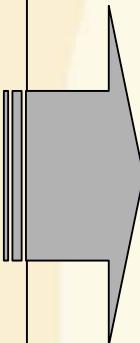
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The only association with the virus in nature is not enough to classify an arthropod as a vector.

## Type of vectors

- Possible vector
- Probable vector
- Proven vector



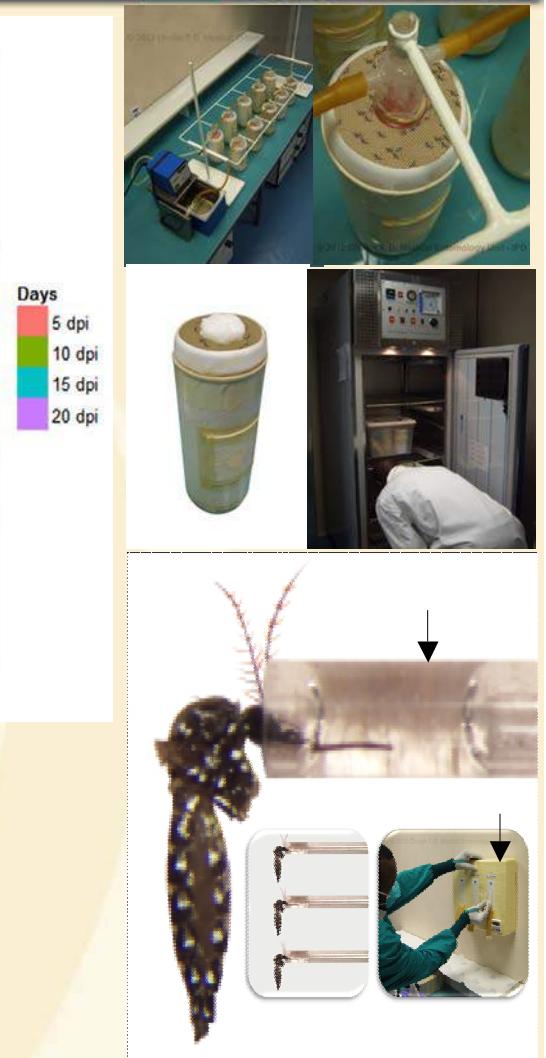
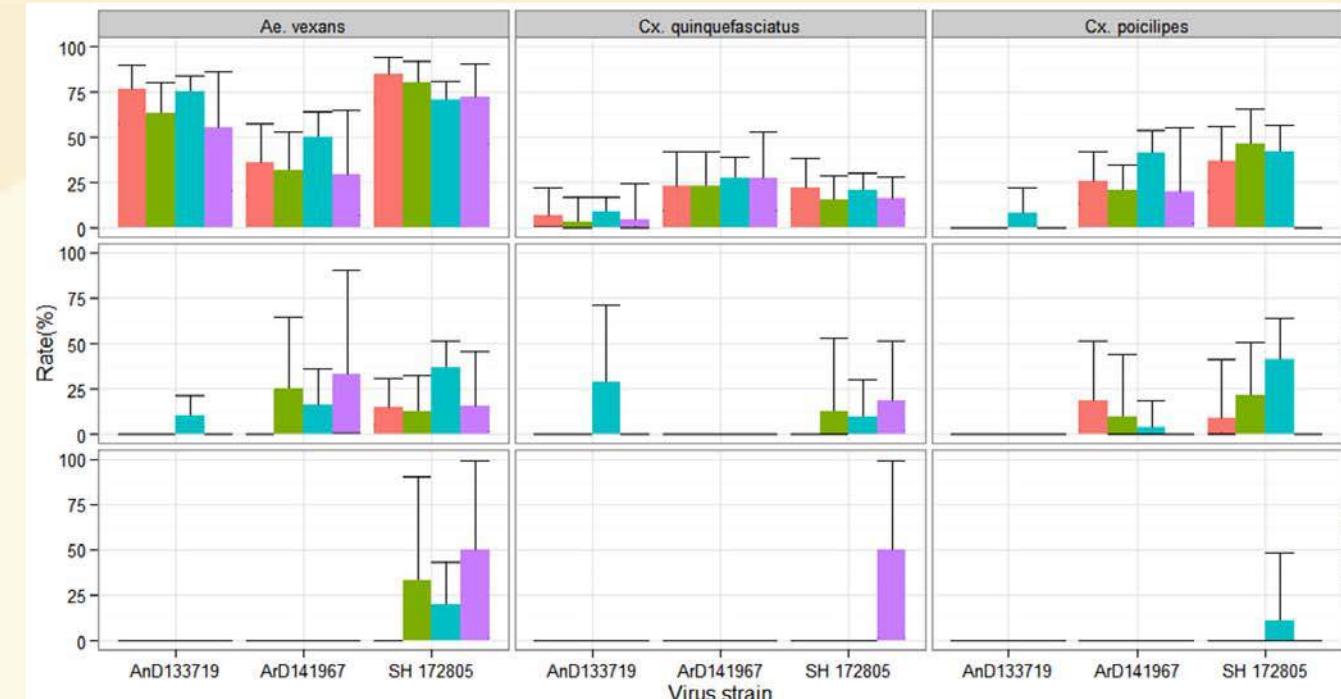
## Parameter to be study

- Vector competence
- Population dynamic
- Feeding pattern
- Dispersal activity
- Other entomological parameters impacting vecotrial capacity
- Etc.





# Vector competence to RVF virus strains isolated from Human, Mosquito and Animal



## Main findings

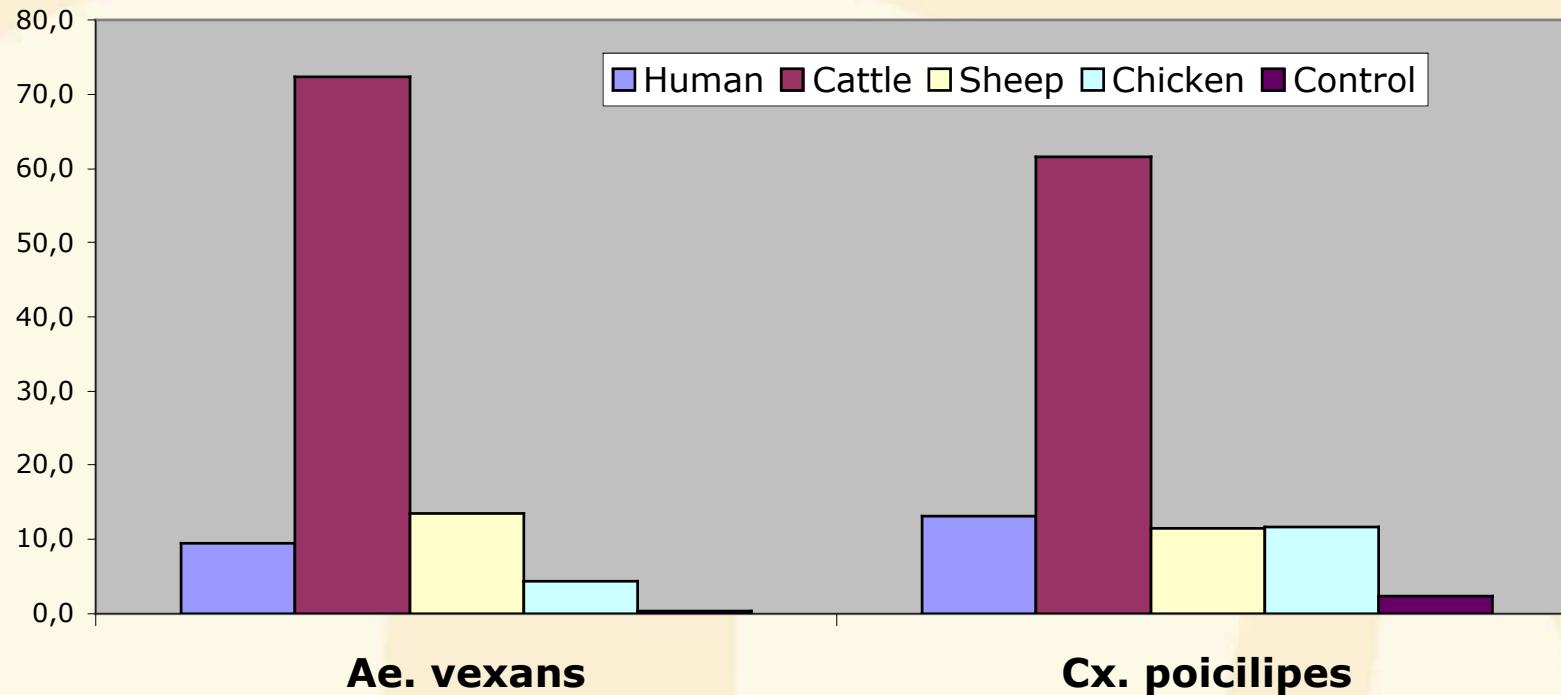
- **Culex less susceptible to RVFV than Aedes**
- **The « animal » strain less infectious**
- **The Human strain (East African lineage) the only virus strain transmitted**



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## Feeding pattern/Attractiveness

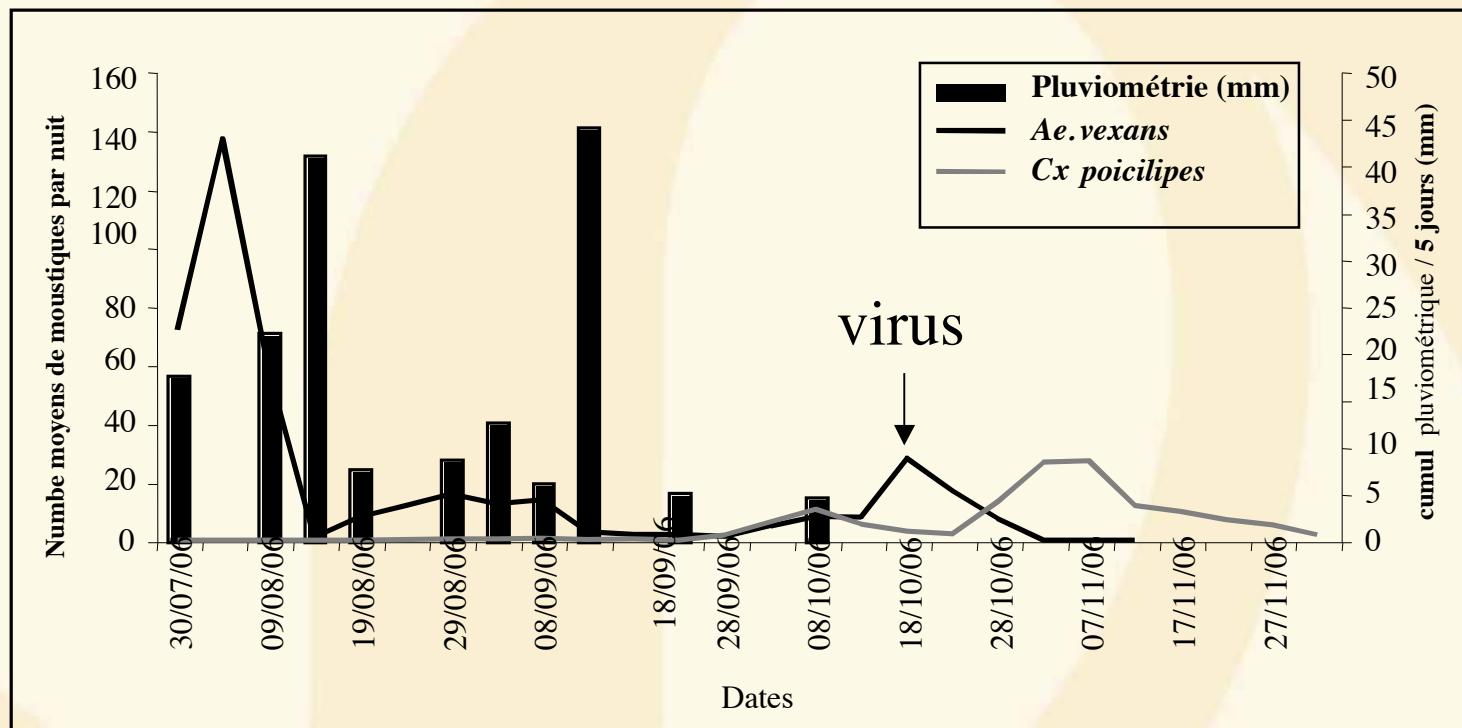




# Population dynamic



- Temporal dynamic of the vectors (daily, fortnight, monthly / period)
- A better appreciation of Rainfall impact in contradiction with the concepts developed in East Africa.
- Rain distribution/break as the key element (most important than surplus)



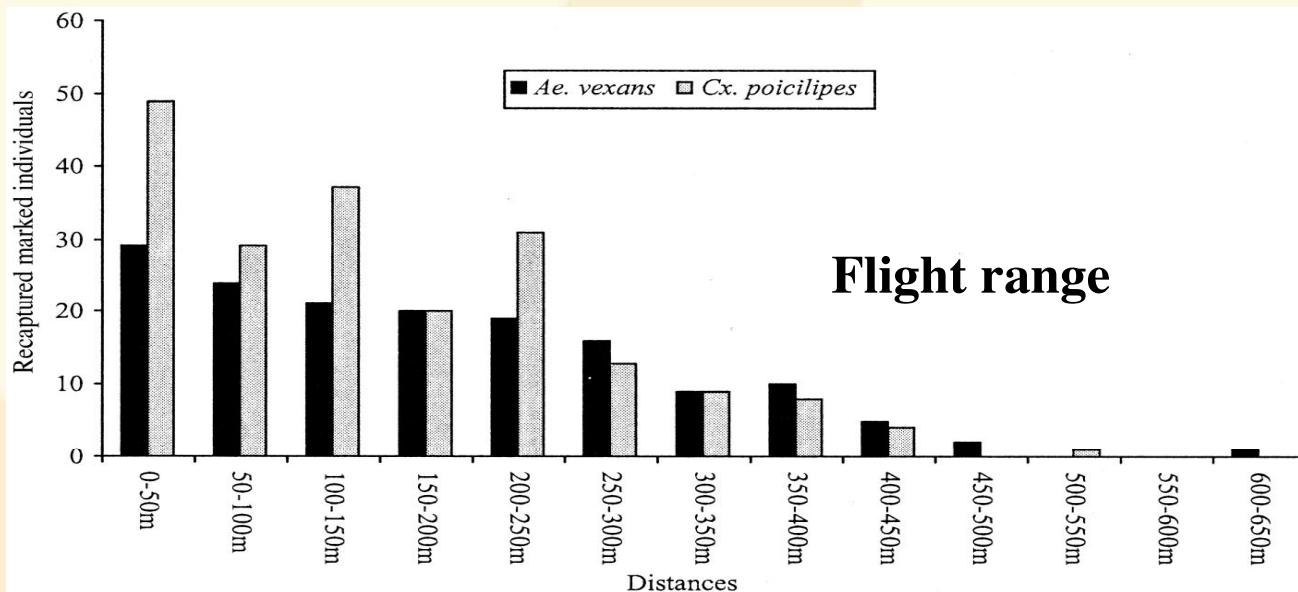


# Dispersal activity

## Mark -release-recapture



- ✿ Maximum distance the first night of release (Day 0) were :
  - ✿ 400m for *Ae. vexans*
  - ✿ 550m for *Cx poicilipes*
- ✿ The longest flight range of *Ae vexans* was 650m
- ✿ For *Cx. poicilipes* it was 550 m

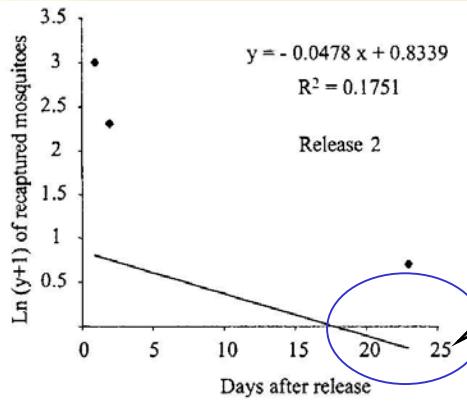
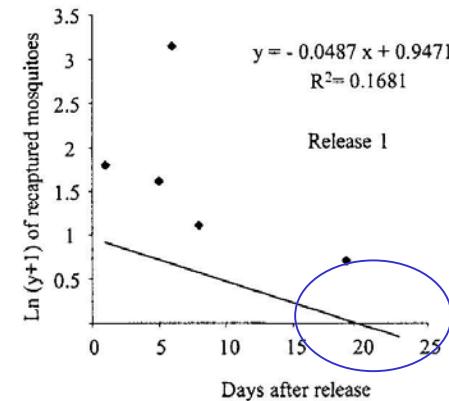


- Fluorescent powder
- color for each release.
- One site for release
- Exposition to U.V of recaptured looking for marked specimens

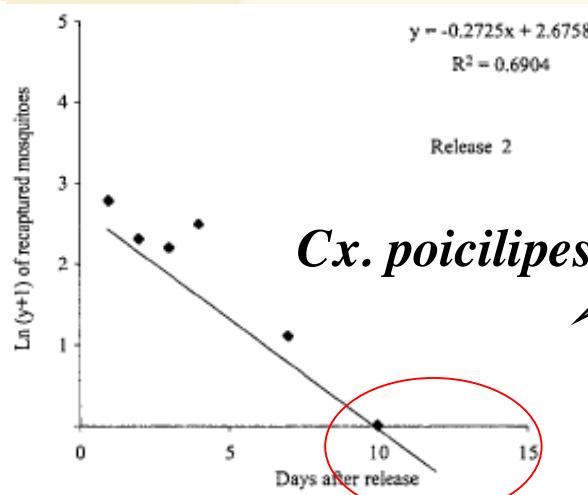
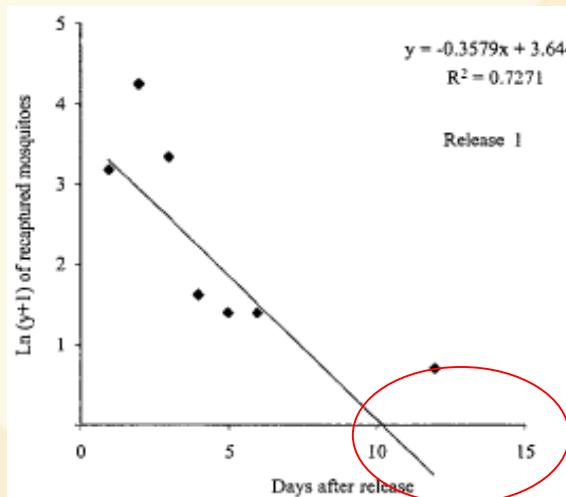




# Longevity/ Survival rate



$\ln(y+1) = -0.384x + 3,836$   
 $e^a = 0,86$   
**Survival rate = 86%**



$\ln(y+1) = -0.384x + 3,836$   
 $e^a = 0,68$   
**Survival rate = 68%**

Aspects of Bioecology of Two Rift Valley Fever Virus Vectors in Senegal (West Africa): *Aedes vexans* and *Culex poicilipes* (Diptera: Culicidae)

YAMAR BA,<sup>1</sup> DIAWO DIALLO,<sup>1</sup> CHEIKH MOUHAMED FADEL KEBE,<sup>2</sup> IBRAHIMA DIA,<sup>1</sup> AND MAWLOUTH DIALLO<sup>1</sup>

J. Med. Entomol. 42(5): 739-750 (2005)

**Low Survival rate & longevity for Cx. poicilipes**



# Population size of RVFV Vectors



## *Ae. vexans*

Release	Dates	Populations size	mean
1	17/8/02	11 505 600	
	21/08/02	5 295 840	
	24/08/02	356 072	4 907 044
2	26/08/02	2 470 666	
	27/08/02	2 390 560	2 411 745
3	5/09/02	2 432 930	
	6/09/02	4 633 222	
	7/09/02	2 626 400	
	9/09/02	1 417 733	2 586 451
4	13/09/02	2 563 842	
	14/09/02	619 650	
	16/09/02	1 189 575	
	17/09/02	76 500	1 112 391
5	13/10/02	207 050	
	14/10/02	999 900	
	15/10/02	747 400	
	16/10/02	2 340 675	
	17/10/02	35 865 100	
	18/10/02	9 648 025	
	19/10/02	8 251 700	8 294 264

## *Cx. poicilipes*

Dates	Populations size	mean
4/11/02	156 906	
5/11/02	75 193	
6/11/02	133 000	
7/11/02	173 460	
8/11/02	341 162	
9/11/02	350 962	205113
16/11/02	133 165	
17/11/02	200 595	
18/11/02	157 905	
19/11/02	170 387	
22/11/02	586 950	249 800
24/11/02	39 750	
25/11/02	23 400	
26/11/02	28 600	
27/11/02	13 050	
28/11/02	37 200	28 400





# Vectors recorded elsewhere



## Arthropodes naturally infected by Rift Valley fever virus (RVFV)

Espèces	Pays	Références bibliographiques
<i>Aedes</i>		
<i>cunimmissii</i>	Burkina Faso	Saluzzo <i>et al.</i> , 1984
	Kenya	Linthicum <i>et al.</i> , 1985
<i>dalzielii</i>	Sénégal	Fontenille <i>et al.</i> , 1998
<i>ochraceus</i>	Sénégal	Fontenille <i>et al.</i> , 1995
<i>vexans arabiensis</i>	Sénégal	Fontenille <i>et al.</i> , 1995
<i>dentatus</i>	Arabie Saoudite	Jupp <i>et al.</i> , 2002
<i>tarsalis</i>	Zimbabwe	McIntosh, 1972
<i>durbanensis</i>	Ouganda	Smithburn <i>et al.</i> , 1948
<i>circumluteolus</i>	Kenya	Mulligan, 1937
	Ouganda	Weinbren <i>et al.</i> , 1957
	Afrique du Sud	Kokernot <i>et al.</i> , 1957; Jupp <i>et al.</i> , 1983
<i>mcintoshi</i>	Zimbabwe	McIntosh, 1972
	Afrique du sud	McIntosh <i>et al.</i> , 1980
	Kenya	Linthicum <i>et al.</i> , 1985
<i>palpalis</i>	Rép. Centre Africaine	Digoutte <i>et al.</i> , 1974
<i>Ochlerotatus</i>		
<i>caballus</i>	Afrique du Sud	Gear <i>et al.</i> , 1955
<i>caspicus</i>	Egypte	Turell <i>et al.</i> , 1996
<i>juppi</i>	Afrique du Sud	McIntosh <i>et al.</i> , 1980
<i>Stegomyia</i>		
<i>africanus</i>	Ouganda	Weinbren <i>et al.</i> , 1957
<i>dendrophilus</i>	Ouganda	Smithburn <i>et al.</i> , 1948
<i>Diceromyia</i>		
<i>groupe furcifer</i>	Burkina Faso	Saluzzo <i>et al.</i> , 1984
<i>Anopheles</i>		
<i>coustani</i>	Zimbabwe	McIntosh <i>et al.</i> , 1972
<i>coustani and fusicolor</i>	Madagascar	Clerc <i>et al.</i> , 1982
<i>Cinereus</i>	Afrique du Sud	McIntosh <i>et al.</i> , 1980
<i>pauliani and squamosus</i>	Madagascar	Clerc <i>et al.</i> , 1982
<i>christyi</i>	Kenya	Linthicum <i>et al.</i> , 1985
<i>pharoensis</i>	Kenya	Linthicum <i>et al.</i> , 1985
<i>Culex</i>		
<i>antennatus</i>	Kenya	Linthicum <i>et al.</i> , 1985
	Nigeria	Lee, 1979
<i>antennatus, annulioris gp., simpsoni, and vansomereni</i>	Madagascar	Clerc <i>et al.</i> , 1982
<i>antennatus, simpsoni, and vansomereni</i>	Kenya	Linthicum <i>et al.</i> , 1985
<i>pipiens</i>	Egypte	Hoogstraal <i>et al.</i> , 1979; Meegan <i>et al.</i> , 1980
<i>neavei</i>	Afrique du Sud	McIntosh <i>et al.</i> , 1983
<i>poicilipes</i>	Sénégal	Diallo <i>et al.</i> , 2000
	Mauritanie	Diallo <i>et al.</i> , 2005

## Arthropodes experimentally competent for RVFV in the laboratory

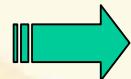
Espèce	Mode de transmission	Références bibliographiques
<i>Aedes</i>		
<i>Ae. mcintoshi</i>	Biologique	McIntosh <i>et al.</i> , 1980
<i>Ae. circumluteolus</i>	Biologique	McIntosh <i>et al.</i> , 1983
<i>Ae. caballus</i>	Biologique	Gear <i>et al.</i> , 1955
<i>Ae. Juppi</i>	Biologique	McIntosh <i>et al.</i> , 1980
<i>Ae. unidentatus</i>	Biologique	Jupp & cornell, 1988
<i>Ae. dentatus</i>	Biologique	Jupp & cornell, 1988
<i>Ae. fowleri</i>	Biologique	Turell <i>et al.</i> , 1988 a
<i>Ae. vexans arabiensis</i>	Biologique	Jupp <i>et al.</i> , 2002
<i>Ae. caspius</i>	Biologique	Gad <i>et al.</i> , 1987; Turell <i>et al.</i> , 1996
<i>Ae. triseriatus</i>	Biologique	Gargan <i>et al.</i> , 1988
<i>Ae. argenteopunctatus</i>	Biologique	Jupp & cornell, 1988
<i>Ae. taeniorhynchus</i>	Biologique/mécanique	Hoch <i>et al.</i> , 1985; Gargan <i>et al.</i> , 1988 McIntosh <i>et al.</i> , 1980; Hoch <i>et al.</i> , 1983
<i>Ae. aegypti</i>	Biologique/mécanique	1985
<i>Ae. aegypti formosus</i>	Mécanique	Gillet & Mims, 1956; Jupp <i>et al.</i> , 1984
<i>Ae. albopictus</i>	Biologique	Turell <i>et al.</i> , 1988 b
<i>Ae. canadensis</i>	Biologique	Gargan <i>et al.</i> , 1988
<i>Ae. cantator</i>	Biologique	Gargan <i>et al.</i> , 1988
<i>Ae. excrucians</i>	Biologique	Gargan <i>et al.</i> , 1988
<i>Ae. sollicitans</i>	Biologique	Gargan <i>et al.</i> , 1988
<i>Ae. notoscriptus</i>	Biologique	Turell & Hay, 1998
<i>Ae. vigilax</i>	Biologique	Turell & Hay, 1998
<i>Anopheles</i>		
<i>Anopheles bradleyi-cruciatus</i>	Biologique	Gargan <i>et al.</i> , 1988
<i>An. multicolor</i>	Biologique	Gad <i>et al.</i> , 1987
<i>An. pharoensis</i>	Biologique	Gad <i>et al.</i> , 1987
<i>Coquillettidia</i>		
<i>Cq. versicolor</i>	Biologique	Daubney & Hudson, 1933
<i>Culex</i>		
<i>Cx. pipiens</i>	Biologique/mécanique	Turell <i>et al.</i> , 1996; Hoch <i>et al.</i> , 1985
<i>Cx. peregrinus</i>	Biologique	Turell <i>et al.</i> , 1996
<i>Cx. poicilipes</i>	Biologique	Jupp & cornell, 1988
<i>Culex salinarius</i>	Biologique	Gargan <i>et al.</i> , 1988
<i>Cx. tarsalis</i>	Biologique	Gargan <i>et al.</i> , 1988
<i>Cx. territans</i>	Biologique	Gargan <i>et al.</i> , 1988
<i>Cx. annulirostris</i>	Biologique	Turell & Hay, 1998
<i>Cx. quinquefasciatus</i>	Biologique/mécanique	Turell & Hay, 1998; Jupp <i>et al.</i> , 1984
<i>Cx. antennatus</i>	Biologique	Turell <i>et al.</i> , 1996
<i>Cx. neavei</i>	Biologique	McIntosh <i>et al.</i> , 1973
<i>Cx. theileri</i>	Biologique	McIntosh <i>et al.</i> , 1973, 1980
<i>Cx. tritaeniorhynchus</i>	Biologique	Jupp <i>et al.</i> , 2002
<i>Cx. univittatus</i>	Biologique	McIntosh <i>et al.</i> , 1980
<i>Cx. zombaensis</i>	Biologique	McIntosh <i>et al.</i> , 1983
<i>Eretmapodites</i>		
<i>E. chrysogaster</i>	Biologique	Smithburn <i>et al.</i> , 1949
<i>E. quinquevittatus</i>	Biologique	McIntosh <i>et al.</i> , 1980



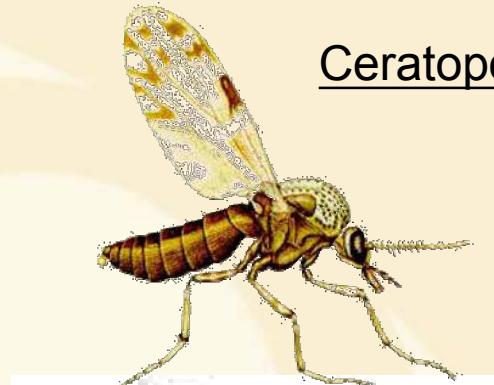


## *Insects other than mosquitoes and RVFV*

- other arthropods hematophagous found infected in nature
- Vector Competence not proven
  - Culicoides,
  - Simulies
  - tiques....



**Possible role in mechanic transmission**



Ceratopogonide



Simulie



Tique





# RVFV vectors

## *Other African regions*



### Other vectors identified

South Africa	Egypt	Madagascar	CAR
<i>Ae. caballus</i>	<i>Cx. pipiens</i>	<i>An. squamosus</i>	<i>Ae. palpalis</i>
<i>Ae. circumluteolus</i>		<i>An. pauliani</i>	<i>Ma. africana</i>
<i>Ae. mcintoshi</i>		<i>An. ziemanni</i>	
<i>Ae. juppi</i>		<i>Culex spp.</i>	
<i>Cx. Zombaensis</i>		<i>Ma. uniformis</i>	
<i>Cx. Theileri</i>		<i>Cq. grandidieri</i>	
<i>An. cinereus</i>			

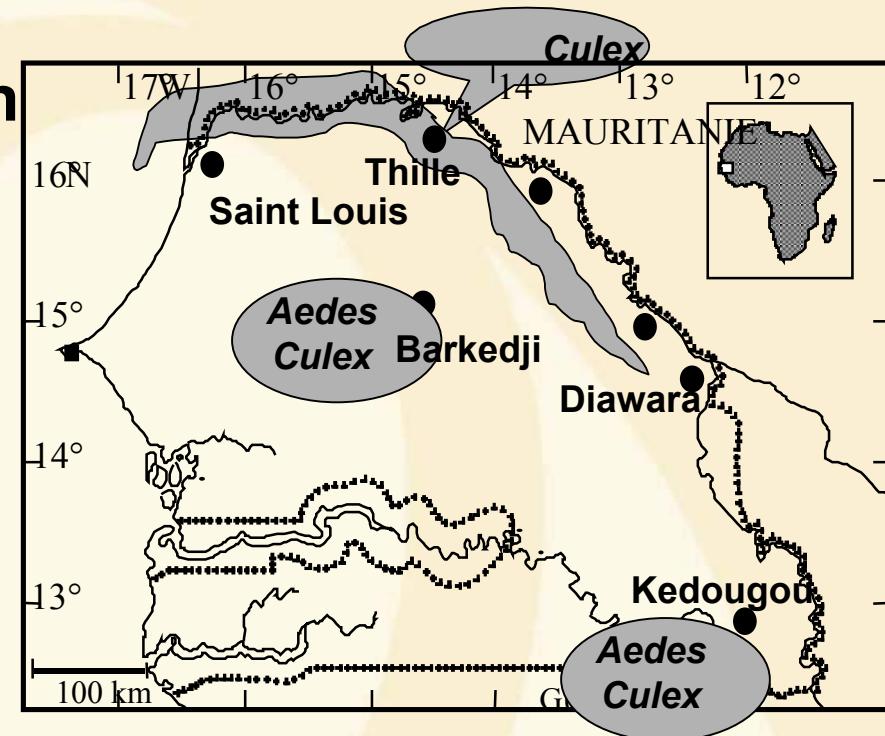




# Problematic of the transmission cycle

Not applicable to all geographic and ecological context

- Case of Egypt where the main vector was *Cx. pipiens*
- Madagascar *Culex sp*, *Anopheles sp* and *Ma. uniformis* unique vectors
- Senegal river where biggest outbreaks were recorded in West Africa with only *Culex*



Main question : The origin of the virus in these geographic contexts



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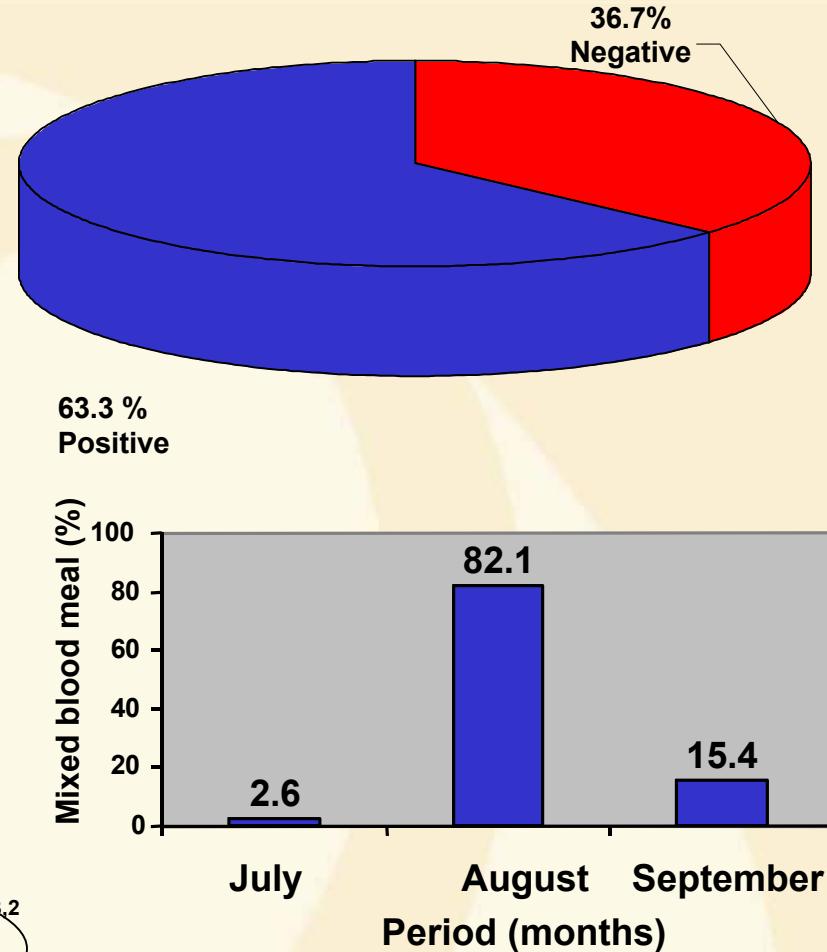
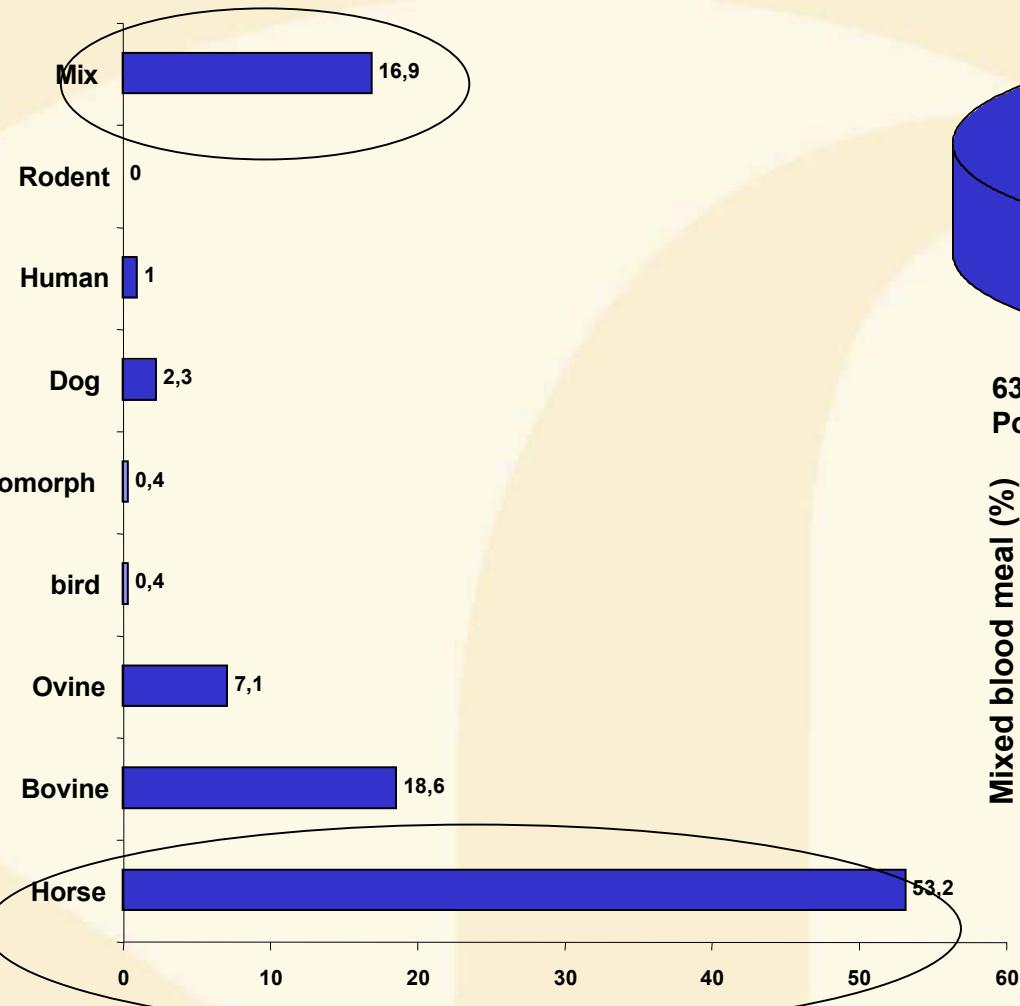
# Hypothesis. Existence of reservoirs

- Rodents highly suspected
  - abundance
  - promiscuity with human and domestic ruminants
  - Serologic record
    - *Aethomys namaquensis* from South Africa
    - *Arvicanthis niloticus* in Sénégal
- Bats also suspected
  - FVRV isolation in Guinea (Boiro et 1987)  
*Micropteropus pusillus, Hipposideros abae, Hipposideros caffer*
  - South Africa
  - *Miniopterus schreibersii & Eptesicus capensis*





# Feeding pattern of Ae. vexans



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# RVF and wild animals



## Recent evidence of the affection of wild ruminant



**Epizooty in Dorcas gazelles, Gueumbeul reserve, Saint-Louis, Sénegal in 2013**

- Frequency of abortion of dorcas since 2009
- High level of abortion in 2012-2013



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# RVF and Wild Ruminants

In South Africa in 2010 exotic and indigenous animals developed for the first time perceptible signs.

• Indigenous species affected :

- springbok (*Antidorcas marsupialis*),
- blesbok (*Damaliscus dorcas dorcas*),
- bontebok (*D. dorcas phillipsi*),
- waterbuck (*Kobus ellipsiprymnus*),
- African buffalo, sable (*Hippotragus niger*),
- kudu (*Tragelaphus strepsiceros*),
- nyala (*Tragelaphus angasii*)
- gemsbok (*Oryx gazella*).

• Exotic species affected :

- fallow deer (*Cervus dama*),
- llama (*Lama glama*),
- alpaca (*Lama pacos*),
- Asian buffalo (*Bubalus bubalis*)
- ibex (*Capra ibex*).



Pienaar NJ & Thompson PN, 2013



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## RVF and other domestic/wild animal



### Camel



160 deaths RIM 2010



### Bufalo

- Susceptibility to infection proven
- Abortion and Mortality reported
- Serologic evidence in African Bufalo in Botswana (2010-1011)



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# Prevention and Control



## 1. Absence of specific treatment (Treatment is symptomatic)

## 2. Efficient Human inactivated vaccine

- Inadequate for mass campaigns (high cost, 3 doses for protection)
- Use restricted to staffs at risk (lab, military operating in endemic areas)

## 3. Animal vaccines (MP12, Smithburn, Clone13, R566)

- Abortive properties of some vaccines
- Stability after passage into hosts still questionable

## 4. Absence / limited efficacy of Vector control

- Difficult to treat large open space or water surface
- Large diversity of species, increasing the number of target
- Mosquitoes Resistance to insecticides



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# Prevention and Control

- Human Surveillance quasi absent
- Disease unknown by physicians
- No collaboration between physician and vet
- Entomologic surveillance
- Skill in entomology
- Animal surveillance
- Using sentinel animals
- Periodic sampling to follow up seroconversion
- Constraint : System difficult to implement ; High cost for the follow up ; Coverage / Sensitivity not always suitable; Herds mobility in some contexts



Major shortcoming of all these systems : They just inform about the virus circulation

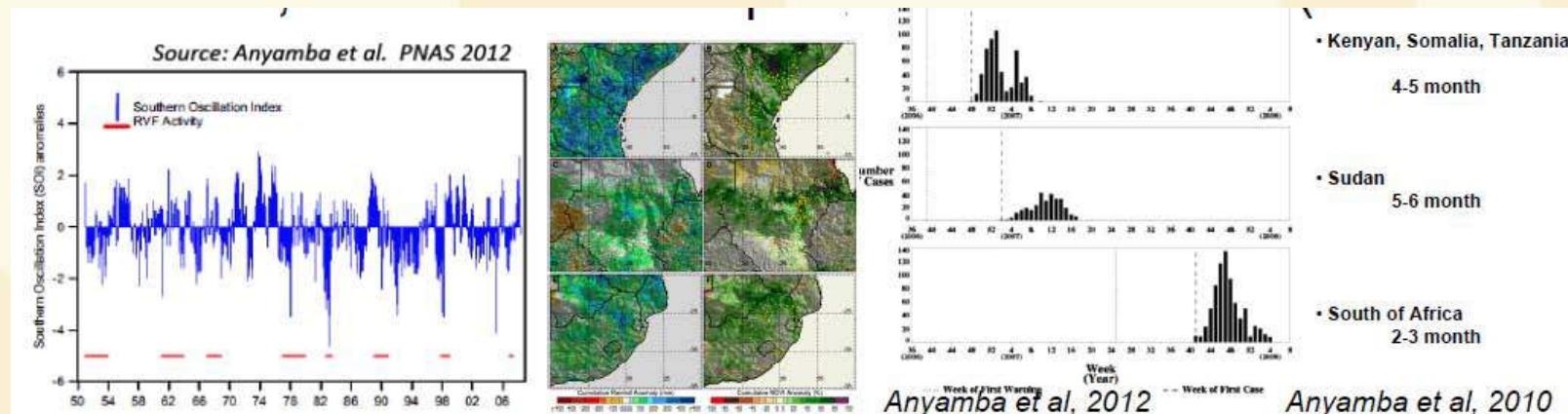


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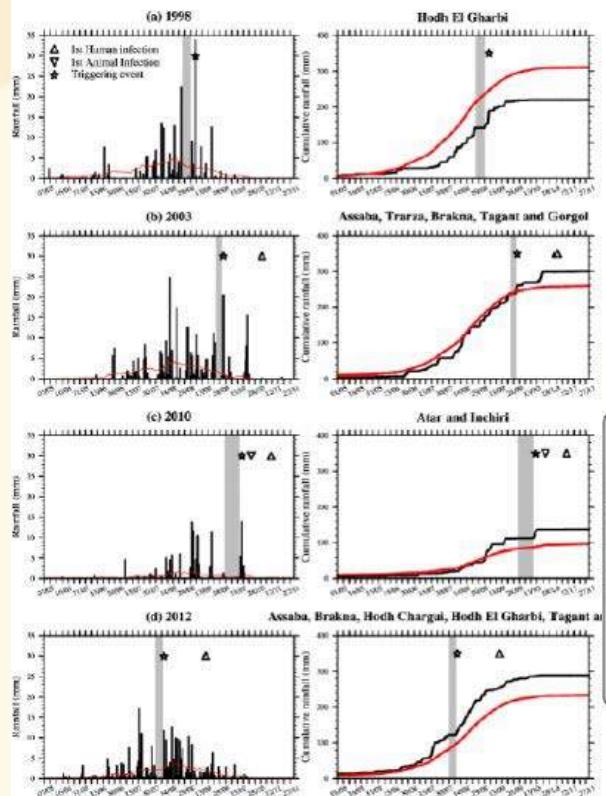
# Early Warning system

- *Objective* : To predict based on climate and environmental factors several weeks or month the occurrence of outbreak
- *Finality and relevance* : To develop preventive vaccine campaign or vector control strategies before the virus emergence
- *Main parameters used alone or in combination* : Rainfall, NDVI (Normalized difference vegetation index) anomalies, Variations of temperature sea surface (El Niño impact)



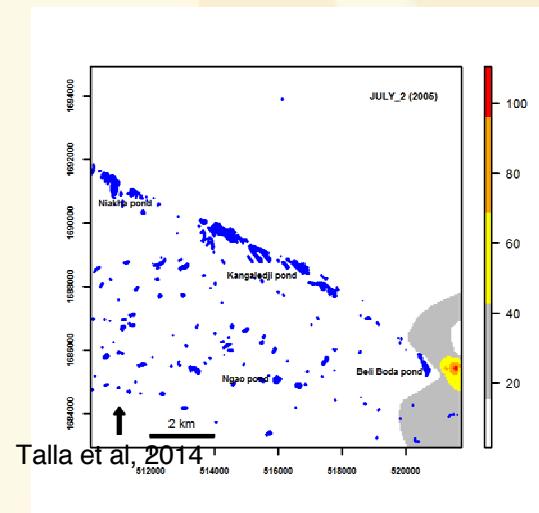


# Early Warning system



- A different profile compared to East Africa
- No impact of rainfall surplus
- Dry spell followed by rain impacting

Spatial & temporal distribution of vectors to identify hot spot



- 10 days of dry spelling required
- Case 3 weeks after rain succeding dryspell





# Thank you



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