



Meeting brief: Lassa International Conference (LIC)

15 – 19 Jan 2019

Abuja, Nigeria

Background (from LIC website): 50 years since the detection of Lassa fever in Nigeria, outbreaks have been recorded yearly in parts of the country. In 2018, Nigeria experienced the largest reported outbreak of Lassa Fever with 21 of 36 States in the country affected. The 50th year of discovery of the Lassa fever is an opportunity for the scientific community to reflect on what is known, describe gaps that exist and prioritize the research agenda for the future.

Contents

1	Plenary session, Day 1	4
1.1.	Nigeria's 2018 Lassa fever outbreak and lessons for the future	4
1.2.	The Irrua Specialist Teaching Hospital (ISTH)'s role in the fight against Lassa fever in Nigeria	4
1.3.	How a North-South relationship has improved our understanding of Lassa fever globally	4
1.4.	CEPI's role in the opportunity and responsibility for clinical trials in Africa	5
2	Parallel sessions, Day 1:	5
2.1.	Case management	5
2.1.1.	General notes: Case Management	5
2.1.2.	Prevalence and severity of acute kidney injury among children with Lassa fever in Edo State, Nigeria (2009 and 2017).....	5
2.1.3.	Early-onset sensorineural hearing loss in Lassa fever	5
2.1.4.	High mortality rates of Lassa fever in Sierra Leone 2014-2017: A descriptive study	5
2.1.5.	Lassa fever disease severity on presentation at Kenema Government Hospital, Sierra Leone	6
2.1.6.	Neonatal presentation of Lassa fever: Report of three cases.....	6
2.1.7.	Retinal hemorrhage as a diagnostic and prognostic tool in the management of Lassa fever patients.....	6
2.1.8.	Excretion of Lassa fever virus in breast milk and the management of the breastfeeding infants: Case series.....	6
2.1.9.	Clinical and virologic response to Lassa fever treatment with Ribavirin at Irrua Specialist Teaching Hospital, Nigeria.....	6
2.2.	Animal and environmental health response.....	6
2.2.1.	Trial to reduce <i>Mastomys natalensis</i> abundance in homes in rural Sierra Leone	6
2.2.2.	Lassa fever in Guinea and Sierra Leone: Rodent control and seasonal human exposure to rodents (LAROCS project)	7
2.2.3.	Evaluation of rodent control to fight Lassa fever based on field experiments and mathematical modelling.....	7
2.2.4.	Detection of antibody and antigen specific for Lassa virus nucleoprotein in monkeys in southern Nigeria: It is time to cast a wider zoo-surveillance net.....	7
2.2.5.	Insights from an anthropology of domestic space and Lassa fever research in Guinea	7
2.2.6.	LAS-V circulation in natural small mammal populations in Bo District, Sierra Leone	8
2.2.7.	Investigating the use of indigenous rodent control methods in Bo Region, Sierra Leone	8
2.2.8.	The rural environment and Lassa fever endemicity in Edo State Nigeria, 2008-2014: A spatial regression	8
2.2.9.	Land use and natal multimammate mouse abundance in Lassa fever-endemic villages in eastern Sierra Leone	8
2.2.10.	Phylogenetic analysis and prevalence of Lassa virus in multimammate mice within the highly endemic Edo-Ondo hotspot for Lassa fever, Nigeria	8

2.2.11. Biosocial dimensions of human contact with potential hemorrhagic fever virus reservoirs through the bushmeat trade.....	8
2.2.12. Impact of climate change on Lassa fever: a 10-year trend analysis of Lassa fever incidence and climatic elements in Edo State, Nigeria	9
2.3. Laboratory surveillance and diagnostics.....	9
2.3.1. Reliable detection of Lassa virus using a combination of two RT-PCR assays targeting S and L gene segments	9
2.3.2. Variation in lineage II of Lassa fever virus in Nigeria	9
2.3.3. Genetic characterization of Lassa virus strains isolated from 2012 to 2016 in Southeastern Nigeria	10
2.3.4. Real time tracking of Lassa virus genome evolution in Nigeria using Nextstrain.....	10
2.3.5. Metagenomic analysis of blood samples obtained from patients infected with Lassa virus in Nigeria.....	10
2.3.6. Methgenomic sequencing at the Epicenter of Nigeria 2018 Lassa fever outbreak. Irrua, Edo State.....	11
2.3.7. Modelling the triage of suspected Lassa cases using ReLASV antigen rapid test during January -March 2018 Lassa fever surge at Irrua Specialist Teaching Hospital, Edo State, Nigeria	11
2.3.8. Characterization of virus specific memory T cell responses from Nigerian and Sierra Leone Lassa fever survivors.....	11
2.3.9. A system biology approach to determine correlates of Lassa fever survival: the center for viral systems biology.....	12
2.3.10. How Lassa virus GP is targeted by protective antibodies	12
2.3.11. The role of mobile Laboratory in the containment of 2013-2016 Ebola virus disease outbreak in West Africa: experience of Nigerian-European consortium.....	12
2.3.12. Performance evaluation of Pan-Lassa fever virus rapid diagnostic test (relevant MRTD) kit in Irrua specialist teaching hospital .	13
2.4. Vaccines and innovations	13
2.4.1. CEPI supported vaccine development on Lassa Fever using Inovio's enhanced DNA platform technology	13
2.4.2. T-705-modified SSRNA in complex with Lassa virus nucleoprotein exhibits nucleotide splaying and increased water influx into the RNA-binding pocket	13
2.4.3. Lassa-glycoprotein processing enzyme (site-1 protease) in Pf429242 bound state: Computational kinetics and dynamics of reversible binding	13
2.4.4. Multivalent hemorrhagic vaccine for Lassa, Ebola and Marburg viruses protects against lethal challenge.....	13
2.4.5. Development of safe and effective single dose vaccines for hemorrhagic fever viruses: Preclinical efficacy data for Lassa fever and Ebola as examples.....	14
2.4.6. A chimpanzee adenovirus-vectored vaccine confers protection against lethal Lassa fever	14
2.4.7. Post-exposure protection against contemporary Nigerian isolates of Lassa fever virus in cynomolgous macaques with human monoclonal antibodies	14
2.4.8. Advancement of a Lassa fever vaccine clinical trial candidate based on the live vesicular stomatitis virus chimera platform	15
2.4.9. Quadrivalent filovirus/Lassa vaccine demonstrates protection against challenge in nonhuman primates.....	15
2.4.10. A broadly-protective Lassa fever vaccine as an effective tool for fighting Lassa fever epidemics and endemicity	15
2.4.11. Development of safe and effective vaccine against Lassa fever in Africa.....	15
2.4.12. Molecular docking studies of compounds from medicinal plants on Lassa fever virus	16
3 Plenary session, Day 2	17
3.1. Lassa fever: A historical perspective and contemporary development in Sierra Leone.....	17
3.2. New approaches in shaping the global response to VHFs	17
3.3. What do we really know about the <i>Mastomys</i> as host?.....	17
3.4. Using genomic sequencing to fight outbreaks in Africa.....	18
3.5. WHO R&D Blueprint: Global Lassa fever research priorities and the role of Nigeria.....	18
4 Parallel sessions, Day 2:	19
4.1. Epidemiology and surveillance	19
4.1.1. Contact tracing and profile of Lassa fever contacts in Edo State: Implications for the control of LF outbreaks.....	19
4.1.2. Lassa Fever Outbreak in Enugu State, Nigeria, August 2018: the role of contact tracing.....	19
4.1.3. Burden and trend of LF in Nigeria: a secondary data analysis 2012-2017.....	20
4.1.4. Lassa Fever Sentinel Surveillance System evaluation – Kenema district, Sierra Leone, October 2016 – September 2017.....	20

4.1.5. Detection of Chikungunya virus among febrile patients in Lagos, Nigeria	20
4.1.6. Epidemiology of LF in Sierra Leone	21
4.1.7. Lassa Fever Surveillance data analysis, Liberia, 2016-2017.....	21
4.1.8. The role of bio-surveillance in rumor capture and validation of LF cases between Jan-Oct 2018 in Nigeria.....	21
4.2. Policy and coordination of response	21
4.2.1. General notes: Policy and coordination of response.....	21
4.2.2. Imported Lassa fever: A review of the literature and implications for international collaboration	22
4.2.3. Preparedness of hospitals to handle emerging and re-emerging infectious diseases in Ekiti state	22
4.2.4. As assessment of states' preparedness to respond to Lassa fever outbreaks in Nigeria, 2016.....	22
4.2.5. Nigeria Lassa fever After Action Review: Lessons learnt and way forward	22
4.2.6. An innovative One Health model for mitigating perennial outbreaks of Lassa fever at the human-animal-ecosystem interface in Nigeria	23
4.2.7. Catastrophic direct medical cost of Lassa fever care by patients managed in Irrua Specialist Teaching Hospital, Irrua Edo State ..	23
4.2.8. The role of incident management system in the containment of the large 2018 Lassa fever outbreak in Nigeria	23
4.2.9. Towards a forecasting system for Lassa fever in Nigeria.....	23
4.3. Infection prevention and control.....	23
4.3.1. Infection prevention and control in a treatment center during a Lassa fever outbreak in Southeastern Nigeria-January 2018.....	24
4.3.2. Occupational acquisition of Lassa fever: an intervention study in Nigeria	24
4.3.3. Containment of Lassa fever outbreak in a southeastern Nigerian burn center without healthcare workers infection: the role of institutionalized infection prevention and control practices	25
4.3.4. Knowledge and compliance with infection prevention and control among health workers in primary health care facilities in a Lassa fever endemic LGA of Edo State, Nigeria.....	25
4.3.5. Management of confirmed Lassa fever cases in a make-shift isolation facility: implications for establishment of Lassa fever endemic situation in an area that is Lassa fever free	25
4.3.6. Knowledge of Lassa fever and infection prevention and control among proprietary and patent Medicine vendors in endemic Local government areas in Edo State: implications for Lassa fever control	25
4.3.7. Assessment of knowledge, attitude and practice of health professionals on Safe disposal of corpses of Lassa fever cases in Southwest, Nigeria.....	26
4.3.8. Knowledge, attitude and practice of post exposure prophylaxis of Lassa fever among health care workers in a tertiary health institution in South-South Nigeria.....	26
4.4. Risk communications and community engagement.....	26
4.4.1. The role of a connect center in public engagement during the 2018 Lassa fever outbreak in Nigeria.....	26
4.4.2. Determine the level of awareness and knowledge of Lassa fever among Nigerians.....	27
4.4.3. Stigma association with Lassa fever among Healthcare workers in Ondo State, Nigeria	27
4.4.4. Healthcare seeking behavior in Lassa fever endemic communities in Edo state.....	27
4.4.5. Knowledge, attitudes and practices to Lassa fever among healthcare workers in Guinea.....	28
4.4.6. Community engagement for Lassa Fever epidemiological studies.....	28
4.4.7. Community engagement: Lessons from the Ebola response	28
4.4.8. Community burial practices in Nigeria and Lassa fever Control	29
5 Side meetings	30
5.1. Meeting with Simone Agwale re Lassa ML29 vaccine.....	30
5.2. Meeting with Chima Oluwabunwo, Executive Director – AFENET.....	30
5.3 Core protocol and next steps: Targeted Lassa epidemiology studies	30
5.4. NCDC/GOARN research meeting on Lassa fever community transmission project in Nigeria	30

LIC Day 1: 16 Jan 2019

1 Plenary session, Day 1

Chaired by Sunday Omilabu (University of Lagos) and Joshua Obasanya (NCDC)

Notes by Nadia Tornieporth

1.1. Nigeria's 2018 Lassa fever outbreak and lessons for the future

Presenter: Elsie Ilori (NCDC)

- Hot spot states in Nigeria: Ondo, Edo, Ebonyi states (80% of outbreak burden 2018)
- The 2018 outbreak lasted all year (week 1-52) with emergency phase week 4-20; shift in seasonal pattern with high spike early 2018
- In total: 3498 suspected cases; 633 confirmed (45 HCWs); CFR 27% and suspected cases reported from all 36 states and FCT
- Outbreak response: community centered
- National emergency operation center activated by NCDC with support of states' EOCs; weekly situation report
- Nat'l guidelines for case mgt: designation of treatment centers and referral flow chart; development of tools; deployment of experts to the states; rapid gap assessment and addressing; capacity building/training; safe burial teams
- Improved surveillance through early case detection; incl cross-border surveillance
- Deployment of EDC reporting system SORMAS; unified data base; reporting template for active case search and contact tracing
- Standard testing algorithm; lab cap bldg.; national sample transportation logistics mgt framework
- Logistics: online tracking tool – continuous monitoring; cap bldg. for logistics officers
- Communications: social media; radio&TV; NCDC situation room radio Nigeria every Monday

Lessons learned:

- Impact of early activation of national and state EOCs
- Inter-agency /partner collaboration
- Functioning lab network and sample mgt system
- Dedicated treatment centers / cap bldg.
- Proactive use of risk communication platforms

Post-outbreak:

- Transition from EoC to TWG
- Natl LF R&D roadmap
- Review VHF IPC guidelines
- Advocacy

The 5 yr strategic plan for Nigeria: reduce CFR to less than 10%.

1.2. The Irrua Specialist Teaching Hospital (ISTH)'s role in the fight against Lassa fever in Nigeria

Presenter: Sylvanus Okogbenin (ISTH)

- WHO had recommended centers of excellence be established in affected countries. To date only 4 exist: LF center in Kenema, Irrua STH (since 2002), FMC Owo and center in Abakaliki, Nigeria.
- Institute of LF research and control established in Irrua in 2007 to reduce external dependence (eg for samples analysis); new bay for suspected cases set up recently with support from ALIMA
- CFR reduction focuses on dialysis – the hospital established a critical care and dialysis center, with critical supportive care, ventilation, blood products to reduce mortality including in patients who present late
- BSL3 lab since 2008; RT-PCR (now Altona 2.0 real-time with short 5-hour turnaround time; quantitative viral load readout) and sequencing (since 2018); 85% of confirmed cases in recent outbreak tested at Irrua; sequencing showed no change in virus – focus on rodent control and reduction of exposure as predominantly rodent to human transmission.

1.3. How a North-South relationship has improved our understanding of Lassa fever globally

Presenter: Stephan Günther (BMITM)

- Diagnostics at ISTH: 1000-2000 samples/yr (not sure of exact numbers); 95% of LASV tests in Nigeria, now other labs are coming online. Supply chain issues remain on the critical path.

- Renal and LFTs are prognostic of severe outcome/death; study ongoing to look at kinetics of viral load and outcome
- Genotype III in the North, II in the South; no or very limited human to human transmission
- Study to investigate 1444 samples with information on date and linked to satellite weather data and rainfall seems to indicate increase in case with increased temperature, decrease with increased rainfall
- Two mobile labs deployed cross country for capacity bldg.

1.4. CEPI's role in the opportunity and responsibility for clinical trials in Africa

Presenter: Richard Hatchett (CEPI)

2 Parallel sessions, Day 1:

2.1. Case management

Notes by Nicole Lurie and Kola Salami

2.1.1. General notes: Case Management

- Role of early dx; case management and presentation may differ in kids (MSF)
- 40% AKI prevalence in kids. Acute kidney injury is a predictor of death in kids, with very high case fatality rates (retrospective chart review of 10 years of data)
- Review of dialysis experience at Irrua in retrospective observational study. Experience w dialysis
- Sensorineural hearing loss caused from immunologic rxn caused by Lassa ab on hair cells; cochlear calcification also happens-cochlear implants are difficult here
- High risk of dying amongst very old and very young
- High affinity of virus for placental tissue; presentation in pregnant women is different. Poor prognostic signs are indications for 'evacuation'
- Presentation of attempts at creating severity indices
- Look at staging system-does stage at presentation affect mortality? No, but AKI high
- Presentation w retinal bleeding in some cases
- Lassa in lactating women; seen in breast milk but clears milk. May be a mechanism for P2p transmission. Need guidelines.
- Final paper looked at clinical parameters and viral load w Ribavirin rx.

2.1.2. Prevalence and severity of acute kidney injury among children with Lassa fever in Edo State, Nigeria (2009 and 2017)

Presenter: Adewale Adetunji

- Objective was to determine the prevalence and severity of acute kidney injury (AKI) in Lassa fever patients.
- Retrospective case control study. 40 LF confirmed children enrolled and characterised using the KDIGO criteria, out of which 16 had AKI. This (40%) prevalence is higher than observed in Dengue, but less than Ebola.
- Most were stage 1 KDIGO. 53.6% of children with AKI died. Intra-dialysis complications are a major cause of mortality. Pre-dialysis blood pressure major indicator of mortality.
- All children administered Ribavirin

2.1.3 Early-onset sensorineural hearing loss in Lassa fever

Presenter: Titus Ibekwe

- Immunologically mediated.
- Calcification of the cochlea is common and makes placement of hearing aid arduous.
- Prospective case control study with 37 LF confirmed patients recruited. Early onset SNHL diagnosed by PTA in 5. RT-PCR +ve in ALL. IgM +ve in 3, IgG +ve in 1 case.
- Ribavirin had no impact on occurrence and severity of SNHL.

2.1.4 High mortality rates of Lassa fever in Sierra Leone 2014-2017: A descriptive study

Presenter: Amara Alhaji Sheriff

- Longitudinal study with surveillance date 2014-2017
- 120 confirmed cases. 20 years is the median age. 73 females affected. Incidence was 5/100,000. CFR is 71.4%.

- Higher incidence in Dodo and lower Banbarra regions.

2.1.5 Lassa fever disease severity on presentation at Kenema Government Hospital, Sierra Leone

Presenter: John Schieffelin

- Increased transaminases and immunological markers of end-organ failure correlated with mortality.

2.1.6 Neonatal presentation of Lassa fever: Report of three cases

Presenter: Qasim Salau

- Fever is common to all cases. Features of sepsis are common.
- LF mimics meningitis and should be considered as a cause of meningitis during an outbreak
- LF in neonatal life progresses rapidly with very fatal outcomes.

2.1.7 Retinal hemorrhage as a diagnostic and prognostic tool in the management of Lassa fever patients

Presenter: Wilson Ovienria

- Retinal bleeding should be looked for in all cases of LF.
- Conjunctival bleeds are well documented findings in LF patients and should therefore raise a high index of suspicion where there is a diagnostic dilemma

2.1.8 Excretion of Lassa fever virus in breast milk and the management of the breastfeeding infants: Case series

Presenter: Chikwuyem Abejegah

- 3 confirmed LF cases reviewed. LASV shedding in breastmilk in all. 2 children LF -ve and 1 LF +ve on admission.
- All children placed on ribavirin and weaned off breastmilk.

2.1.9 Clinical and virologic response to Lassa fever treatment with Ribavirin at Irrua Specialist Teaching Hospital, Nigeria

Presenter: Ephraim Ogaini-Emovon

- Prospective study involving 152 confirmed LF patients on Ribavirin
- Steady declining in viral load observed with Ribavirin treatment.
- Viral load at presentation increased the duration of treatment by increasing time to virus clearance.
- Duration of illness prior to commencement of treatment significantly associated with treatment outcomes

2.2. Animal and environmental health response

Notes by Alison Bettis and Kwasi Amfo

2.2.1. Trial to reduce *Mastomys natalensis* abundance in homes in rural Sierra Leone

Presenter: Alexandra Jaouiche

- 20 village trial – 40 households (4 groups)
 - Household hygiene – eliminate attractants in and around house, received water, concrete cover, rubbish pit (with consultation from WASH experts). Results – stayed in good condition, valued by residents, but
 - Structural Exclusion – patch and fill holes, concrete thresholds at household entrances. Results – filling holes is low cost, not very effective (doors left open during the day), cement expensive and not long-lasting
 - Extermination – each household received 2 snap traps (local encouraged), poison (preferred method of rodent control - indomethacin). Safe disposal education carried out by community advocates
 - Control
- The use of indomethacin (poison) seems to be the best and preferred control for rodents that carry LV compared to others (traps, proper refuse management, etc.)
- One community started providing extermination services (for small fee) as some residents didn't want to handle carcasses

- Rodent-proof containers were popular. Integrated pest management likely most effective and sustainable approach. Research needed on Lassa infection/transmission in cats to see if they are a viable, natural control method
- Possibility of using ecological methods of control such as biological control using animals that prey on *Mastomys*? Possible unintended consequences could be a problem.

2.2.2. Lassa fever in Guinea and Sierra Leone: Rodent control and seasonal human exposure to rodents (LAROCS project)

Presenter: Elisabeth Fichet-Calvet (LAROCS)

- Study to investigate seasonality of rodent dynamics and rodent-to-human transmission
 - Incidence and seroconversion
 - Seroprevalence by age and sex
 - Effectiveness of rodent trapping
 - Anthropology/acceptability
- 12 study sites in overlapping clades in Sierra Leone (6 villages in Faranah and 6 in Bo districts)
- PCR, serology, sequencing (Sanger, NGS)
 - 85% IgG seroprevalence in Faranah, about 23% in Bo (and significant variation between villages)
 - 30 – 62% of seroconversion – IgG positive in these sites studies
- Rodent control by poisoning, trapping – lower *M. natalensis* abundance in Bo
- Partial geographical clustering (3 sublineages in Faranah)
- Anthro: Children most likely to come into contact with rats, rodents that are normally nocturnal can behave diurnally in dark homes, etc.

2.2.3. Evaluation of rodent control to fight Lassa fever based on field experiments and mathematical modelling

Presenter: Joachim Marien (LAROCS)

- Relationship between transmission in rodent pop and abundance? What is the ideal threshold of rodent population density below which Lassa does not persist?
- Assumes SEIR model
- Conclusions: Yearly control is inefficient, continuous control more efficient (60% continuous control seems to be effective), rodent vaccination is efficient. There is no magic number – though 80% reduction seems to have an impact.
- His studies also explored the possible use of a hypothetical veterinary vaccine to control rodents. Why hasn't the Lassa fraternity explored veterinary vaccines?

2.2.4. Detection of antibody and antigen specific for Lassa virus nucleoprotein in monkeys in southern Nigeria: It is time to cast a wider zoo-surveillance net

Presenter: Bamidele Ogunro

- Screening of monkeys (ELISA) as part of regular surveillance, investigating possible sylvatic transmission cycles.
- 6/62 monkeys IgG positive (Edo state), one positive for IgG and positive to Lassa virus antigen, none to IgM. Planning to carry out PCR on the positive samples (currently stored)
- Monkeys regularly approach human dwellings, feed at refuse dumps (lots of opportunity for contact with rats and humans)
- Advocating for more zoonotic surveillance (not just in rats)

2.2.5. Insights from an anthropology of domestic space and Lassa fever research in Guinea

Presenter: Almudena Mari Saiez (LAROCS)

- *Mastomys* nocturnal, but rodents are still active during the day (behind closed doors, in shadows)
- Rainy vs dry season
- Rodents are captured/controlled opportunistically – when you see one, captured by children, etc. (Need to include children in public health campaigns)
- Rodents found to return a few weeks after rodent control/poison applied
- Empty houses are a focal point for rodent concentration
- Treatment requires cooperation of entire village (otherwise rodents just move next door)

2.2.6. LAS-V circulation in natural small mammal populations in Bo District, Sierra Leone

Presenter: Umaru Bangura (LAROCS)

- Rodent sampling in 6 villages, every 3 months for about 2 years – virology (PCR) and serology (IFA)
- 41/1473 positives (28%) – only 28 of them were *M. natalensis*

2.2.7. Investigating the use of indigenous rodent control methods in Bo Region, Sierra Leone

Presenter: Dan Brunson

- 2 villages and 4 markets, looking at what methods are being used for rodent control and what are the preferred methods (and what do people think is effective)?
- Qualitative – ethnography and quantitative – cross-sectional survey
- 4 categories
 - i. Infrastructure
 - ii. Biological – cats (2nd most common)
 - iii. Chemical – most common and cheapest
 - iv. Traps – 3rd most common (only use one piece of bait, often rodents just go for food stores instead, only catch one rodent at a time)
- Seemed that perceived effectiveness was against ease of access/affordability

2.2.8. The rural environment and Lassa fever endemicity in Edo State Nigeria, 2008-2014: A spatial regression

Presenter: Samuel Owiocho

- Suspected and confirmed cases in households
- Confirms Edo state (site of Prof Sylvanus Okogbenin) as hotspot for Lassa. Not uniform as there seems to be “hotspots within hotspots” - important for future trials sampling – need and importance of our epi studies.
- On site conversion with Prof Okogbenin (IRRUA Hospital – Edo state Nigeria). He confirmed that cases are all year round in his hospital. As at the week of the conference – his 50 bed admissions facility was full with Lassa patients.
- 80% households with positive cases near forest, 73% surrounded by rice farms

2.2.9. Land use and natal multimammate mouse abundance in Lassa fever-endemic villages in eastern Sierra Leone

Presenter: Johana Teigan

- Land use types: farmhouse, forest, mining, different crops, swamp, etc.
- 10 different rodent species documented
- Higher trap success in peri-urban rather than rural (except in Aug/Sep)
- Peak abundance coincides with times of significant human-driven land perturbation
- Possible cross-cutting with agricultural sector?

2.2.10. Phylogenetic analysis and prevalence of Lassa virus in multimammate mice within the highly endemic Edo-Ondo hotspot for Lassa fever, Nigeria

Presenter: Adetunji Adesina

- Hotspots within hotspots observed
- LASV II lineage is maintained in multiple reservoirs

2.2.11. Biosocial dimensions of human contact with potential hemorrhagic fever virus reservoirs through the bushmeat trade in Nigeria

Presenter: Sagan Friant

- Long-term study in Cross River Natl Park, biodiversity hotspot
- Roughly 60 species of bushmeat, bushmeat highly preferred over domestic meat
- Bushmeat plays an important role in food security (rodents being particularly important)

2.2.12. Impact of climate change on Lassa fever: a 10-year trend analysis of Lassa fever incidence and climatic elements in Edo State, Nigeria

Presenter: Emmanuel Osagiede

- Seasonal shift in occurrence/distribution was observed with a reduction in rainfall associated with increase in incidence of LF

2.3. Laboratory surveillance and diagnostics

Notes by Gunnstein Norheim and Solomon Yimer

2.3.1. Reliable detection of Lassa virus using a combination of two RT-PCR assays targeting S and L gene segments

Presenter: Lisa Oestereich (ISTH/BNITM)

- Worked on development and validation of two different RT-PCR assays for LASV detection
- Diagnostic workflow for conventional and RT-PCR explained
- ISTH has conventional PCR (GPC PCR) which is targeting the S (small) segment of the LASV genome coding a glycoprotein. This is also where the RT-PCR (GPC PCR Altona 1.0) is binding. Nikissin PCR is binding to different target, the L segment of the LASV genome.
- The two PCRs (Altona GPC and Nikissins) are targeting different coding of the virus increasing the confidence of detecting both the S and L segment of the virus.
- Evaluation of Altona 1.0 and Nikissins PCRs was done in 2017. A total of 820 samples out of 850 samples collections were tested in three months at field level. This was transferred to Laboratory diagnostics: Sensitivity and specificity were evaluated at ISTH: More analytical tests were also done in Hamburg, Germany.
- At the end of 2018, Altona 2.0 kit which contains PCR assays of both GPC and L was evaluated with 200 samples in the field. The kit was then optimized again, and clinical evaluation was done in Nigeria in Oct 2018 and sensitivity and specificity were evaluated in Hamburg under analytical condition. Moreover, there has been a trial in Europe as part of the *efficient response to highly dangerous and emerging pathogens at EU level* (EMMERGE) project.
- The performance of GPC and Nikissins assays have been assessed with various virus isolates, cell culture isolates, and with all the different lineages of LASV that are currently circulating in West Africa (lineages I, II, III from Nigeria; lineage IV from Sierra Leone, Liberia and Guinea; Lineage V from Mali and Lineage VI from Togo). All reacted very well with both assays, but there were some differences between individual assay performance. Some strains are very detectable with the "L" assay and some with GPC assay. Therefore, use of both assays is essential to be sure that most of the LASV-positives samples are detected.
- The assays were also tested for cross-reactivity with other viruses such as flavivirus, and other diseases including malaria, hepatitis A, B and C strains. The assays were found to be none cross-reactive.
- For all samples that tested positive for LASV, CT values were compared, and all turned to have similar CT values, with a little bit higher for the GPC assay.
- Altona 2.0 Assay evaluation result
 - Of the total 174 samples tested, 154 were positive with combined GPC and L assay. The number of positive LASV samples for individual assays showed significant difference. For the GPC assay, 142 samples were positive for LASV and 130 were positive for the L assay. Altona 2.0 sensitivity was 89.5%
- **Conclusion:** Altona 2.0 gives the highest sensitivity for detecting LASV. The assay can be used for all Lassa lineages circulating in various countries in West Africa to date. Validation data has now been submitted to the WHO for Expert Review Panel (ERP). WHO response is expected in 60 days from the time of first submission by the developers.

2.3.2. Variation in lineage II of Lassa fever virus in Nigeria

Presenter: Uche Unigwe

- Lineages II and III LASV are prevalent in Southern and Northern regions of Nigeria, respectively.
- the South central (S.C) and South east (S.E) areas are highly endemic for Lassa fever, and region-specific variations in disease complications, morbidity and mortalities have been observed (CFR of 30% for S.C cases versus 48% of S.E cases). Are there any variations in the LF strains in the SC and SE areas?

- This study performed L and S gene sequencing of LASV. The main finding of this study indicated that lineage II strains have two distinct clades which can be grouped into Lineages IIA and IIB clades based on GPC/S and L/Z gene, south Nigeria variation across the river – in collaboration Nagasaki Univ. Spreading in south?
- A ten-year study of nucleic acid sequences of lineage II strains of LF from Nigeria covering the period 2004-2014 from the genome database pool was conducted
- A total of 79 LASVs (50 from SC and 29 from SE regions of Nigeria) were included in this study
- Diversity among the clades of the SE strains ranged between 18%–21%. The SC strains were of one clade and exhibited good homologous identity of 97-100%.
- Less diversity of the SC strains than the SE strains. The SC and SE strains exhibited diversity of up to 20%
- 2005, 2008, 2011 there was Lassa epidemic, 40% mortality in the 2016 epidemic in Nigeria. Nigeria experienced the largest epidemic ever in 2018. What is really happening with this? Something is responsible for the increase in morbidity and mortality from Lassa. The reason for this should be investigated. Is this a viral drift? Is there something related with the host? Environment?

2.3.3. Genetic characterization of Lassa virus strains isolated from 2012 to 2016 in Southeastern Nigeria

Presenter: Olamide Oloniyi

- The study focuses on the lineage II Lassa strains from southern Nigeria.
- Sequencing done on LASV positive samples reported at Ebonyi and Enugu hospitals between 2012 and 2016.
- 29 out of 123 suspected cases were positive for LASV
- Whole genome sequencing was performed for 11 out of the 29 LASV positive strain
- Phylogenetic analysis of the sequences of four viral proteins showed that lineage II strains are broadly divided into two genetic clades (Lineage IIA and Lineage IIB) that diverged from a common ancestor 195 years ago. Lineage IIA, consisting of strains from Ebonyi and Enugu, was more conserved than the other from Irrua
- The results suggested that the viruses of these clades have been distinctively evolving in geographically separate parts of southern Nigeria.
- Conclusion: the evolution of LASV in southern Nigeria may have implications for vaccine development, diagnostic assay design, and LF outbreak management.

2.3.4. Real time tracking of Lassa virus genome evolution in Nigeria using Nextstrain

Presenter: Paul Oluniyi

- Nextstrain is applied to understand epidemic origins
- Performed evaluation of LASV over the 12 years using Nextstrain platform in Nigeria
- Nextstrain consists of a database of a number of viral genomes and is an interactive visualization platform. Nextstrain makes possible due time analysis of genomic data. It is a bioinformatics tool kit.
- Nextstrain integrates sequence data with other data types including geographic information, serology, or host species
- Nextstrain helps for real-time monitoring of surveillance and visualization of patterns of spread of LASV Shows how the virus has spread in different states over time.
- In this study, full genome analysis was done for more than 200 samples. LASV phylogenetic analysis - modified Nextstrain to do transmission analysis for real-time use in contact tracing. Found a different lineage: new lineage IIB
- More information about Nextstrain is available in the link below: <https://nextstrain.org/>

2.3.5. Metagenomic analysis of blood samples obtained from patients infected with Lassa virus in Nigeria

Presenter: Judith Oguzie

- This study attempted to address the implications of coinfections in Lassa fever patients. In a place with high Lassa disease burden in Nigeria, what is the proportion of coinfection with other pathogens? How does that impact patient outcome?
- Next generation metagenomic analysis gives nucleotide sequence of everything in the sample, which is unbiased. Possible to identify all pathogens in a sample
- Illumina was used for metagenomic sequencing on identification of coinfections among LF cases
- In addition to LASV, the metagenomics analysis identified other pathogens such as plasmodium falciparum (31 out of 92 samples), salmonella, gonococcus, GB Virus C, *Mycobacterium tuberculosis* and HIV-2

- Conclusion: the study established possible coinfection of LASV; Helps for future preparation of studies on the implication of coinfection on Lassa patient outcome

2.3.6. Methgenomic sequencing at the Epicenter of Nigeria 2018 Lassa fever outbreak. Irrua, Edo State

Presenter: Sophie Durafour

- Objective: To understand the molecular epidemiology LASV circulating during the 2018 outbreak,
- Performed metagenomic nanopore sequencing from patient specimen. Specifically, MinION metagenomics analysis was used to perform the LASV genetic analysis. The MinION is a small, sequencing device which is appropriate for the genetic analysis of pathogens in resource-limited settings.
- Liana, PHE/Liverpool started preparatory mission in Nov2017, surprised by an outbreak, then started to sequence.
- Prof P Lemey, Leuven. Bioinfo support UK. Viral loads variation in samples.
- A total of 120 samples were sequenced, of these were 36 real-time shared with NCDC and the WHO.
- 36 LASV genomes were analyzed in real-time and were confirmed using 120 samples already sequenced in the country of origin.
- The sequences of the 36 strains revealed extensive diversity,
- Overall, the result showed that rodent to human transmission was main cause.
- No evidence of human to human transmission.

Questions:

- Did they have paired isolates primary-secondary case to estimate genetic distance for human transmission?
- What is the natural within host nucleotide variation.
- What is the data to support setting two Nucleotides as limit to decide on transmission?
- Everything was done at ISTH, no export of samples, data sharing with NCDC WHO easy.
- This study is published, and for more information please visit the link below:
<http://science.sciencemag.org/content/363/6422/74.full?ijkey=CBaN7HY8.ZgGk&keytype=ref&siteid=sci>

2.3.7. Modelling the triage of suspected Lassa cases using ReLASV antigen rapid test during January -March 2018 Lassa fever surge at Irrua Specialist Teaching Hospital, Edo State, Nigeria

- ReLASV DX consist of RDT, molecular Dx, serology (IGG, IGM ELISA)
- The RDT turnaround time is 15 minutes, and with higher titer (viremia) signals could be ready in 2 minutes. This is the second-generation product
- The first-generation product was based on a monoclonal antibody system which is very specific to lineage IV. Recently validated and published in scientific reports- 95% Sensitivity and 97% specificity vs combined standard ELISA and PCR
- The current triage study was conducted during the 2018 Lassa outbreak. The evaluation data was based on 445 samples collected during the outbreak
- Comparison was made against Rt-PCR Altona 1.0 and Nikisins assays and Illumina sequencing
- RDT antigen ELISA detected approximately 20% of those 445 samples, and the IGM ELISA detected one third of the 445 samples with reduced case fatality rate
- Looking for acute Lassa in IGG sero-negatives in the blood, triage performance of 92% sensitivity and 97% specificity was achieved
- Conclusion: by incorporating RDT complementary to PCR, you get a much more accurate triage of acute versus sub-acute cases

2.3.8. Characterization of virus specific memory T cell responses from Nigerian and Sierra Leone Lassa fever survivors

Presenter: Brian Sullivan

- T-cell response is critical for clearing any infection
- T-Cell response for Lassa virus infection is poorly understood, characterized
- Discovered 40 new HLA seqs in Sierra Leone, remain poorly characterized in African populations.
- Used VSV based antigen delivery system, replaced Josiah GPC and LP. Incubated PBMCs with rVSV Lassa. CD4, CD8, cytokine profiles for TNFa and IFNg. Stimulated cells with predicted peptides of Ag.
- Sampled from Sierra Leone Lassa survivors
- Found poor CD8+ for S (1/5th good for Nigeria (3/5th?)) (NB clinical difference?). Stronger T cell responses for Lineage II GP? Human component - HLA? Hypothesis:

- Nigerians have been better evolved to develop a strong T cell response due to longer exposure to Lassa (1000 years vs SL?)
- Lots of cross reactivity between epitope regions between lineage II and IV stimulated T cells.
- 37 new Lassa virus CD8+ T cell epitopes discovered T cell responses correlates with sequelae.

2.3.9. A system biology approach to determine correlates of Lassa fever survival: the center for viral systems biology

Presenter: Mathias Pauthner

- Why do some people survive Lassa infection, get Lassa disease and develop sequelae after Lassa disease? What factors determine the outcome of Lassa infection? Do differences in the composition of the human antibody repertoire, evolution, and function, T cell dynamics, HLA type affect this? Are there other factors? Systems biology approach is needed to address all these questions, what affects severity of infection,
- Virus: 250 LF virus wgseq (human + rodent). Antibody therapy mAb LF - starting same as for Ebola (Gunn et al 2018). Differences in HLA, Difference in LF survivors, deceased. Infected vs non-infected. Kenema Donald Grant.

2.3.10. How Lassa virus GP is targeted by protective antibodies

Presenter: Robert Garry

- Why are not more neutralizing antibodies raised during infection with LASV? Is this related to stability of GP and glycosylation?
- Four variants of conformations of wild type GP, abs against all induced in infection - but rarely to the whole complete trimer and therefore nAbs are rare. Polyclonal non-neutralizing Abs can be protective? Neutralizing mAbs recognized mainly the full trimer, not the 3 other variants.
- A vaccine using the stabilized GP should be more effective in inducing nAbs than "regular". NB should be included in LF vaccines?! Preclinical evidence?

2.3.11. The role of mobile Laboratory in the containment of 2013-2016 Ebola virus disease outbreak in West Africa: experience of Nigerian-European consortium

Presenter: Donatus Adomeh

Objective: to describe the experience of mobile laboratory performance during the last Ebola outbreak

- The mobile laboratory consists of 14 boxes containing a BSL-3 lab glove box accessory, two smart cyclers, a collapsed master -mix tent and a laptop. The mobile unit is based in Irrua.
- Main finding and conclusion
- In this mobile lab model, a total of 7477 specimens were tested in Nigeria and Sierra Leone (1231 whole blood and 6246 oral swabs)
- Sierra Leone: 287/ 7443 (3.9% +ve for EBV; Nigeria: 2/34 (5.8%) +ve for EBV
- Turnaround time for sample test was 8 hours
- There were 4 field missions: 2 in Nigeria and 2 in Sierra Leone, the deployment period lasted over 515 days between 2014-2016.
- Desd bucca swabs cepheid GeneXpert and several rapid test kits for EBOV (OraQuick rapid Ebola antigen, Sd Q line Ebola Zaire Ag, Corgenix REEBOV antigen Rapid test were used

Challenges:

- Deployment: Logistics, immigration, customs and cost of freight
- Lengthy bureaucracy for trans-border transport of laboratory equipment and consumables, power supply, and security of staff
- required huge funding to remunerate and maintain persons in the field
- Restrictions of commercial airlines flights to West Africa
- Need for frequent equipment replacement
- Burn-out among staff because of change of environment
- Shortage of Kits and reagents for immediate deployment
- Lack of stand-by generator for power supply essential to run the freezer for storage of reagents and samples

Conclusions:

- The deployment of mobile laboratory unit contributed to early detection of Ebola cases, post-mortem DX monitoring of patient care and supported surveillance
- The mobile laboratory initiative should be strengthened for a large-scale outbreak within and across borders future outbreak response

2.3.12. Performance evaluation of Pan-Lassa fever virus rapid diagnostic test (relevant MRTD) kit in Irrua specialist teaching hospital

Presenter: Ikonmwosa Odia

2.4. Vaccines and innovations

Notes by Nadia Tornieporth and Richard Hatchett

2.4.1. CEPI supported vaccine development on Lassa Fever using Inovio's enhanced DNA platform technology

Presenter: Kate Broderick (Inovio)

- Brief general description of Inovio DNA vaccine technology and Celectra delivery device
 - Highlighted thermostability, rapid deployment capabilities demonstrated with Zika (7 months btw virus and product); experience with Phase 1 studies Zika, Ebola, HIV, MERS
 - Celectra device has previously received regulatory approval for studies in 6 continents incl Africa
- Description of Inovio consortium, including Dr. Gary Kobinger and Heinz Feldmann
- INO-4500 NHP data – 100% effective, no clinical s/sx, no viremia
- Josiah strain v Clades I and II: robust B and T cell responses
- Study start of Phase I was disclosed as Jan 2019; Phase II IQ2020

2.4.2. T-705-modified SSRNA in complex with Lassa virus nucleoprotein exhibits nucleotide splaying and increased water influx into the RNA-binding pocket

Presenter: Olaposi Omotuyi

- Two woes of ribavirin
- T-705-RTP is incorporated in LASV ssRNA, promoting water permeation into the binding cleft, altering torsion around the sugar-base bond and causing nucleotide splaying
 - Destabilizes binding and exposes viral ssRNA to host RNases – supports anti-Lassa virus potency – results published
- Alteration of structure results in antiviral activity.
- Centre for Biocomputing and Drug Development in partnership with the Centre for Genomics Research and Innovation: screening of novel anti-Lassa compounds based on binding properties
- Adaptive simulation data identifies compounds as key to ligand stability in fully bound state (published in Drug Research 2018)

2.4.3. Lassa-glycoprotein processing enzyme (site-1 protease) in Pf429242 bound state: Computational kinetics and dynamics of reversible binding

Presenter: Olaposi Omotuyi

- Search for a small molecular weight antiviral against Lassa
- FDA-approved drug screening strategy employed, identified 3 candidates
- Site 1 protease allows virus to enter nucleus

2.4.4. Multivalent hemorrhagic vaccine for Lassa, Ebola and Marburg viruses protects against lethal challenge

Presenter: Jonathan Heeney

- Multivalent hemorrhagic vaccine for Lassa, Ebola and Marburg viruses protects against lethal challenge – could provide protection against VHF across the endemic HF belt
 - Provides a compelling case for a multivalent hemorrhagic fever vaccine.
- InnovateUK/University of Cambridge DIOSYNVAX insert design to produce libraries of antigen
- Pan-EBOV neutralization titers achieved in vector with a large payload (MVA)
- Has demonstrated proof of concept in guinea pigs for Ebola and Lassa
- Funders: InnovateUK, BBSRC, ACEGID, University Hospital Southampton
- OVEL: One Health for Accelerating Vaccines for Ebola and Lassa
- DioSynvax insert design based on immune correlates

- DIOS synthetic vaccine inserts funded to proceed to Phase I of trivalent vaccine (poster PL76) (One Health vaccine grant, Innovate UK, ACEGID)

2.4.5. Development of safe and effective single dose vaccines for hemorrhagic fever viruses: Preclinical efficacy data for Lassa fever and Ebola as examples

Presenter: Farshad Guirakhoo

No presentation.

2.4.6. A chimpanzee adenovirus-vectored vaccine confers protection against lethal Lassa fever

Presenter: Sarah Gilbert

- Replication-deficient, safe in all ages, including immunocompromised
- Highlighted that the vector is replication-deficient – safe, tested in pregnant sheep and goats in the RVF program
- Highly adaptable platform and highly immunogenic (typically immunizes after a single dose)
- ELISA titrations against Lassa GP at day 28 and at day 51 after 1-2 doses.
- 100% effective in Lassa GP challenge model (homologous); T-cell responses cross-protective against clades I, II and III in outbred mice; plans to repeat heterologous challenge in GP
- High neutralizing abs and CD4/8 cells
- Thermostable 45 for 6 months
- Protective across a number of diseases after a single dose
- Live Lassa virus detected in tissues in control animals only (suggests good TCR?)
- T-cell responses to Lassa are cross-reactive in outbred mice. Seems to work against other lineages (I to III)
- Need to perform a NHP study

Q&A round 1

- Vasee Moorthy: I don't see the sense of urgency that I think is warranted. Doing Phase 1s in the US and only then moving to countries isn't incorporating the lessons from Ebola. A short period after P1 trials in US or other Western countries, followed by rapid movement to West Africa would be much better.
 - Panel responds in a generally sympathetic way
 - Kate Broderick: Seeking to accelerate.
 - Sarah Gilbert ready to accelerate clinical testing; other partners need to do their part, trial designs need to be agreed on, sites need to be ready
 - Jonathan Heeney: Continuous learning process – collecting information on immune response and risk factors
 - Melanie Saville: CEPI working with developers should be done in parallel with cap bldg. of clinical trial sites; leverage US and EU experience with regulatory support to the region as well
- Els Torrele (Director, MSF campaign): Access and affordability are critical to take into account early in the development process. Curious to hear how you are thinking about this. Unless we think about this throughout the process we are going to fail.
 - Melanie Saville: CEPI dedicated to equitable access, examples: thinking about cold chain much earlier in the process; sometimes better to spend time developing suitable formulation early vs accelerating
 - Sarah Gilbert: COGs are low for ChAd
- Dicky Akanmori, AVAREF – offers AVAREF platform to increase the efficiency of the regulatory process. AVAREF – track record of facilitating parallel track review Ebola and joint reviews for multi-country trial protocols; pre-proposal trial scientific and design advice. Vaccine developers invited to meeting of AVAREF in Feb 2019.
 - Melanie Saville: Support is appreciated.
- Marion Gruber – is vaccine goal for prophylaxis or for use in outbreak setting? Do you evaluate duration of protection?
 - Sarah Gilbert: Haven't done duration of protection studies yet for LF vaccine, but with other simian adenoviruses we have seen durability of at least three years (good persistence of T and B cell responses)
 - Jonathan Heeney: Not just the duration but the breadth of response is important.
 - Kate Broderick: Durability done in GP protection after a year; will also be done in NHPs.

2.4.7. Post-exposure protection against contemporary Nigerian isolates of Lassa fever virus in cynomolgous macaques with human monoclonal antibodies

Presenter: Robert Cross

- UTMB and VHF Consortium program
- Data presented on 3 isolates: Nigeria 1, 2, 3; protection demonstrated across at least 2 clades thus far for 3 ab cocktail and bi-partite cocktail
 - Two Nigerian isolates fatal – Nigeria 2 didn't produce mortality for some reason
- Cites Nat Med 2017; 23:1146-49 paper on efficacy of Lassa mAbs delivered in cocktails. Different treatment cohorts (d0,3,6 – d3,6,9 – d6,9,11 – d8,11,14)
- Therapeutic protects across at least two different clades
- Conclusions: clade 2 isolates do not have uniform virulence in macaques; immunotherapeutic cocktail effective against phylogenetically distant clades – model and approach need refinement

2.4.8. Advancement of a Lassa fever vaccine clinical trial candidate based on the live vesicular stomatitis virus chimera platform

Presenter: Swati Gupta

- Brief background on IAVI: discovery labs, product development center, epi/clinical research network, global access
- Describes preclinical program, showed outline of path from research vaccine to clinical trial candidate; plans include further investigation of immunological and gene expression responses associated with protection from challenge in NHPs
- Investigating cross-neutralization in lineages I-VI via PRNT using serum from vaccinated macaques
- Planning a LASV NHP challenge study in 2019
- Increased likelihood of success highlighted based on Ebola vaccine from Merck
- Cross-neutralization investigations important: PRNT across lineages I-IV; additional clades reported from Mali and SL (V and VI)

2.4.9. Quadrivalent filovirus/Lassa vaccine demonstrates protection against challenge in nonhuman primates

Presenter: Rong Xu

- EBOV, SUDV, MARV GPs, LASV GPC
- Challenge study 4 arms (1 per virus, 8 NHPs per arm: 3 controls, 5 challenge)
 - Tested in cynos: 2 doses at 0, 56 with challenge on Day 84, tested antibody and T-cell responses (T cell responses in 100% of animals only after 2nd dose). Protection against distant lineage clade II
 - Serum IgG good for all but lags in LASV (goes up at d66)
 - PRNT and Ifn ELISpot show T cell responses by d66 for all viruses
 - Shares clinical chemistry, gross pathology findings (vaccinated monkeys do well, controls don't)
- Phase 1 trial end 2019 or early 2020

2.4.10. A broadly-protective Lassa fever vaccine as an effective tool for fighting Lassa fever epidemics and endemicity

Presenter: Abdulalami Nasidi (former CEO for NCDC, Background on LF, 2018 outbreak)

- Reviews history of Arena Virus vaccines (starting with Junin)
- Reviewed preclinical data from the ML29 candidate (in development since 1997)
- Genetic diversity of Lassa
- 2017 WHO TPP: acceptability
- Rational approach (ML29) v platform-based approach (all others)
- ML29 genetically stable (but no FDA-required track records on all passages of ML29). Solution: reverse genetics to rescue virus (from cDNA clones ML29bi). Need to improve manufacturing controls.
- Low protection dose 1x10³ PFU in NHP
- ML29 has demonstrated activity against Nigerian strains
- Goal is to advance the rML29 vaccine into clinical trials in Nigeria (no timeline provided)
 - Pushed for in-country manufacturing

2.4.11. Development of safe and effective vaccine against Lassa fever in Africa

Presenter: Simon Agwale

- Partnership between Merck and Innovative Biotech LTD with a goal to create an integrated vaccine development and production platform in Nigeria.
- First will build a fill/finish facility; second will build up vaccine development capability for HIV, EBOV, LASV

- Developing ML29 vaccine in collaboration with Medigen and Univ of Maryland; post challenge experiments in GP – indicate potential for preventive AND therapeutic applications of the vaccine since protection shown when given eg 2 days post challenge; 100% protection in marmosets: conclusion that theirs is the only vaccine to have shown protection against LASV variants currently circulating in Nigeria
- Live reassortant Mopeia Virus
- ML29 also demonstrated activity
- Planning manufacture of cGMP material for P1 clinical trial in Nigeria
 - GMP MCB and WCB available and CMO identified – clinical testing planned – no timelines provided.
- Innovative Biotech, University of Louisville, UMD, Medigen
- Stated that this is the only vaccine not funded by CEPI

2.4.12. Molecular docking studies of compounds from medicinal plants on Lassa fever virus

Presenter: Amaka Ubani

- Seven medicinal plant ligands were docked into NP structure using software
- Have low docking energy with good binding affinity
- Compounds randomly selected from list of medicinal plants known to have antiviral activities ag HCV
- Ligands docked into NP structure of LASV; potential to inhibit the activity of NP of LASV
- ADME and QSAR of the molecules can be considered for further studies
 - Could be considered for development as antiviral drugs

Q&A round 2

- Does VSV leave the injection site? Is it safe for the immunocompromised?
 - Simon Agwale: Yes
 - Rong Xu: Our vaccine construct has been shown safe in immunocompromised
 - Swati Gupta: We would demonstrate safety after P1
 - What is being done to understand the risk of immune-mediated sensorineural hearing loss?
 - Swati Gupta: Hearing loss will be tested in Phase 2 trials (IAVI)
 - (For Simon Agwale) Will locally produced vaccines be affordable?
 - Simon Agwale: Cost should not be the main issue; you need something that works, and THEN you worry about costs. In terms of timelines, when would you move to P1/P2 for ML29? Will take about 24 months.
 - (For Simon Agwale) Are there any COP for your vaccine?
 - COP so far is CMI
-

LIC Day 2: 17 Jan 2019

3 Plenary session, Day 2

Chaired by Adebola Olayinka (WHO) and Ephraim Ogbaini (ISTH)

Notes by Richard Hatchett and Nadia Tornieporth

3.1. Lassa fever: A historical perspective and contemporary development in Sierra Leone

Dan Bausch (UK-PHRST)

- Almost impossible to differentiate Lassa from other non-malarial febrile illnesses by s/sx alone
- Anecdote about UN rodent spinning
- Mano River Union Lassa Fever Network built capacity and organized work across Liberia, Sierra Leone, and Guinea, mainly at Kenema.
- Training via Tulane/KGH: over 60 trainees since 2001
- Facility constructed with US government funds
- UK Public Health Rapid Support Team
- ASTMH meeting in DC November 20-24, 2019

3.2. New approaches in shaping the global response to VHFs

Pierre Formenty (WHO)

- Overview of advances in epidemiology, diagnostics, etc. for VHFs, with reference to West Africa Ebola epidemic
 - We need better Dx and licensed commercial products that are easy to use.
- VHF diagnostics: many PCR-based (but potentially non-validated) tests in use
 - Should we use the same approach across VHFs? Should we copy the Ebola approach for Lassa?
- TPP for Lassa serology (IgG and IgM) under development
- Phylogenetic analysis shows limited evidence of H2H in 2018 epidemic but general similarity to known lineages.
- More work needed on therapeutics.
- Vaccines: summary of priorities for different VHFs
 - Animal vaccine for RVF
 - Rodent control for Lassa
 - Antitick vaccines for CCHF
- We need better epi data; vaccines may not be the answer.

3.3. What do we really know about the *Mastomys* as host?

William Ampofo (Noguchi Memorial Institute for Medical Research, Ghana)

- *Mastomys natalensis* as host of Lassa (natal multimammate mouse)
- LASV maintained by multiple reservoirs
- Multiple transmission pathways:
 - Touching objects contaminated with rodent urine
 - Breathing aerosolized infectious particles
 - Being bitten by or consuming rodents
- Risk mapping potential for wide spread of LASV, corresponds mainly with distribution of rodent (WHO African Region Technical Report 2016)
- Country-specific information:
 - Ghana: two cases in Amansie West and one case in West Akim in 2011; two imported cases in May 2013 among Ghanaian peacekeepers returning from deployment to rural Liberia
 - Benin: has mapped distribution of rodents, snakes (pythons)
 - Ghana: Dr. Franklin Asiedu-Bekoe, Disease Surveillance, Ghana Health Service, Accra
 - Guinea and SL seasonal human exposure to rodents – rodent ecology (A. Mari Saez et al 2018)
 - Knowledge base study: 81 % in SL know about Lassa Fever but only 32 % knew that rodents are vectors (Bonwitt et al. 2016, 2017);
 - Guinea: Exposure increases if houses are kept dark, children exposed (Kelly & A. Mari Saez 2018)

- People welcome rodent control interventions and provide feedback
- LF Nigeria Research Plan identifies questions about behavioural risk factors, etc.
- Genomic analysis of Lassa during an increase of cases in 2018 – Happi NEJM
- Knowledge gaps:
 - Lassa incidence and seroprevalence
 - Ecologic investigations and modelling

3.4. Using genomic sequencing to fight outbreaks in Africa

Christian Happi (Redeemer's University, Nigeria)

- Many of the technological and economic benefits of genomic revolution have yet to reach Africa
- African Centre of Excellence for Genomics of Infectious Disease (ACEGID) brings together Harvard, Broad, Cambridge, centers in West Africa, including ISTH, Redeemer's University. ACEGID played a key role in 2018 outbreak.
- 9/27/08 @ 9:15p – first onsite molecular diagnostic of Lassa fever in Nigeria. ISTH still celebrates Lassa Fever Day every year on 27 Nov.
- 1st generation RDTs had low sensitivity, due to diversity of virus.
- NextGen sequencing of Lassa Virus genomes – ancient origins of Lassa virus emerged ~1060 years ago in SW Nigeria and circulated for 600 years before moving west
- Novel rhabdoviruses (?)
- Over 400 full genome sequences of viruses from 2018: genetic diversity is structured geographically, along major river basins.
- Growing demand for local sequencing capacity: white powder at US embassy, monkeypox outbreak, viral discovery and diagnosis, Lassa in rodent reservoirs.
- Scanning human genome for evidence of viral resistance (LARGE protein).
- Over 850 trainees in last 5 years.

3.5. WHO R&D Blueprint: Global Lassa fever research priorities and the role of Nigeria

Vasee Moorthy (WHO)

- WHO's new technical strategy (GPW13): achieving impact for people at country level
- WHO priorities: Healthier Populations; Health emergencies; Universal health coverage
- R&D Blueprint: Strengthening research capacity before and during epidemics
- Key strategic shifts:
 - Global roadmaps → national research plans → continuous improvements in measures to prevent and control outbreaks and in research capacity
 - Research better integrated into outbreak response
 - Research pillar in incident mgt system
 - Integration of systems btw research and response
 - Link at end of outbreak into multi-year research
- Nigeria LF plan is prime example of maturing locally-led research aligned to local health priorities.
- WHO wants to challenge the concept of peacetime and maintain the sense of urgency in the interepidemic periods. WHO fully supports the move to multi-year research preparedness plans.
- Demonstrating tangible progress each year will drive donor confidence and enable resources for capacity and infrastructure.
- Beneficial to take on the hard work to agree on master protocols that can be used from one outbreak/season to another – consult with WHO and AVAREF early.

Q&A

- Dicky Akanmori: how many LF cases are we missing due to lack of validated Dx? How different does a disease present in different countries?
 - Dan Bausch: Standardization and validation of assays still to be done
 - Dan Bausch: Case definitions do need to be harmonized across countries - ongoing
 - Vasee Moorthy: Surprising how little funding goes into lab and Dx support – not valued enough (compared to investment in vaccines R&D); standardization work incredibly important yet under-resourced; lab infrastructure strengthening key for sustainable capacity strengthening
- Prof Nasidi: Concern about human to human transmission – adaptability of the virus to human cells?
 - Christian Happi: human to human Tx exists but only in small clusters; LASV evolves much more slowly than eg EBOV (published 2018)

- Sustainability of control efforts, how to build indigenous capacity and reduce dependence on overseas support? Need integrated control efforts for HFs eg YF outbreak last year as well
 - Christian Happi: pushing for accredited YF lab in Nigeria given the size of the country
 - William Ampofo: Continent-based initiative to produce vaccines locally – CEPI supporting NCDC – they will continue to push local manufacturing
- Chikwe Ihekweazu emphasized the One Health approach

Parallel sessions, Day 2:

4.1. Epidemiology and surveillance

Notes by Tom Verstraeten, Josie Skufca, Lamprini Veneti

4.1.1. Contact tracing and profile of Lassa fever contacts in Edo State: Implications for the control of LF outbreaks

Presenter: Faith Ireye, WHO

Dr Ireye presented the contact tracing during the 2018 outbreak in the Edo State, which has the highest number of Lassa Fever (LF) cases in Nigeria. In the LF outbreak in 2018, contact tracers were deployed to find persons having a contact with the LF cases. Contact line lists and forms on contact's information were filled in Excel, including how many contacts there were per case (CPS). In total, 200 cases and 2527 contacts were found. Most of the contacts were females (63%), adults 18-64 years (73.5%), most from the community (>60%) and 37% in health-care facilities. Of in total 2,527 contacts found, 2.7% were symptomatic (of which 23% PCR positive) and 97.3% non-symptomatic. More than one third of contacts were the health care workers (HCWs), indicating nosocomial transmission. Number of cases and mortality due to LF declined rapidly after the contact tracing began, including the active case search and sensitization about the LF. Early detection of cases helped in surviving the LF.

Table 1. Relationship between number of contacts per case and selected variables

Variable	Mean	p-value
Edo North	13.10	<0.001
Edo Central	10.78	
Edo South	23.67	
Case outcome		<0.001
Survived	11.13	
Died	20.53	
Cases with symptomatic contacts		
Yes	17.90	0.014
No	11.67	
Cases with PCR positive symptomatic contacts		
Yes	12.73	0.981
No	12.63	

4.1.2. Lassa Fever Outbreak in Enugu State, Nigeria, August 2018: the role of contact tracing

Presenter: Christian Akpa

Dr Akpa presented the contact tracing during the 2018 outbreak in the Enugu State in Nigeria. On the 31 July 2018 a suspected LF case was detected, which was confirmed on 4th August 2018 when consequently an outbreak was confirmed and emergency operation center (EOC) began the control measures. There was 1 confirmed, 1 probable and 10 suspected LF cases. The following case definitions were used: a) Suspected case: any person residing in Enugu state presenting with any of malaise, fever, headache, sore throat, cough, vomiting, diarrhea, myalgia, chest pain, hearing loss and a history of contact with excreta of rodents or with a case of LF between July and August 2018; b) Confirmed case: a suspected case of LF with laboratory confirmation; c) Probable case: any suspected case who died without collection of specimen for laboratory test; d) Contact: a person having a close contact with the patient or testing the laboratory specimens of a patient in 3 weeks after the onset of illness. Contact tracing was conducted among family members, health workers and communities. Nine contact tracing teams and supervisors were trained. Contacts were categorized according to risk level: a) high risk contacts (category 3 – if in direct contact); b) low risk contacts (category 2); c) non-risk contacts (category 1). Follow-up of contacts was conducted by active search: temperature monitoring of contacts through home visits for 21 days

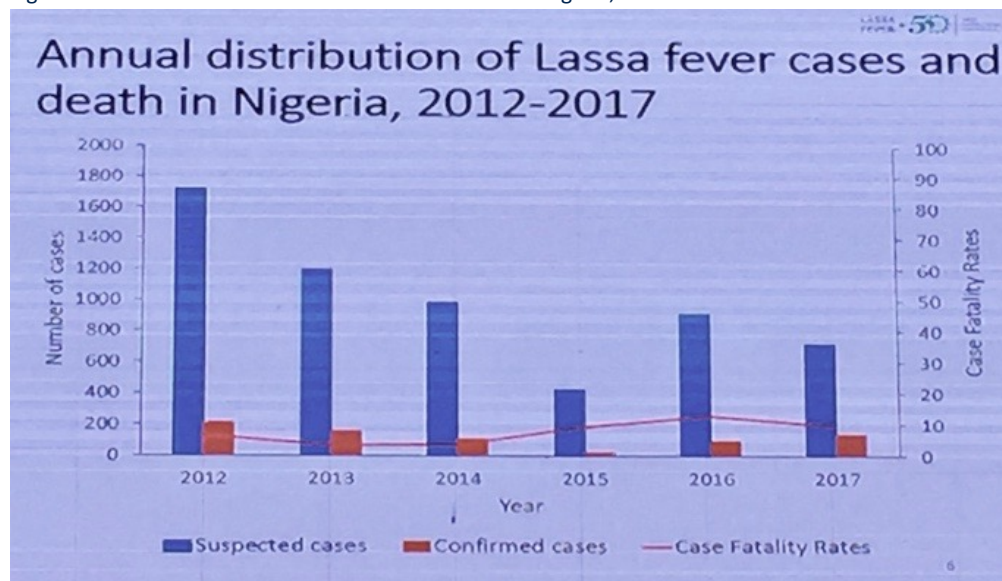
from the date of last exposure. There were in total 101 contacts found, of which 97 (96%) were followed-up for all 21 days. Four were not traced due to incomplete/incorrect addresses. Of all contacts, 57.4% (n=58) were of age 20-39 years and majority 71.3% (n=72) were HCWs. 17 (16.8%) contacts became symptomatic during follow-up but symptoms resolved within follow-up. Moreso, serum PCR was done for 6(35.3%) of the symptomatic cases and all were negative for LASV.

4.1.3. Burden and trend of LF in Nigeria: a secondary data analysis 2012-2017

Presenter: Onyebuchi Okoro

Dr Okoro presented the trends of LF in Nigeria from 2012 to 2017 using the IDSR data. Overall, the surveillance data showed that South of Nigeria is most affected, having most confirmed LF cases. The Edo State has the highest number of cases. The peak of LF cases was from January to March. The attack rate of LF cases (per 1,000,000) decreased from 2012 to 2015, from about 12/mill in 2012, 8/mill in 2013, 7/mill in 2014, 3/mill in 2015 and then increased again to 6/mill in 2016 and 5/mill in 2017. There is a low percentage of laboratory confirmed cases, indicating that laboratory capacities must be improved.

Figure 1. Annual distribution of LF cases and deaths in Nigeria, 2012-2017



4.1.4. Lassa Fever Sentinel Surveillance System evaluation – Kenema district, Sierra Leone, October 2016 – September 2017

Presenter: Amara Alhaji Sheriff

Dr Amara Alhaji Sheriff presented the results of the evaluation of surveillance system (LFSSS) in Kenema district, which has been established and in function for about three decades. There are approximately 40 cases of LF per year in Kenema, Sierra Leone. The team in Kenema evaluated the LFSSS data from October 2016 to September 2017. The semi-structured questionnaires based on the CDC guidelines for surveillance system evaluations were developed. Twenty-one key people were interviewed: 3 district surveillance officers, 3 LF-based laboratorians, 6 clinicians and 9 community members. Also, case forms, surveillance reports and the LF database at the district level were reviewed to determine the predictive positive value (PVP), timeliness and data quality. The content of the qualitative data was analyzed to assess the simplicity, acceptability, stability and usefulness of the surveillance system. Results: even though more than 2/3 of the respondents found the LFSSS to be simple, acceptable and stable, it was not useful in guiding control efforts because the case definition was not sensitive to guide control measures. It is recommended that the MOH and partners consider a modification of the current case definition to make it more sensitive, to organize inter-service trainings for HCWs on LF case management and to initiate processes to improve data quality and to harmonize data management among LF unit and district health management teams.

4.1.5. Detection of Chikungunya virus among febrile patients in Lagos, Nigeria

Presenter: Sylvester Ibemgbo

Dr Ibemgbo presented the Chikungunya virus (CHIKV) cases in Lagos, Nigeria. The CHIKV was first detected in 1969. There are no vaccines available against CHIKV. A cross-sectional study was conducted in Alimosho and Orile-Agege local

government areas of Lagos state. Selected into the study were all patients who were of age above one year and with symptoms of fever (>37.5 degrees Celsius) and with more than one or equal to one of the following symptoms: headache, myalgia, arthralgia, hemorrhage, and rash. The 5 ml of whole blood samples were collected from patients who met the study criteria, over a period of 5 months from April to August 2018. An RNA extraction was done using the E.Z.N.A Viral RNA kitR68740-01 (Omega Bio-ten) and RT-PCR was carried out (described before in study of Pfeffer et al. 2002). Results: A total of 130 outpatients with fever were enrolled in the study, of which 76 (58%) were females. The age of all participants was 1-60 years of age, mean age 13.3 years. Of all serum samples, 6.9% (9/130) were positive for CHIKV RNA. Of all 9 positive samples, 4 out of 56 (7.1%) were among males and 5 out of 74 (6.8%) were among females. Although the rate of infection was among males was slightly higher than in females (7.1% vs. 6.8%), the difference was not statistically significant ($p>0.05$).

4.1.6. Epidemiology of LF in Sierra Leone

Presenter: John Schieffelin

Dr Schieffelin presented the epidemiology and LF study conducted in Kenema, Sierra Leone. The Kenema Government Hospital (KGH) is an important site for LF research and surveillance since 1970-80s. After 1993 the LF program was hindered by the blood diamonds civil conflict. A new VHF ward with 50 beds was established within the KGH. The center collaborates with the Viral Hemorrhagic Fever (VHF) Ecology team, which collects data on environmental factors and test rodents, and with the VHF Outreach team that conducts active case finding, community sensitization and informs the community for LF related activities that are planned or ongoing. The KGH is in charge for passive and active LF surveillance, included in e-IDSR. A bilateral hearing loss in LF survivors is also recorded. A large (>11,000 subjects) LASV seroprevalence/incidence study was conducted on house and village level assessment in 20 endemic communities of Kenema, 20 emerging communities in Tonkolili and 20 non-endemic communities in Port Loco. All households in community were counted and then households were randomly selected (20+ households from each of three communities, and in household 1 each in 5 age groups were selected). Information was collected on demographics, global positioning system (GPS) on location of the participants and households. Dried blood spots samples were collected for IgG testing by ELISA. Results: Total of 150 suspected LF cases were reported, of which 57% (84/150) were males. Median age of suspected cases was 24 years (range: 7 months-68 years) and incidence rate was 0.9 per 100,000 population. Of all cases, 28% (42/150) were confirmed LF cases. Of all confirmed cases, 55% (23/42) were females. Median age of confirmed cases was 15 years (range: 1-67 years). Overall case fatality rate was 38% (16/42) and case fatality rate among hospitalized was 33% (n=14).

4.1.7. Lassa Fever Surveillance data analysis, Liberia, 2016-2017

Presenter: Oscar Gberr

Dr Gberr presented the LF surveillance data from Liberia in years 2016 and 2017. In Liberia, the LF is under notifiable surveillance system and has to be reported immediately. One LF case is a definition of an outbreak. There was an increased trend of LF cases in the 2-years period. Incidence rate of LF continues to be high in 3 endemic counties. Liberia is divided into 15 counties and during 2016-2017, most of the suspected LF cases (10 cases and above) were reported from 3 counties in the middle of Liberia: Bong (n=60), Grand Bassa (n=20) and Nimba (n=39). The LF has a seasonal trend. Most of the cases were recorded at the beginning of the year from January to June (similar to findings in Nigeria in 2017). Among confirmed cases, there were more females (comparable to findings in Ondo State, Nigeria in June 2016). Case fatality was high among confirmed cases (similar to findings in Ondo state, Nigeria in June 2016 – described in Iserere et al. 2018).

4.1.8. The role of bio-surveillance in rumor capture and validation of LF cases between Jan-Oct 2018 in Nigeria

Presenter: Adachioma Ilhuez

Dr Ilhuez presented the concept of the bio surveillance in Nigeria. The monitoring of chemical, agricultural, and biological threats is critical to both public health and national security. Chemical agents, engineered diseases and agricultural threats can cause widespread panic, and kill hundreds of thousands of people (example: Ebola in Nigeria 2004). A bio surveillance system is in place, so that the government is better equipped to identify and eliminate threats before reaching the public. Some cases were identified, which were not in the classical surveillance systems.

4.2. Policy and coordination of response

Notes by Nicole Lurie and Dawn O'Connell

4.2.1. General notes: Policy and coordination of response

- Hospital preparedness-half have IPC unit; most hospitals did not have plans, especially staff continuity or for regular assessment
- State preparedness-attack rate 5.1 per million overall in Nigeria
- AAR: policy gaps, human resource gaps, most states had no functional EOC, stock out of reagents, multiple reporting tools and channels, not enough lab testing, now have a plan
- Things that went well: EOC, response structure, comms; interesting discussion about disease specific vs a generalizable system and metrics
- One health approach
- Some patients went broke
- Discussion of IMS
- Modeling-main temporal predictor is 3 months after heavy rainfall, although rainfall may be a proxy

4.2.2. Imported Lassa fever: A review of the literature and implications for international collaboration

Presenter: Colin Brown

- Lassa is the most exported VHF that we are aware of. Exported all the way to Japan and the US.
- Lots of endemic countries have historic ties to the US and UK and Europe. So increased exportation.
- Of 35 exported cases: 74% to US, UK, and Germany. 71% survived.
- 80% of exported cases from Sierra Leone, Nigeria, and Liberia.
- Despite increase travel no obvious increase in # of cases exported. Likely because of increased ability to diagnose within endemic country.
- Of the exported cases: 1/3 were HCW, 14% aid workers; 11% engineers. 9% soldiers. 9% tourists.
- For every exported case, there are on average 124 contacts to trace.
- Conclusion: need increased in-country capacity to diagnose and report cases.
- Public Health England putting program in place to strengthen these capabilities in Nigeria and Sierra Leone.

4.2.3. Preparedness of hospitals to handle emerging and re-emerging infectious diseases in Ekiti state

Presenter: Olagoke Okimi

- Study looked at preparedness to handle EIDs in 6 hospitals in Ekiti.
- 3 of 6 hospitals had Infection Prevention and Control units in place
- Most hospitals (83.3%) not prepared in terms of Administration/operational support and essential support services.
- Only 1 had plan in place to quarantine staff.
- Only 1 had plan in place to assess level of preparedness for EIDs.
- Conclusion: Most hospitals not prepared and need to prioritize IPC. A standard should be put in place by which to review and judge readiness, etc.

4.2.4. An assessment of states' preparedness to respond to Lassa fever outbreaks in Nigeria, 2016

Presenter: Abiodun Ekwuenu

- In 2016, 28 states had a case of Lassa—Doubled from 2015.
- 2016: 932 cases. Most cases in January.
- Most states in North had higher mortality
- South better prepared than north.
- Over ½ states do not have adequate surveillance staff or budget.
- NCDC has developed guidelines to coordinate outbreak response. EOC's being set up in most states.
- Conclusion: States need budgets set aside for epi surveillance.

4.2.5. Nigeria Lassa fever After Action Review: Lessons learnt and way forward

Presenter: Malgwi Arhyel

- In 2018, 432 cases of Lassa, 108 deaths. 5,353 contacts identified.
- 21 states had a Lassa case in 2018.
- After Action Review (AAR) was conducted with 65 participants from core stakeholders (CDC, UNICEF, etc.) Used WHO standard tool for AAR.
- 14 actions identified including the need to stand up EOC's
- Gaps Identified: inadequate policies, no functional EOC's, no reagents available, multiple reporting channels

- After the AAR—follow up with states to assess the level of planning and intensify the high-level advocacy to the Minister of Health, etc.
- Conclusion: Pleased with participation by stakeholders in the AAR.

4.2.6. An innovative One Health model for mitigating perennial outbreaks of Lassa fever at the human-animal-ecosystem interface in Nigeria

Presenter: Daniel Oluwayelu

- Lassa has a long incubation period (7-10 days) which increases the risk of exportation
- Propose one-health holistic approach to take into account expertise of animal/human/environmental experts to work together.
- Model would include surveillance of Lassa in endemic populations; combined with study of genomes and evolution of strains; and known rodent populations. Include zoologists; taxonomists, vets, physicians, molecular biologists, virologists, ecologists, etc.

4.2.7. Catastrophic direct medical cost of Lassa fever care by patients managed in Irrua Specialist Teaching Hospital, Irrua Edo State

Presenter: Emmanuel Osagiede

- A fundamental function of health systems is to put in place a health financing system to protect populations according to WHO
- Some patients with Lassa have high Direct Medical Costs (DMC)
- Median age of a Lassa patient is 34 years old. Most are semi-skilled. Median income is 80,000 Naira. Out of pocket to be treated for Lassa: average DMC is 100,000 Naira.
- 53% borrowed money to pay healthcare costs. 1/10 sold property to pay—which further worsens their financial situation. Some pay \$10 a day to settle debt. This is 10x the critical minimum poverty level.
- Conclusion: The Nigerian government should take over the DMC for Lassa treatment.

4.2.8. The role of incident management system in the containment of the large 2018 Lassa fever outbreak in Nigeria

Presenter: Chioma Dan-Nwafor

- Incident Management System (IMS) was activated on 1/22/2018. Daily EOC meetings. Action plans. Standard testing algorithms, safe burials, SOP's and rapid response teams all put into place.
- Use of IMS led to containment of the outbreak.
- Conclusion: Use IMS in future outbreaks and establish State PHEOC, early deployment of rapid response teams, animal surveillance, encourage collaborations among states.

4.2.9. Towards a forecasting system for Lassa fever in Nigeria

Presenter: Gibb Rory

- Clear seasonal cycle to Lassa with spike in the early part of the year.
- Study looked at social, environmental, climate correlates of Lassa outbreaks to create a forecast.
- Main temporal predictor of a Lassa outbreak is rainfall 3 months prior. Mastomys increase population during rain.
- Conclusion: with more data, an early warning system can be established based on human/rat interaction patterns.
- Similarly in East Africa rainfall is used to determine crop damage from Mastomys rats.

4.3. Infection prevention and control

Notes by Solomon Yimer and Frederik Kristensen

Summary by moderators:

Infection prevention and control intervention is an essential component of the Lassa prevention and control strategy in Nigeria. All the studies presented in the session are important to identify gaps on IPC and propose appropriate interventions in the respective study areas. However, the main limitation of the studies is that all have not used

standardized method (questionnaires) so that the study results cannot be compared against each other. The WHO has prepared a standard questionnaire on IPC and can be used for future similar studies.

The study findings have shown important gaps in the implementation of IPC by health workers, which should be addressed appropriately. The NCDC is currently planning to collaborate with the CDC on recruiting student for postgraduate diploma in infection and prevention control for the future. Health workers who are interested in this initiative will be invited to apply for the course soon.

The experience of mobile lab may be applied to CEPs epidemiology work in West Africa. We may need to set up mobile labs to access lab diagnostics for Lassa suspects in remote communities.

4.3.1. Infection prevention and control in a treatment center during a Lassa fever outbreak in Southeastern Nigeria-January 2018

Presenter: Odekunle Odegbemi

Objective: to assess IPC practice among health workers

Method: cross-sectional study, systematic sampling, sample size 30, self-administered questionnaire used

Study population: nurses, doctors, laboratory scientists and pharmacists participated

Results:

- Nurses accounted for 43%, of the study participants
- 51.9% of the health care workers did not wash hands before patient contact
- 78% of health workers did not wash after patient contact
- Gloves were available only 50% of time
- face masks were available 25% of the time
- 14% of the time had soap for hand washing
- At 66% of the time they never had PPE at a Lassa treatment center
- Knowledge: Most have good, but still practice is low

4.3.2. Occupational acquisition of Lassa fever: an intervention study in Nigeria

Presenter: Stephen Abah

Objective: apply evidenced based criteria to reduce the effect of Lassa on health care workers through effective implementation of IPC

- Occupational acquisition of Lassa fever among health workers (HW) in endemic countries is the biggest challenge resulting in high morbidity and mortality (as high as 36-65% mortality according to available literature
- During the 2015-16 Lassa outbreak in Nigeria, 6% of the HW died, and in 2018, 8% confirmed cases were HW resulting in a CFR of 26%. This showed high morbidity and mortality among HW from Lassa suggesting that hospital precautions against Lassa should be emphasized.

Method: Intervention research at the Irrua Specialist Teaching Hospital, Irrua, Edo State.

The study focuses on quality improvement processes which utilizes a set of standards and compare them with HWs practice. The study used the WHO IPC facility assessment tool, which contain four criteria.

1. Data collection was done through observation of HW practice and compared this with the standard
2. HWs practice related to the following were evaluated against the standards set by WHO: Hand hygiene, surface disinfection, use of PPPE, training, water supply, communications, routine disinfection, waste segregation, Post-exposure prophylactics, Water supply
3. Scoring system was applied using 0-2 marks: 0 does not meet the minimum standard; 1= somehow meet the minimum standard; 2 =adequately meets the standard
4. Pre-post intervention assessment. Total score from 13 to 18 (20 max)

The gaps identified were categorized into three domains

- Reinforce prequestionnaire measures
- Implement the standard
- Mange contacts
- IPC should be institutionalized

Conclusion:

- Possible to reduce occupational accusation of Lassa through the application of simple cost-effective practices
- Infection control should be institutionalized, and costs included in the operational budget

4.3.3. Containment of Lassa fever outbreak in a southeastern Nigerian burn center without healthcare workers infection: the role of institutionalized infection prevention and control practices

Presenter: Ifeanyichukwu Onah

Objective: Assess the role of institutionalized IPC

- Active infection control unit since 2012. With monthly monitoring.
- Before LF: Wound dressing protocol. Multiple hand wash points, some with elbow taps etc.

Method: Compliance monitoring using the Mayo clinic IHI hand hygiene and glove use monitoring form.

Results: better in Ebola time, then slump, then better again in 2018; missing boots (only 12,5%)

Conclusion: IPC institutionalization helps a lot. Risk communication helped. Training and re-training required.

4.3.4. Knowledge and compliance with infection prevention and control among health workers in primary health care facilities in a Lassa fever endemic LGA of Edo State, Nigeria

Presenter: Martha Okonofua

Objective: Assess health workers knowledge and compliance on IPC

Method: Cross-sectional study, sample size 153, self-administered questioner (True/False) used for data collection; hand hygiene, use of PPE, injection safety and water management were assessed

Result: Good practice associated with age (over 50), more than 10 years' service, males, knowledge.

Conclusions: Continuing education, continual supply of PPE and other items, need for programme to be institutionalized
There was a question on how the sample size was calculated and the author defended well.

4.3.5. Management of confirmed Lassa fever cases in a make-shift isolation facility: implications for establishment of Lassa fever endemic situation in an area that is Lassa fever free

Presenter: Tope Ojo

- Provision of hyper-chlorinated water system and a waste management system.
- + contact tracing and surveillance. Training. Draft treatment protocol.
- One case managed, using the resources they had, no nosocomial transmission
- Need better preparation to manage more cases

4.3.6. Knowledge of Lassa fever and infection prevention and control among proprietary and patent Medicine vendors in endemic Local government areas in Edo State: implications for Lassa fever control

Presenter: Ekaete Tobin

Objective: Assess KAP on IPC among proprietary and patent Medicine vendors

- Proprietary and patent medicine vendors are persons without formal training in pharmacy. These are informal HCWs, including patient diagnosis. They are very well patronized.
- Method: cross-sectional study, sample size 94, two-stage sampling technique, self-administered questionnaire used, SPSS used for analysis

Result:

- Most had secondary level education
- Only 44,4% knew that LF agent is a virus, and 80% that the vector is the rodent.
- 30% think they can recognize a case of LF
- 2/3 see themselves at risk of infection.
- 22 % given an injection in the past six months. 75% recap needles.
- Hand hygiene was poor for 2/3
- Most common practice was providing antimalarials
- Only 14% always used gloves when touching potentially infected material.

Conclusion: Opportunity for early recognition and referral of Lassa suspected cases. To be included in IPC training and referral of suspects

4.3.7. Assessment of knowledge, attitude and practice of health professionals on Safe disposal of corpses of Lassa fever cases in Southwest, Nigeria

Presenter: Bamidele Oni

Objective: asses KAP of health professionals on safe disposal of corpses

Method: cross-sectional study, self-administered questionnaire; sample size 300 HW, ¾ responded

Result:

- 65% had knowledge about LF burial practices. Only 5% got it right.
- Environmental health officers should be responsible for burial.

Conclusion: Few have been trained, and few have participated. Need of training and certification of responsible officers to minimize spread of LF

4.3.8. Knowledge, attitude and practice of post exposure prophylaxis of Lassa fever among health care workers in a tertiary health institution in South-South Nigeria

Presenter: Francis Erah

Objective: Assess health workers' KAP on post-exposure prophylaxis of Lassa fever

- NCDC recommendation of use of ribavirin for 10 days among high risk groups (HW)

Method: cross-sectional study, self-administered questionnaire used,

Results:

- Post exposure prophylactics knowledge and practice was assessed using scoring.: < 50% score = Negative, > 50% = positive
- 86 % had tertiary education
- Knowledge: 75% good
- Attitude: 2/3 good
- Practice: 31% Good
- Knowledge & attitude highly correlated.

Conclusion: Calls for training and retraining with respect to PEP to improve practice.

Discussion: should look at morticians, not e.g. lab technicians.

4.4. Risk communications and community engagement

Notes by Nadia Tornieporth and Jodie Rogers

4.4.1. The role of a connect center in public engagement during the 2018 Lassa fever outbreak in Nigeria

Presenter: Favour Makava (NCDC)

Favour presented the work of the NCDC Risk Communications Team (a sub-team of their wider Comms Team) which aims to ensure that cases of diseases are monitored and responded to. They work on logging rumours and debunking false news surrounding diseases such as Lassa. They use social media and work with the media to do this.

During the 2018 outbreak last year, various false reports came through suggesting sugarcane cures Lassa Fever (various other rumours were also circulated during the outbreak). NCDC Risk Comms Team came up with a public health campaign to debunk news and they used social media to do this.

NCDC has a connect centre that serves as a platform for community engagement and disease response. They use various channels to get information in from the community and dispense information out:

- Whatsapp message
- SMS
- Social Media
- Phone (toll-free) – some calls ask how do we prevent Lassa, what are the signs and symptoms. They serve as a NHS 111 helpline for people experiencing symptoms but not being sure of what this may be. They notify health teams and second responders to follow up.
- Every Tuesday, they gather all the reports from the health facilities. Pharmacies also must send through antibiotic use for the week.

They work with the wider Comms Team to debunk rumours and ensure the public get the right scientific information.

They received a number of queries during the peak of the Lassa outbreak from Jan-Apr 2018. They received and responded to phone calls, SMS and WhatsApp messages (103 in total).

To resolve rumours, they work with Twitter and Facebook. They also engage the media on this. It is useful as serving as a way for the public to check their symptoms and get the right info and for information to be sent over.

THEIR RECOMMENDATIONS – Public health organisations should partner with telecommunication firm to establish similar connect centres to support surveillance (e.g. NCDC there is a toll-free line available 24/7)

4.4.2. Determine the level of awareness and knowledge of Lassa fever among Nigerians

Presenter: Oloche Owoicho

- Meta-analysis of 28 studies conducted in different geopolitical zones of Nigeria – among students, health workers, traders and community members. All studies were looking at the level of awareness and knowledge of Lassa fever among Nigerians.
- Knowledge and attitude among health workers – 61.2% of health workers had good knowledge.
- Overall, **93.1% were aware of Lassa fever, 61% had good knowledge of it.** There is no correlation between awareness and knowledge.
 - Additional studies among students (college and secondary school) and traders (some of whom are food handlers: 90% had poor knowledge; 77% were aware of LF)
 - Community: 4-20% had adequate knowledge of the disease
- In conclusion, knowledge of Lassa fever in the country is generally poor and more work needs to be done to build upon this – this includes starting young and engaging with school pupils so that they understand the importance of this. Awareness of LF is higher than the level of knowledge about the disease.

4.4.3. Stigma association with Lassa fever among Healthcare workers in Ondo State, Nigeria

Presenter: Ifeoma Idigbe

- There are several sociocultural factors that drive stigma among healthcare workers providing treatment and care to Lassa fever patients.
- Strategies to raise awareness and educate people have not been recognised and we need to do much more of this as stigma around the disease leads people not to report their symptoms, which in turn allows the greater spread of disease.
- They held 4 focus groups and 10 in-depth interviews in private rooms. They had question guides to explore health worker perceptions and experiences of working during the on-going Lassa fever outbreak, their coping mechanisms and asking how to create resilience.
- 58% had little knowledge about Lassa fever and managing the patients.
- 74% said they would be reluctant/embarrassed to tell their relatives or friends.
- 42% scared to have their samples taken.

THEMES THAT EMERGED:

SELF-STIGMA

- Fear of infection
- Lack of trust – many community members believe Lassa fever was spread by health workers who had contact with patients
- Healthcare workers also said that patients did not report true symptoms.
- This resulted in healthcare workers being feared and resulting in isolation

Findings highlight the need to educate people and create awareness. Treatment and support programmes need to be improved and tailored to specific communities.

4.4.4. Healthcare seeking behavior in Lassa fever endemic communities in Edo state

Presenter: Alphonsus Aigbiremolen

- Edo state is a hotspot for Lassa fever
- Seeking early care is critical for successful treatment of LF
- Lassa fever shares many symptoms with diseases like malaria, typhoid fever and respiratory infections, meaning that people can often not distinguish whether symptoms relate to the Lassa virus or another pathogen

- Researchers interviewed adults in Edo state among 300 participants asking about their health seeking behaviour (cross-sectional study design, 18 yrs and above, resident in community for >1yr, sampling technique)
 - 78% seek care in hospital, 26% seek care in drug store, 4% self-care, <2% seek care from a traditional healer
 - When asked, where would you go for treatment if you thought you had Lassa fever? Most people said the hospital or a health centre – some suggested self-medication and traditional healers
 - When asked, ‘how soon would you report to the health care facility?’, many said after self-medication had not worked
- People may also delay seeking treatment due to inadequate funds, it is too expensive, nobody to take me (correlated with socio-economic status)
- Females, tertiary education and Lassa knowledge are more likely to show health-seeking behaviour

4.4.5. Knowledge, attitudes and practices to Lassa fever among healthcare workers in Guinea

Presenter: Mory Cherif Haidara

- High case fatality rate in Guinea, among other West African countries
- Aimed to determine the factor that influence knowledge, attitudes and practices around Lassa fever in Guinea
- Descriptive cross-sectional study with quantitative approach:
 - They used 5 health facilities in Guinea – hospital, 2 urban area, 2 rural areas (included all types of healthcare workers)
 - 195 respondents (80% Muslim, mean age 30, 57% women)
 - 33% have not heard of Lassa fever. 48% had adequate knowledge. >95% had positive attitude toward suspected cases (associated with urban location and availability of PPE)
- Rural health facilities had more negative attitudes towards Lassa fever.
- General low level of knowledge among healthcare workers.

4.4.6. Community engagement for Lassa Fever epidemiological studies

Presented on behalf of Danny Asogun

- Reference to vaccine trial being informed by disease epidemiology – requires studies to be conducted in endemic communities. If you are to collect epidemiological data, it is crucial to engage the community
- Experience reported here is from the pilot studies completed by Irrua Specialist Teaching Hospital (w/ BNITM)– selected three endemic communities with high Lassa endemicity
 - Formal engagement of community: meetings of senior leaders. Traditional head, then trad head and senior elders or opinion leaders etc.
 - Lecture on LF and details of research to be conducted Q&A
 - They were aware Lassa was endemic in their communities
 - They would get the entire research team and community council of elders and women and youth leaders together to discuss actions
 - Supplied wine, gin and food
 - Community liaisons accompanied the study teams (e.g. during blood sampling), which showed reduced stress of community members
 - High attendance of elders and working together resulted in 95-100% of data collection

4.4.7. Community engagement: Lessons from the Ebola response

Presenter: Akintoye Akinrinade

- Narrative review looking at first-hand ethnographic data and response to the 2014/5 Ebola outbreak in West Africa
- Reports were assessed through documents from epidemic response anthropology platform (hosted by LSHTM)
- Public health workers lagged behind community during Ebola outbreak – cultural gaps, language barrier
- Social and behaviour change increased knowledge in the first 6 months of the outbreak
- Knowledge is power. If you know what something is, you know how to respond. You don’t know what you don’t know.
- We cannot have 100% control of an outbreak without human interaction and recognising human interaction as core to responding to epidemics.
- Socio-cultural norms remain crucial to responses.

- Community engagement can save lives – as a disease prevention and control strategy

4.4.8. Community burial practices in Nigeria and Lassa fever Control

Presenter: Anastacia Ojimba

- Case fatality rate is higher in pregnant women as opposed to non-pregnant women
- The corpse of a positive Lassa fever patient remains infective after death and should be buried in a non-contagious method that is culturally acceptable
- It is considered taboo in most of S and SE Nigeria to bury a pregnant woman with fetus in situ.
- There were 2 cases of pregnant women who died after Lassa fever:
 - **Case A:** 23 years old, succumbed to the disease on second day of admission. She was buried according to NCDC guidelines. As soon as they left, the community buried the baby separate to the mother.
 - **Case B:** 27-year-old housewife in her second community, presented Lassa at 31 weeks of gestation. She died on the second day of admission. Her family said they could not bury her if she still had her baby. They waited 3 months due to disputes. After a stakeholder meeting, they conducted a post mortem caesarean section into two separate body bags.
- Study conducted to review impact of cultural consideration: Sample population included all stakeholders.
- **Recommendation:** Case A put community at risk – as such, cultural beliefs and practices should always be taken into consideration in planning and implementation of LF control.

Extra comments:

- Role of the media is a very powerful tool – sharing this message via the media
- Media role in debunking Yellow Fever debunking – media got in touch with NCDC
- We should start young and engage more patients
- Robin Nandy – outbreaks are good because they expose cracks in the health system and that's how we develop

Q&A:

- Was there any contact tracing in the case of exhumation of the pregnant woman?
 - Yes, they went to the community and informed the Ministry of Health; they will continue to visit and study that community.
- Did you use the media in these cases to spread the message?
 - They deal with rumors all the time and should be engaged early.
- The NCDC toll-free CC number was requested by the audience

5 Side meetings

5.3 Core protocol and next steps: Targeted Lassa epidemiology studies

15 Jan 2019

- Presentations:
 - Review of outcomes of Ghana workshop (November 2018), including overview of key objectives, take-aways, and issues to still be addressed.
 - Review of protocols (cohort study and seroprevalence study), highlighting areas for finalization.
 - Further harmonization needs: Laboratory testing and exploratory objectives.
 - Introduction of LF EpiData Knowledge Initiative.
 - Process to project implementation, including next steps.
- Key outcomes:
 - We will concentrate on the cohort study for now (one protocol). Initial site visit for the cohort study can act as a seroprevalence survey.
 - Case definition and follow-up frequency need further refinement, as well as clear instructions for how participants will be expected to do in cases of fever (e.g. when to report to healthcare facility).
 - We should tie these activities to existing surveillance structures as much as possible (for capacity building, reducing duplications of effort).
 - Pregnant women should be fully integrated into the study.