UMR Unité des Virus Émergents

UVE

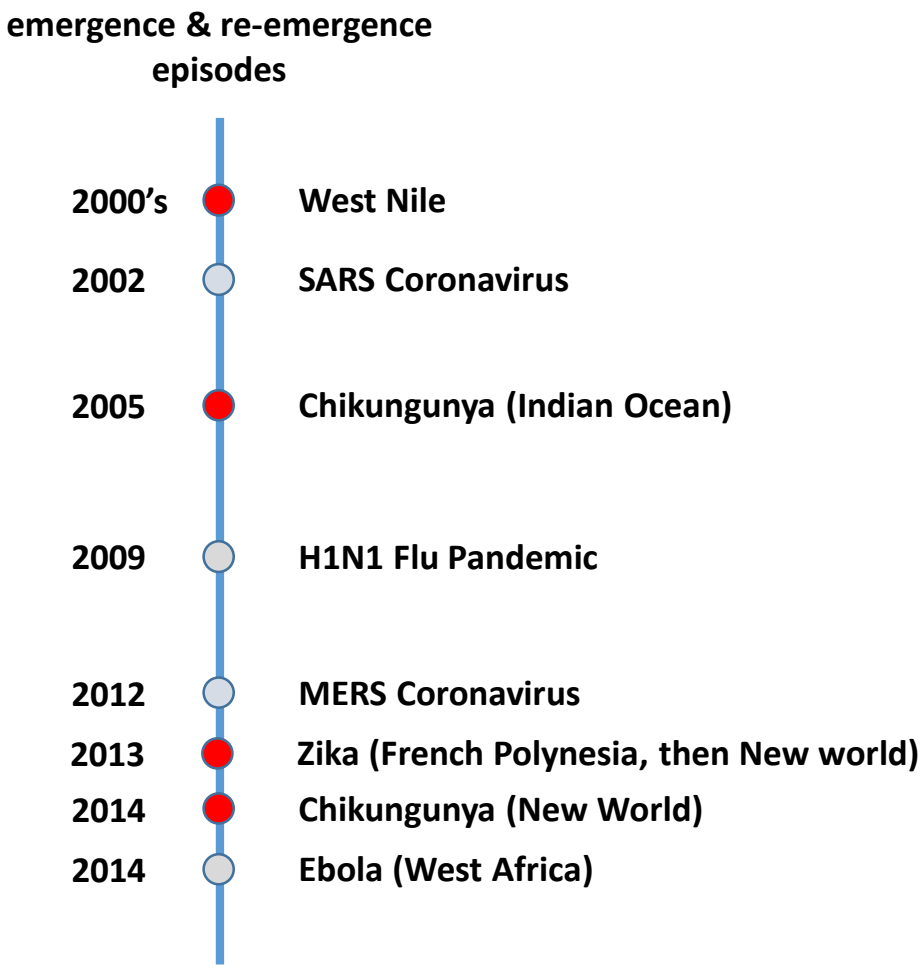
IRD 190 - Inserm 1207

Diagnostics and emergence potential of arboviruses

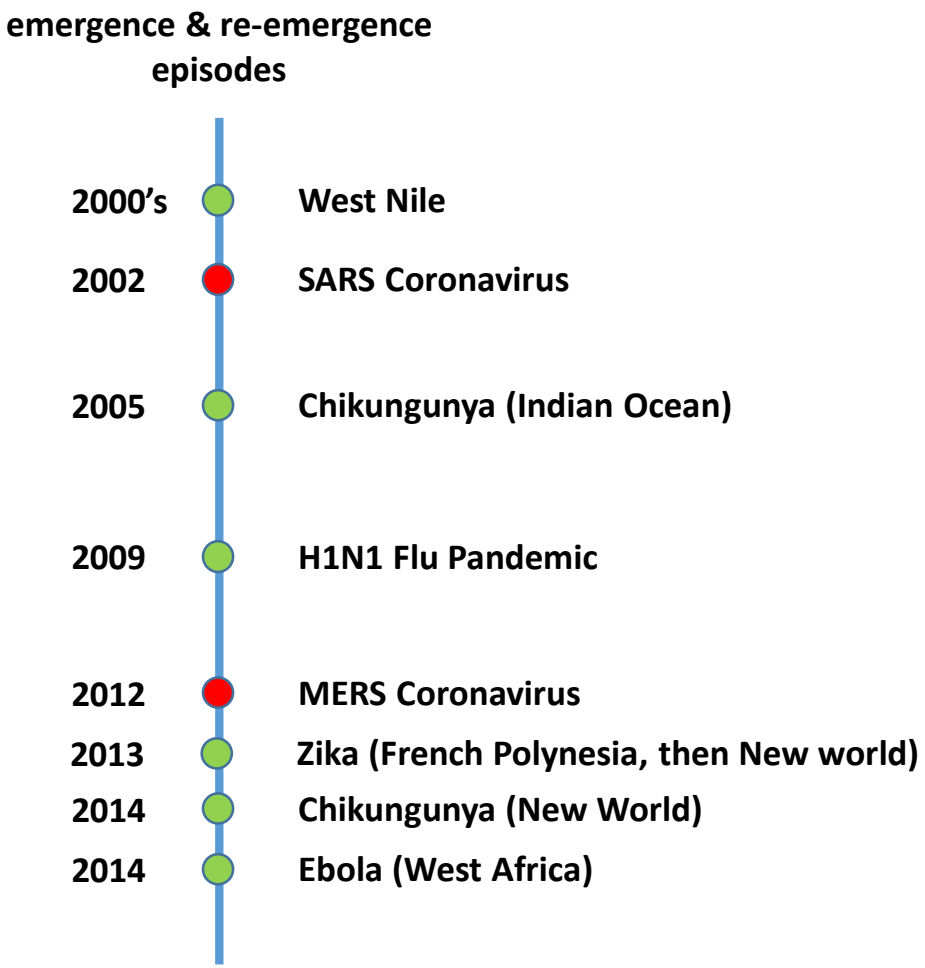
X de Lamballerie

Emergence potential of arboviruses

Recent (arbo)viral emergence events



+ DENV, YFV, TBEV, ALKV, EV71 …
& POWV, TOSV, RVFV …



+ DENV, YFV, TBEV, ALKV, AEV71 …
& POWV, TOSV, RVFV …

Emergence potential of arboviruses

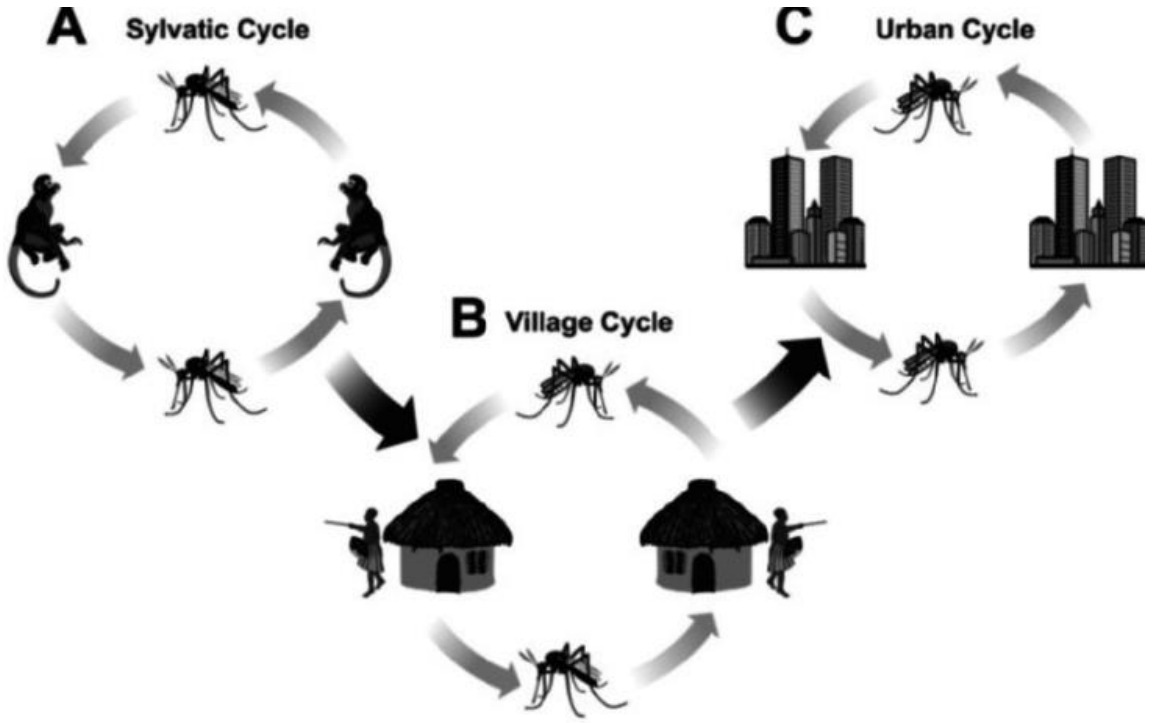
Lessons:

- *Specific importance of arboviruses among emerging pathogens*

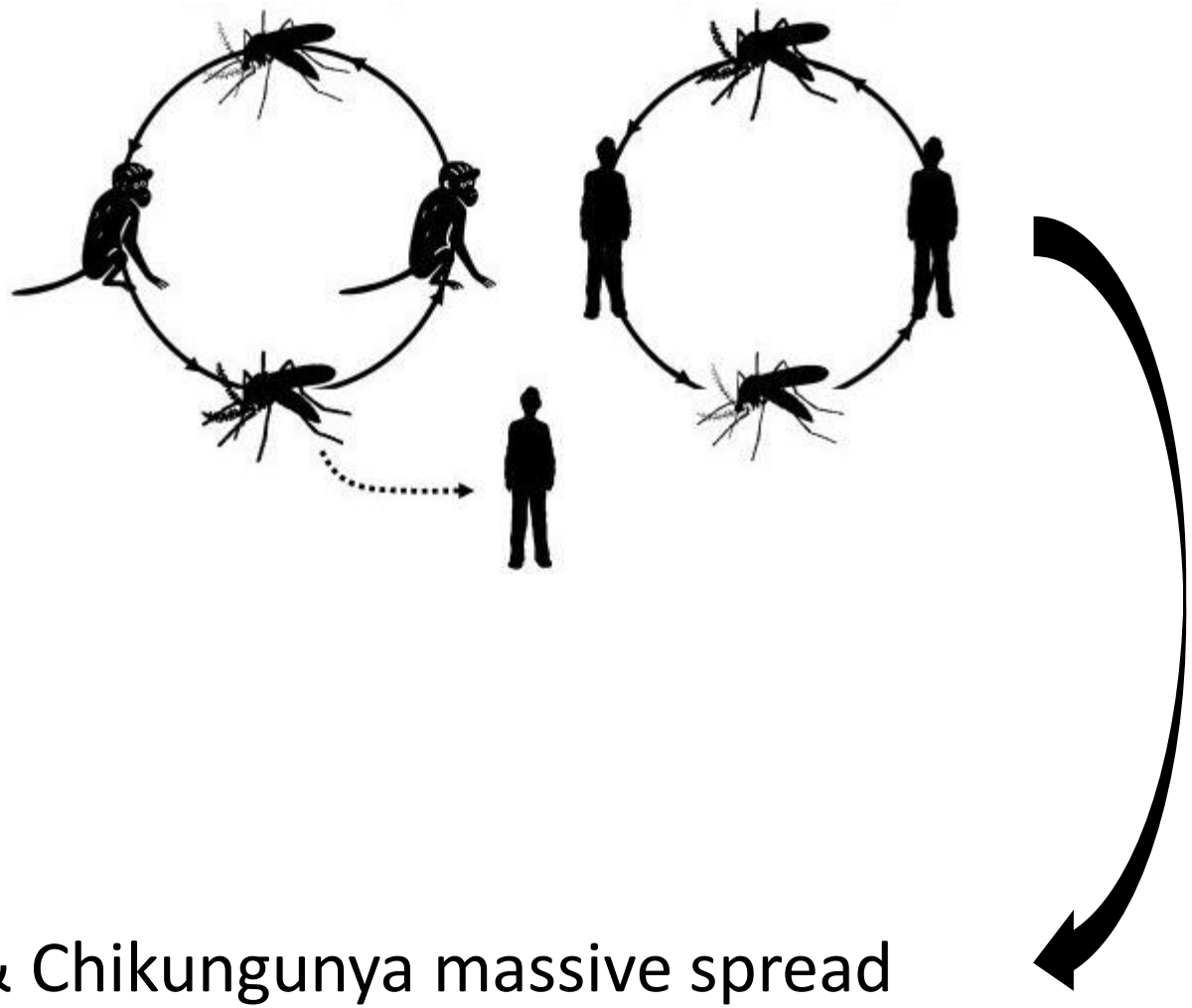
- *Re-emerging pathogens represent the greatest part of the public health burden of « emergence »*

Emergence mechanisms
(i) « anthropisation » of the transmission cycle: from forests to cities

A well established model based on the case of *Aedes* borne viruses



First described for YFV



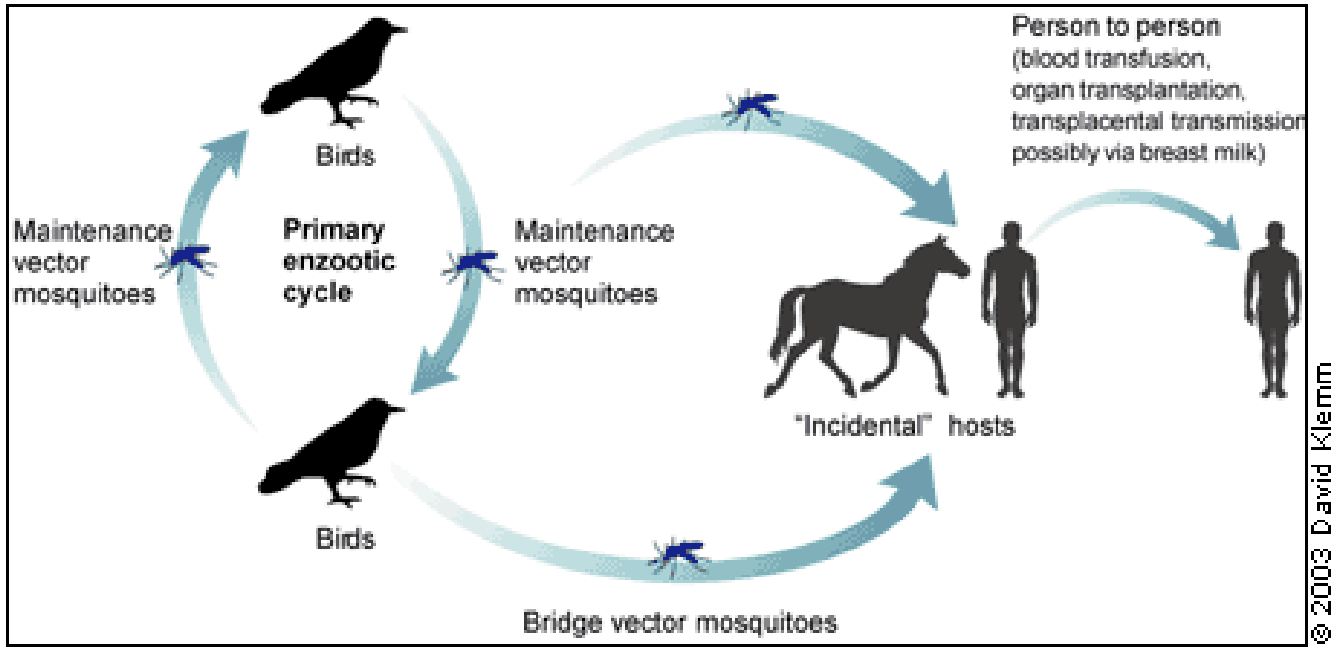
Dengue, Zika & Chikungunya massive spread

Emergence mechanisms (ii)
« non-anthropisation » of the transmission cycle

Imagine a mosquito-borne virus :

- That gives low viremia in humans
- For which humans are dead-end hosts
- That can be transmitted to humans only by mosquitoes that are both ornithophilic and anthropophilic and which have previously bitten an infected bird (in the close environment of humans since such mosquitoes fly over very short distance)

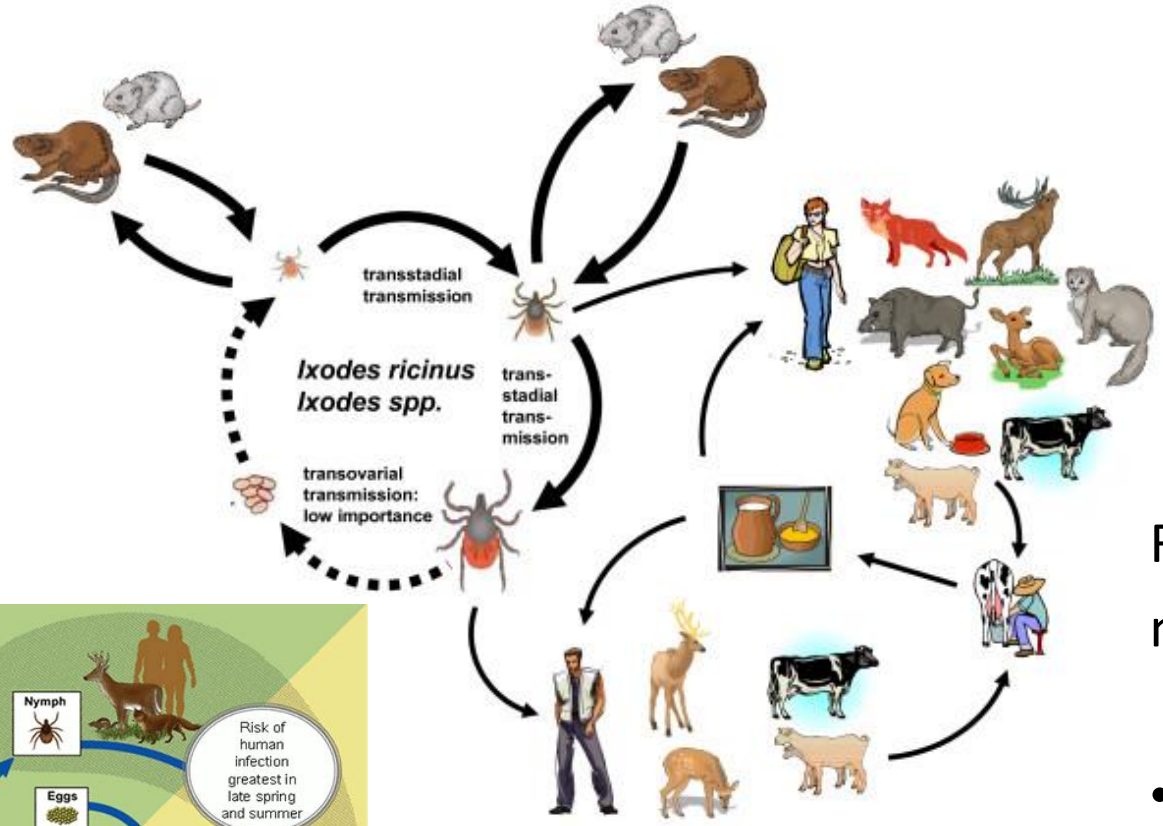
It seems not likely that this virus would be responsible for many cases –even less in urban areas

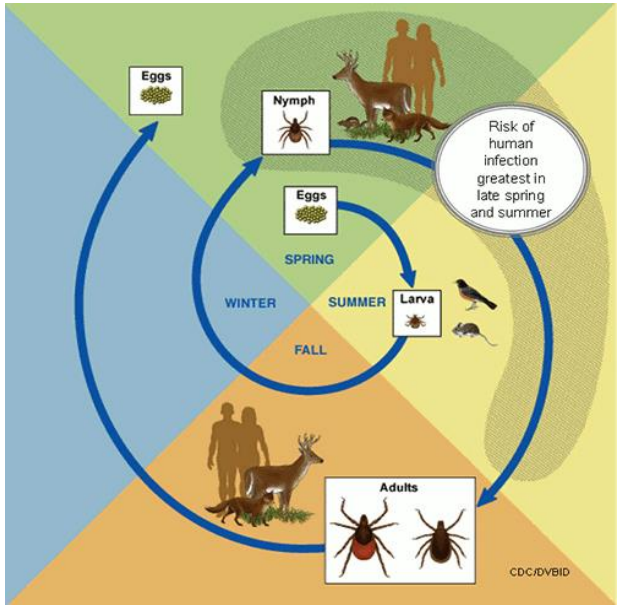


West Nile virus

Such a virus was able to invade the North American continent, infect a large panel of mosquitoes, birds and vertebrates, and finally provoke hundred thousands cases of human infections –starting in a urban environment

Emergence mechanisms (iii)
« non-anthropisation » of the transmission cycle: from cities to forests





The case of Tick-borne encephalitis

From 1974 to 2003, a 400% increase in TBE morbidity had been observed in Europe.

- Ecology of ticks:
  - climate change
- Increased contact with ticks:
  - Poverty
  - Leisure habits

Emergence potential of arboviruses

Lessons:

- *Understanding of emergence determinants and evaluation of « emergence potential »*
  - *There is no systematic scheme of emergence*
  - *A few « accepted » scenarii identified, many exceptions and counterexamples*
    - *CHIKV in Europe*
    - *CHIKV in the Americas*
    - *ZIKV vs CHIKV efficient spread*
    - *YFV in Brazil…*
  - *The actual precise mechanisms remain essentially unknown*

➔ *A lot of modesty required*

- *Viruses previously identified as natural* human and NHP pathogens can be considered potential emerging agents*

Name	Acronym	Host
Barmah Forest virus	BFV	H
Chikungunya virus	CHIKV	NHP, H
Eastern equine encephalitis virus	EEEV	H
Everglades virus	EVEV	H
Mayaro virus	MAYV	H
Middelburg virus	MIDV	H
Mucambo virus	MUCV	NHP, H
Ndumu virus	NDUV	NHP
O'nyong-nyong virus	ONNV	H
Ross River virus	RRV	H
Semliki Forest virus	SFV	H
Sindbis virus	SINV	NHP, H
Tonate virus	TONV	H
Una virus	UNAV	H
Venezuelan equine encephalitis virus	VEEV	H
Western equine encephalitis virus	WEEV	H

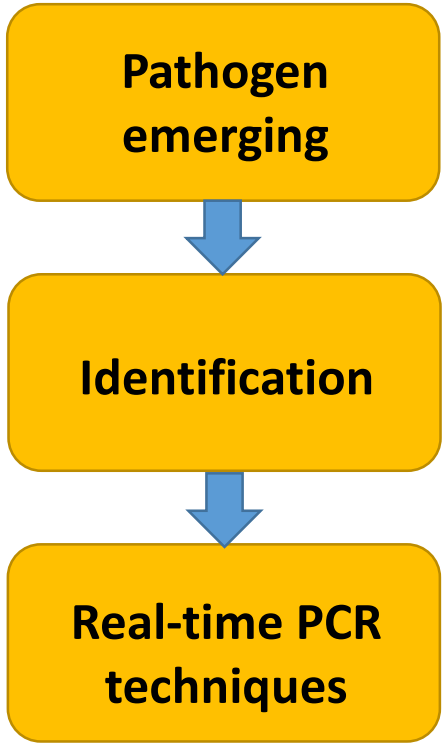
Name	Acronym	Host
Omsk haemorrhagic fever virus	OHFV	H
Powassan virus	POWV	H
Tick-borne encephalitis virus	TBEV	H
Kyasanur Forest disease virus	KFDV	H
Dengue virus 1	DENV-1	NHP, H
Dengue virus 2	DENV-2	NHP, H
Dengue virus 3	DENV-3	NHP, H
Dengue virus 4	DENV-4	NHP, H
Kedougou virus	KEDV	H
Zika virus	ZIKV	NHP, H
Banzi virus	BANV	H
Bouboui virus	BOUV	H
Edge Hill virus	EHV	H
Sepik virus	SEPV	H
Uganda S virus	UGSV	NHP
Wesselsbron virus	WESSV	H
Yellow fever virus	YFV	NHP, H
Aroa virus	AROAV	H
Aroa virus	BSQV	NHP, H
Cacipacore virus	CPCV	H
Japanese encephalitis virus	JEV	H
St Louis encephalitis virus	SLEV	H
Usutu virus	USUV	H
West Nile virus	WNV	NHP, H
Murray Valley encephalitis virus	MVEV	NHP, H
Ilheus virus	ILHV	NHP, H
Ntaya virus	NTAV	H
Entebbe bat virus	SOKV	H
Modoc virus	MODV	H
Rio Bravo virus	RBV	H
Dakar bat virus	DBV	H

Diagnostic preparedness efforts

Real emergence

The iconic example remains SARS (2003)

A robust and still valid scenario was elaborated



➔ different tools but nowadays dominent place of NGS techniques

➔ genomic characterisation, nearly-immediate release of real-time PCR detection techniques

➔ rapid availability to the medical community

Real emergence

Why real-time (RT-)PCR ?

- Easy design
- Intrinsic high sensitivity and specificity
- Widespread generic technology
- Rapid availability of primers and probes

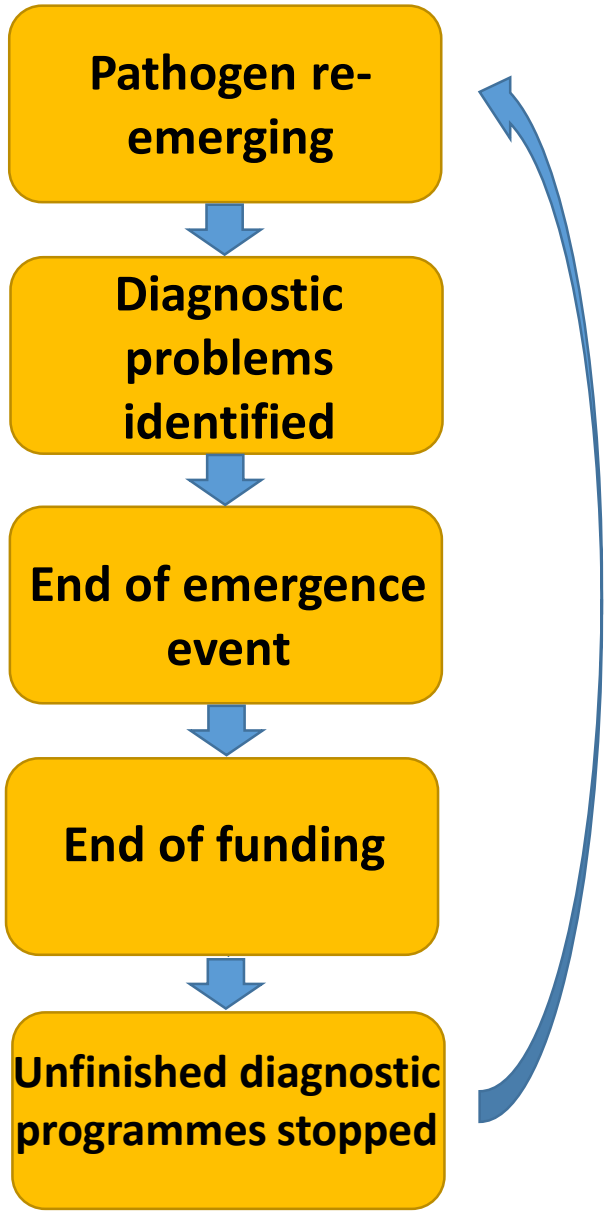
Of note:

- Individual use requires positive and negative controls (*cf.* European Virus Archive)
- Enzymes and other reagents now stabilized at room temperature

Serology on the short term:

- Old fashioned ELISAs or IF tests
- Possible rapid production of recombinant antigens
- Validation difficult

Re-emergence



➔ Very slow evolution of the situation regarding diagnostics

➔ Poorly evaluated molecular tests and low-performance serological tests

➔ For serious pathogens, bedside inactivation of samples needed, at least for inaugural molecular diagnosis

➔ What is needed is preparedness, and systematic improvement of diagnostic tools before the pathogens re-emerge

Chikungunya, O'Nyong Nyong & Mayaro
GLOPID-R Working group

Brasil, Patricia - Oswaldo Cruz Foundation (Fiocruz), Rio de Janeiro, Brazil
Busch, Michael P. - Blood Systems Research Institute, San Francisco, USA
de Lamballerie, Xavier - Marseille university, France
de Sousa Ribeiro, Guilherme - Oswaldo Cruz Foundation (Fiocruz), Salvador, Bahia, Brazil
Diamond, Michael - Washington University School of Medicine, St. Louis, USA
Drebot, Michael - Public Health Agency of Canada and the University of Manitoba
Drexler, Jan-Felix - Institute of Virology, Charité – Universitätsmedizin, Berlin, Germany
Failloux, Anna-Bella - Institut Pasteur, Paris, France
Gallian, Pierre - Etablissement Français du Sang, Marseille, France
Jaenisch, Thomas - Dept. of Infectious Diseases, Heidelberg University Hospital, Germany
Kohl, Alain - MRC-University of Glasgow Centre for Virus Research, UK
LaBeaud, Desiree - Stanford University, USA
Lecuit, Marc - Institut Pasteur, Paris, France
Lourenço-de-Oliveira, Ricardo - Oswaldo Cruz Foundation (Fiocruz), Rio de Janeiro, Brazil
NeytsJohan - Rega Institute for Medical Research, University of Leuven, Belgium
Ng, Lisa - Agency for Science, Technology and Research (A*STAR), Singapore
Reusken, Chantal - Department of Viroscience, Erasmus MC, Rotterdam, the Netherlands
Rodriguez-Morales , Alfonso J. – Univ. Tecnologica de Pereira, Pereira, Risaralda, Colombia
Sall, Amadou - Institut Pasteur de Dakar, Senegal
Simmons, Graham - Blood Systems Research Institute, San Francisco, USA
Simon, Fabrice - French Military Medical Service, Marseille, France
Siqueira, André - Oswaldo Cruz Foundation (Fiocruz), Rio de Janeiro, Brazil
Weaver, Scott - University of Texas Medical Branch, USA

Pezzi, Laura – Scientific secretariat

SG1	Diagnosis & Epidemiology
SG2	Clinics, treatment & blood transfusion incl. Acute & Post-Chik
SG3	Entomology
SG4	Fundamental research
SG5	Disease burden

Methodology

- Review /assessment
- Identification of gaps of knowledge
- Experts' recommendations
- Tools

”There is a clear need for a meaningful ”peace-time” research response strategy, defined as preparedness research in between epidemics, leading to the development of a strong and permanent global emerging disease research capacity”

Thank you for your attention