Diagnostics and emergence potential of arboviruses

X de Lamballerie
Emergence potential of arboviruses
Recent (arbo)viral emergence events

emergence & re-emergence episodes

2000’s  •  West Nile
2002    •  SARS Coronavirus
2005    •  Chikungunya (Indian Ocean)
2009    •  H1N1 Flu Pandemic
2012    •  MERS Coronavirus
2013    •  Zika (French Polynesia, then New World)
2014    •  Chikungunya (New World)
2014    •  Ebola (West Africa)

emergence & re-emergence episodes

2000’s  •  West Nile
2002    •  SARS Coronavirus
2005    •  Chikungunya (Indian Ocean)
2009    •  H1N1 Flu Pandemic
2012    •  MERS Coronavirus
2013    •  Zika (French Polynesia, then New World)
2014    •  Chikungunya (New World)
2014    •  Ebola (West Africa)

+ DENV ●, YFV ●, TBEV ●, ALKV ●, EV71 ●... & 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
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
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
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

<table>
<thead>
<tr>
<th>Name</th>
<th>Acronym</th>
<th>Host</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barmah Forest virus</td>
<td>BFV</td>
<td>H</td>
</tr>
<tr>
<td>Chikungunya virus</td>
<td>CHIKV</td>
<td>NHP, H</td>
</tr>
<tr>
<td>Eastern equine encephalitis virus</td>
<td>EEEV</td>
<td>H</td>
</tr>
<tr>
<td>Everglades virus</td>
<td>EVEV</td>
<td>H</td>
</tr>
<tr>
<td>Mayaro virus</td>
<td>MAYV</td>
<td>H</td>
</tr>
<tr>
<td>Middelburg virus</td>
<td>MIDV</td>
<td>H</td>
</tr>
<tr>
<td>Mucambo virus</td>
<td>MUCV</td>
<td>NHP, H</td>
</tr>
<tr>
<td>Ndumu virus</td>
<td>NDUV</td>
<td>NHP</td>
</tr>
<tr>
<td>O’nyong-nyong virus</td>
<td>ONNV</td>
<td>H</td>
</tr>
<tr>
<td>Ross River virus</td>
<td>RRV</td>
<td>H</td>
</tr>
<tr>
<td>Semliki Forest virus</td>
<td>SFV</td>
<td>H</td>
</tr>
<tr>
<td>Sindbis virus</td>
<td>SINV</td>
<td>NHP, H</td>
</tr>
<tr>
<td>Tonate virus</td>
<td>TONV</td>
<td>H</td>
</tr>
<tr>
<td>Una virus</td>
<td>UNAV</td>
<td>H</td>
</tr>
<tr>
<td>Venezuelan equine encephalitis virus</td>
<td>VEEV</td>
<td>H</td>
</tr>
<tr>
<td>Western equine encephalitis virus</td>
<td>WEEV</td>
<td>H</td>
</tr>
<tr>
<td>Omsk haemorrhagic fever virus</td>
<td>OHFV</td>
<td>H</td>
</tr>
<tr>
<td>Powassan virus</td>
<td>POWV</td>
<td>H</td>
</tr>
<tr>
<td>Tick-borne encephalitis virus</td>
<td>TBEV</td>
<td>H</td>
</tr>
<tr>
<td>Kyasanur Forest disease virus</td>
<td>KFDV</td>
<td>H</td>
</tr>
<tr>
<td>Dengue virus 1</td>
<td>DENV-1</td>
<td>NHP, H</td>
</tr>
<tr>
<td>Dengue virus 2</td>
<td>DENV-2</td>
<td>NHP, H</td>
</tr>
<tr>
<td>Dengue virus 3</td>
<td>DENV-3</td>
<td>NHP, H</td>
</tr>
<tr>
<td>Dengue virus 4</td>
<td>DENV-4</td>
<td>NHP, H</td>
</tr>
<tr>
<td>Kedougou virus</td>
<td>KEDV</td>
<td>H</td>
</tr>
<tr>
<td>Zika virus</td>
<td>ZIKV</td>
<td>NHP, H</td>
</tr>
<tr>
<td>Banzi virus</td>
<td>BANV</td>
<td>H</td>
</tr>
<tr>
<td>Boubouli virus</td>
<td>BOUV</td>
<td>H</td>
</tr>
<tr>
<td>Edge Hill virus</td>
<td>EHV</td>
<td>H</td>
</tr>
<tr>
<td>Sepik virus</td>
<td>SEPV</td>
<td>H</td>
</tr>
<tr>
<td>Uganda S virus</td>
<td>UGSV</td>
<td>NHP</td>
</tr>
<tr>
<td>Wesselsbron virus</td>
<td>WESSV</td>
<td>H</td>
</tr>
<tr>
<td>Yellow fever virus</td>
<td>YFV</td>
<td>NHP, H</td>
</tr>
<tr>
<td>Aroa virus</td>
<td>AROAV</td>
<td>H</td>
</tr>
<tr>
<td>Aroa virus</td>
<td>BSQV</td>
<td>NHP</td>
</tr>
<tr>
<td>Cacipacore virus</td>
<td>CPCV</td>
<td>H</td>
</tr>
<tr>
<td>Japanese encephalitis virus</td>
<td>JEV</td>
<td>H</td>
</tr>
<tr>
<td>St Louis encephalitis virus</td>
<td>SLEV</td>
<td>H</td>
</tr>
<tr>
<td>Usutu virus</td>
<td>USUV</td>
<td>H</td>
</tr>
<tr>
<td>West Nile virus</td>
<td>WNIV</td>
<td>NHP, H</td>
</tr>
<tr>
<td>Murray Valley encephalitis virus</td>
<td>MVEV</td>
<td>NHP, H</td>
</tr>
<tr>
<td>Ilheus virus</td>
<td>ILHV</td>
<td>NHP, H</td>
</tr>
<tr>
<td>Ntaya virus</td>
<td>NTAV</td>
<td>H</td>
</tr>
<tr>
<td>Entebbe bat virus</td>
<td>SOKV</td>
<td>H</td>
</tr>
<tr>
<td>Modoc virus</td>
<td>MODV</td>
<td>H</td>
</tr>
<tr>
<td>Rio Bravo virus</td>
<td>RBV</td>
<td>H</td>
</tr>
<tr>
<td>Dakar bat virus</td>
<td>DBV</td>
<td>H</td>
</tr>
</tbody>
</table>
Diagnostic preparedness efforts
Real emergence

The iconic example remains SARS (2003)
A robust and still valid scenario was elaborated

- Different tools but nowadays dominant 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
Pathogen re-emerging

Diagnostic problems identified

End of emergence event

End of funding

Unfinished diagnostic programmes stopped

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 Lambererie, 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
Lourengo-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