Lassa fever in Guinea: epidemiological study and implication for preparation of clinical trials

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Plan

• Introduction
• Laboratory capacity and resources
• Research studies
• Case definition
• Capacity building
Introduction (1/2)

• The Haemorrhagic Fever Project in Guinea, the BNITM in Hamburg and RKI in Berlin, conduct joint research on LF in Guinea for more than two decades.
• Research has been focussed on: Diagnostics, Ecology, and Epidemiology of LF.
• One on-going project (LAROCS project) investigates:
  • The association of LASV prevalence in the rodent reservoir and seroprevalence in humans.
  • The impact of rodent control measures on both parameters in villages around Faranah.
  • The project also implements an anthropological component on the perception of the disease and the intervention in rural communities.
• Preliminary data of the consortium indicate a high seroprevalence in the communities despite low incidence of acute Lassa fever in hospitals.
• We express our interest to further explore this specific epidemiological pattern of LF in Guinea, to estimate the burden of Lassa fever in the country, and built capacity for clinical and epidemiological research.
Laboratory capacity and resources

• **In Conakry:** The HFP in Guinea (PFHG in French) was established in 1999 with the help of grants from the Volkswagen Foundation of Germany, the European Community, WHO, the Harvard Hughes Medical Institute, German Foundation for Research (Deutsche Forschungsgemeinschaft).

• **In Faranah:** There is no possibility to do the LF tests in Faranah Regional Hospital.

• **In Gueckédou:** The laboratory in Gueckedou is in operation for two years. It is fully equipped with instruments for molecular and serological testing, including conventional and real-time PCR cyclers, class II cabinet and glove-box with negative pressure for inactivation of samples.
Master mix
Two Class 2 biosafety cabinets
Biobank
Cold chain and liquide nitrogen Tank
Real-time PCRs
Class 3 glove box
Research studies – historical

Epidemiology

• In Guinea, the first seroprevalence studies were undertaken in 1990 by Lukashevich et al. (1993), who showed that seroprevalence was high (40%) along the border with Sierra Leone, and low (5%) in the north.

• Our recent findings show a high human seroprevalence in Faranah district, we are on the process to establish surveillance system in health facilities
Faranah, Guinea: Seroprevalence by village

- Total seroprevalence: very high: 84.0%
- No difference between males and females (data not shown)
- Modest differences between villages (70.5% to 91.9%)

<table>
<thead>
<tr>
<th>Village</th>
<th>N</th>
<th>Seroprevalence %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yerewalia</td>
<td>210</td>
<td>74.3</td>
</tr>
<tr>
<td>Damania</td>
<td>202</td>
<td>89.1</td>
</tr>
<tr>
<td>Dalafilani</td>
<td>210</td>
<td>79.5</td>
</tr>
<tr>
<td>Sokourala</td>
<td>211</td>
<td>89.1</td>
</tr>
<tr>
<td>Sonkonia</td>
<td>235</td>
<td>91.9</td>
</tr>
<tr>
<td>Birissa</td>
<td>234</td>
<td>70.5</td>
</tr>
<tr>
<td>TOTAL</td>
<td>1302</td>
<td>84.0</td>
</tr>
</tbody>
</table>
Research studies – historical

Virology

• To improve diagnostic tests, research has been undertaken on cellular immunity to produce a new recombinant immunoblot (ter Meulen et al 1998, 1999, 2004).

• Studies on the viral evolution were carried out in Faranah and Guékédou thanks to the strains detected in the reservoir. Values indicate emergence between 50 and 100 years (Lalis et al., 2012, Fichet-Calvet et al., 2016).
Research studies – historical

Ecology

• Based on investigations conducted by Lukashevich et al., research on reservoir ecology has been undertaken since the 2000s. Thus, 2 species, *M. natalensis* and *M. erythroleucus* have been found LASV positive in Guinea (Lecompte et al., 2006, Olayemi et al. 2016).

• They are highly infected in areas where human seroprevalence is high (Demby et al. 2001, Lecompte et al., 2006). In the hyperendemic zone of Faranah, *M. natalensis* varies seasonally in abundance and alternately frequents human habitat such as the surrounding fields (Fichet-Calvet et al., 2007, Mariën et al., 2018).
Research studies – historical

Anthropology

Some studies identified human behavior and risk factors for LASV transmission:

– Hunting and rodent capture, and the use of syringes, would be conducive to virus transmission in forested areas (Ter Meulen et al., 1996, Kerneis et al., 2009).

– In Upper Guinea, maintaining darkness in homes would promote daytime activity of the reservoir in addition to nocturnal activity (Kelly & Mari Saez, 2018).
Research studies – ongoing

- **In Faranah:** works are focused on human and rodent cohabitation and control of the disease (LAROCS project), its objective is to investigate patterns or LASV migration, household determinants of rodent-to-human transmission, the potential of rodent control to prevent LF in humans, and the disease burden.

- **In Gueckedou:** hospital-based studies are focused on patients presenting with symptoms of viral hemorrhagic fever
Lassa local surveillance

- We are on the process to establish surveillance system in health facilities where LAROCS project is active by setting up sentinel sites for screening of patients seeking care in health centers.
- Lassa fever suspect cases will be admitted at the isolation unit for epidemic diseases in Faranah Regional Hospital. If the test is positive for LASV the patient will be treated with Ribavirin and contacts followed and put under prophylaxis with oral Ribavirin.
Case definition

Possible case

Criteria (Conditions required):

• Absence of a known exposure to another probable or confirmed case of Lassa fever
• Fever > 38°C for less than three weeks
• No remission 48 hours after anti-malaria treatment
• broad-spectrum antibiotic therapy
• Absence of signs of local inflammation
• 1 Major sign or 2 minor signs without a major sign.

The possible cases are those with a low probability of a diagnosis of Lassa fever. They are included in this activity as part of the research.
Case definition

Probable case

• Probable case without epidemiological link.
  
  Criteria (Conditions required):
  Fever $> 38 \, ^\circ\text{C}$ for less than three weeks
  and No remission 48 hours after anti-malaria treatment
  and broad-spectrum antibiotic therapy
  and Absence of signs of local inflammation
  and 2 + Major Signs or 1 major sign and 2 + minor Signs.

• Probable case with epidemiological link Criteria (Conditions required): Known exposure to another probable or confirmed case of Lassa fever and Fever $> 38 \, ^\circ\text{C}$ or bleeding.

The probable cases are those with a high probability of a diagnosis of Lassa fever
Case definition

Confirmed cases

• Confirmed cases are possible or probable cases with confirmation of the diagnosis in the laboratory.

• Criteria (Conditions required):
  • Prior status of possible cases or probable case and
  • Positive PCR result for Lassa fever.
Signs for the case definition

Major signs:
• bleeding,
• swelling of the neck or face,
• conjunctivitis or sub-conjunctival haemorrhage,
• spontaneous abortion,
• petechial or haemorrhagic eruption,
• tinnitus or hearing impairment,
• persistent hypotension

Minor signs:
• headache,
• sore throat,
• vomiting,
• diffuse abdominal pain/abdominal tenderness,
• chest pain and retro sternal,
• cough,
• diarrhoea,
• generalized myalgia or arthralgia,
• profuse weakness.
Filoviridae

- 2 membres dans la famille :
  - Marburg ==> 1 sous-type
  - Ebola ==> 4 sous-types :
    - EBOV-Zaire
    - EBOV-Soudan
    - EBOV-Reston Philippine
    - EBOV-Côte d'Ivoire
VHF: Sample preparation

- Patient material: Serum (plasma)

- Centrifugation & pipetting only with personal protection!
Yellow fever diagnostics in Conakry

Yellow fever: IgM – ELISA from WHO

- Quality control: Pasteur Institute Dakar & Lyon
Lassa fever diagnostics in Conakry

- RT/PCR
- IIF (IgM, IgG)

- Quality control: Inst. of Virology, Marburg
Research studies – proposed

• To continue with rodent control implementation and epidemiological surveillance.

• To involve primary health centers in the surveillance program to better understand the specific epidemiological pattern and the range of disease manifestation of Lassa fever in Guinea.
Capacity building

- In Conakry some academic training are needed in virology and molecular biology.
- Since Faranah district is endemic, we would like to have community and HCWs trained on Lassa cases management.
- To include LF in the national surveillance system.
- To have local expertise through the involvement of young Guinean students in training in domains related to the project implementation.
- Capacity building is essential to close this gap.
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