

Ebola Virus where the Hell are the reservoirs ?

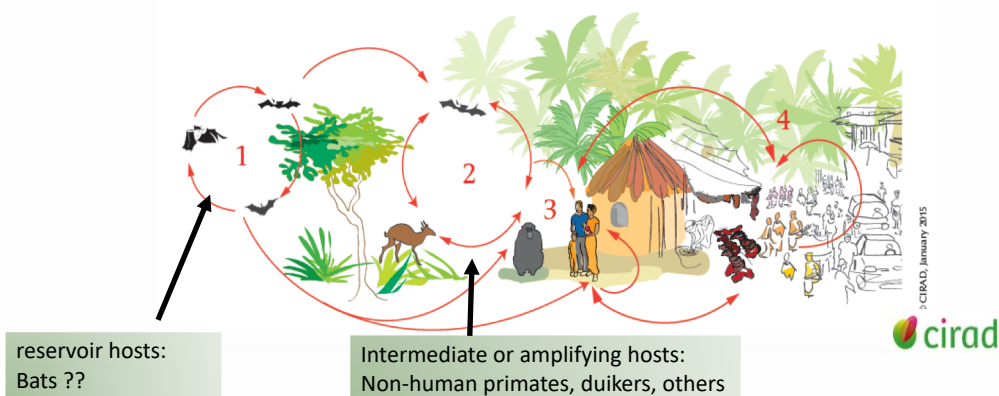
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Kasetsart University
Workshop « Reservoir Hosts »
21- 23 November 2018

EBOLA: complex zoonotic disease

Each outbreak in humans = independant zoonotic transmission event

Ebola virus circulation and transmission within a forest socio-ecosystem:
(1) bats (2) wildlife (3) contact between man and wildlife (4) human
communities © D. Guard-Lavastre/CIRAD, after CDC;
<http://www.cdc.gov/vhl/ebola/resources/virus-ecology.html>



How can humans become infected?

Bushmeat and hunting:

Reservoir and intermediate reservoir species

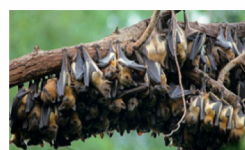
Exposure to blood and/or infected tissues

Non-human primates, bats, duiker, ..



bats : infected saliva, faeces

On fruits, other..



Mango tree in Yaoundé, May 2015

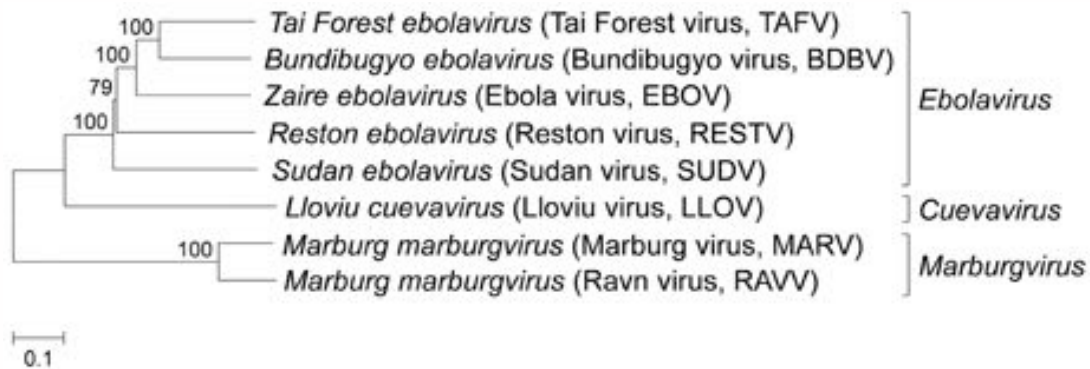
EBOLA: complex zoonotic disease



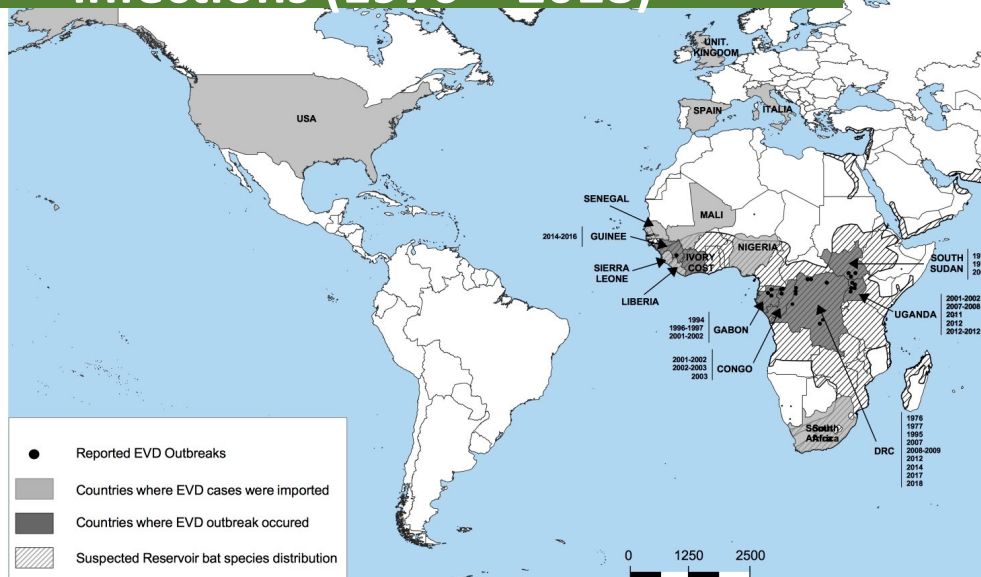
Filoviridae's family includes **three genera** (Kuhn et al. 2010; Negredo et al. 2011; Kuhn et al. 2013; Maruyama et al. 2014):

- **Ebolavirus** (EBOV) with five distinct species: *Sudan ebolavirus* (SUDV), *Zaire ebolavirus* (ZEBOV), *Tai Forest ebolavirus* (TAFV), *Bundibugyo ebolavirus* (BDBV) and *Reston ebolavirus* (RESTV)
- **Marburgvirus** (*Marburg marbugviruse*), with only one species consisting of two viruses, Marburg virus (MARV) and Ravn virus (RAVV);
- **Cuevavirus**, a new genus recently reported with one species, *Lloviu virus* (LLOV).

EBOLA: complex zoonotic disease



32 epidemics and/or sporadic case infections (1976 – 2018)



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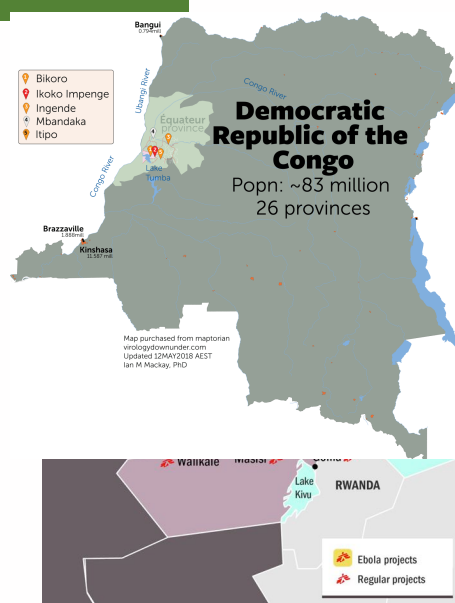
In 2018 : 2 Outbreaks in RDC :

May outbreak : 54 cases (33 deaths – 61 % mortality)

– Ongoing Ebola Outbreak in RDC (18 Nov 2018):

Total cases: 373 (323 Confirmed)

Total Death : 217 (170 Confirmed, 40 probable)



West Africa outbreak

- 2014 – 2016
- Single zoonotic spill over event (2-year-old boy, Guinea).
- March 2014, the outbreak was reported in Guinea by the WHO's
- May 2014, the disease crossed the borders and Liberia and Sierra Leone
- More than 26 000 Human cases (25 to 66 % of mortality)

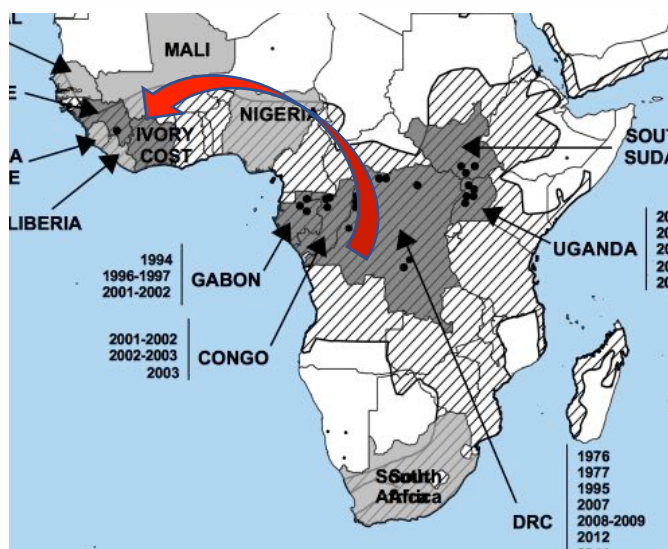
West Africa outbreak

- Outbreak was caused by a **new strain of ZEBOV** distinct of those incriminated in Central Africa
- with a **most recent common ancestor estimated at 10 years** with ZEBOV circulating in Central Africa

Questions ?

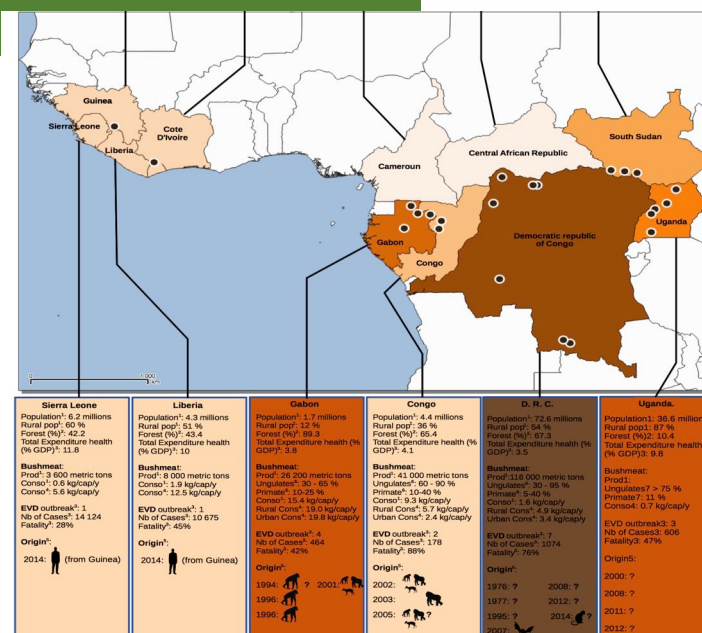
- Is EBV Zaire widespread across Africa ?
- For a long time?
- Recent spread?
- How the virus went from central to West Africa ?

ZEBOV Most Recent common Ancestor: 10 Years



Zoonotic origin identified in 9/32 EBV outbreaks

- Guinea : bats ?
- Ivory Coast : Chimp
- South Sudan (bats ?)
- Sierra Leone and Liberia: human Transmission
- Gabon: Apes And Multiple animals?
- Congo: Multi species, Gorilla,
- RDC: Bats,



Chimpanzees and gorillas : not a natural reservoir species for EBV

High mortality rates of EBV in apes

>25% mortality:

Ebola_virus outbreak among wild chimpanzees living in a rain forest of Côte d'Ivoire. (Formenty et al, 1999)

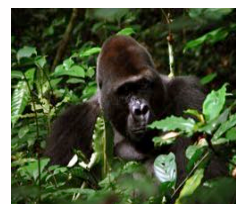


99% reduction in nest counting sites:

NE Gabon after EBV outbreaks (Walsh et al, 2003)

90% mortality in habituated gorillas:

Lossi Park, NE Congo (Bermejo et al, 2006)



EBV outbreaks with different strains:

multiple introductions and most likely not natural host (Leroy et al 2006)

Ebola Outbreak Killed 5000 Gorillas

Magdalena Bermejo,^{1,2*} José Domingo Rodríguez-Tejedor,² Germán Illera,¹ Alex Barroso,² Carles Vilà,³ Peter D. Walsh⁴

How chimpanzees and gorillas become infected?

CHIMPANZEES:

Hunting and/or bats/other species ?

Tai Forest, Côte d'Ivoire, well documented behaviour data on Chimp (Formenty, Boesch et al, 1999)

- infants from infected mothers
- meat consumption (red colobus represent >80% of hunted animals by Chimp)

Central Africa

- chimpanzees hunt duikers and monkeys (ex. EBV RNA detected in carcass) (Rouquet et al 2005)



How chimpanzees and gorillas become infected?

GORILLAS:

Transmission via chimpanzees and/or bats/other species ?

herbivorous, no hunting

sympatric species with chimpanzees

exchanges and contacts possible: infected carcasses,
feed in same fruit trees (Walsh et al, 2007)

ex.others pathogens exchanged (SIV)



Are other non-human primates (NHP) natural hosts for EBV?

West Africa: Tai Forest

red colobus monkey at origin of EBV in chimpanzees?

>80% of meat (estimated 250 kg in lifespan)

red colobus not a natural host, because no other outbreaks

Central Africa: captive but wild captured monkeys Gabon and Cameroon

EBV antibodies: 12% chimpanzees, 6% in gorillas also in
drills, mandrills, baboons, De Brazza monkey

EBV also in Cameroon without EBV outbreak?

Is there non-lethal infections in chimpanzees and other NHPs?



Morbidity and mortality of wild animals between EBV outbreaks 1994-2003 in Gabon (Lahm et al 2006)

397 carcasses in 35 outbreaks of animal mortality

NHPs: gorillas, chimpanzees, 12 – 17 outbreaks
 mandrills 13 outbreaks
 white nosed and mustached guenon, 3-7 outbreaks
 black and guereza colobus 1-3 outbreaks

Antilopes: duiker and sitatunga 1-3 outbreaks

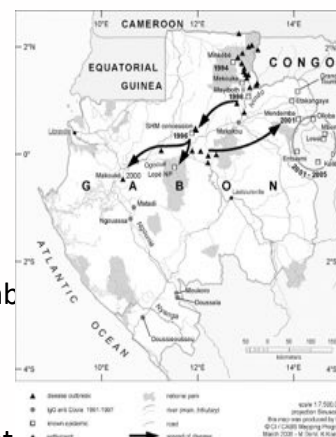
Other: Bush pigs, porcupines, civet 1-10 outbreaks

Mortality: single cases but also in groups or >2; ex 10 mandrills in timber concession

Morbidity: animals (monkeys) with diarrhea, vomiting, bleeding, ..

Seasonality: dry season and transitional months between dry and wet seasons

Caution: no laboratory confirmation done on these samples



Actual knowledge on EBV in Bats

Bats suspected to be the reservoir for Ebola (Leroy et al 2005)

3 fruit bat species in Gabon (*Hypsignathus monstrosus*, *Epomops franqueti* et *Myonycteris torquata*): wide geographic range

EBV RNA (3%-19%), cluster in Zaire EBV

EBV antibodies (7%-24%)

Additional studies in bats

at least 9 bat species were found with antibodies (<5% to >20%, 40% for some species)

Gabon and Congo (Pourrut et al, 2007)

Ghana (Hayman et al 2008)

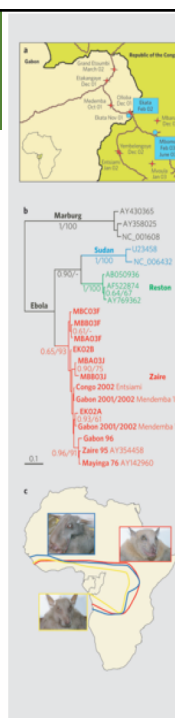
Zambia (Ogawa et al 2015)

Also in bats from Asia:

China (Yuan et al, 2012)

Bangladesh (Olival et al, 2013)

Only RNA detection in 3 species, no virus isolation, Asymptomatic, bat mortality? enough data?



Role of bats identified in 2 of 32 EBV outbreaks (epidemiological evidences)

- **Exposure to bushmeat**

In 2007 in Luebo, DRC



- **Indirect exposure to infected bats:**

2013 Guinea

the burnt tree that housed a bat colony in Meliandou where the index case (2years old child) could have been infected



Role of bats in other outbreaks?

Direct or indirect exposure, or via intermediate/amplifying host?

(Marí Saéz et al. EMBO Mol Med. 2015)

More than 32 EBV outbreaks than those reported between 1976-2018 ??

West Africa: 2 outbreaks (not Human to Human transmission)

Central Africa: 25 outbreaks

- no major spread (except outbreak in Guinea)
- Between 1- 400 fatal cases for each outbreak

EBV antibodies in central Africa in populations living in areas without EBV outbreak

(Iahm et al 2006, Nkoghe et al 2011, de Nys et al 2018)

1% to >30% in forest areas in Gabon and Congo

Guinea : up to 18 % ; Ghana : up to 11%; Cameroun : 7%

Other epidemics not detected/recognized?

Ex.1956 in Buni DRC (Colebunders et al 2015)

Existence of less pathogenic variants?

Remaining questions on EBV reservoir

Incomplete understanding of ecology of EBV

- extend of EBV infection in animals (limited number of studies, limited geographic areas covered)
- role of reservoir species and amplifying hosts.

Role of bats:

- how many species are infected
- how widespread is EBV in bats across Africa
- how many ebola species in bats
- how is virus maintained in bat populations

Remaining questions on EBV reservoir

Role of non-human primates:

- often identified as source (hunting and bushmeat)
- high mortality in chimpanzees and gorillas
- mortality rates in other NHP species?
- asymptomatic infections? How widespread across Africa

Role of other animals ?



Perspective

Ebola Virus Maintenance: If Not (Only) Bats, What Else?

Alexandre Caron ^{1,2,3,*}, Mathieu Bourgarel ^{1,2}, Julien Cappelle ^{2,4,5}, Florian Liégeois ⁶,
Hélène M. De Nys ^{2,5,7} and François Roger ^{2,5}

Futur EBV cross-species transmission ?

Depends on contact between humans and infected animals

- frequency of contacts
- prevalence of EBV in animals
- modes of transmission.

Determine role of bushmeat and hunting for futur EBV transmissions:

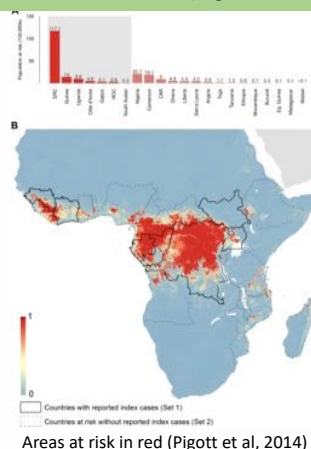
- direct exposure to infected blood and tissues (higher probability of contamination?)

Determine role of bats for futur EBV transmissions

- direct exposure to infected blood and tissues as bushmeat
- exposure to infected faeces and/or saliva

Need for studies on EBV at interface between wildlife and humans

22 million individuals in 22 countries at risk for EBV contamination (Pigott et al, 2014)



In countries with know EBV outbreaks but also in countries where risk for cross-species is estimated to be high

Study EBV infection in bushmeat

- primates, bats, antilopes etc..



Study EBV infections in humans involved in hunting and bushmeat

- antibody and/or RNA detection
- existing sample collections
- prospective studies



Ecological approach of EBV to understand underlying mechanisms

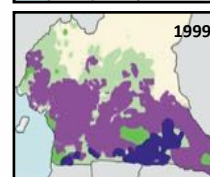
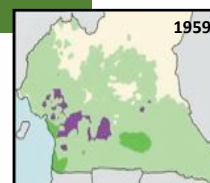
Can we expect higher frequency of futur EBV outbreaks with higher impact?

Increasing demand for bushmeat in cities
bat bushmeat consumption seems to increase

Increasing human presence in forest areas:
logging and mining concessions
road constructions,

Acces to previously inaccessible areas
increasing hunting in these areas

Deforestation and changing bat distribution
humans closer to infected bats?



Logging concession
(purple) in Central Africa
(Global Forest Watch)

