Arboviruses and hemorrhagic fevers in Africa: implications and lessons for global health

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Outline

• Background

• Case studies:
  • YF, dengue, Zika

• Way forward

• Conclusion
What are arboviruses and viral hemorrhagic fever?

- Arbovirus and viral hemorrhagic fevers
  - Caused by viruses
  - Hemorrhagic (clinical symptom)
  - Fever (clinical symptom)
  - Arthropod Borne Virus (ecological definition)

- Clinical and ecological definition encompassing a wide diversity:
  - Burden
  - Viruses
  - Syndromes & clinical presentation
  - Transmission and reservoir
  - Diagnostics, treatment, prevention and public health
### Significant viral hemorrhagic fever and arboviruses

<table>
<thead>
<tr>
<th>Diseases</th>
<th>Cases/year</th>
<th>Transmission</th>
<th>Letality %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ebola, Marburg</td>
<td>100</td>
<td>Bats ?</td>
<td>50-90</td>
</tr>
<tr>
<td>Dengue fever</td>
<td>50 000 000*</td>
<td>Mosquitoes</td>
<td>0,5</td>
</tr>
<tr>
<td>Lassa fever</td>
<td>100.000</td>
<td>Rodents</td>
<td>7-10</td>
</tr>
<tr>
<td>Crimean Congo Hemorrhagic Fever</td>
<td>100</td>
<td>Ticks</td>
<td>3-40</td>
</tr>
<tr>
<td>Yellow Fever</td>
<td>200.000*</td>
<td>Mosquitoes</td>
<td>Up to 50</td>
</tr>
<tr>
<td>Rift Valley Fever</td>
<td>10 (100.000)</td>
<td>Mosquitoes</td>
<td>50% of severe</td>
</tr>
</tbody>
</table>
AVHF most common clinical presentation

- High fever (40°C/ 104°F)
- Joint pain (lower back, ankle, knees, wrists or phalanges)
- Joint swelling
- Rash
- Headache
- Muscle pain
- Nausea
- Fatigue
AVHF are major public health problem at the global level ...

- August 2014: Declaration of a Public Health Emergency of International Concern (PHEIC) for Ebola Virus Disease
- February 2016: Declaration of a Public Health Emergency of International Concern (PHEIC) for Zika associated with severe neurological syndrome
- May 2016: Meeting of the Emergency committee for examination of yellow fever epidemic to declare it as a PHEIC
...with high political level of involvement...

Dengue Cape Verde 2009

Rift Valley Fever Mauritania 2010

EVD Sierra Leone 2014

EVD Guinea 2014
... media reporting...
... social economic impact

Riots for Ebola in 2014-15
associated with deaths, prisoners

Rio Olympics Games in 2016
Yellow fever epidemic in Angola in 2016

Distribution of suspected cases in Luanda Province reported up to 01/03/2016

Market «attraction» from all part of the city. People are bitten there and then disseminate the virus in the rest of the city with contamination of “naïve” mosquitoes in those new places & local amplification.
Reemergence of an old strain 1971

Angola YFV 2015-2016
Yellow fever epidemics in Africa in 2016

> 3,867 cases/369 deaths
16 of 18 provinces reported cases
16M people vaccinated/25 M
International spread of yellow fever epidemic from Angola in 2016
International spread of yellow fever epidemic from Angola in 2016: DRC outbreak

- **KIN:** Fractionated doses 8 M in 32 HZ
- **Border:** 3 M in 16 HZ
### China: map and data

<table>
<thead>
<tr>
<th>Location</th>
<th>No. of cases</th>
<th>Population (million)</th>
<th>March Lo-Hi Temp (°C)</th>
<th>Past reports of Dengue</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beijing</td>
<td>4</td>
<td>11.51</td>
<td>-1 to 11</td>
<td>-</td>
</tr>
<tr>
<td>Fuzhou</td>
<td>2</td>
<td>2.124</td>
<td>9 to 19</td>
<td>2015</td>
</tr>
<tr>
<td>Shanghai</td>
<td>3</td>
<td>14.35</td>
<td>5 to 13</td>
<td>-</td>
</tr>
</tbody>
</table>

Source: MoH, China Meteorological Administration
Yellow fever in Angola

- Yellow fever is endemic in Angola with occasional outbreaks
  - Luanda 1971 and 1988
  - Sporadic cases of YF identified in routine surveillance

- YF vaccine integrated in routine immunization in 1980
  - 2008-2013: coverage 40%-65%
  - 2014: coverage 77% (WHO/UNICEF estimations)

- Angola has never implemented mass vaccination of YF
Challenges: urbanization, travel, trade, social impact

- Increased risk of large urban yellow fever outbreaks with international spread

- Angola and DRC yellow fever crises
  - Limited surveillance and laboratory confirmation capacity worsen the epidemic burden
  - Epidemic management and control is very resources-intensive
  - Impact goes far beyond epidemic figures (health and economic indicators)
  - The world is a global village (In Angola: 400,000 migrants workers from DRC, at least 220,000 Portuguese, and about 260,000 Chinese, 2008 estimates)
Zika and dengue in Cape verde islands
Zika in Cabo verde 2015-2016
Epidemic curve and spread for Zika Virus

1st microcephaly
Situation for Zika at late May 2016

- 962 suspect cases tested
  - Santiago, Maio, Fogo, Brava, Boa Vista and Sao Vincente
  - Age from 2 days to 86
  - Females > Males
- 219 positifs for IgM and/or PCR
  - Sex ratio F/M: 1.82
- Pregnant women
  - 87 tested and 19 identified as Zika infected
  - Santiago, Fogo and Maio
  - Majority 16-30 years
- Microcephaly
  - 9 cases
Confirmed cases of Zika in Cape verde islands
Entomological investigation for Zika in Cape Verde in 2015-16
Mission conjointe
Entomologie-Virologie
investigation
épidémie dengue,
Cap – Vert,
Janvier – Février 2017
Îles de Santiago, Fogo et Maio

➢ Sérums humains:
640 sérums testés:
• 35 sérums positifs recherche génome viral et IgM DENV
• Analyse séquences dengue sérotype 3

➢ Moustiques:
157 lots moustiques testés:
Recherche génome viral de la dengue NEGATIF
Introduction of Dengue 3 in Cape Verde 2009

Cape Verde samples (in red boxes)

Senegal samples (in blue boxes)
Way forward: Vaccines in an integrated approach

• **Integrating vaccine as part of a more comprehensive strategy**
  • Understand better the epidemiology, factors of emergence and transmission dynamics.

• **Anticipating on vaccines against Emerging viruses**
  • Innovative flexible platform
  • Establish an ecosystem for development and evaluation of candidate vaccine
  • Financing and access to vulnerable populations

• **Involve the first line exposed populations and countries in the strategy**
Estimated Global supply 2017-2026 (Risk adjusted)

- **Total volume 2017-2026**
  - Approx. 1,488 million doses
  - 800-900 million people vaccinated

Source: GAVI and WHO
Yellow fever: management of vaccine shortage

1. Request sent through WHO
2. Secretariat contacts ICG members
3. Approval of request
4. Clarifications may be sought through Secretariat
5. UNICEF SD ships vaccines as requested by ICG

Requesting country

ICG Secretariat

UNICEF SD

UNICEF authorised to ship the vaccines to the country

Global Stockpile

ICG consensu

Dx

Global Stockpile
Risk for yellow fever urban epidemics

- **26 high risk countries**
- **8 moderate risk countries**
- **12 countries with potential for YF transmission**

Source: WHO
Way forward: integrated surveillance sentinel sites (4S Senegal)

"Back to the field"
Dengue epidemic in Mbour (Senegal): 2016-2017

Novembre 2016

- Identification d’une flambée d’arboV à travers 4S (Mbour et Louga)
- Confirmation de dengue chez 11 cas en provenance des cliniques privés de Dakar: Dengue type III

Janvier 2017

- Investigation Entomo-Viro
  - 445 suspects ou contacts dont 32 confirmés (IgM ou PCR)
- Entomologie: présence de vecteur

<table>
<thead>
<tr>
<th>Genre et espèce</th>
<th>Sexe</th>
<th>Nombre Mos</th>
<th>Nombre lot</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Aedes aegypti</em></td>
<td>Femelle</td>
<td>216</td>
<td>33</td>
</tr>
<tr>
<td></td>
<td>Mâle</td>
<td>136</td>
<td>23</td>
</tr>
<tr>
<td></td>
<td>Larve</td>
<td>226</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>Nymphe</td>
<td>23</td>
<td>5</td>
</tr>
<tr>
<td><em>Culex quinquefasciatus</em></td>
<td>Femelle</td>
<td>3125</td>
<td>135</td>
</tr>
<tr>
<td></td>
<td>Mâle</td>
<td>3264</td>
<td>85</td>
</tr>
<tr>
<td><em>Culex cinctus</em></td>
<td>Femelle</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Mâle</td>
<td>8</td>
<td>3</td>
</tr>
</tbody>
</table>
Surveillance of Rift Valley fever among domestic animals
Rift Valley fever activity in Senegal
Way forward: integrated surveillance observatoire sites

Surveillance
- Vectors
- Humans
- Non-human primates
- Wildlife
- Environment
- Early detection
- Pathogen discovery

Emergence and maintenance factors
- POC diagnostics
- Multidisciplinary approach
- Entomology
- Virology
- Geography of health
- Medical Anthropology
- Climatology
- Modeling

"Back to the field"
Surveillance from febrile cases

Geographic distribution of DENV, CHIKV et YFV cases

- **DENV 2**
  - October-December 2008
  - 20 confirmed cases
  - Mild clinical form

- **CHIKV**
  - October-December 2009
  - 20 confirmed cases
  - Mild clinical form

- **YFV**
  - June –November 2010 et 2011
  - 13 confirmed cases
  - 10 probable cases
Malaria and arbovirus co-infections

- (20/41) 48.7% of patients coinfected with malaria and arboviruses
  - (3/16) 18.7% CHIKV-P. falciparum
  - (7/12) 58.3% YFV-P. falciparum
  - (8/9) 88.9% ZIKV-P. falciparum
  - (1/3) 33.3% DENV-P. falciparum
  - (1/1) 100% RVFV-P. falciparum

- Higher frequency of circulation of ZIKV comparatively to other arboviruses in the region

- Co-infection is strongly correlated with higher temperature (>40°C)
Way forward: Entomological surveillance

"Back to the field"
Modeling of amplification and emergence

"Back to the field"
Zika virus sylvatic circulation
Zika virus Emergence in Kedougou, 2011

Geographical Distribution of Zika virus in Kedougou from October to December 2011
Emergence of Yellow fever in 2010-2011 at Kedougou

Mosquitoes in 2010
- 3477 batches collected
- 63 batches (1.8%) positive for YF virus
- Distribution of species
  - *Ae. furcifer*: 55.5%
  - *Ae. luteocephalus*: 33.3%
  - *Ae. taylori*: 6.3%
  - *Ae. africanus*: 3.2%
  - *Ae. vittatus*: 1.6%

Table 3: Repartition of positive Monkey sera according to species and age during catching season 2010 and 2011.

<table>
<thead>
<tr>
<th>Season</th>
<th>Species</th>
<th>caught monkeys</th>
<th>Number</th>
<th>Juvenile</th>
<th>Adult</th>
<th>Unknown</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>2010*</td>
<td>AGM</td>
<td>44</td>
<td>1</td>
<td>-</td>
<td>7(41%)</td>
<td>10(59%)</td>
<td>17</td>
</tr>
<tr>
<td></td>
<td>PP</td>
<td>103</td>
<td>0</td>
<td>3(8%)</td>
<td>33(89%)</td>
<td>1(3%)</td>
<td>37</td>
</tr>
<tr>
<td></td>
<td>EP</td>
<td>11</td>
<td>0</td>
<td>-</td>
<td>1(100%)</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>158</td>
<td>1</td>
<td>3(4%)</td>
<td>41(76%)</td>
<td>11(20%)</td>
<td>55</td>
</tr>
<tr>
<td>2011*</td>
<td>AGM</td>
<td>70</td>
<td>0</td>
<td>17(25%)</td>
<td>51(75%)</td>
<td>-</td>
<td>68</td>
</tr>
<tr>
<td></td>
<td>PP</td>
<td>127</td>
<td>0</td>
<td>50(48%)</td>
<td>55(52%)</td>
<td>-</td>
<td>105</td>
</tr>
<tr>
<td></td>
<td>EP</td>
<td>23</td>
<td>0</td>
<td>14(70%)</td>
<td>6(30%)</td>
<td>-</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>220</td>
<td>0</td>
<td>81(42%)</td>
<td>112(58%)</td>
<td>-</td>
<td>193</td>
</tr>
</tbody>
</table>

* Monkey were caught from January to May
AGM=African Green Monkey, PP= Papio Papio, EP= *Erythrocebus patas*
Table 5: Adults mosquitoes collected in the field or obtained from emergence of collected larvae

<table>
<thead>
<tr>
<th>Species</th>
<th>Human catching</th>
<th>Emergence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aedes aegypti</td>
<td>39</td>
<td>1742</td>
</tr>
<tr>
<td>Aedes descentropunctatus</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Aedes dalzieli</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Aedes furcifer</td>
<td>112</td>
<td>0</td>
</tr>
<tr>
<td>Aedes fowleri</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Aedes hirsutus</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>Aedes luteocephalus</td>
<td>0</td>
<td>37</td>
</tr>
<tr>
<td>Aedes minutus</td>
<td>28</td>
<td>0</td>
</tr>
<tr>
<td>Aedes vexans</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Aedes vittatus</td>
<td>35</td>
<td>127</td>
</tr>
<tr>
<td>Total Aedes</td>
<td>217</td>
<td>1914</td>
</tr>
<tr>
<td>Total Anopheles</td>
<td>15</td>
<td>10</td>
</tr>
<tr>
<td>Total Culex</td>
<td>81</td>
<td>815</td>
</tr>
<tr>
<td>Eretmapodites chrysogaster</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>Ma uniformis</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>316</td>
<td>2744</td>
</tr>
</tbody>
</table>
Take home messages

- Preparedness is critical
  - What is the next threat?

50,000 vertebrate species. Even if each has only 20 endemic viruses, we can predict 1,000,000 vertebrate viruses. Given current state of knowledge, >99% of vertebrate viruses remain to be discovered!

Large potential for future zoonotic emergence
Other arboviruses with potential for urban emergence

Source: DJ Gubler
Conclusion

• AVHF will relentlessly emerge and need:
  • Understanding factors of emergence at local and global level
  • Delivery of medical countermeasures to the right people at the right time and in right quantity
  • Focus on needs of countries with weakest system is necessary to prevent and control large scale emergence
  • Sustainable surveillance and preparedness is needed
• Regional and national champions should be focused on « priority » diseases
• Coordination in research and response
• Innovation in medical countermeasures (Diagnostics, vaccines, therapies) should be prioritized
Acknowledgements

- IP Dakar
  - Virology, Entomology, Epidemiology, G4, Immunology
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- French Embassy in Dakar
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- World Health Organization
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