

NATIONAL GUIDELINES FOR LASSA FEVER CASE MANAGEMENT

NOVEMBER, 2018

Foreword

The large Lassa fever outbreak in Nigeria between January and May 2018, increased our awareness of the need to have well-detailed and easily accessible guidelines, for response activities.

Although the Nigeria Centre for Disease Control (NCDC) had coordinated the development of these guidelines in 2017, the 2018 outbreak highlighted some lessons.

We were fortunate to have contained the outbreak at the time. However, those events highlighted the potential loss of life that can occur if we were not better prepared.

The After-Action Review conducted in July 2018, demonstrated critical gaps that need to be filled to protect us from the next outbreak. These results have helped to guide the review of the national guidelines for Lassa fever case management.

This guideline provides details on how to identify a suspected case of Lassa fever, clinical and laboratory diagnosis, clinical management of Lassa fever cases including in special populations.

It is important to remember that the recommended treatment approach provided in this document are based on the best evidence available, and in consistent with the already existing WHO guidelines. We acknowledge however, that there are a lot of knowledge gaps that will require further research. Comments that aim to improve these treatment guidelines will be appreciated.

We encourage all stakeholders to carefully review this document and use it as a countryowned guide for Lassa fever management. We hope that the national guidelines for Lassa fever case management can contribute to our joint efforts, to reduce the transmission and mortality of Lassa fever in Nigeria.

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Table of Contents

Chapter 1: Background	7
1.1 Case Definition of Lassa Fever	7
1.1.1 Alert case	7
1.1.2 Suspected case	7
1.1.3 Probable case (Clinical)	8
1.1.4 Supporting Laboratory evidence:	8
1.1.5 Confirmed case	8
Chapter 2:	10
Clinical SCREENING AND TRIAGING FOR Lassa fever	10
2.1. Triaging and Initial management modalities	10
2.1.1 Suspected case	10
2.1.2 Probable Case	11
2.1.3 Confirmed Case	11
2.1.4 Severe Lassa fever	11
Chapter 3: DIAGNOSIS AND CLINICAL MANAGEMENT OF LASSA	FEVER . 12
3.1.1 Diagnostic Investigations	12
3.1.2 Confirmatory Investigations	12
3.1.3 Supportive Investigations	12
3.1.4 Monitoring Investigations	13
3.2 Drug Treatment of Lassa fever	13
3.2.1A Adults including non-pregnant adults (McCormick regimen)	13
3.2.1B Adults including non-pregnant adults (Irrua regimen)	13
3.3 Management of Lassa fever in Pregnant Women	14
3.3.1 ISTH Regimen for Pregnant women (Modified McCormick regimen)	14
3.3.1A Prognostic Features	15
3.3.1B Considerations	15
3.3.1C Management Modalities	15
3.3.2 Lassa Fever in Puerperium	17
3.3.3 Bundle of Care of Infected Pregnant Woman	

NATIONAL GUIDELINES FOR LASSA FEVER CASE MANAGEMENT

3.4 Management of Lassa fever in Children	18
3.4.1 Neonatal Care	18
3.4.1A Contra-indications to Breastfeeding	18
3.4.1B Treatment Regimen	19
3.5 Management of Suspected cases awaiting lab results	19
3.6 Precautions to take when treating cases of Lassa fever	19
3.7 Poor Prognostic Indicators	19
3.8 Supportive Care	20
3.8.1 Basic requirements for all types of support needed	20
Chapter 4: Management of Complications of Lassa fever	24
4.1 Management of Acute Kidney Injury (AKI)	24
4.2 Management of Severe dehydration (from vomiting or diarrhoea)	26
4.2.1 Features of Hypovolemic Shock	26
4.2.2 Management of Hypovolemic Shock	27
4.3 Management of Sepsis/Septic Shock	27
4.3.1: Phases of Septic Shock	27
4.4 Management of Encephalopathy	32
4.5 Management of Acute Respiratory Failure	33
4.6 Management of Severe bleeding/Anaemia	34
Chapter 5: Infection Prevention and Control in Lassa fever Management.	36
5.1: Introduction	36
5.2: Use of PPE in the care of Lassa fever Patients	36
5.2.1: Who must wear protective clothing	36
5.3: Hand Hygiene and Glove Disinfection when caring for Lassa fever patients	39
5.3.1: Carrying out Hand Hygiene	40
5.3.1A: Hand hygiene with Alcohol-based Hand-rub	40
5.3.1B: Handwashing with soap and water	40
5.3.2: How to Change Gloves	41
Chapter 6: Identification and management of Lassa fever Contacts	42
6.1 Who is a contact?	42
6.2 Considerations for Post-exposure prophylaxis with Ribavirin	45

Chapter 7: Discharge Criteria for Lassa fever	
Chapter 8: Safe Burial for Lassa fever Cases	47
8.1: Introduction	47
8.2: How to prepare the dead body in the health facility	47
Chapter 9: Appendices	50
a. List of Treatment Centres in Nigeria	50
b. WHO 5 Moments of Hand Hygiene	
c. Steps in performing Hand Hygiene using ABHR	53
d. Steps on how to Handwash	54
References	55
LIST OF REVIeWERS	

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Er loni

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Acronyms

ABG	Arterial Blood Gas	INR	International Normalized Ratio
ACE	Angiotensin-converting enzyme	IPC	Infection Prevention and Control
AKI	Acute Kidney Injury	ISTH	Irrua Specialist Teaching Hospital
ALT A	Alanine Aminotransferase	IUFD	Intra Uterine Foetal Demise
ARDS A	Acute Respiratory Distress Syndrome	IV	Intravenous
AST A	Aspartate Aminotransferase	IU	International Unit
AVPU A	lert-Voice-Pain-Unresponsive	LFT	Liver Function Test
BCS I	Blantyre Coma Scale	LF	Lassa Fever
Ca (Calcium	LGA	Local Government Area
CNS (entral Nervous System	mEQ	Milliequivalent
CPAP C	ontinuous Positive Airway Pressure	MRI	Magnetic Resonance Imaging
CPR	Cardiopulmonary Resuscitation	MVA	Manual Vacuum Aspiration
C/S	Caesarean Section	NSAIDs	Non-Steroidal Anti-Inflammatory Drugs
CrCL	Creatinine Clearance	PCR	Polymerase Chain Reaction
CSF	Cerebrospinal Fluid	PCV	Packed Cell Volume
СТ	Computer Tomography	PEP	Post Exposure Prophylaxis
CTG	Cardiotocography	PPE	Personal Protective Equipment
EBT	Exchange Blood Transfusion	РТ	Prothrombin Time
ECG	Electrocardiography	RBS	Random Blood Sugar
EEG	Electroencephalogram	RDT	Rapid Diagnostic Test
E/U/Cr	Electrolyte Urea & Creatinine	RRT	Renal Replacement Therapy
FBC	Full Blood Count	RT-PCR	Reverse Transcription Polymerase Chain Reaction
FFP	Fresh Frozen Plasma	SBP	Systolic Blood Pressure
GCS	Glasgow Coma Scale	SpO2	Peripheral Capillary Oxygen Saturation
GIT	Gastrointestinal Tract	μG	Microgram
ICP	Intracranial Pressure	VBG	Venous Blood Gas
ICU	Intensive Care Unit		

CHAPTER 1: BACKGROUND

1.1 Case Definition of Lassa Fever

Preamble: The case definitions in this document are for **CLINICAL DECISION MAKING** to guide management of Lassa fever cases in health facilities.

1.1.1 Alert case

Any person who has an unexplained *fever (i.e., malaria and other common causes of fever have been ruled out), with or without bleeding.

OR

Any person who died after an unexplained severe illness with fever and bleeding.

1.1.2 Suspected case

Patient with *fever for 3-21 days with a measured temperature of 38°C or more with one or more of the following: vomiting, diarrhea, sore throat, myalgia (muscle pain), generalized body weakness, abnormal bleeding, abdominal pain.

OR

In Neonates: Maternal Lassa fever +/- signs and symptoms.

Any of the following scenarios should raise the index of suspicion:

- a. Patient has not responded to standard anti-malaria treatment and treatment for other common infectious causes of fever within 48-72 hours
- b. History of recent contact with a probable or confirmed case of Lassa fever within 21 days of onset of fever
- c. Patient with history of fever and history of travel to high risk/burden area of Lassa fever
- d. Contact with body fluids or tissues of a dead patient with a febrile illness, symptoms and signs highly suggestive of Lassa fever leading to death.

Abnormal Bleeding: mucosal bleeding, punctures sites bleeding, uncontrolled intra operational and/or immediate post operational bleeding, irregular

**Fever:* Measuring temperature within 24 hours without the use of antipyretics for patients who present with apparently normal temperature.

1.1.3 Probable case (Clinical)

A suspected case who has **one or more** of the following complications

- a. Hearing loss
- b. Facial or neck swelling
- c. Seizures
- d. Restlessness
- e. Confusion
- f. Hypotension (SBP< 90mmHg in adults and <70mmHg in children)
- g. Oliguria (<0.5ml/kg/h for 6 hours)
- h. Abnormal bleeding

and **ANY** of the following supporting laboratory features:

1.1.4 Supporting Laboratory evidence:

- a. Proteinuria and/or microscopic hematuria
- b. Elevated urea $\ge 45 \text{ mg/dl}$ or creatinine $\ge 2 \text{ mg}$
- c. Elevated transaminases (liver enzymes, ALT & AST)
- d. Reduced platelets count ≤ 90,000 cells/ml³

* Absence of the above listed complications and laboratory evidence does not rule out LF

1.1.5 Confirmed case

A suspected or probable case with a positive laboratory test using real time polymerase chain reaction

Case Identification and Detection

History	 History of contact with rat urine and droppings or history of handling/consumption of rats.
	• All age groups are susceptible.
	 Children, pregnant women, adults >40 years and those with comorbidities have a greater risk of severe illness. Close contact (e.g. family members, caretakers, traditional healers,
	participants in traditional burial rites) of a Lassa fever patient within 3 weeks of date of onset of their illness.
	 Receiving health care from a provider who is also treating patients infected with Lassa fever.
	 Sexual partner of a known or suspected case (virus can be present in semen for up to 3 months after clinical recovery).
Clinical	Non-specific clinical features: early diagnosis difficult.
Assessment	- High index of suspicion advised.
	 Detailed clinical examination advised as patients may present with complications.
	• The incubation period is 2-21 days.
	 Severity of illness may depend on several factors including the body's
	natural immune response, mode of transmission, duration of exposure, viral infecting dose, phase of illness in the case, and possibly even the virus strain.
	 Swollen face and neck, sore throat and hearing loss are suggestive of Lassa fever.
	• Hemorrhage seen in only about 20% of Lassa fever patients.
	- Exclude other common causes of fever.
Laboratory diagnosis	 Early laboratory diagnosis of Lassa fever is important to have a good outcome with ribavirin administration. This is also important for the early institution of appropriate public health control measures.
	• All samples must be considered as highly infectious.
	 Confirmation of Lassa fever requires highly specialized aboratories with appropriate biosafety levels
	• Exclude other common causes of fever through appropriate investigations.

CHAPTER 2: CLINICAL SCREENING AND TRIAGING FOR LASSA FEVER

Preamble: The clinical management of patients should be based on the classification of cases to either suspected, probable and confirmed.

Clinical Screening Criteria

- Fever more than 48hrs or less than 3 weeks
- Any symptoms: sore throat, malaise, cough nausea, vomiting diarrhea, retrosternal pain, hearing loss or a woman with abnormal vaginal bleeding;

OR

- Any complications, such as encephalopathy (seizure, coma, irritability, confusion), shock, bleeding, Acute Kidney Injury, spontaneous abortion
- Travel to an endemic area less than 21 days AND contact with rodents
- History of contact with Lassa Fever patient less than 21 days before presentation

Indications for screening a newborn: Maternal Lassa fever+/- signs and symptoms

2.1. Triaging and Initial management modalities

2.1.1 Suspected case

- a. Put patient in a holding area and institute infection prevention measures
- b. Alert the relevant authorities: infectious disease team or responsible physician
- c. Notify relevant public health authorities e.g. State Epidemiologist, LGA Disease Surveillance and Notification Officer)
- d. Start rehydration. Commence Fluid therapy (see guidance on fluid replacement in Chapter 4)
- e. Monitor vital signs every 4 hours (Pulse Rate, Blood Pressure, Respiratory Rate, Temperature)
- f. Monitor Urinary output
- g. Carry out dipstick urinalysis for protein and blood
- h. Test for presence of malaria parasites preferably through RDT, and check full blood count including platelets count, serum electrolytes, urea and creatinine and liver function test (LFT)

i. Take blood to laboratory for diagnostic testing (RT-PCR) or Serology using RDT

2.1.2 Probable Case

In addition to steps listed under suspected case,

- a. Transfer patient to suspect bay of the treatment unit/centre
- b. Commence supportive care (See Chapter 3)
- c. Start treatment with Ribavirin. See Chapter 3 for approved treatment protocol
- d. Assess Patient for possible complications and manage accordingly (See Chapter 4)
- e. Review Ribavirin treatment with PCR result. If PCR is negative, continuation of treatment with Ribavirin is at the discretion of the Managing Physician

2.1.3 Confirmed Case

- a. Transfer patient to the treatment unit/centre
- b. Commence supportive care
- c. Continue treatment with Ribavirin if patient has been on it prior to confirmation
- d. Start treatment with Ribavirin, if patient is newly confirmed for Lassa fever
- e. Assess patient for possible complications and manage accordingly (See Chapter 4)

In Treatment Centers where it is practicable, all cases (suspected, probable and confirmed cases) further separated into 'wet' and 'dry' categories.

- 'Wet'- Bleeding, vomiting, diarrhoea, coughing, sneezing
- 'Dry'- Patients without wet symptoms

2.1.4 Severe Lassa fever

Lassa fever is said to be severe when any of the following complications are present.

- a. Acute kidney injury (AKI): Increased serum creatinine ≥ 0.3 mg/dl (or \geq 26.5 mmol/l within 48 hours or reduced urine output (<0.5 ml/kg/h for 6hours), or no urine for at least 6hours
- b. Severe central nervous system features (seizures, restlessness, confusion and coma)
- c. Severe Bleeding
- d. Respiratory distress
- e. Severe Anaemia requiring blood transfusion
- f. Sepsis/ hypovolemic Shock

Mild Lassa fever: A confirmed case without any of the signs and symptoms listed above.

CHAPTER 3: DIAGNOSIS AND CLINICAL MANAGEMENT OF LASSA FEVER

3.1.1 Diagnostic Investigations

- a. Lassa virus Reverse Transcriptase Polymerase Chain Reaction (RT-PCR)
- b. Serology including RDT

3.1.2 Confirmatory Investigations

a. Lassa virus Reverse Transcriptase Polymerase Chain Reaction (RT-PCR)

3.1.3 Supportive Investigations

Supportive investigations to be carried out will depend on the severity of the illness, i.e, if mild or severe.

- a. Mild Illness
 - i. Full blood count including platelets
 - ii. Liver Function Test
 - iii. Urinalysis
 - iv. Malaria Parasite test
 - v. Pregnancy test (For all women of child bearing age)
- b. Severe Illness

Investigations are same as in mild illness **PLUS** the following underlisted

- i. Electrolyte, Urea and Creatinine
- ii. Random Blood Glucose
- iii. Quantitative PCR (For monitoring)
- iv. EEG for unconscious patient
- v. ECG for patients with suspected pericarditis
- vi. ICP monitoring for unconscious patients
- vii. Central Venous Pressure (CVP) monitoring for those with shock or other forms of cardiovascular instability
- viii. Radiological test depending on the clinical presentation (e.g., Abdominal Ultrasound scan if abdominal tenderness is present, CT or MRI if encephalopathy, Chest X-ray if in respiratory distress)

- ix. Other tests based on clinical suspicion
- x. Blood Culture
- xi. Prothrombin time
- xii. Blood Gases
- xiii. Serum calcium.

*The frequency of the above investigations for monitoring will depend on the clinical state of patient at presentation and at the discretion of the managing physician

3.1.4 Monitoring Investigations

- a. Laboratory: E/ U Creatinine every 5 days or as required by the managing physician
- b. PCV/Haemoglobin every 5 days or as required by the managing physicians
- c. Viral load every 5 days to monitor response to therapy

*Monitoring investigations must be carried out daily or not later than every 48hours in severely ill patients

3.2 Drug Treatment of Lassa fever

The drug of choice for the treatment of Lassa fever is intravenous Ribavirin. Intravenous Ribavirin is administered over a period of 10 days as seen in the table below. Outcome is more favorable if treatment is commenced within six days of onset of symptoms.

3.2.1A Adults including non-pregnant adults (McCormick regimen)

Period	Dose	Frequency
Loading Dose	33mg/kg (maximum dose of 2.64 g)	Stat
Day 1-4 16mg/kg (maximum dose of 1.28 g)		6 hourly
Day 5-108mg/kg (maximum dose of 0.64g)8		8 hourly

*For patients who require dialysis, give IV ribavirin 4 hours before dialysis session

3.2.1B Adults including non-pregnant adults (Irrua regimen)

Period	Dose	Frequency
Loading Dose	100mg/kg (maximum of 7g)	In 2 divided doses: $2/3$ given stat & $1/3$ given 8 hours later
Day 2-7	25mg/kg	Daily (single dose)
Day 8-10	12.5 mg/kg	Daily (single dose)

Day two commences 24 hours after first component of the loading dose and subsequent daily dose follow same dosing pattern

3.3 Management of Lassa fever in Pregnant Women

The general principles for managing Lassa fever in Pregnant Women

- a. A high index of suspicion is essential for identifying suspected cases of Lassa fever in pregnant women particularly in the context of fever occurring with unexplained pregnancy loss(es)
- b. All confirmed cases of Lassa fever in pregnancy must be managed in a dedicated Lassa fever treatment centre with restricted access to all unauthorized staff.
- c. Strict adherence to IPC measures is advised.
- d. Nursing care to be provided by trained nurses experienced in management of Lassa fever in pregnancy.
- e. Nurse all pregnant women particularly in third trimester in left or right lateral position.
- f. Commence IV ribavirin (see dosing below) while awaiting PCR results for all probable cases
- g. Evaluate for co-morbidities such as malaria, typhoid fever, urinary tract infection etc., and treat appropriately
- h. Treat associated complications
- i. If during conservative management, foetal demise occurs, commence immediate evacuation of the uterus

3.3.1 ISTH Regimen for Pregnant women (Modified McCormick regimen)

Management of Lassa fever in Pregnant women is carried out using the modified McCormick Regimen, irrespective of the gestational age of the pregnancy

Period	Dose	Frequency
Loading Dose (Day 1)	100mg/kg	In 2 divided doses. $2/3^{rd}$ of loading dose given stat and after 8 hours, remaining $1/3^{rd}$ is given
Day 2-5	16mg/kg	6 hourly
Day 6-10	8mg/kg	8 hourly

For a pregnant woman who weighs 70kg, total calculated dose will be 7000mg. 2/3rd of the total calculated dose (4700mg) will be given stat and balance of 2300mg given 8 hours later). From day 2-5, total calculated daily dose will be 1120mg given 6 hourly and from Day 6-10, total calculated daily dose will be 560mg given 8hourly

Please Note:

- Each Dose must be given as slow intravenous push over 5-10 minutes
- Day 2 commences 24 hours after first component of the loading dose and subsequent daily dose follow same dosing pattern

3.3.1A Prognostic Features

Good

- a. Viable Foetus
- b. Breast Engorgement without expressible breastmilk discharge

Poor

- a. Extra-vaginal Bleeding (Bleeding from orifices apart from the vagina)
- b. Seizures in Pregnancy
- c. Non-viable pregnancy
- d. Acute Kidney Injury in Pregnancy

3.3.1B Considerations

- a. For women with viable foetus, conservative management with intravenous ribavirin (as stated above) improves maternal and fetal outcome
- b. For women with non-viable foetus, active and immediate measures must be taken to achieve uterine evacuation along with the use of IV ribavirin
- c. Lassa fever in pregnancy is not an indication for Caesarean Delivery. However, if there are core indications for a C/S, this must not be delayed.

3.3.1C Management Modalities

- a. Routine screening for Lassa fever is advised for all febrile pregnant women in Lassa fever endemic areas who have been unresponsive to anti-malarials and antibiotics treatment.
- b. A Pregnant woman with confirmed LF must be transferred to a designated LF treatment centre where she will be cared for by a multi-disciplinary team made up of obstetricians, virologists, intensivists, neonatologists and anaesthetists that can provide a bundle of care to standardize and optimize clinical management.
- c. Patients who present with viable foetus(es) either presenting early or with mild disease, often do well with conservative management with good maternal and foetal outcome
- d. A pregnant woman who is PCR Lassa virus positive and is on conservative management, close foetal monitoring for viability is recommended on admission and at least twice daily with hand-held foetal Doppler.
- e. Pregnant woman with LF and viable foetus(es), should be treated conservatively with the following bundle of care elements: ribavirin, antibiotics, and supportive care. Safe management of labour, including timing and method of delivery, should be based on foetal maturity, mother's severity of illness, and presence of other obstetric factors.
- f. Post-ribavirin treatment, Patients with negative Lassa fever PCR must be admitted into the antenatal ward for intensive foeto-maternal monitoring,

irrespective of the gestational age. This is necessary because of risk of unexplained intra-uterine fetal death which is common among these women. In addition, delivery must not exceed 37 completed weeks.

- g. Prematurity is common. However, use of tocolytics is not advised.
- h. Pregnant women with LF that once tested positive but later became negative after treatment must be delivered in a dedicated delivery room or theatre. This is due to the possibility of residual virus in the placenta bed even when the patient is negative which is a potential source of reinfection for mother and an occupational hazard for the managing team.
- i. Post-delivery, anatomical waste, e.g. placenta, is highly infectious and must be disposed of within the treatment facility.
- j. A Pregnant woman with LF that has a non-viable fetus (spontaneous abortion, intra-uterine fetal demise) must have an immediate evacuation of dead foetus. In addition, also provide other elements of the bundle of care, including: ribavirin, antibiotics, and supportive care. After evacuation, ensure there is no retained placenta.
- k. In twin or multiple gestation with all foetuses alive, manage conservatively. However, the death of any of the foetus will require immediate uterine evacuation

Uterine Evacuation can be achieved uneventfully with misoprostol vaginal insertion. See dosing below:

Indications for Evacuation	Regimen
Missed Abortion in 1 st Trimester	800µg vaginal tablet (max of 2 doses in 24 hours)
Incomplete Abortion	 400-600 µg oral or vaginal misoprostol given as a single dose. Carry out a manual vacuum aspiration (MVA) to evacuate retained products
Foetal demise	 13-17weeks: 200µg vaginal misoprostol 6 hourly for a max of 4 doses in 24 hours 18-26 weeks: 100µg 6hourly for a max of 4 doses in 24 hours >26 weeks-25-50µg max of 6 doses in 24 hours

MVA must be carried out in all cases of retained products as an adjunct to medical termination of pregnancy.

It is also important to ensure complete removal of retained products of conception to prevent deterioration of maternal clinical condition

It is important to note that:

a. Despite the above, most patients in the first or early second trimester will present with an abortive process. This should be completed with antibiotic cover. b. In the late second or third trimester, a patient may present with an IUFD or a viable foetus. In cases of IUFD, the patients are usually severely ill and often develop fulminant disease unless evacuation is carried out as soon as possible.

3.3.2 Lassa Fever in Puerperium

If mother develops unexplained fever in puerperium, a high index of suspicion for LF should be entertained. The following steps must be taken:

- a. Stop Breastfeeding
- b. Isolate Mother from baby
- c. Carry out RT-PCR for mother for confirmation.
- d. Test baby for Lassa fever using RT-PCR
- e. Carry out an Ultrasound scan to rule out retained products of conception
- f. If RT-PCR is positive, Commence bundle of care for infected pregnant woman
- g. Recommence breastfeeding after ribavirin treatment and post treatment RT-PCR (blood and breastmilk) is negative

3.3.3 Bundle of Care of Infected Pregnant Woman

- Apply **IPC** measures always when caring for an infected pregnant woman and during delivery.
- In a pregnant woman with positive Lassa virus PCR who are on conservative management, fetal monitoring with hand-held foetal Doppler on admission and at least twice daily.
- Post treatment, Pregnant women with negative PCR must have intensive fetal monitoring (Biometric and Biophysical fetal surveillance)
 - Appropriate fetal size for gestational age monitoring using Ultrasound scan
 - Monitoring of fetal well-being using hand-held Doppler, Non-stress test with CTG, Biophysical profile and Doppler velocimetry
- Evaluate for co-infection, such as malaria, typhoid fever and urinary tract infection. Treat empirically with appropriate antimicrobials.
- Treat with IV ribavirin using ISTH regimen for pregnant women (Modified McCormick) regimen for 10 days. If mother continues to be ill, then treatment can be extended.
- Provide supportive care as necessary. Pregnant woman in shock must be placed in lateral decubitus position, avoiding supine position. SpO2 must be maintained >95% saturation.
- Safe management of labour and delivery by expert, multi-disciplinary team.
- Early cord clamping and active management of 3rd stage of labour is advised
- After delivery, test the umbilical cord blood and maternal breast milk immediately for Lassa Virus.
- Monitor newborn carefully for development of signs or symptoms of LF/sepsis, re-test if indicated.
- Allow Breastfeeding only when maternal breastmilk, serum and cord blood Lassa virus PCR are negative.

3.4 Management of Lassa fever in Children

The general principles for managing Lassa fever in Children

- a. A high index of suspicion is essential for identifying suspected cases of Lassa fever in Children
- b. Diagnosis of Lassa fever in children is through serum RT-PCR. Other samples that can be tested in Children include CSF especially when there is a strong suspicion of Lassa fever and serum RT-PCR is negative, or there are signs of meningeal irritation (nuchal rigidity, positive Kernig's and Brudzinski signs) or features of encephalopathy (seizures, coma GCS \leq 12)
- c. A suspects' bay/area for children must be set up at points of entry/designated treatment centres to manage suspected cases pending PCR result
- d. A specialized ward within designated treatment centre for managing confirmed paediatric patients
- e. Strict adherence to IPC measures is advised
- f. Nursing care to be provided by trained paediatric/neonatal nurses
- g. Prompt referral to a pediatrician is advised
- h. Commence IV ribavirin (see dosing below) while waiting PCR results
- i. Evaluate for co-morbidities such as malaria, bacteraemia, urinary tract infection, etc, and treat appropriately
- j. Treat associated complications

3.4.1 Neonatal Care

After delivery:

- a. Test newborn (cord blood) and maternal breastmilk immediately for Lassa virus.
- b. Nurse the baby in a designated neonatal section of a treatment centre while awaiting PCR result.
- c. Commence IV ribavirin (see dosing below) in a neonate if Mother is PCR positive at time of delivery. However, if Mother is negative at time of delivery and baby is not symptomatic, Ribavirin can be withheld until investigation results (RT-PCR for Lassa virus) are available

3.4.1A Contra-indications to Breastfeeding

- a. Maternal Breastmilk is Lassa virus PCR positive
- b. Maternal Serum or cord blood is PCR positive
- c. Other contraindications to breastfeeding
- d. If breastmilk testing cannot be carried out

Use of infant formula should be considered as an alternative to breastfeeding if any of the contraindications listed above exist.

3.4.1B Treatment Regimen

McCormick Regimen

Period	Dose	Frequency
Loading Dose	33mg/kg (maximum dose of 2.64g)	After stat dose, the next dose is given 6 hours later irrespective of time of presentation
Day 1-4	16mg/kg (maximum dose of 1.28g)	6 hourly(for 4 days)
Day 5-10	8mg/kg (maximum dose of 0.64g)	8 hourly (for 6 days)

For Neonates and children with Lassa virus disease who require care in designated treatment centres, a caregiver maybe permitted to stay with the patient during treatment. In the event this happens, the managing team should educate and counsel the caregiver on basic IPC measures and other measures to be taken to prevent being infected and commence them on PEP for high-risk contacts (See dosing in Chapter 6)

3.5 Management of Suspected cases awaiting lab results

For a suspected case who has established contact with a confirmed case, commence Ribavirin immediately while awaiting lab result OR if clinical features strongly support the diagnosis of Lassa fever

3.6 Precautions to take when treating cases of Lassa fever

- a. NSAIDS are contraindicated due to risk of bleeding
- b. Avoid intramuscular injections to prevent hematoma formation
- c. Use cotton wool to clean the mouth of patients instead of hard toothbrush
- d. Any skin ulcers must be cleaned and dressed gently
- e. Avoid nasogastric tube, urinary catheter insertion unless strongly indicated
- f. DO NOT remove old blood clots from previous bleeding sites.
- g. NEVER RECAP needles.
- h. For pregnant patients, gentle vaginal examination must be done only infrequently.
- i. Do not enter a patient's room or get in contact with a patient with suspected or confirmed Lassa fever without putting on full PPE.

3.7 Poor Prognostic Indicators

- a. Pregnancy
- b. Abnormal Bleeding
- c. Encephalopathy

- d. Shock
- e. Late commencement of Ribavirin (after the 6th day of onset of illness)
- f. Age less than 5 years or greater than 50 years
- g. Acute kidney injury (AKI) characterized by increase serum creatinine ≥ 0.3 mg/dl (or ≥ 26.5 mmol /l within 48 hours or reduced urine output (<0.5 ml/kg/h for 6hours), or no urine for at least 6hours
- h. Elevated Serum AST \geq 150IU/ml
- i. Seizures
- j. Alteration of consciousness

3.8 Supportive Care

Support needed is dependent on the complications identified and may include any of the following:

- a. Fluid Support
- b. Cardiovascular Support
- c. Haematologic Support
- d. Renal Support
- e. Respiratory Support
- f. GIT Support
- g. CNS Support
- h. Nutritional Support
- i. Neonatal Support
- j. Psychosocial Support

If signs of severe disease are seen at a lower facility of care, patient must be referred to a tertiary site or treatment centre (*See list of treatment centres in appendix*)

3.8.1 Basic requirements for all types of support needed

A. Fluid Support

- Intravenous fluids: Crystalloids preferred
- For Children, the following fluid types can be used for management
 - 4.3% dextrose in 1/5th saline
 - 8% dextrose in 1/5th Saline
 - Ringers' Lactate
 - Normal Saline
- B. Cardiovascular Support (neonate, paediatric and adults sizes)
 - Vasopressors: dopamine, or adrenalin/Adrenaline, dobutamine,
 - Hydrocortisone
 - Central venous catheter, cannula, wide bore canula, iv infusion sets and pumps (

- Pulse oximeter, automated blood pressure machine, cardiac monitor (ECG)
- Portable Echo/Cardiac ultrasound
- Automated Blood Pressure Machines
- Glucometer
- Blood gas machine
- Fluids- Crystalloid

C. Haematologic Support

- Drugs-Tranexamic acid (Tablets and Intravenous fluid)
- Microscopes
- Slides
- Autoheamatocrit analyzer
- Blood Bags
 - Paediatric blood bag (100ml, 250ml) are recommended for use
- Cannula
- Capillary Tubes
- Cold Centrifuge
- Coagulometer
- Blood Transfusion
 - This maybe indicated in any patient who presents with anemia or becomes anaemic at the time of treatment.
 - Erythropoietin and other haematinics for patients who refuse blood transfusion should be considered

D. Renal Support

- Point of care chemistry testing facilities
 - Complete Electrolyte, Urea and Creatinine
- Renal replacement therapy-haemodialysis, haemofiltration. Consumables for heamodialysis in children: paediatric blood lines, paediatric dialyser (F3-F5), double lumen paediatric femoral catheter. Consumables for peritoneal dialysis: diasylate fluids with different dextrose concentrations, Peritoneal Dialysis catheters, Peritoneal Dialysis cycler e.t.c.
- Drugs: Dopamine
- Relevant IPC
- Trained Staff-Nephrologist, Renal Nurses, etc

E. Respiratory Support: (neonates, adults, children)

- Oxygen cylinders
- Ventilators
- CPAP for children/Bubble CPAP
- Suctioning Machine
- Oxygen delivery devices-neonatal and paediatric nasal prongs, non-rebreathing face masks
- Facemasks
- Other consumables-intubation materials (ambu-bag), laryngoscope with neonatal and paediatric blades and endotracheal tubes
- Relevant IPC
- Trained Staff- Anesthesiologist

F. CNS

- Electroencephalogram: to monitor and support diagnosis especially in seizures
- Lumbar puncture sets
- ICP consumables
- Anti-seizure medications
- Cardiac Monitors,
- Ventilators
- Neurologists
- Functioning ICU with Anesthetics

G. Nutritional support

- Feeding tube
- Artificial feeds
- Parenteral nutrition

H. Psychosocial support

Clinical Therapist

I. GI support

- Proton pump inhibitors
- Anti-emetics

J. Neonatal support

- Cots
- Incubators
- Infusions-Infusion pumps, syringe drivers, soluset
- EBT sets
- Phototherapy units
- Angle poise Lamps
- Transcutaneous Bilirubinometer
- Portable X-ray Machine
- Portable Ultrasound Scan
- Cold light
- Suction Machine
- Radiant Warmer
- Multi-parameter monitor for assessing vital signs, SPO_2 and ECG monitoring
- Psychological support for mothers
 - Counselling of mothers on benefits of admission from diagnosis to delivery. Explain to the patient the risk of IUFD which can occur at any gestational age
 - If Mother is negative and baby is positive, isolating the baby from the mother and preventing breastfeeding is important to prevent the possibility of re-infection of the mother and transmission in the community
 - If Mother is positive and baby is negative, isolate mother and counsel on the benefits of isolation from her baby. Breastfeeding is contraindicated.
- Drugs: Broad spectrum antibiotics for severely ill patients
- Foetal monitoring-Sonicaid, CTG, Ultrasound scan

• Co-morbidities which may exist and cause anaemia in the new born should be considered and appropriate management instituted.

K. Infectious Disease Support:

- Drugs-Broad spectrum antibiotics for severely ill patients
- Antibiotics-to be used for the shortest time possible
- Automated blood and other culture machines

CHAPTER 4: MANAGEMENT OF COMPLICATIONS OF LASSA FEVER

It is recommended that in cases of severe or complicated LF, management must be carried out in a dedicated ICU. If this is not available, a facility with automated equipment for monitoring vital signs and resuscitative measures must be provided.

Complications of Lassa fever

- 1. Acute kidney injury (AKI)
- 2. Severe dehydration (from vomiting or diarrhoea)
- 3. Sepsis/septic shock
- 4. Encephalopathy
- 5. Acute Respiratory Failure
- 6. Severe Bleeding/Anaemia

4.1 Management of Acute Kidney Injury (AKI)

In management of AKI, a step-wise approach to management is recommended

- Recognize AKI syndrome
- Secure IV Access
- Correct shock with crystalloid fluids (+/- vasopressors)
- Avoid nephrotoxic agents
- Correct electrolyte disorders
- Consider dialysis if indication(s) established
- a. **Recognize AKI**: increased serum creatinine $\geq 0.3 \text{ mg/dl}$ (or $\geq 26.5 \text{ mmol/l}$ within 48 hours) or reduced urine output (< 0.5 ml/kg/h for 6 hours) (KIDGO Criteria for AKI). Monitor urine output.
- b. Evaluate for reversible causes of AKI and treat accordingly
- c. **Ensure volume status and perfusion pressure**: maintain renal perfusion with adequate crystalloid fluid resuscitation and vasopressors (as needed). Avoid Ringer's lactate in patients with hyperkalaemia (K >5 mmol/L).

- d. **Prevent further injury:** avoid nephrotoxic drugs, such as NSAIDS, aminoglycosides and ACE inhibitors.
- e. **Appropriate drug dosing:** meticulously dose medications on basis of renal dysfunction. The dose of ribavirin should be adjusted by half for patients with renal dysfunction (CrCl <30mls/min in children and <50mls/min in adults)
- f. **Manage hyperkalaemia**: monitor ECG, recheck potassium level after 4 hours. ECG changes evolve as the potassium levels rise: between 5.5.-6.5 mEq/L, peaked T waves are seen; at levels of > 6.5 mEq/L, widened QRS and decrease of P wave is seen and at > 8.0 mEq/L, there is loss of P wave, progressive QRS widening and eventual ventricular fibrillation. Severe hyperkalemia can lead to death.

Adult: - K 5.5 -6.4	Adult	
mmol/L	• Repeat test and monitor. Give IV 10% calcium gluconate 10mls	
Child: - K 5.5-6.0	over 10mins stat.	
mmol/L		
	Child	
	Stop all potassium-containing fluids and food	
	Repeat tests and monitor	
	Stop all nephrotoxic drugs	
Adult: - K > 6.5	Adult:	
mmol/L or Peaked	1. Calcium gluconate 10% 10 mL IV slow push (minutes)	
T waves	2. 10 U insulin bolus + 50 ml 50% glucose (minutes-hours)	
Child:->6 mmol/L	3. Bicarbonate infusion (i.e. 3 ampules of 50 mEq sodium	
	bicarbonate added to 1 litre of D5W, infused as maintenance	
	solution).	
	4. Sodium polystyrene sulfonate 15 grams once and can repeat	
	every 8 hours. Caution: does not have immediate effect and do	
	not use in patients with constipation.	
	Child:	
	Stop all potassium-containing fluids and food	
	Repeat tests and monitor	
	• Stop all nephrotoxic drugs	
	1. Calcium gluconate 10% 1 mL/kg IV slow push	
	AND one of the following:	
	1. Nebulize with salbutamol 5-10mg stat.	
	2. Insulin 0.1units/kg + 1ml/kg 50% glucose IV push	
	3. Bicarbonate 1 mEq /kg IV slow push over 10-15 minutes	
	4. Iron exchange resin at 1g/kg orally or per rectum	

Table 4.1: Management Protocol for Hyperkalemia

NATIONAL GUIDELINES FOR LASSA FEVER CASE MANAGEMENT

Treat acid-base abnormancies: check arterna blood gas, when available		
For	severe	Adult: Start IV bicarbonate infusion (e.g. 3
acidosis	(pH <	ampoules of 50 mEq sodium bicarbonate added to
7.2)		1 litre D5W, infused as maintenance solution)
		Child: Bicarbonate 1 mEq /kg IV slow push over
		10-15 minutes

g. Treat acid-base abnormalities: check arterial blood gas, when available

- h. **Manage volume overload:** if there are signs of volume overload and patient is not hypotensive, then administer diuretic (i.e. furosemide) as needed to assist with fluid removal.
- i. **Renal replacement therapy (RRT**): There are two main modalities of RRT in the ICU, continuous RRT or intermittent haemodialysis.

ine ree, continuous ru	5				
Emergent	• Severe hyperkalaemia unresponsive to				
indications for	medical therapy				
RRT are life-	• Severe metabolic acidosis unresponsive to				
threatening	medical therapy				
changes in fluid,	Severe fluid overload refractory to medical				
electrolyte or	management				
acid-base status	• Severe uraemia-related complications (i.e.				
	encephalopathy, or very rarely pericarditis)				

4.2 Management of Severe dehydration (from vomiting or diarrhoea)

Patients with Lassa fever can become dehydrated from loss of body fluids through vomiting and diarrhoea. It is important to identify ongoing losses and replace accordingly. If not managed promptly, it can progress to hypovolemic shock which can occur in patients with the disease. Hypovolemic Shock can be:

- Compensated: if compensatory mechanisms can maintain a systolic blood pressure within a normal range (i.e., at least the 5th percentile systolic blood pressure for age) in the presence of signs of poor perfusion.
- Hypotensive: when compensatory mechanisms fail and systolic blood pressure declines.

4.2.1 Features of Hypovolemic Shock

- Tachycardia
- Tachypnea without increased effort
- Adequate systolic blood pressure (compensated shock), narrow pulse pressure, or systolic hypotension with a narrow pulse pressure.
- Hypotension terminally (hypotensive shock)
- Weak or absent peripheral pulses

- Normal or weak central pulses
- Delayed capillary refill (>3s in children and >2s in adults)
- Cool to cold, pale, mottled, diaphoretic skin
- Dusky/pale distal extremities
- Changes in level of consciousness
- Oliguria

4.2.2 Management of Hypovolemic Shock

- 1. Stabilization of airway, breathing, and circulation (the ABCs)
- 2. Airway intervention may be necessary, including intubation and mechanical ventilation
- 3. Correct metabolic derangement
- Rapid administration of 20ml/kg of normal saline or Ringer's lactate over 5-20 minutes (use Ringer's lactate with caution if there is consideration of AKI). Up to 3-4 boluses within the first hour (60-80ml/kg) if there is no contraindication (pulmonary edema, heart failure).
- 5. If there is good response to fluid therapy (See Page 28 'b' under Fluid responsiveness), complete correction of fluid deficit, ensure fluid maintenance and correct ongoing loses.
- 6. Commence inotropes for fluid refractory shock.
 - Dopamine is the 1st-line agent or dobutamine must be quickly optimized before the initiation of other agents, (especially in normotensive patient). Dose 3-20 µg/kg/min. Dose > 10 µg/kg/min will cause strong peripheral vasoconstriction with reduction of renal blood flow.
 - For fluid refractory, dopamine/dobutamine resistant shock:
 Cold shock 0.05–3.0 μg/kg/min
 - Warm shock 0.05–1.5 µg/kg/min

4.3 Management of Sepsis/Septic Shock

For patients with severe LF and septic shock syndromes, a step-wise approach to management is recommended.

- Recognize septic shock syndrome
- Start oxygen therapy
- Place IV access and administer targeted resuscitation with crystalloid fluids (+/- vasopressors).

4.3.1: Phases of Septic Shock

Children

Warm Shock: Features are subtle and maybe difficult to recognize because peripheral perfusion may appear to be good. This is characterized by

- Bounding Peripheral Pulses
- Brisk capillary refill
- Warm flushed skin
- Hypotension(SBP <70mmHg) with wide pulse pressure

Cold Shock: This characterized by

- Pale mottled skin with vasoconstriction
- Weak and fast pulse
- Hypotension(SBP <70 mmHg)with a narrow pulse pressure
- Delayed capillary refill(>3s)

Adult:

- SBP <90 mmHg

OR

- Other signs of hypo-perfusion such as delayed capillary refill, cool extremities, respiratory rate > 22/min, reduced urine output, and/or altered mental status

Table 4.2: How to Recognize Cold Phase of Septic Shock

Age	SBP (mmHg)	Capillary refill <3 sec	Urinary Output <0.5-ml/kg/h	Cold Extremities	Fast and thready pulse	Respiratory rate
< 1month	< 50	+	+	+	+	NI
1-12 months	< 70	+	+	+	+	NI
1-12 years.	70 + (2 x age in year)	+	+	+	+	NI
>12 years.	< 90	+	+	+	+	> 22/min

NI-Not Indicated

a. Optimize Oxygen Content of Blood

- **Give oxygen/manage airway and breathing:** Check SpO₂ and if <94% in adults and <90% in neonates, or if pulse oximeter not available and signs of respiratory distress or shock, then give **oxygen therapy** immediately. Titrate based on oxygen requirements of the patient. Use lowest flow rate necessary to reach target SpO₂ >94% in adults and 90-95% in neonates.
- Transfusion may be needed if haemoglobin is low for age and sex
- Facemask with reservoir bag at 15 L/min can be used for adults and children in emergent situation and titrate to lowest flow rate necessary to reach target $SpO_2 > 94\%$ in children and 90-95% in neonates
- Nasal cannula is recommended for children

Table 4.3: Oxygen Flowrate by Age

Nigeria Centre for Disease Control

Age	< 1	1-12	< 6	6-12	Adolescent/Adult
	month	months	years	years	
*Oxygen	0.5-1.0	1-2	1-4	1-6	5 L/min
Flowrate	L/min	L/min	l/min	L/min	

*Oxygen flow rate must be titrated based on oxygen requirements

b. Give crystalloid fluid, using fluid challenge method.

- Crystalloid fluid is recommended as fluid of choice for initial resuscitation and subsequent intravascular volume replacement.
- Ringers Lactate must be considered in the absence of normal saline provided patients do not have features of renal impairment.
- For patients with diarrhoea, vomiting, hypokalaemia with adequate urine output, Ringers Lactate must be used as the preferred fluid. (See table below for constituent of each usable fluid).
- Monitor for volume responsiveness and volume overload after each fluid bolus.
- **Fluid responsiveness** is defined as when fluid therapy improves markers of perfusion as shown below:
 - Normal Heart rate and BP for age
 - Normal pulse
 - Capillary refill <2 secs
 - Warm extremities
 - Normal Mental Status
 - Urine Output >1ml/kg/hour
 - Decrease Serum Lactate
 - Reduce base deficit
 - Central venous oxygen saturation >70%
 - Decrease respiratory rate towards normal

Table 4.4: Constituents of Recommended Intravenous Fluid

Fluid	Sodium	Chlorine	Potassium	Buffer	Calcium
Ringers' Lactate	130 mEq	109 mEq	4 mEq	28 mEq	3 mEq
Normal Saline	154 mEq	154 mEq	0	0	0

- c. For adult patients with shock and without severe dehydration, severe anaemia or severe malnutrition
 - i. Initial bolus is 1 Litre of crystalloid over 15-30 minutes.
 - ii. After each fluid bolus, assess hemodynamic status and markers of good perfusion.
 - SBP >90-100 mmHg
 - Absence of Skin Mottling
 - Improved capillary refill

- Strong pulse
- Warm extremities
- Urine output >0.5 ml/kg/h
- Normal mental status
- iii. If still in shock and no signs of volume overload, repeat fluid challenge (250-500mL) every 30 minutes, if remains fluid responsive by dynamic indices.

Caution: stop fluid challenges under the following conditions:

- When targets of perfusion are met. Then transition to maintenance fluid or oral intake only.
- When no longer fluid responsive (additional fluids are no longer beneficial).
- Any time signs of fluid overload develop i.e. crackles on auscultation, abdominal distension, cardiac failure, pericardial effusion
- iv. For fluid refractory shock (after first -2nd bolus). Initiate vasopressor infusion and titrate to target BP and markers of perfusion.
- Adrenaline/noradrenaline: initiate 0.1 mcg/kg/min, titrate up 0.1 every 10-15 min, maximum is 1.0 mcg/kg/min;
- If noradrenaline/adrenaline is not available, dopamine can be used. Dopamine at a dose of 1-5mcg/kg/min IV and titrated as required can be used in adequately hydrated patients.
- Once stable/improving, reduce inotrope and vasopressor dose, if perfusion BP targets are maintained

Fig 4.1: Algorithm for Management of Septic Shock Syndrome in Children



Additional Treatment:

- 1. Transfuse with fresh O Blood if Haemoglobin concentration is less than 10g/dl.
- 2. Consider IV Hydrocortisone in fluid refractory and vasoactive refractory shock.
- 3. Consider respiratory support (Supplementary oxygen and Positive end expiratory pressure (PEEP).
- 4. ICU Care may be required.
- 5. NOTE: Consider additional fluid boluses if required and no contraindication.

4.4 Management of Encephalopathy

For patients with severe LF and encephalopathy, a step-wise approach to management is recommended

- a. Recognize neurologic emergencies
- b. Secure IV access
- c. Correct glucose and electrolyte abnormalities
- d. Treat seizures if present
- e. Correct shock with crystalloid fluids +/- vasopressors
- f. Avoid unnecessary sedatives unless there is absolute indication(s)
- a. **Recognize patients with neurologic urgencies:** acute confusional state (delirium), lethargy, coma and/or seizures. Use GCS (modified GCS or BCS (for children under 4 years of age) or AVPU to monitor. EEG can be used for monitoring and as a supportive investigation. EEG is contraindicated in a restless patient
- b. **Manage airway and breathing.** Patients with depressed mental status should be placed in the recovery position to avoid aspiration. Consider intubation to protect airway when patient is deeply in coma (GCS \leq 8 or BCS \leq 2). Avoid sedatives.
- c. **Check electrolytes and serum glucose levels:** these are reversible causes of abnormal mental status and need immediate treatment. If unable to check glucose, give emergency glucose:
 - **Child**: If RBS level is <2.8 mmol/l in well-nourished or <3 mmol/l in severely malnourished child or unable to measure, then give 10% glucose: 5mL/kg as bolus and maintain to achieve euglycemia
 - **Adult:** If level is < 3 mmol/l) or if unable to measure, give 50% glucose 25-50 mL as bolus, or 10% glucose 125 to 250 mL as bolus.
- d. **If seizures, treat immediately.** Rapidly administer benzodiazepines (IV diazepam 5-10mg; consider risk of respiratory depression following use), and then load with phenytoin at 15 20 mg/kg in 0.9% N/S over 30 minutes. Aiming to deliver 50mg/min. Consider anesthetics with ICU care if symptoms persist.
- e. Correct shock state with targeted resuscitation. (refer to flowchart on algorithm for managing shock)
- f. **Antimicrobial treatment:** Empiric anti-malarial and antibiotics as coinfection may occur (i.e. ceftriaxone for bacterial meningitis and IV artesunate for severe malaria)
- g. **Further diagnostics on an individual case basis:** consider the risk/benefit of the procedure and if clinical management will be guided with the result.

- Lumbar puncture to evaluate the cerebral spinal fluid. CSF PCR where blood is negative and symptoms highly indicative of Lassa fever encephalitis. LP is Contraindicated in the following instances
 - Presence of infection over the needle entry site
 - Features of markedly increased ICP including those of coning/cerebral herniation or incipient coning
 - Suspicion of Brain Abscess
 - Coagulopathy
- Patients with HIV (unless Cranial CT is normal)
- CT or MRI of brain, if available.
- EEG

4.5 Management of Acute Respiratory Failure

For LF patients with acute respiratory failure, recommendation is to manage using a step-wise approach which includes:

- a. Airway management
- b. High flow oxygen therapy
- c. Intubation followed by lung protective ventilation
- Recognize patient with severe LF that has acute respiratory failure.

-Failure to maintain and protect patent airway (i.e., coma) -Severe hypoxemia SpO2 < 85-90% and/or other clinical indicators of severe respiratory distress despite maximal oxygen therapy (face mask with reservoir bag at 10-15 L/min or CPAP or bubble CPAP in child). -Severe respiratory acidosis

- Perform safe intubation using a rapid sequence induction method.
- Deliver lung protective ventilation strategy (Target tidal volumes 6-8 ml/kg (ideal body weight) and plateau pressure below 30 cm H₂O.

Recognize Patients with acute respiratory distress syndrome (ARDS)

a) Pa SpO₂/ FiO₂ < 315 or PaO2/FiO2 <300

b) Chest film with bilateral infiltrates. If chest film not available, then use lung ultrasound

c) Respiratory failure not exclusively explained by cardiac failure or fluid overload. -If ARDS, then use low target tidal volumes of 6 ml/kg, target plateau pressure < 30 cm H20 and adequate PEEP for degree of oxygen impairment.

- Use national protocol strategies to manage sedation and pain in ventilated patient
- Use national protocol strategy to evaluate ventilated patient for spontaneous breathing trials and physical therapy.
- Ensure all preventative measures are in place while patient is on ventilator.

4.6 Management of Severe bleeding/Anaemia

For patients with severe LF and severe bleeding, a step-wise management approach is recommended:

- Recognize massive bleeding (evidenced by cardiorespiratory decompression i.e., tachycardia, bounding pulse, hypotension, breathlessness and features of heart failure to guide further intervention)
- Secure IV access using 2 large bore cannula
- Collect blood samples for grouping and cross-matching
- Give Oxygen if SpO₂ is <94%
- Transfuse pack cells at a dose of 15-20mls/kg in pediatric patients, for adult patients transfuse as required under frusemide cover. Transfusion must be completed within four hours of set up
- Ensure antihistamine, hydrocortisone and normal saline are readily available before commencement of transfusion
- Monitor patient for signs and symptoms of transfusion reaction
- Give crystalloid fluid and start transfusion with packed red blood cells (PRBC), platelets and plasma according to national transfusion policies
- Consider transfusion of other blood products
 - Platelet over 30-60min per unit
 - FFP-at a dose of 15ml/kg over 30-60 min
 - Cryoprecipitate a dose of 15ml/kg over 30-60 min
 - \circ For patients who decline blood transfusion, see below for other options
- a. **Recognize and manage massive haemorrhage:** patients with large amount of bleeding that is causing hemodynamic instability are having life-threatening haemorrhage. These patients need rapid blood transfusion of PRBC, with plasma and platelets to replace all factors and cell lines that are lost with massive haemorrhage.
 - Commence blood transfusion in the presence of massive bleeding
 - Transfuse with plasma and platelets using a 1:1:1 ratio, if possible (i.e. 4 units Red Blood Cell, 4 units plasma, 1 pool platelets [4 units]).
 - If cold stored whole blood is used, supplementation of platelets and plasma is still needed because of the short lifespan of platelets and coagulation factor, fresh whole blood should be considered for bleeding patients in centres where facilities for blood products are not available.
- b. **Stop haemorrhage:** control bleeding with direct pressure and bandages when possible. All invasive procedures need to be carefully considered. Provide appropriate PPE for staff performing procedure

c. Transfusion in non-massive haemorrhage syndromes

- Transfuse with packed red blood cells as needed to keep Haemoglobin > 7.0g/dl or haematocrit >20%.
- Transfuse with fresh plasma to maintain target INR < 1.5 (while bleeding)

- Transfuse with platelets needed to maintain target: Platelets ≥ 50,000/mm³ (while bleeding)
- d. **Tranexamic acid**: some patients can also receive 1 b gram IV tranexamic acid administered over 10 minutes followed by 1 gram over 8 hours, based on extrapolation of evidence from other patient populations. For women with post-partum hemorrhage, recent trial found administration of 1 gram, repeated if bleeding continued at 30 minutes or if re-bleeds within 24 hours. The dose should be reduced in AKI.
- e. **Multivitamin/vitamin K/ESA administration:** Many malnourished or ill patients with diminished oral intake, and those treated with antibiotics, have mild vitamin-K deficiency, which may predispose to bleeding. Give vitamin K (e.g. 1-5 mg orally daily for 3 days) at admission or vitamin K 10 mg intravenously for those unable to take pills. Efficacy in LF patients is unknown. Vitamin K may be considered for patients with deranged clotting profile e.g. PT/INR. Erythropoietin stimulating agent (ESA) (Erythropoietin 50-100 units/kg IV or S.C three time weekly), intravenous iron supplement must be considered for patients who decline blood transfusion
- f. **Keep patient warm:** Patients with massive bleeding and hypothermia should be kept warm, with a blood warmer used if available. If not available, blood products can be warmed with a blood warmer or water bath before transfusion.
- g. **Monitor for hypocalcaemia**: Hypocalcaemia is rare but can occur in severely ill patients receiving large quantities of blood products. Check calcium level especially in the setting of signs of low calcium (i.e. arrhythmias, tetany).
CHAPTER 5: INFECTION PREVENTION AND CONTROL IN LASSA FEVER MANAGEMENT

5.1: Introduction

Infection Prevention and Control(IPC) is an essential aspect of clinical management of Lassa fever. Healthcare workers involved in managing Lassa fever cases are at risk of being infected and as part of management must implement IPC measures always. The focus for this guideline will be on use of PPE and Hand hygiene in the care of Lassa fever patients.

5.2: Use of PPE in the care of Lassa fever Patients

Healthcare workers who work in the treatment centre must be proficient in donning and doffing PPE and this requires specific training for this. The donning and doffing of PPE must be done under constant supervision. All Healthcare workers (including wardaides and cleaners) must wear **full set of PPEs** when providing **direct care to patients or managing medical or patient wastes, handling deceased bodies or cleaning.** A **full set of PPEs** must be put on in a **dedicated donning zone**, before entering the isolation area and must be removed in a dedicated doffing area after use.

5.2.1: Who must wear protective clothing

Different types of PPE apply to the various activities and locations within the treatment centre

- All doctors, nurses, and health workers who provide direct patient care to suspected or confirmed LF patients.
- All support staff who clean the isolation room, handle contaminated supplies and equipment, launder re-usable supplies, and collect and dispose of infectious waste from Lassa fever patients.
- All laboratory staff who handle patient specimens and body fluids from suspected Lassa fever cases.

- Laboratory support staff who clean and disinfect laboratory equipment used to test Lassa fever specimens.
- Safe burial teams who remove bodies of deceased Lassa fever patients and prepare them for burial.
- Family members who care for Lassa fever patients.

The PPE is to be worn systematically prior to entry into isolation area, regardless of the tasks to be performed (care, cleaning, distribution of meals, etc.) and to be removed before leaving the isolation area

PPE	Characteristics and Description on how to use		
Eye	Face shield or goggles can be used.		
protection	 Adequately protects the healthcare worker's conjunctival mucous membranes from splashes. Reading glasses are not acceptable as PPE for eye protection Goggles must fit comfortably and securely, and person must have his/her own goggles/face shield with their name on them. It must be sterilized with 0.5% for subsequent use. Condensation of the goggles may occur and can impair the user's vision. This can be minimized by anti-fog spray. Goggles or face shields need to be disinfected by the person wearing them, washed with water and then hung outside the changing room to dry. 		
Mouth and	• N95 respirator is acceptable. If unavailable, surgical mask can be used.		
nose	• Healthcare workers must cover the mucous membranes of the nose and		
protection	mouth to avoid body fluid splashes and droplet spread.		
	 Medical-surgical mask must be Fluid-resistant with a structured design that does not collapse against the mouth (i.e. duck bill or cup shape). Ideally, a face shield must be worn over the mask/respirator. 		
Gloves	 Correctly sized latex or non-sterile examination (nitrile) gloves must be used to protect hands against both direct and indirect contact. In all instances in the care of Lassa fever patients, double gloving (i.e. two layers of gloves) should be used to decrease virus transmission. 		

Table 5.1: Types of PPEs and how to use them

	• Inner glove worn under the gown/coverall cuff, outer glove worn over			
	the cuff, reaching well above the wrist.			
	• Outer glove must be "nitrile" to resist disinfectant chemicals.			
	• DO NOT touch eyes, nose or mouth areas with gloved hands.			
	 A new pair of (outer layer) gloves must be used for each patient. 			
	 As a rule, if the risk is to the patient then 'Sterile' gloves are required. If the 			
	risk is to the user, then 'Non-sterile' gloves will probably be sufficient.			
	• When handling chemical disinfectants, it may become necessary to wear			
	industrial or domestic gloves.			
Protective	Scrubs are preferred over dress uniforms to avoid exposed legs.			
body wear	 Disposable gown or coverall should be made of fabric that is tested for 			
	resistance to penetration by blood or body fluids or blood borne pathogens.			
	The disposable gown should be placed over scrubs.			
Apron	Aprons should be worn over the gown or coverall.			
-	Rationale is that when risk of splashes from patient's vomiting,			
	diarrhoea or bleeding is high, an apron is easier to replace than a			
	soiled gown or coverall.			
	 Fluid proof aprons provide extra protection of the front part of the body. 			
	• Ideally disposable aprons must be used, but if non-disposable apron is used,			
	it should be disinfected with 0.5% hypochloride by the user.			
	(This must include cleaning to remove gross contamination, disinfection and			
	then hanging to dry in the sun).			
Footwear	• Water proof boots, Rubber or gum boots are preferred over closed shoes			
	because they are easier to clean and disinfect, provide optimal protection			
	when floors are wet, and protect from sharp injuries.			
	• If not available, then wear closed shoes with impermeable shoe			
	covers.			
	• Boots should also be cleaned to remove gross contamination and then			
	disinfected prior to re-use.			
Head cover	• The purpose of head covers is to protect the skin and hair from virus			
	contamination with subsequent unrecognized transmission to the mucosa of			
	the eyes, nose or mouth.			
	the eyes, nose or mouth.			
	the eyes, nose or mouth.A head cover that also protects the neck and sides of the head (leaving no or			

Heavy-duty	• Used when handling infectious waste (i.e. solid waste or any secretion or	
rubber gloves	excretion of with visible blood) by cleaners, launderer and hygienists	
	• Used for movement of human remains or performing environmental cleaning activities.	

Before exiting isolation area, carefully remove PPE and dispose in waste containers in a **designated doffing/contamination area**.

- Do not recycle any single-use PPE.
- Remove PPE under supervision of a buddy.
- Avoid any contact with soiled items and areas of the face or non-intact skin.
- Place rubber boots, goggles/face shield in bins with chlorine-containing solutions.
- Place reusable equipment in bin for decontamination.

5.3: Hand Hygiene and Glove Disinfection when caring for Lassa fever patients

- Alcohol-based hand-rub (ABHR) is the standard of care when hands are not visibly soiled. ABHR must be made available at every point of care (i.e. at the entrance and within the isolation rooms/areas).
- If hands are visibly soiled, use soap and water to perform hand hygiene.
- Ensure the availability of hand hygiene products (clean water, soap, single-use clean towels and ABHR).

The practice of performing hand hygiene with 0.05% chlorine should not be encouraged because:

- Chlorine has not been shown to be as effective as hand hygiene with soap and water or alcoholbased hand-rub (ABHR)
- Chlorine needs a longer skin contact time to be effective
- Repeated washing with chlorine can irritate and/or damage skin, which can increase the chance of Lassa fever entering the body through broken skin.

5.3.1: Carrying out Hand Hygiene

Before and after any direct contact between a Healthcare worker and a patient, and contact between patients, hand hygiene must be performed in the following scenarios, regardless of if gloves were worn or not:

- Upon entry into the isolation area, before putting on PPE and gloves.
- Before performing clean or aseptic procedures on patient.
- After any exposure risk or actual exposure to patient blood or body fluid.
- After touching contaminated surfaces/items/equipment in patient's surroundings.
- Upon leaving the isolation area, after removal of PPE.

Important points to note in carrying out hand hygiene.

- All Healthcare workers (including aides and cleaners) and visitors must be trained/instructed in hand hygiene.
- Instructions should be displayed at the point of entry into the isolation unit/room.
- Perform hand hygiene with an alcohol-based hand-rub solution (20-30 seconds) or soap (preferably liquid soap), running water and single-use towels (40-60 seconds), applying recommended techniques (*see Appendix for Steps in performing hand hygiene using ABHR*).
- Always perform hand hygiene with liquid soap and water when hands are visibly soiled.
- Alcohol-based hand rubs must be made available at every point of care.

5.3.1A: Hand hygiene with Alcohol-based Hand-rub

- ABHR containing 60-80% alcohol is effective for removing microorganisms including Lassa fever virus from the hands. However, ABHR **does not** remove soil or organic matter. If hands are visibly soiled or contaminated with blood or body fluids, they must be washed with soap and water.
- For hand hygiene with ABHR to be effective, approximately 3-5 ml (about a teaspoonful) of ABHR must be used.
- The solution must be rubbed until it completely dries (20-30 seconds). The steps are seen in the appendix of this document (*Steps in performing hand hygiene using ABHR*) and must be followed when performing hand hygiene or cleaning gloves

5.3.1B: Handwashing with soap and water

Hands must be washed when visibly soiled. Clean water must be supplied and used regularly to prevent microorganisms from water contaminating the hands. Proper hand washing requires that soap be rubbed on all surfaces of both hands followed by rinsing and drying. The World Health Organization(WHO) recommends that this process takes between 40-60 seconds. The procedure is the same when performing hand hygiene and when cleaning gloved hands.

5.3.2: How to Change Gloves

Changing gloves between patients and performing hand hygiene is considered best IPC practice. Glove change can be safely performed by following a two-step procedure:

- Disinfect the outer gloves before removing them safely.
- Keep the inner gloves on and disinfect them before putting on a fresh outer pair.

Alcohol-based hand-rubs are preferred when disinfecting gloved hands. However, if

this is unavailable, soap and water or bleach/chlorine solutions are acceptable.

Points to note

- Never perform hand hygiene by dipping hands into basins containing standing water.
- Do not add soap to a partially empty liquid soap dispenser. The practice of topping up dispensers can lead to microorganism contamination of the soap.
- If there is no running water, a bucket with a tap can be used.

CHAPTER 6: IDENTIFICATION AND MANAGEMENT OF LASSA FEVER CONTACTS

6.1 Who is a contact?

A contact is defined as a person who has been exposed to an infected person, or to an infected person's secretions, excretions, or tissues within three weeks of last contact with a confirmed or probable case of Lassa fever

It is a public health responsibility to:

- Identify, assess and categorize contacts of patients with Lassa fever.
- Ensure the appropriate monitoring of high-risk contacts.
- Arrange further evaluation for contacts who develop a temperature of $\geq 38^{\circ}$ C within 21 days of the last possible exposure.
- Consider and arrange antiviral prophylaxis, as necessary

Contacts are categorized into:

- Category 1: No-risk
- Category 2: Low-risk
- Category 3: High-risk

Table 6.1: Categorization of Contacts

Category	Description	Follow up Action
Category 1: No-risk contacts (including pregnant women)	 No direct contact with the patient or body fluids. Casual contact, e.g., sharing a room with the patient, without direct contact with body fluids or other potentially infectious material. Handling of laboratory specimens under contained conditions 	• Monitor for at least 21 days

Category 2: Low-risk contacts (including pregnant women)	 Direct contact with the patient, e.g.,routine medical/nursing care, OR Handling body fluids wearing appropriate personal protective equipment, OR Breach of laboratory containment without direct contact with specimen 	• As above
Category 3: High-risk contacts (including pregnant women)	 Unprotected exposure of broken skin or mucous membranes to potentially infectious blood or body fluids and secretions (including splash injury) clothing and bedding. This includes: unprotected handling of clinical/laboratory specimens; mucosal exposure to splashes; penetration of skin by contaminated sharp instrument e.g. needle-stick injury and kissing and/or sexual contact; breastfeeding. HCWs involved in emergency/exposure prone procedures i.e. surgery/CPR/ intubation /suctioning on confirmed cases and without use of appropriate PPE. Prolonged (i.e. for hours) and continuous contact in an enclosed space without use of appropriate PPE Infant of a RT-PCR Lassa virus positive mother 	 Commence PEP and monitor patients Conduct a RT-PCR for Lassa virus if they develop signs and symptoms of Lassa fever

All contacts should be identified by responsible authorities e.g. Hospital emergency teams, Public Health institution or infection control team or managing team.

Although experience is limited, post-exposure prophylaxis with Ribavirin should be considered for high-risk contacts of confirmed cases. The prophylactic regimen is **Ribavirin 500mg by mouth every 6 hours for 7 days.**

Options for PEP with ribavirin for high risk contacts are:

- a. IV ribavirin 100mg/kg stat, and then switch to oral dose as highlighted above
- b. Oral Dosing as stated above

Use of any of these options is dependent on patient's preference

- Oral ribavirin must be started immediately after the high-risk exposure, but not before counseling the patient
- The patient must be informed that the efficacy of PEP for Lassa fever is unknown and that minor adverse effects often occur.
- The drug must be taken with food.
- The index case must be tested for Lassa fever, with cessation of ribavirin if the test results are negative.

For Pregnant women who are high risk contacts:

• Intravenous daily dose regime (ISTH Irrua regime) is recommended as seen in the table below:

Period	Dose	Frequency
Day o(Loading Dose)	100mg/kg	In 2 divided doses. $2/3^{rd}$ of loading dose given stat and after 8 hours, remaining $1/3^{rd}$ is given
Day 1-4 (Commence Day 1 dose 24 hours after 1 st 2/3 rd of loading dose is given)		Daily
Day 5-7	12.5mg/kg	Daily

Regimen is best started immediately after exposure. RT PCR for Lassa virus must be done at the completion of therapy and temperature/foetal monitoring continued for 21days. Therapy and follow up monitoring can be done on an outpatient basis.

It is recommended that pregnant women who receive ribavirin in **first trimester** should have screening for anomalies using biochemical investigations and ultrasound.

6.2 Considerations for Post-exposure prophylaxis with Ribavirin

- PEP must be administered on a case basis.
- High risk patients must be counseled and commenced on ribavirin
- Pre-PEP counseling should be considered, and specialized counselors engaged to counsel persons with high exposure risk. Commence treatment with ribavirin after informed consent.
- Surveillance officers must monitor the contacts and then link them to a health care facility (See appendix for list of facilities and contacts).
- All contacts must be counseled and monitored for 21 days.
- PCR testing for Lassa Fever should be reserved for contacts that develop fever ≥ 38°C or other signs and symptoms of Lassa fever within 21days of the last possible exposure.

CHAPTER 7: DISCHARGE CRITERIA FOR LASSA FEVER

The decision to discharge a patient should be taken on clinical grounds and supported by laboratory results. A negative PCR means that the virus can no longer be detected in the blood and the patient is unlikely to be infectious with casual contact.

A patient should be discharged if any of the following criteria is met:

- 1. RT- PCR testing carried out at day 10 is negative and patients is afebrile.
- 2. In centers without facility for RT-PCR, discharge patients in the absence of signs and symptoms after 10 days of treatment
- 3. For symptomatic patients with negative RT-PCR discharge into appropriate ward for subsequent management
- 4. RT-PCR is positive after treatment but there are no symptoms suggestive of Lassa Fever for 72 hours post treatment (patient should however be followed up and oral ribavirin must be given at 500 mg 6 hourly for seven days)

If patient is still RT-PCR positive at day 10 and still symptomatic, treatment can be extended for 5-10 days.

Recommendations for Follow Up:

- Patients should be followed up weekly for the first 3 weeks and monthly for the next 3 months.
- After discharge, patient should be evaluated consistently for hearing loss and other complications
- Nursing mothers should not commence breastfeeding until breast milk tests negative. Supportive nutrition is encouraged for babies whose mother's breast milk tests positive
- Semen should be tested after 3 months and patient advised to avoid unprotected sexual intercourse during this period.
- If semen remains positive, patient should be counseled on the use of condom

CHAPTER 8: SAFE BURIAL FOR LASSA FEVER CASES

8.1: Introduction

There is a major risk of transmission when a patient dies of Lassa fever, as the dead body remains contagious for several days after death. The family and members of the community are also at risk, if the burial rites involve manipulation and cleaning of the body.

The body and immediate environment of the deceased are likely to be heavily contaminated with the Lassa virus, and therefore scrupulous attention to appropriate PPE and cleaning procedures is required. Attention and care must be taken to avoid injuries from sharp objects in or around the body.

8.2: How to prepare the dead body in the health facility

- a. Gather the necessary materials (PPE, coverall, plastic apron, fluid resistant mask, eye protection goggles, disposable gloves, heavy duty gloves, rubber boots) 2 body bags, disinfectant (0.5% chlorine), leak proof puncture resistant sharps box, two leak-proof infectious waste bags: one for disposable material (destruction) and one for reusable materials (disinfection) and ensure transport.
- b. Before going in to bag the body, use an indelible marker to mark the top surface of the outer bag with the deceased's name, age, and Identification number and clearly mark it to show that the deceased is a suspected or confirmed case of Lassa fever.
- c. At least four members of the burial team should wear full body PPE with heavyduty gloves (in the PPE donning area) including rubber boot
 - i. An apron must be worn over the PPE because of the increased likelihood of significant contamination with blood or other body fluids).

- ii. Use thick rubber gloves as the second pair (or outer layer) of gloves.
- d. The body must be properly prepared at the site of death. It should only be moved after this has been completed, and the outer surface of the body bag or other outer covering has been disinfected.
- e. Any person required to identify the body must not have direct contact with the dead body. Viewing should be done from a separate room through a see-through door or through a window. Anyone entering the room must wear appropriate PPE.
- f. Before a body is handled, use a surgical mask to cover the nose and mouth of the deceased. During manipulation and handling of bodies (e.g. while they are being placed into body bags), fluids can be expelled from body cavities. A mask should reduce the risk that fluids will travel any distance from any upper body cavities.
- g. The body SHOULD NOT be washed, sprayed or embalmed. Any practice of washing the remains in preparation for "clean burials" must be discouraged. Identify a family member who has influence with the rest of the family and who can make sure family members avoid dangerous practices such as washing or touching the body.
- h. Leave any medical devices (tubes, drips) in place. DO NOT attempt to remove them.
- i. If any family member is present at this point, the person may be asked to say a prayer if they wish.
- j. Place the body in the first body bag and close the bag
- k. Wipe the entire surface of the outside of the second bag with 0.5% chlorine solution
- 1. Once the body bag has been disinfected, move to the doffing area to take off PPE and follow the sequence for doffing PPE.
- m. Decontaminate the boots
- n. Place the body in a coffin, outside the ambulance where appropriate and if a coffin is provided.
- o. Disinfect the coffin with 0.5% chlorine
- p. If no coffin is available, the body bag should be gently placed in the ambulance.
- q. Transport the body to the burial place as quickly as possible or to the morgue in the treatment centre if immediate burial is not possible.

- r. After the body of the deceased patient has been moved: The patient care area must be thoroughly disinfected with 0.5% chlorine solution, by a trained staff while wearing full PPE.
- s. Entry into the mortuary is restricted to health-facility staff and burial team members wearing appropriate PPE. Family members must not touch, handle or touch the body bag with the dead body.

CHAPTER 9: APPENDICES

a. List of Treatment Centres in Nigeria

S/N	TREATMENT CENTRE	TC FOCAL PERSON CONTACT
1	ADAMAWA	DR. SATI KLEIN AWANG
	Federal Medical Centre, Yola,	08034999791
	Adamawa State	<u>awangsati@yahoo.com</u>
2	BAUCHI	DR. IBRAHIM MAIGARI
	Abubakar Tafawa Balewa	08061551992
	University Teaching Hospital	Ibmega05@yahoo.co.uk
	(ATBUTH), Bauchi.	
3	EBONYI	DR. UCHE UNIGWE
	Federal Teaching Hospital	unigweus@yahoo.com
	(FETHA) - Abakaliki	
		Dr. DAMIAN NWIDI
		08039536145 ugomascot@yahoo.com
4	EDO	DR. OGBAINI EPHRAIM
4	Irrua Specialist Teaching Hospital,	08032424965
	Irrua (ISTH), Edo State	epogbaini@yahoo.com
5	FCT, ABUJA	DR. FALODUN
	National Hospital, Abuja (NHA),	08028794965
	Abuja	lanrefalo@yahoo.com
		DR. OSIOGBU (COORDINATOR LASSA
		FEVER COMMITTEE)
		08066377980
		ogogbu@yahoo.com
6	KANO	DR. M B ABDULLAHI
	Yargaye Isolation Centre along	07036033077
	Wudil Road, Kano State.	muhdba@yahoo.co.uk
7	KOGI	DR MONDAY AJODOH
	Kogi State Specialist Hospital,	07034831875
	Lokoja, Kogi State	

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b. WHO 5 Moments of Hand Hygiene

C. Steps in performing Hand Hygiene using ABHR

How to Handrub?

RUB HANDS FOR HAND HYGIENE! WASH HANDS WHEN VISIBLY SOILED

Ouration of the entire procedure: 20-30 seconds





Apply a palmful of the product in a cupped hand, covering all surfaces;

Rub hands palm to palm;



Right palm over left dorsum with interlaced fingers and vice versa;



Palm to palm with fingers interlaced;



Backs of fingers to opposing palms with fingers interlocked;



Rotational rubbing of left thumb clasped in right palm and vice versa;



Rotational rubbing, backwards and forwards with clasped fingers of right hand in left palm and vice versa;



Once dry, your hands are safe.

d. Steps on how to Handwash

How to Handwash?

WASH HANDS WHEN VISIBLY SOILED! OTHERWISE, USE HANDRUB

Ouration of the entire procedure: 40-60 seconds





all hand surfaces:

Wet hands with water;



Right paim over left dorsum with interlaced fingers and vice versa;



Rotational rubbing of left thumb clasped in right paim and vice versa;



Dry hands thoroughly with a single use towel;



Paim to paim with fingers interlaced;



Rotational rubbing, backwards and forwards with clasped fingers of right hand in left palm and vice versa;



Use towel to turn off faucet;



Rub hands paim to paim;



Backs of fingers to opposing palms with fingers interlocked;



Rinse hands with water;



Your hands are now safe.

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