Clinical Presentation and Complications of Lassa Fever

Daniel Bausch, MD, MPH&TM
Director, UK Public Health Rapid Support Team
Public Health England/London School of Hygiene and Tropical Medicine
London, UK

Daniel.Bausch@phe.gov.uk
Lassa Fever

- Hemorrhagic illness caused by the arenavirus Lassa
- First discovered in Nigeria in 1969
- Endemic in areas of West Africa
  - 300,000-500,000 infections/year (?)
  - 5,000 deaths/year
- Rodent reservoir
  - Mastomys natalensis ("multimammate rat")
- Occasional nosocomial outbreaks
- Case fatality rate: 20-25% of hospitalized cases
- Effective treatment with ribavirin (?)
Lassa: Clinical Presentation at Admission

Bausch et al., Vector Borne and Zoonotic Diseases, 2001

- Lassa fever (n=21)
- Non-Lassa febrile illness (n=268)
Associated with Poor Prognosis in Lassa Fever

- High viremia
- Serum AST level >150 IU/L
- Bleeding
- Encephalitis
- Renal disease
- Edema
- Pregnancy, especially third trimester
Lassa Fever: Complications

- Renal disease
- Sensorineural deafness (up to 30%)
- Encephalitis
- Pleural and pericardial effusion
- Spontaneous abortion
- Shock
Clinical Management

- **Supportive treatment**
  - Intensive care unit if possible
  - Limit movement of patient
  - Fluid and electrolyte balance, supplemental O2, ventilation, pressors, dialysis
  - Consider capillary leak and risk of pulmonary edema when rehydrating
  - Steroids NOT indicated

- **Specific antiviral therapy**
Lassa fever: Clinical Questions and Challenges (I)

- Development/validation/standardization of diagnostic tools
  - Acute disease (RNA, antigen, virus)
  - Serology/antibody (IgM, IgG)
- Enhanced clinical and laboratory surveillance for evidence-based estimates of endemicity and incidence
- Case definitions
- True infection-to-disease ratio
- Significance of strain variation
Lassa fever: Clinical Questions and Challenges (II)

- Effect of mode of transmission on disease manifestation
- Incidence of re-infection and associated clinical manifestations
- Pathogenesis and causes of death
- Sequelae and delayed virus clearance
- Optimal supportive care
- New treatments to replace or add to ribavirin
- Clinical trial capacity in Africa
Lassa Diagnostics

- Cell culture
- Complement fixation
- IFA
- ELISA (Ag and IgM)
  - Antigens from cell lysates
  - Recombinant antigens
- PCR (numerous assays/targets)
- Lateral flow and other rapid tests
Five Lineages of Lassa Virus
(Manning 2015)
218 *M. natalensis* trapped in southeastern Sierra Leone

- 41 LASV isolates

Heterogeneity:
- ~10% nt (L)
- ~4% aa (GP)
Sensorineural Hearing Loss in Lassa Fever (Yun 2016)

- Stat1<sup>−/−</sup> mouse model
- Mild damage to cochlear hair cells
- Auditory nerve spiral ganglion degeneration
- T-cell mediated?
District map of reported Lassa fever virus cases from 1989 to 2016 (WHO 2016)
New Kenema Government Hospital Lassa Ward (and Clinical Research Center)
Mastomys natalensis ("Natal multimammate rat")

- Peri-domestic
- Inhabits fields and cleared forest
- Prolific breeder (~8-12 pups/litter)
- Infected at birth and become chronic asymptomatic carriers of Lassa virus
- Shed virus in the urine and feces
Housing equity: Rights-based approach to Lassa fever control (Kelly 2013)