FOUR DECADES OF EBOLA OUTBREAKS EXPERIENCE IN DEMOCRATIC REPUBLIC OF CONGO (DRC):

GLOBAL EBOLA VACCINE IMPLEMENTATION TEAM.
REGIONAL WORKSHOP


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DG Nat.Inst.Biomedical Research.
Order Mononegavirales

Family Filoviridae

Genus Marburgvirus
Species Marburg marburgvirus
Virus 1: Marburg virus
Virus 2: Ravn virus (RAVV)

Genus Ebolavirus
Species Tai Forest ebolavirus
Virus: Tai Forest virus (TAFV)
Species Reston ebolavirus
Virus: Reston virus (RESTV)
Species Sudan ebolavirus
Virus: Sudan virus (SUDV)
Species Zaire ebolavirus
Virus: Ebola virus (EBOV)
Species Bundibugyo ebolavirus
Virus: Bundibugyo virus (BDBV)

Genus Cuevavirus
Species Lloviu cuevavirus
Virus: Lloviu virus

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Circulation of Ebola viruses in Africa

*FILOVIRIDAE*

*EBOLA*

- Ebola Soudan
- Ebola TAI
- Ebola Zaïre
- Ebola Bundibugyo

Map showing the circulation of different strains of Ebola virus in Africa, with highlighted areas indicating regions affected by each strain.
Mysterious disease of Yambuku, 1976

- Ecology: region of tropical forests.
  - Typhoid fever?
  - Yellow fever?
- Severity of situation: « from 5 to 22 September 30 cases, 22 deaths ».
- National response: 23 Sept mission to investigate the nature of the deadly disease.
Mysterious disease of Yambuku: bacteriological investigations, 24 Sept.

Collected blood specimens from 6 patients for:

- Blood culture processed at the university of Kinshasa: negative.
- Widal test at the university of Kinshasa:
  - 1. Mb., wife of the index case:
    - TO=1/10; TH=1/20. blood sample of 17 September.
    - TH= 1/160; TH= 1/80 blood sample of 24 September.
  - 2. Ng., sister of an Ebola patient
    - TO: 1/320; TH: 1/160.
  - 3. Ma., pregnant woman (chloramphenicol)
    - TO=1/80; TH: 1/160.
  - 4. Ab., child 5 years old, his mother was sick.
    - TO= 1/40; TH= 1/40.
  - 5. Mba., woman (chloramphenicol)
    - TO= 1/40; TH= 1/40.
  - 6. Suk., nurse (chloramphenicol)
    - TO= 1/320; TH= 1/640.
Mysterious disease of Yambuku: pathology investigations.

☐ 3 Post-mortem liver samples collected on 24 Sept 1976 and processed at the University of Kinshasa.

1. Anangi A35/76: histological aspect compatible with Yellow fever.
2. Amene A37/76: histological aspect compatible with active liver congestion.
Mysterious disease of Yambuku: efforts to determine the cause of the outbreak

24 Sept, I travelled with a sick Belgian nun who cared for patients in Yambuku hospital. Blood specimen was collected and sent to ITM/Antwerp/PPiot A Marburg like virus was isolated. Ebola = name of a small river near the catholic mission of Yambuku. Mysterious disease was named: Ebola outbreak.
Aperçu sur l’épidémie de Fièvre hémorragique Ebola à Yambuku, 1976

- 318 cas, 280 décès.
- Décès de 11 des 17 agents de santé.
- Cas index le 5 Sept, le dernier cas décédé le 5 novembre 1976.
- Equipe internationale avec matériel de protection, le 18 Octobre (WHO/CDC/IMT/IPP/NICD).
- Modes de transmission: syringues réutilisées et participation à des funérailles traditionnelles.
- Dissémination: 55 villages affectés et virus introduit à Kinshasa (2 cas).
19 YEARS AFTER YAMBUKU EBOLA OUTBREAK: **KIKWIT OUTBREAK, 1995**

- **525Km, East of Kinshasa.**
- **400,000 inhabitants**
- **Kikwit 2 hospital: 60 beds.**
- **Kikwit general hospital: 300 beds.**
- **Health Centers: 42.**
- **The alert of bloody diarrhea and fever 27 April 1995.**
- **Several deaths in communities and among health care workers.**
- **Severity of the situation: even European nuns died of the mysterious disease**

<table>
<thead>
<tr>
<th>NATURE</th>
<th>NUMBER</th>
<th>NEGATIVE</th>
<th>POSITIVE</th>
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<tr>
<td>STOOL CULTURE/SHIGELLA</td>
<td>97</td>
<td>93</td>
<td>4</td>
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<tr>
<td>BLOOD CULTURE/S.TYPHI</td>
<td>9</td>
<td>9</td>
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Epidémie de Kikwit: distribution par âge et par sexe des cas de diarrhée au 1er Mai, 1995.

<table>
<thead>
<tr>
<th>AGE</th>
<th>HOMME</th>
<th>FEMME</th>
<th>TOTAL</th>
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<tr>
<td>&lt;1</td>
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<td>3</td>
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<tr>
<td>1-10</td>
<td>4</td>
<td>2</td>
<td>6</td>
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<td>11-20</td>
<td>21</td>
<td>8</td>
<td>29</td>
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<td>21-30</td>
<td>16</td>
<td>12</td>
<td>28</td>
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<td>&gt;30</td>
<td>20</td>
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<td>40</td>
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<tr>
<td>TOTAL</td>
<td>62</td>
<td>44</td>
<td>106</td>
</tr>
</tbody>
</table>
Epidémie de Kikwit: investigations épidémiologiques.

**QUI?**

- Techniciens de labo (2).
- Infirmiers.
- Médecins.
- Autres.

**QUAND?**

- 10 Avril, 1995.
- Post-chirurgical.
- Soins intensifs

**OÙ?**

- Hôpital KKT2
- Hôpital général de KKT
- Hôpital de Mosango.
- Hôpital de Bonga-Yassa.
National response: epidemiological links between cases.

Kimfumu M 36 ans
Laborantin KK2
Transféré HGK 9/4/95
Opéré 10 et 11/4/95

Mubiala M
Anesthésiste
Malade 15/4/95
Décédé 26/4/95

Palata
Médecin
Malade 1/5/95

Ofur
Médecin
Malade 5/5/95

Dina R
Médecin
Malade 1/5/95

Daniella
Médecin
Malade 30/4/95

Clara
Malade 30/4/95

Rde Floralba
Infirmière S.O.
Malade 14/4/95
Décédée 25/4/95

Kingansi
Infirmier S.O.
Malade 14/4/95
Décédée 26/4/95

Musiela F O
Anesthésiste
Malade 1/5/95

Beya
Médecin
Malade 2/5/95

Kimfumu M 36 ans
Laborantin KK2
Transféré HGK 9/4/95
Opéré 10 et 11/4/95

EBOLA KIKWIT: sœurs victimes
National/International response: virological investigations

14 blood samples collected on 4 May, 1995.

Kinshasa, 5 May

itm/Antwerp, 6 May

12 May, arrival of international team: WHO, CDC, IPP.

Kikwit, 10 May, 1995.

CDC/Atlanta, 9 May
Aperçu sur l’épidémie de Fièvre hémorragique Ebola à Kikwit, 1995

- 317 cas (75 personnel de santé).
- 250 décès (60 personnel de santé).
- Convalescents: 70.
- Familles affectées: 180; orphelins: 727.
- Extension: 25 villages et 1 cas à Kinshasa.
The seven outaks of EVD in DRC, 2014.
No link between the two outbreaks in West Africa and Boende according to the results of sequencing of the two viruses. EBOV Boende showed 99.2% identity with the isolate of Kikwit and 96.8% identity to EBOV variant of West Africa.

- Social mobilization community dialogue & engagement
- Psychosocial support
- Water, Hygiene, sanitation
- Mobile laboratory , research
- Epidemiological surveillance
- Logistics
- Case management
- Safe burial
- CICTS
- Family's members wearing gloves, are participating in the burial
Control measures: community approach

- Community approach aims at early community engagement and early ownership for implementing Ebola prevention and control measures.
- The pluridisciplinary technical teams have to work closely with:
  - APA: administratives/political/Privates local leaders.
  - Other opinion leaders (priests, pastors, traditionnal healers).
  - RECO: community relay (community delegates for health)
  - IT: nurse responsible of the Health zone.
Control measures: community approach

- Roles of APA, RECO and IT:
  - Sensitization of community members
  - Role of Ebola survivors for prevention and management of community resistance by disseminating their messages in the communities.
  - Dialogue and negociation with communities and affected families.
  - Promotion of Ebola survivors to reintegrate their communities.
  - Guided visit of the Ebola treatment centers (ETC), because regarded as a « place for dying ».
  - Implementation of negociated solutions with communities members.
Characteristics of Ebola outbreaks in DRC, 1976-2014

<table>
<thead>
<tr>
<th>Year</th>
<th>Location</th>
<th>Cases (% death)</th>
<th>Risk factors (index cases)</th>
<th>Nosocomial infection</th>
<th>Delay in response</th>
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</thead>
<tbody>
<tr>
<td>1976</td>
<td>Yambuku</td>
<td>318(88)</td>
<td>Bushmeat contact</td>
<td>++++</td>
<td>4 months</td>
</tr>
<tr>
<td>1977</td>
<td>Tandala</td>
<td>1(100)</td>
<td>?</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>1995</td>
<td>Kikwit</td>
<td>315(88)</td>
<td>Farming activities</td>
<td>++++</td>
<td>5 months</td>
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<tr>
<td>2007</td>
<td>Mweka</td>
<td>264(71)</td>
<td>Bats preparation?</td>
<td>+</td>
<td>4 months</td>
</tr>
<tr>
<td>2008</td>
<td>Mweka</td>
<td>32(42)</td>
<td>Bats preparation?</td>
<td>0</td>
<td>21 days</td>
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<tr>
<td>2012</td>
<td>ISIRO</td>
<td>77 (49)</td>
<td>?</td>
<td>++++</td>
<td>4 months</td>
</tr>
<tr>
<td>2014</td>
<td>Boende</td>
<td>66 (70)</td>
<td>Dead monkey</td>
<td>++</td>
<td>15 days</td>
</tr>
</tbody>
</table>
## Characteristics of Ebola outbreaks in DRC, 1976-2014

<table>
<thead>
<tr>
<th>Year</th>
<th>Location</th>
<th>Alert</th>
<th>Ebola type</th>
<th>Ecology</th>
</tr>
</thead>
<tbody>
<tr>
<td>1976</td>
<td>Yambuku</td>
<td>Typhoid Fever, Yellow Fever</td>
<td>Ebola Zaire</td>
<td>Rural, Region of tropical forests</td>
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<tr>
<td>1995</td>
<td>Kikwit</td>
<td>Typhoid Fever, Shigellosis</td>
<td>Ebola Zaire</td>
<td>Urban, Région of savannah</td>
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<tr>
<td>2007-08</td>
<td>Mweka</td>
<td>Typhoid fever and shigellosis</td>
<td>Ebola Zaire</td>
<td>Rural, Region of savannah with forested galeries</td>
</tr>
<tr>
<td>2012</td>
<td>Isiro</td>
<td>Malaria and bacteremia</td>
<td>Ebola Bundibugyo</td>
<td>Urban, region of tropical forests</td>
</tr>
<tr>
<td>2014</td>
<td>Boende</td>
<td>Gastroenteritis</td>
<td>Ebola Zaire</td>
<td>Rural, Region of tropical forests</td>
</tr>
</tbody>
</table>
EVD in DRC were confined at the outbreaks epicenters (1976-2014)

<table>
<thead>
<tr>
<th>Locations</th>
<th>Num cases (%)</th>
<th>Number cases transferred to Kinshasa</th>
<th>Secondary Infections</th>
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</thead>
<tbody>
<tr>
<td>YAMBUKU, 1976</td>
<td>318(88%)</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Tandala (1977)</td>
<td>1(100%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>KIKWIT, 1995</td>
<td>315(88%)</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>MWEKA, 2007</td>
<td>264(71%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Mweka, 2008</td>
<td>32(42%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>ISIRO, 2012</td>
<td>77(49%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>BOENDE, 2014</td>
<td>66(70%)</td>
<td>0</td>
<td>0</td>
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</tbody>
</table>
Challenge for early clinical diagnosis of the EVD.

- Haemorrhage
- Hiccups
- Somnolence, delirium, coma
- Severe sore throat
- Chest and abdominal pain
- Skin rash
- Diarrhoea, vomiting

Infectivity

- Fever
- Severe headache
- Myalgia
- Extreme fatigue
- Conjunctival injection

CFR 25-90%

<50%
Challenge for laboratory diagnosis: local lab facilities for the confirmation and case management

1976-2007

INRB
Challenge to have an adequate social mobilisation to overcome the socio-cultural aspects of EVD outbreak

- Resistance of population to accept control measures.
- Engagements of community leaders.
- Traditional funeral practices.....
- Social mobilization : radio, mass gathering
Challenge to give a safe and dignified burial.

Kikwit 1995

Family's members wearing gloves, are participating in the burial.

Isiro 2012
Logistic challenge to reach the epicenter of EVD outbreak in DRC.
Challenge to manage Ebola cases

- Late recognition of EVD by HCW.

- Isolation ward: most Ebola patients were reluctant to stay at the isolation wards because far away from the city, surrounded by black plastic, no running water, no electricity, no toilets. Sometime old morgue is used as an isolation ward.

- Shortage of PPE and disinfectants.

- Lack of local laboratory facilities for triage and follow up of hospitalized Ebola patients.
Challenge for the treatment of EVD: use of blood transfusion from Convalescent Patients

- No effective anti Ebola treatment.
- Only palliative treatment.
- And treatment to avoid cardiovascular collapse and renal insufficiency.
- Lethality >80%
- A nurse who cared for Ebola infected Italian nuns, became infected......
- Decision was made by Congolese team to treat her with blood transfusion from convalescent Ebola patients.
### CHARACTERISTICS OF THE CONVALESCENT BLOOD DONORS

<table>
<thead>
<tr>
<th>DONORS</th>
<th>AGE Years</th>
<th>Sex</th>
<th>Nº of days between onset of symptoms and Blood Donation</th>
<th>EBOLA STATUS</th>
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<tr>
<td></td>
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<td></td>
<td></td>
<td>Ag</td>
</tr>
<tr>
<td>1</td>
<td>27</td>
<td>M</td>
<td>37</td>
<td>_</td>
</tr>
<tr>
<td>2</td>
<td>33</td>
<td>M</td>
<td>45</td>
<td>_</td>
</tr>
<tr>
<td>3</td>
<td>32</td>
<td>F</td>
<td>45</td>
<td>_</td>
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<tr>
<td>4</td>
<td>30</td>
<td>F</td>
<td>55</td>
<td>_</td>
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<tr>
<td>5</td>
<td>27</td>
<td>F</td>
<td>65</td>
<td>_</td>
</tr>
</tbody>
</table>

M=Male
F=Female
<table>
<thead>
<tr>
<th>DONOR</th>
<th>AGE (Years)</th>
<th>Sex</th>
<th>N° of days between onset of symptoms and transfusion</th>
<th>Blood Volume</th>
<th>Donor n°</th>
<th>Outcome</th>
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<tbody>
<tr>
<td>1</td>
<td>27</td>
<td>F</td>
<td>7</td>
<td>400cc</td>
<td>1</td>
<td>Alive</td>
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<td>2</td>
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<td>11</td>
<td>150cc</td>
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<tr>
<td>3</td>
<td>15</td>
<td>F</td>
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<td>150cc</td>
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<tr>
<td>4</td>
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<td>F</td>
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<td>250cc</td>
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<td>5</td>
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<td>6</td>
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<td>8</td>
<td>48</td>
<td>F</td>
<td>4</td>
<td>400cc</td>
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<td>Dead</td>
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F=Female
Patient n°1 : 27 Y-O : nursing care of 2 italians nuns died of Ebola

<table>
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<tr>
<th>Days</th>
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<th>1-06</th>
<th>2-06</th>
<th>4-06</th>
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<th>14-06</th>
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<tr>
<td>Fever</td>
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What conclusion?

- With adequate symptomatic treatment, the Ebola case fatality rate may drop significantly.
- **Transfusions are probably usefull**
  - For treatment or prevention of shock.
  - For providing coagulation factors to stop or to prevent bleeding manifestations.
  - For providing protective passive anti Ebola IgG and IgM.
Major limitation of our study and perspective

- **Limitation**
  - Small number of patients in our study.
  - Lack of control subjects
  - Lack of specific dose (volume of blood needed)

- **Perspective**
  - Further evaluation of passive immune therapy:
    - Natural
    - Feasable everywhere in Africa
    - Not expensive

Contrôle de l’épidémie de MVE par simples mesures de santé publique, Kikwit 1995.

12 May, arrival of international team with PPE

- Non health care workers
- Health care workers

315 cases
250 (80%) deaths
Research priorities: Ebola virus transmission from animal to human

Must we ban consumption of bushmeat?

But we can promote behaviours changes of hunters/farmers

Universal Precautions

Behaviours change
Research priorities: discovery of new pathogens associated with Acute Hemorrhagic Fever in Africa

- On the African continent, viral hemorrhagic fever are usually caused by four families of enveloped, single stranded RNA viruses:
  - Arenaviridae
  - Bunyaviridae
  - Filoviridae
  - Flaviviridae.
- In 2009, by deep sequencing, we discovered a novel rhabdovirus associated with an outbreak of viral hemorrhagic fever, in Mangala village, Boma Bungu HZ Bas Congo Province, DRC.

Source: PLoS Pathog 8(9): e1002924.doi:10.1371/journal.ppat.1002924
CONCLUSION.

- Ebola outbreaks in DRC more and more frequent due to a better surveillance system and consumption/handling of bushmeats.
- Both Ebola Zaire and Ebola Bundibugyo strains are circulating in DRC.
- Late recognition because of the poor acknowledge of the disease by doctors and nurses who confuse and treat EDV like malaria and typhoid fever.
- National expertise in managing Ebola outbreaks (skils in epidemiology, mobile lab, case management, coordination)
- In DRC Ebola outbreaks are localised without expansion and under control by using simple public health control measures based on community approach.
Conclusion

- Une coordination rigoureuse de l’ensemble des partenaires sous l’autorité du gouvernement constitue la clé de réussite.
- Mise en place d’un système d’alerte précoce grâce au renforcement du système national de surveillance et de capacité de diagnostic de laboratoire.
- Un engagement sans faille des communautés aux mesures de lutte.
- Ressources humaines et financières nationales facilement mobilisables.
- Travail en équipes multisectorielles comprenant médecins hygiénistes, anthropologues, psychologues.
EBOLA GREETINGS SAVED LIVES

THANK YOU FOR YOUR ATTENTION