WINNING THE FIGHT AGAINST LASSA FEVER IN ONDO STATE

By

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- LASSA FEVER VIRUS IS ONE OF THE SIX HAEMORRAGIC FEVR VIRUSES IN NIGERIA

HAEMORRHAGIC FEVER VIRUSES IN NIGERIA

Virus	Vector/Reservoir
Yellow fever virus	Mosquito
Dengue (types 1-4) viruses	Mosquito
Rift Valley fever virus	Mosquito
Crimean-Congo Haemorrhagic Fever	Tick
Lassa Fever Virus	Rat
(Ebola)-Imported	?Bat

- IN THE LAST TWO DECADES, LASSA FEVER VIRUS IS THE MOST ACTIVE HAEMORRHAGIC FEVER VIRUS IN THE NIGERIAN POPULATION WITH AT LEAST 15 REPORTED OUTBREAKS SINCE 1969

LASSA FEVER IN ONDO STATE

- Several Outbreaks in Ondo State in recent years
- Outbreaks occur more frequently than before
- More cases now than before
- Cases occur in dry and wet seasons
- More LGAs affected now than before

LASSA FEVER IN ONDO STATE- THE 2017 OUTBREAK

- No. of Cases: 102
- No. of LGAs Affected: 8 - Owo, Ose, Akoko south-west, Akure north, Akure south
- No. Confirmed (positive cases): 36
- No. of Deaths: 9

LASSA FEVER: DEFINITION

- An acute disease caused by Lassa virus, a rat-borne virus characterized by high fever accompanied by myalgia and severe prostration, and signs of the involvement of the respiratory and gastrointestinal tracts cardiovascular and nervous systems and a case fatality rate of up to 25%
- Mild cases are common
- Subclinical Infections are also common

HISTORICAL PERSPECTIVES

- First outbreaks were described in the 1950s
- Virus was first identified in Nigeria during an outbreak in 1969 in Lassa Village, Bornu State
- Virus was named after the original location of isolation –Lassa, the village where the first patient came from.

HISTORICAL PERSPECTIVES:THE 1969 OUTBREAK

- Two nurses became ill and died at Evangel hospital, Jos; the first nurse was infected in Lassa village and was evacuated to Jos. The second was infected while looking after the first.

- The third nurse (Ms. Pinneo) was evacuated to the USA where she recovered after a severe and prolonged illness.

HISTORICAL PERSPECTIVES: INFECTION OF A PATHOLOGIST

- Dr. Jeanne Troup, Pathologist got Infected while performing autopsy on one of the dead patients
- Died

LABORATORY INFECTION AT YALE UNIVERSITY, USA

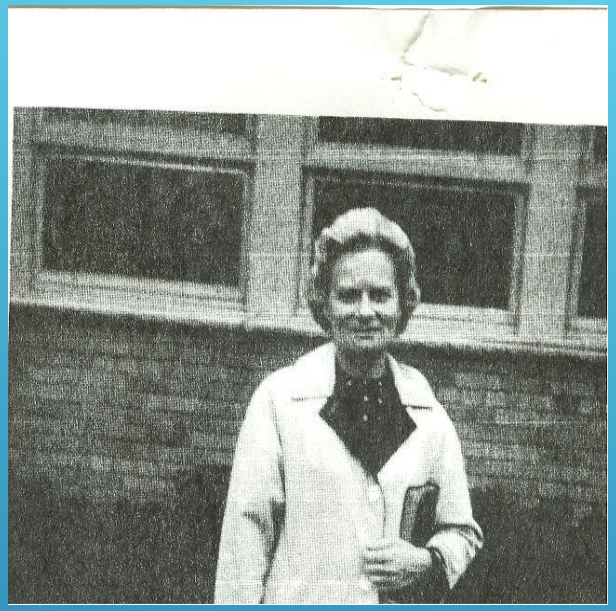
- Professor Jordi Casals isolated Lassa fever Virus from the specimen obtained from patients
- He was infected and became seriously sick and almost died.

HISTORICAL PERSPECTIVES: LABORATORY-ACQUIRED INFECTION AT YALE (CONTD)

- He was treated with the serum obtained from the only surviving nurse (Ms. Pinneo).
- A second laboratory-acquired infection occurred at Yale in a junior laboratory worker

Evangel Hospital

HOSPITAL STAFF



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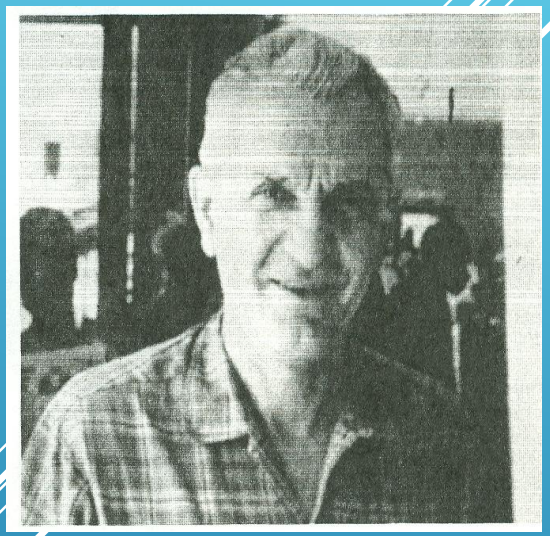


JC

Dr. Troup

DR. JEANETTE M. TROUP

December 24, 1923 - February 18, 1970

"Therefore, my beloved brethren, be ye steadfast, unmovable, always abounding in the work of the Lord, forasmuch as ye know that your labor is not in vain in the Lord."

I Corinthians 15:58 Jeanette's Life Verse

HISTORICAL PERSPECTIVES-1974 OUTBREAK

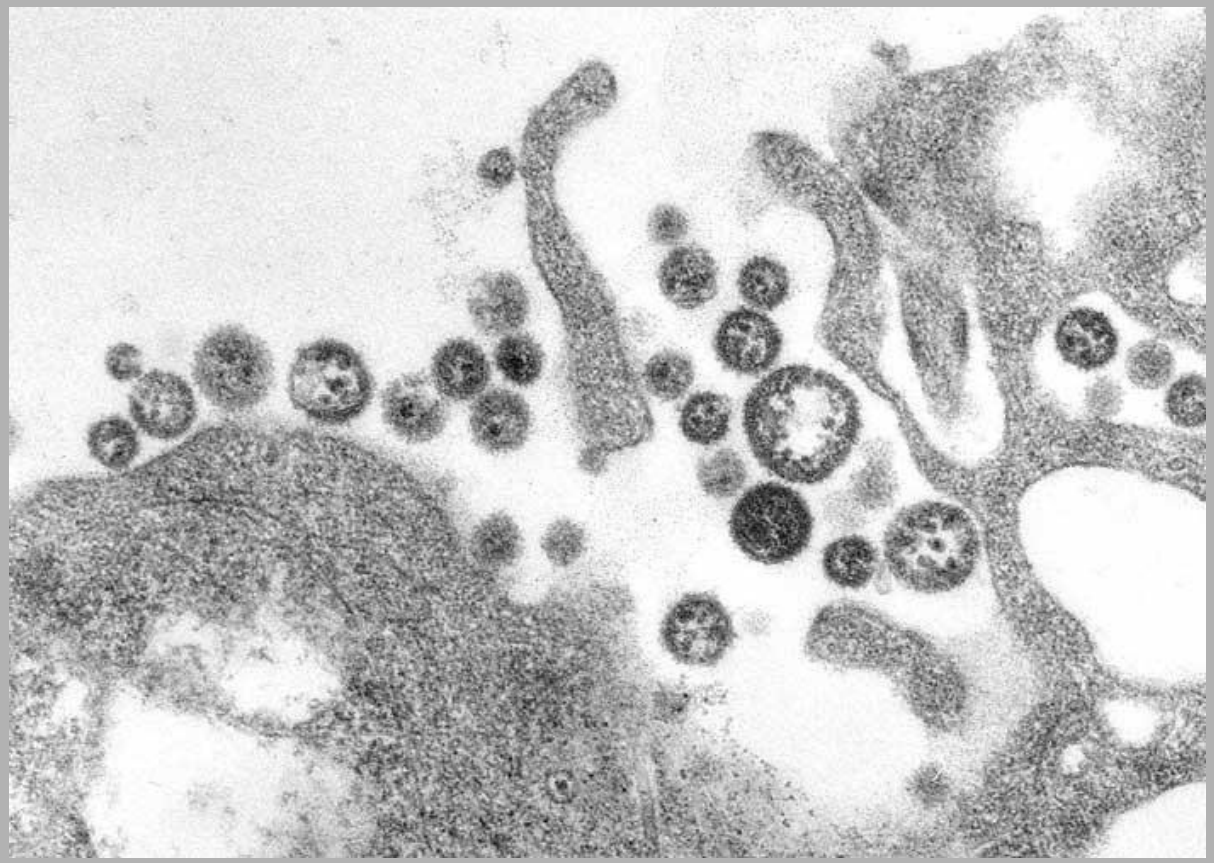
- A German medical officer contracted Lassa fever from a patient at Onitsha
- Died
- His colleague who cared for him became infected and was seriously sick
- He was evacuated to Ibadan
- Professor Casals was flown to Ibadan from the USA and serum was collected from him to treat the German doctor

- Lassa fever virus belongs to the family Arenaviridae
  - *Arenosus*= sand

LASSA FEVER VIRUS

WHAT DOES IT LOOK LIKE UNDER THE ELECTRON MICROSCOPE?

Lassa Virus



EFFECT OF HEAT ON LASSA FEVER VIRUS

Virus can be killed by:

- Heating to 60 degrees Celsius for 1 hr
- Boiling water within 1 minute
- Incineration/burning

EFFECT OF CHEMICALS ON LASSA FEVER VIRUS

Virus can be killed by:

- Bleach (10%)- 0.5 sodium hypochlorite
- Dettol, Lysol –(Phenol)
- Formalin
- Other chemicals: Ether, chloroform, glutaraldehyde etc.

EFFECT OF LASSA FEVER VIRUS ON ANIMALS

▸ Adult Mice	Severe Disease and Death
▸ Guinea Pigs	Severe Disease and Death
▸ Monkeys:	
Rhesus	Severe disease and death
Cynomolgus	Severe disease and death
Squirrell	No disease
Capuchin	No disease
▸ Baboons	Severe disease/Death
▸ Cats	????

TRANSMISSION LASSA FEVER VIRUS

BREAK TIME!!!

TRANSMISSION

- Mastomys Rats-to-human:
  - Ingestion of food and drink contaminated with rat urine or droppings
  - Use of materials and utensils/cutleries contaminated with infected rat urine and droppings
  - Catching and preparing *Mastomys* as a food Direct contact with blood tissues, saliva, droppings, urine of infected rats

-Inhalation of aerosolized virus

Transmission

- Human-to-human:

- Direct contact with blood, tissues, secretions or excretions of infected humans

Others:

-Needlestick injuries or cuts,

-Sexual -virus in semen for up to 3 months post recovery

Mastomys species complex

- *M. natalensis*
- *M. huberti*
- *M. erytholeucus*
- Others

MASTOMYS NATALENSIS RAT RESERVOIR

- "Multimammate rat"
- Prolific breeder (~8-12 pups/litter)
- Infected at birth and become chronic asymptomatic carriers of Lassa virus
- Shed virus in the urine and feces
- Major agricultural Pest

HABITATS OF MASTOMYS NATALENSIS

- Peridomestic sites-Around homes
- Cultivated farms: Maize and rice farms
- Fallow farms
- Savannah
- Grassland
- Others-Bush

BREEDING CHARACTERISTCS OF MASTOMYS NATALENSIS

- Life span 339 days
- Age at first litter 130 days
- Frequency of litter 61.5 days
- Average size of litter 8
- Ratio of male:female

In litter 4.5: 5.5

- No. of litters in lifespan 4

FACTORS CAUSING INCREASE IN POPULATION OF M. NATALENSIS

- All Year Round Breeding
- Abundance of Food (Maize And Other Cereals)
- Abundance of food in raining season leads to Increased Breeding Rate During Rainy Season
- High Birth Rates During Rainy Season

Result in

Very high Population of Adult M. natalensis in the dry season

Mulungu et al (2013); Coetzee et al (1965)

OTHER RODENT HOSTS OF LASSA FEVER VIRUS

- *Rattus rattus*
- *Mus musculus*
- *Mus minutoides*

Agbonlahor et al (2017)

Wulff (1975)

- *Mastomys erythroleucus*
- *Hylomyscus pamfi*

Olayemi et al (2016)

CLINICAL FEATURES OF LASSA FEVER

- Gradual onset of fever, headache, malaise and other non-specific signs and symptoms

- Pharyngitis, myalgias, retro-sternal pain, cough and gastrointestinal symptoms typically seen

- A minority present with classic symptoms of bleeding (gums, eyes and nose, mucosal bleeding), neck/facial swelling and shock
- Case fatality of hospitalized cases: 15-20%
- Particularly severe in pregnant women and their offspring
- Deafness a common sequela

Lassa Fever in Children and Infants

- Significant cause of pediatric hospitalizations in some areas of West Africa
- Signs and symptoms most often similar to adults
- "Swollen Baby Syndrome" -Edema/Anasarca

  - Abdominal distension and Bleeding
  - Poor prognosis

DISEASES THAT COULD BE CONFUSED WITH LASSA FEVER

- Malaria
- Typhoid fever
- Streptococcal pharyngitis
- Leptospirosis
- Bacterial sepsis
- Bacterial meningitis
- Arboviral infection
- Anicteric hepatitis
- Enterovirus infection
- Bacterial or viral conjunctivitis
- Dengue HF
- Yellow Fever
- Ebola

HOW ARE SUSPECTED CASES OF LASSA FEVER CONFIRMED?

Laboratories equipped to confirm Lassa fever cases in the country are very few.

Rapid confirmation of cases required for early commencement of treatment

HOW ARE SUSPECTED CASES OF LASSA FEVER CONFIRMED ?

- Specimen: Blood, CSF, Pharyngeal Secretions, Urine, Acute and Convalescent sera

- HANDLING OF LASSA FEVER SPECIMENS REQUIRES A BIOSAFETY CABINET LEVEL 2 AND PPE FOR THE LABORATORY PERSONNEL

- Working with un-treated specimen or live virus requires a BSL-4

LABORATORY SAFETY

Personal Protective Equipment (PPE) utilized in the inactivation room.

LABORATORY TESTS FOR LASSA FEVER

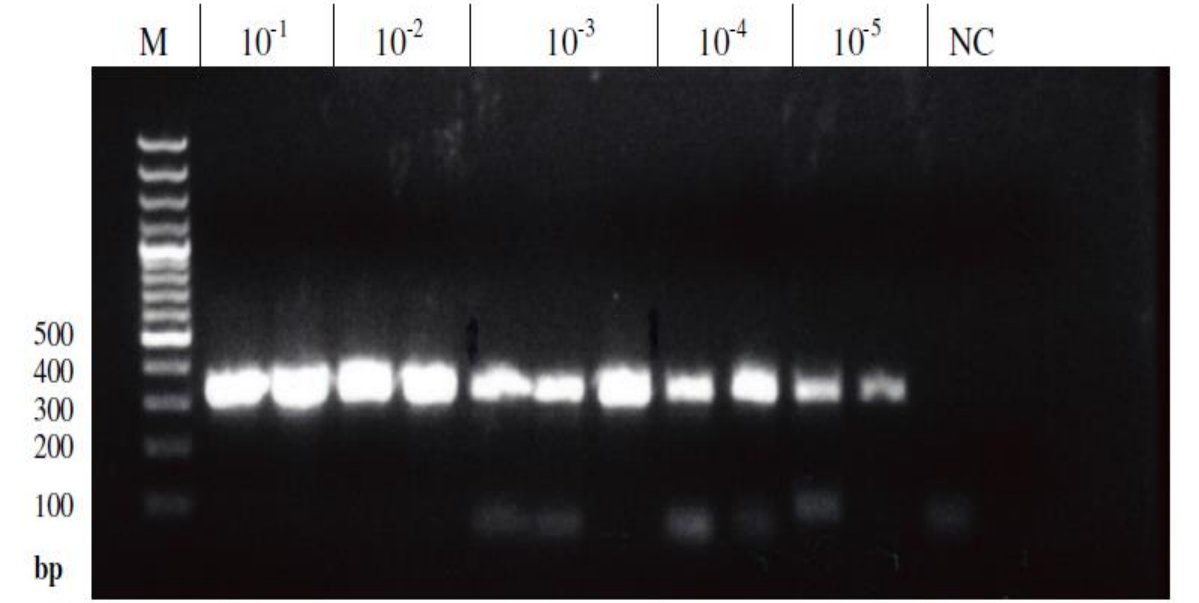
- Direct detection
  - Virus Isolation and Identification
  - RT-PCR
  - Antigen Detection
- Indirect: Antibody detection
  - IgG and IgM immunofluorescence
  - IgM ELISA

VIRUS ISOLATION IN BIOSAFETY LEVEL 4 (BSL-4) LAB

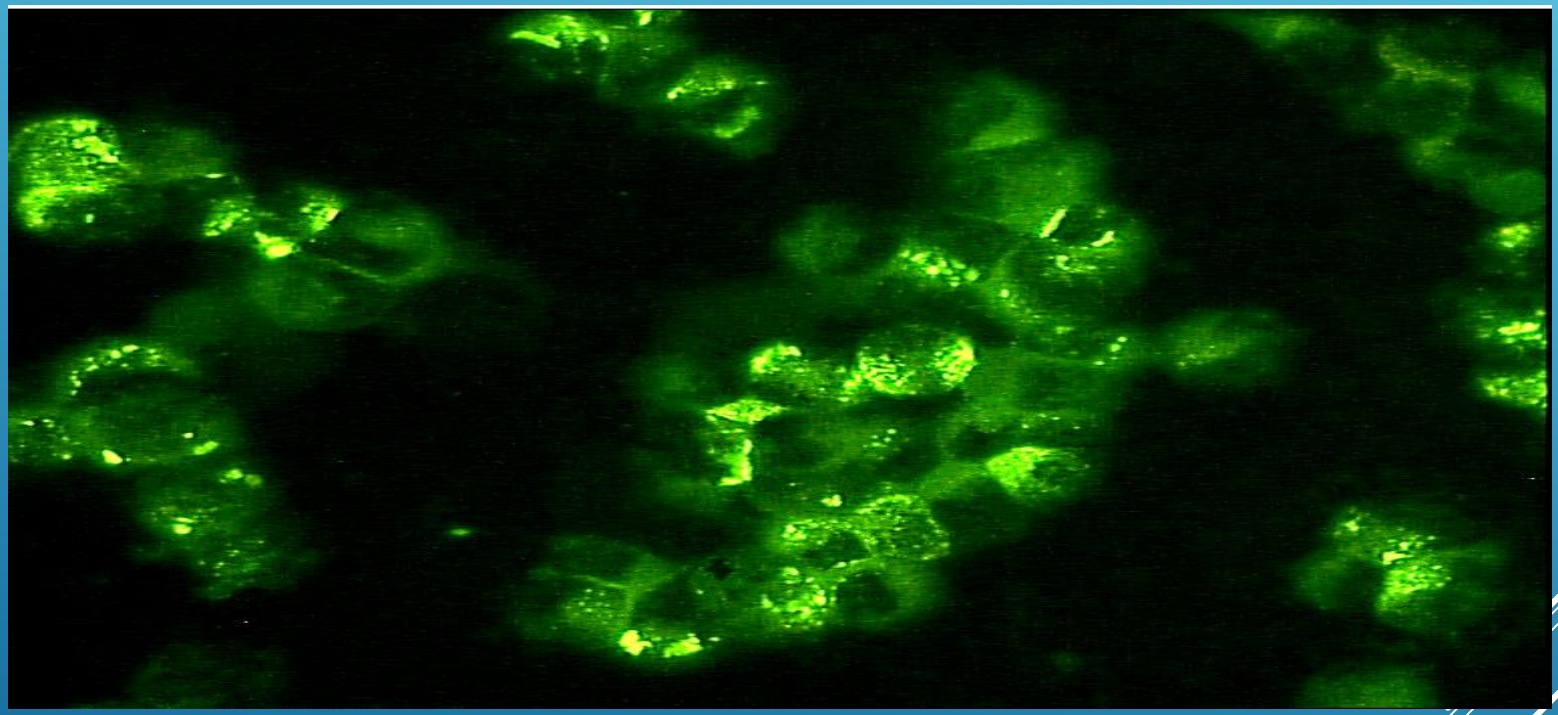
Advantages:
- Independent of genetic variability
- Detailed characterization of isolate.

Disadvantages:
- Time and labour intensive
- Expensive infrastructure
- Requirement for a BSL-4 Facility

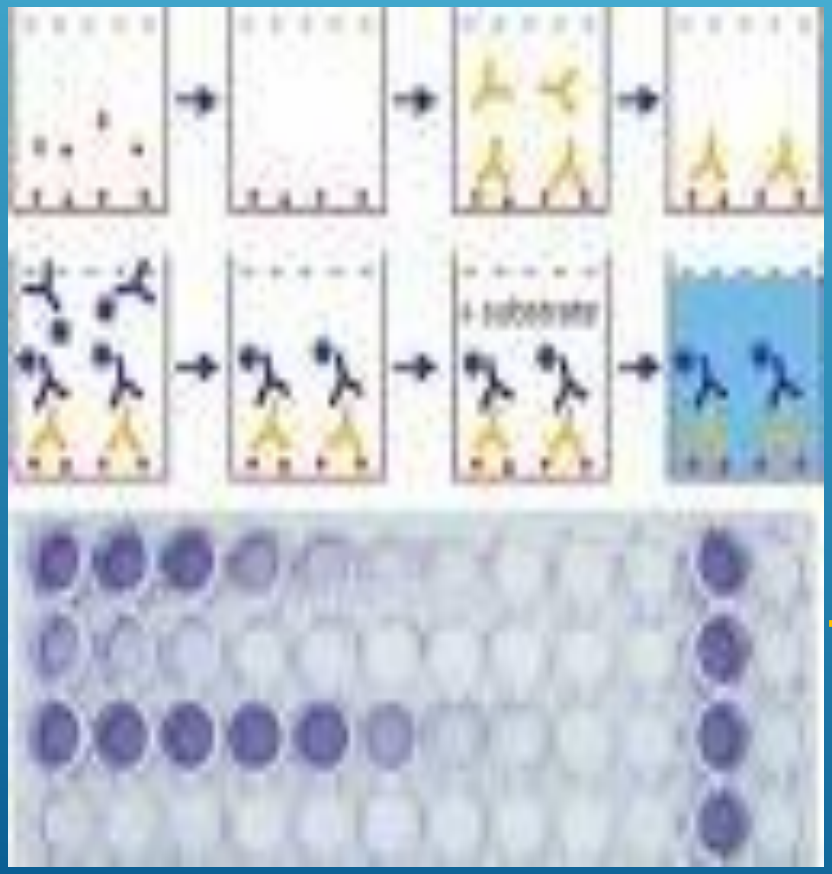
POLYMERASE CHAIN REACTION

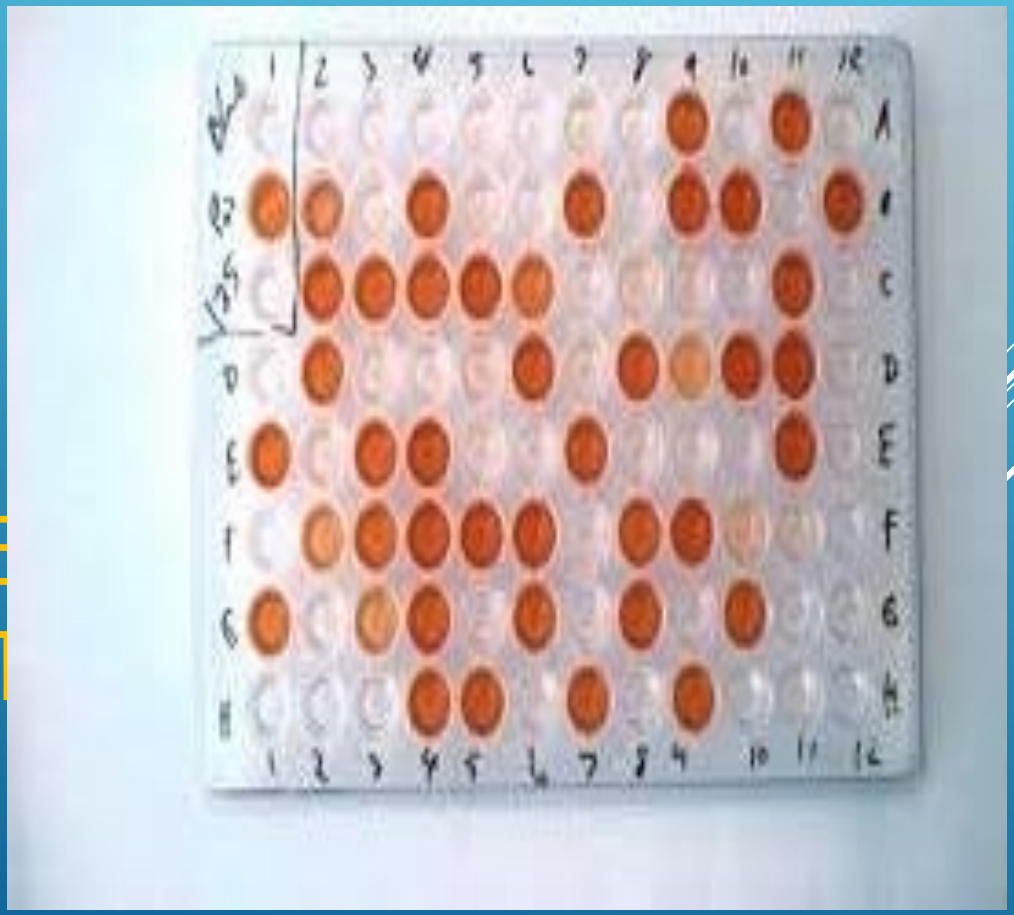


LASSA VIRUS-ANTIGEN DETECTION BY IMMUNOFLUORESCENCE



Lassa viral antigens seen as granules/dots within the cytoplasm


+ substrate



HOW ARE LASSA FEVER PATIENTS TREATED

- Supportive measures
- Ribavirin
  - Most effective when started within the first 6 days of illness
  - Major toxicity: mild hemolysis and suppression of erythropoesis. Both reversible
  - Presently contraindicated in pregnancy, although may be warranted if mother's life at risk
  - Does not appear to reduce incidence or severity of deafness

HOW CAN LASSA FEVER BE PREVENTED: VACCINATION

- Most Practical Approach to Prevention
- No licensed vaccine
- Vaccine Development: Two types of vaccines approved for clinical trials

WHAT TO DO TO AVOID INFECTION

Divided into 6 parts:

- Personal Hygiene and Environmental Sanitation
- Foods
- Utensils, Cutleries, etc
- Healthcare workers and Caregivers
- Sexual Intercourse after recovery
- Rat Control

PREVENTIVE MEASURES

v

Personal Hygiene and Environmental Sanitation

- Wash your hands frequently with soap and water
- Clean your house always
- Disinfect floors that may be contaminated with rat urine and droppings with 10% household bleach or dettol
- Don't touch rat droppings or dead animal with bare hands. Disinfect them with bleach or dettol, remove and discard or incinerate
- Clean home surroundings-no garbage and bush

PREVENTIVE MEASURES

Food

- Do not eat food that has been eaten by rats or that is contaminated with urine or droppings of rats
- Cook all foods very well before eating
- Store food and grains in rodent-proof containers (tough plastics or metal containers).
- Remove food such as rice, gari, semolina etc from bags and cartons and store them in these containers. Containers must have tight fitting covers

PREVENTIVE MEASURES

Food (contd)

- Do not sun-dry food, grains and other farm produce by the road side
- Do not drink gari. If you must, heat it in a frying pan.
- Do not taste gari in the market
- Wash fruits with vinegar before eating
- Avoid catching of rats and preparing them as food

PREVENTIVE MEASURES

Utensils and Cutleries

- Disinfect utensils, plates, spoons, drinking cups and other cutleries that may be contaminated with rat urine or droppings using very hot water or 10% household bleach
- Incinerate disposable materials contaminated with rat urine or droppings

PREVENTIVE MEASURES

Health care workers, Other care-givers, and burial of patients

- As a health care worker, you should adhere to infection prevention and control procedures
- If you are relative assisting in caring for a Lassa fever patient, you should take extra precautions
- States should ensure safe and dignified burial practices for patients that die of Lassa fever

SEXUAL INTERCOURSE AFTER RECOVERY

- Virus clearance from semen takes 3 months after recovery
- Virus has also been detected in vaginal secretions
- Sexual Intercourse after recovery from Lassa fever should be delayed for 3 months

PREVENTIVE MEASURES- RAT CONTROL

- Very difficult but very crucial to preventing spread of Lassa fever virus because hundreds of thousands or millions of Lassa fever virus-infected rats are produced every year
- Reduction of rat population will reduce the level of rat-human contact
- To be effective, rat control effort should be intensive and sustained

PREVENTIVE MEASURES-RAT CONTROL

You can eliminate rats from your house or reduce their population in your community and LGA by:

- Trapping
- Killing with Rat poisons
- Other methods-Contraception and use of predators (Cats): No data on infection of cats by Lassa fever virus

RECOMMENDATIONS TO GOVERNMENT

- 1. Continue the current efforts of raising awareness of the general public and health personnel on how Lassa fever virus is transmitted and how to avoid being infected

2. RAT CONTROL

Government should develop a permanent rat management policy in the Ministry of Health that will include:

- A sustained and intensive effort to reduce the rat population by trapping, poisoning and other methods, around homes, in the bush and on the farms
- Support for communities in rat control efforts by supplying them rat traps and rat poisons free of charge or at subsidized prices.

2. RAT CONTROL

- Creation of anti-rat scouts in all LGAs that will be used to execute the rat control activities
- Coordinate the rat control efforts with neighboring states

3. OTHER RECOMMENDATIONS

- Legislate against sun-drying of food and grains by the roadside and other practices that promote contact of rats with food
- Teach people alternative methods of drying food and grains
- Legislate against bush-burning

- Build a Maximum or High Security Virology Laboratory for UNIMED. Will facilitate early diagnosis and prompt treatment of confirmed cases
- Annual training and workshops for Health personnel on infection prevention and control to reduce nosocomial infections

3. OTHER RECOMMENDATIONS

- Support Research on the biology and behavior of Mastomys natalensis in Zoology departments of the 3 state universities

- Federal Government should award scholarship/Fellowship to train Nigerians on Vaccine development against Lassa fever and other Nigerian haemorrhagic fever viruses

Acknowledgement

Gratitude to Professor S. A Omilabu, Department of Medical Microbiology & Parasitology, LUTH, Idi-Araba for providing many of the slides used in this presentation.

THANK YOU FOR LISTENING

EVIL SHALL NOT COME YOUR WAY AMEN