Animal origin agents that have emerged into « high public health impact » zoonoses

HIV/SIV

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HIV/AIDS: The most important infectious disease to have emerged in the past century.

- First cases of unusual immune deficiency among gay men in USA, HIV identified as the cause of AIDS
- HIV-2 identified in West Africa
- In Africa, a heterosexual AIDS epidemic is revealed
- 2009: 33.2 (30.6 – 36.1) million (1/180) living with HIV/AIDS
- 25 million deaths
Two types of HIV

HIV-1
Global spread

HIV-2
West Africa
Origin of HIV
Cross-species transmission of SIV from non-human primates

HIV-2 from SIVsmm in sooty mangabeys in West Africa

HIV-1 from SIVcpz/SIVgor in chimpanzees and gorillas in Central Africa

Phylogenetic relation, viral structure
Geographical coincidence habitat and HIV-1 and HIV-2 epicenters
Contact between primates and humans
How did SIV cross-species transmission occur?

Cutaneous or mucous membrane exposure to infected blood or other secretions

- Hunting
- butchering;
  injury from butchering
- pets: biting or other injuries, contact with body fluids?
How many cross-species transmissions?

Each HIV-1/HIV-2 group represents a zoonotic transmission
8 transmissions for HIV-2 4 transmissions for HIV-1

Global epidemic
< 20 in Cameroon

2 Cameroonians
1% of HIV-1 in Cameroon

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When did these cross-species transmissions occur?

- HIV-1 M: MRCA: 1921 (1915-1941)
- HIV-1 O: MRCA: 1920 (1890-1940)
- HIV-2 A and B: MRCA: 1940-1945
- 1959 1960: HIV-1 M Kinshasa DRC
- 1964: HIV-1 O: Norwegian sailor infected in Cameroon
- 1960: Oldest HIV positive samples in Africa
- HIV1 (M/O) and HIV-2 started to diverge in the human population 1920-1940

Cross-species transmissions occurred before these dates. How many before? After?

HIV-1 N and P more recent transmissions?
Where are the reservoirs of the HIV-1/2 ancestors?

Identify the prevalence and genetic diversity of SIVcpz and SIVsm in wild mangabey and chimpanzee/gorilla populations?

Primates are highly endangered species,

Large scale studies only possible using non-invasive approach
Detection of SIV infection in faecal samples
(B.Hahn, UAB, USA)

Storage: Max 3 weeks in the field at ambient temp in RNA-later, -80° in the lab

- Faecal samples in RNA-Later
- Faecal samples

Antibody detection after dialysis

Viral RNA detection: RT-PCR, Sequence and phylogenetic analysis

mtDNA:
- species/subspecies
- Microsatellite analysis: Enumeration of SIV positive samples
Where are the reservoirs of HIV-2?

Two epidemic groups of HIV-2 (A and B) most closely related to SIVsmm from the Tai Forest, Eastern Ivory Coast

Non-invasive sampling of SIV from sooty mangabeys
Santiago et al. (2005)

Tai Forest, Cote d’Ivoire
Where are the reservoirs of HIV-1?

Chimpanzees from West central Africa are the reservoir for HIV, but also for SIV in gorillas

No SIVcpz infection

Chimpanzees
N >5000

Gorillas
N>2500

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Cross-species transmissions and emergence of viruses

- Exposure/contact
  - frequency of contacts
  - prevalence in host
  - transmission mode

- Infection in the new host
- Adaptation and replication in the new host
- Spread from human to human

- From single cross-species transmission to epidemic?
Why multiple cross-species transmissions with SIVsmm and SIVcpz/gor in this areas?

- **Many contacts between primates and humans**
  - mangabeys: 50% of primate bushmeat in West of Ivory Coast
  - Chimpanzees and gorillas: bushmeat, ....

- **High SIV prevalence:**
  - SIVsm: 50% in wild mangabeys
  - SIVcpz: 30% in wild chimpanzees infected with M and N ancestors
What are the potential risks of transmission of SIVs other than SIVcpz/SIVgor and SIVsmm from NHPs to humans?

Evidence of SIV infection in at least 40 African non-human primates (NHP), 32 confirmed by sequence.

Ongoing exposure to SIVs through hunting, butchering and handling of NHPs.

Cross-species transmission of other retroviruses has also been documented among hunters (Mahieux et al., 1998; Wolfe et al., 2004, Switzer et al, 2010).

Study more in detail the SIV in primate bushmeat allows to evaluate to what extent humans are exposed to SIV infected primates.
Extensive survey on the prevalence of SIVs in primate bushmeat in Cameroon (Aghokeng et al, Virology 2006; Aghokeng et al, IGE 2009).

DBS from fresh hunted or confiscated primates
2586 samples
7 different sites in southern Cameroon
SIV lineage specific Elisas

SIV prevalence in bushmeat = 2.93%.

Most frequently hunted species (>90%): low prevalence or absence of SIV infection

11 species, 3-5 predominate
Wild living adult red colobus represent a substantial SIVwrc reservoir in Côte d’Ivoire (Locatelli et al, IGE 2008)

Red colobus, diana monkeys and sooty mangabeys: most extensively NHP hunted by the human population

SIV infection possibly reaching 50% of the adult red colobus population living in Tai Forest

BUT NO EVIDENCE YET for transmission of SIV from red colobus to humans!

Two epidemic groups of HIV-2 (A and B) most closely related to SIVsmm from the Tai Forest
Limited knowledge on SIV diversity and prevalences

> 30 species not tested

Most likely sample bias!! Samples from limited geographic regions only

- 4 in West Africa
- 12 in West Central Africa
- 4 in East Africa
- 2 in Central Africa
- 1 en Afrique du sud

1000 Km
From cross-species transmissions to epidemic?

Combination of several factors

- Pathogenic potential of the virus
- Host specific differences
- Social, demographic, and environmental factors
- *Role of iatrogenic factors?*

Not all SIVcpz/SIVsmm became epidemic
Ongoing risk for new SIV transmissions

- Humans continue hunting of primates for bushmeat!!
- Other transmission(s) not yet recognized due to long incubation period?
- New SIV variants not detected by actual HIV screening assays
A new human immunodeficiency virus derived from gorillas

Jean-Christophe Plantier, Marie Lenoir, Jonathan E Dickerson, Fabienne De Oliveira, François Cordemier, Véronique Lemoine, Florence Dambourné, David I. Robertson & François Simon

We have identified a new human immunodeficiency virus in a Cameroonian woman. It is closely related to gorilla simian immunodeficiency virus (SIVgor) and shows no evidence of recombination with other HIV-1 lineages or with chimpanzee SIV (SIVcpz). This new virus seems to be the prototype of a new HIV-1 lineage that is distinct from HIV-1 groups M, N and O. We propose to designate it HIV-1 group P.

HIV-1, the virus principally responsible for the AIDS pandemic, arose through cross-species transmission of a retrovirus (SIVcpz/Pot) found in

related to SIVgor in a Cameroonian chimpanzee (major or main), N (non-M, non-O) and O. Since 2001, a French network monitoring HIV genetic diversity is suspected when RNA viral load is negative in an individual with a history of antiretroviral therapy. As part of a previous study, serial samples from a 6-year-old girl (RBE168) who was found to be negative in her birth family and subsequently became infected with HIV-1 were analyzed.

Several HIV-1 screening tests were performed in these patients; all showed positive results. The virus has been isolated from the patient's blood and confirmed to be of HIV-1 group M. The sequence of the virus has been compared with other isolates of HIV-1 group M.

Supplementary Methods and Supplementary Figure S1. The virus has no signs of AIDS, remains undetectable, and has a viral load of about 1000 copies per ml. The patient's CD4 cell count has been consistently high since the diagnosis of infection.
## Increasing demand and trade of bushmeat

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<th>Topic</th>
<th>Details</th>
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<td>Bushmeat hunting</td>
<td>Longstanding common practice of rural household economies</td>
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<td>Commercial logging</td>
<td>Road constructions into remote forest areas</td>
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<td>Hunters in previously inaccessible forest areas</td>
<td>New infrastructure to capture and transport bushmeat</td>
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<td>High HIV prevalences in rural villages around logging concessions</td>
<td>(&gt;20%)</td>
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<td>High potential for dissemination of new HIV, recombination between HIV and SIV.</td>
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The 4 HIV-1 groups have their origin in West Central Africa

Origin of virus is different to origin of epidemic

Only SIVcpz/gor transmissions in Cameroon?

First aids cases identified in the US
Study whether other cross-transmissions occurred?

- develop approach for large scale screening with the different SIV antigens?

- continue to identify SIVs?

- Target population?
  - Screen human populations at risk for new SIV infections, hunters?
  - In rural areas and around logging concessions with high hunting pressure?
  - In urban areas?