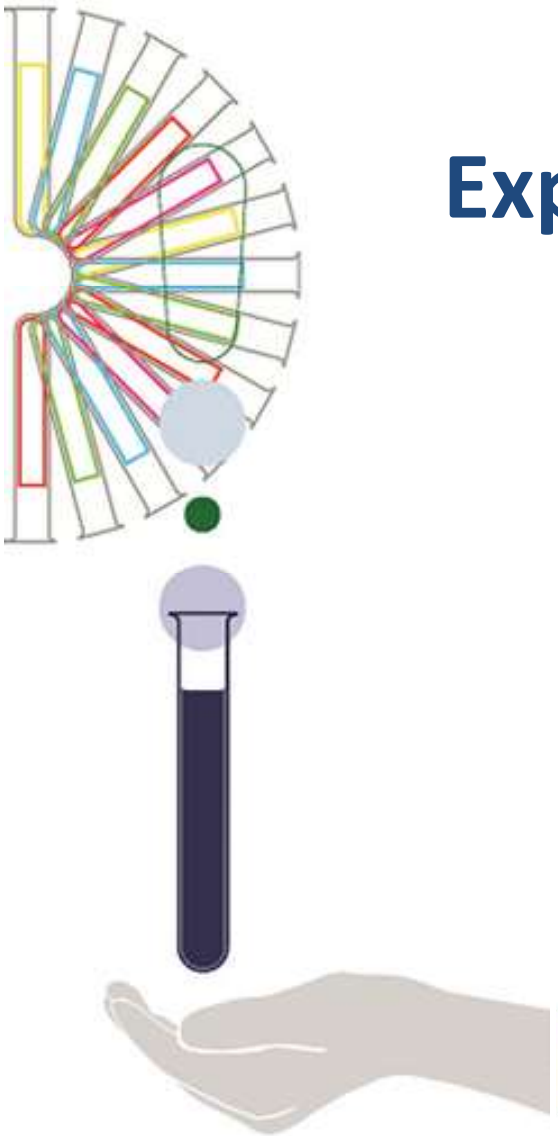
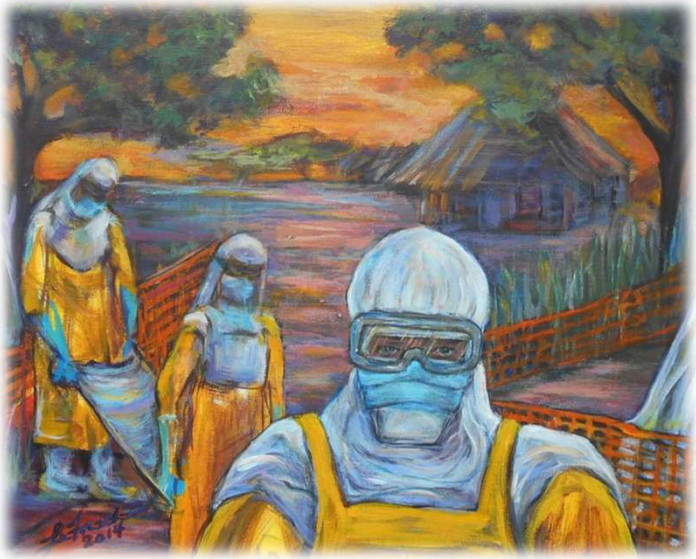


The Bleeding Continent: Exploring Viral Haemorrhagic Fevers in Africa



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Dr Michelle Naidoo
Medical Virologist

SEPTEMBER 2025

The Returning Traveller

e.g. 48-year-old patient with recent travel to West Africa. Now presenting with fever and malaise

- Malaria?
- Typhoid Fever?
- Traveller's Diarrhoea?
- Cholera?
- Other (e.g. Influenza, SARS-CoV-2)?
- VHF?

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The Returning Traveller

- Which country and city?

(What's endemic there? Current transmission/outbreak?)

- Dates
- Activities/exposures:

- Animal exposures
- Water exposures
- Sick contacts
- Occupation

- Residence: Rural or urban
- Immunizations and prophylaxis taken

Within the last 3 weeks

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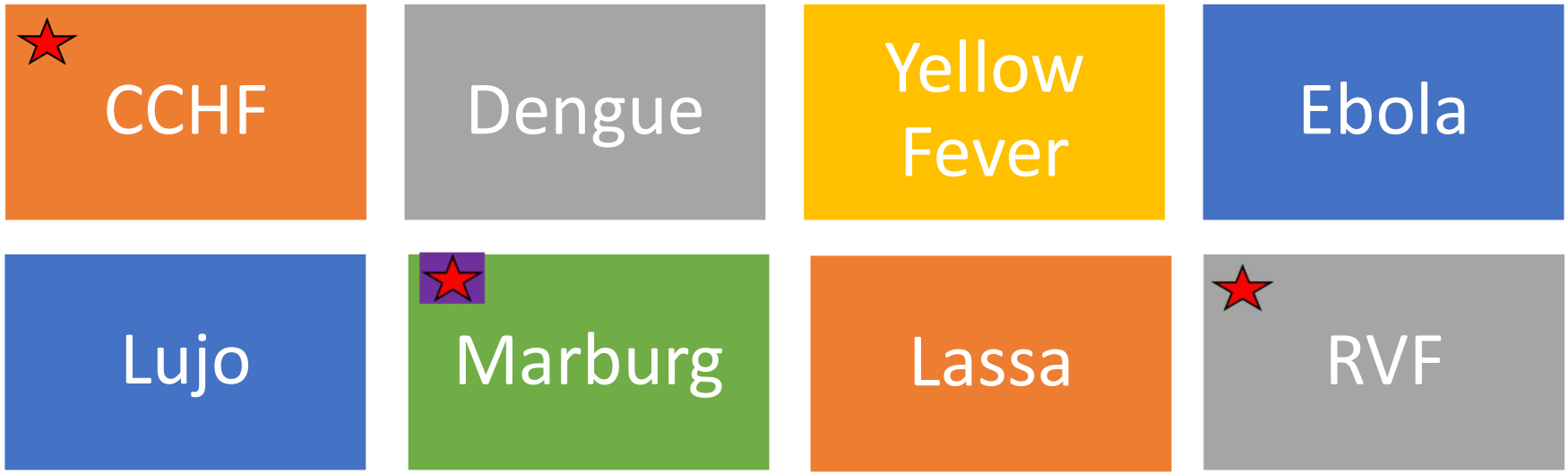
Viral haemorrhagic fevers (VHFs) in Africa



- Group of illnesses caused by several families of viruses:
- Filoviridae, Arenaviridae, Flaviviridae, Nairoviridae, Phenuiviridae
- Enveloped, RNA viruses
- Zoonotic (reservoirs/vectors in animals)

- Geographically restricted
- Overlap of symptoms and signs
- Overlap in general laboratory findings
- Overlap in management * with exceptions
- Major Public Health implications for most

Public Health Bulletin
South Africa

Surveillance of viral haemorrhagic fevers, Rift Valley fever and yellow fever in humans, South Africa, 2019-2023

Naazneen Moolla[1], Ednah Baloyi[2], Jessica Coertse[1], Antoinette Grobbelaar[1], Mabatho Mogadime[2], Veerle Msimang[1], Wayne Ramkrishna[2], Mbavhalelo Skandukani[2], Jacqueline Weyer[1]

[1]Centre for Emerging Zoonotic and Parasitic Diseases, National Institute for Communicable Diseases of the National Health Laboratory Service, Sandringham, South Africa

[2] Cluster: Communicable Diseases, National Department of Health, South Africa

Disease	Year					Total confirmed per disease
	2023	2022	2021	2020	2019	
EVD	0 (1)	0 (2)	0 (1)	0 (1)	0 (6)	0 (11)
MVD	0 (0)	0 (2)	0 (1)	0 (0)	0 (5)	0 (8)
LF	0 (2)	1(3)	0 (1)	0 (0)	0 (2)	1 (8)
Lujo fever	0 (0)	0 (2)	0 (1)	0 (0)	0 (2)	0 (5)
New World arenaviruses	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
CCHF	1(7)	3(15)	1(10)	2 (11)	3 (34)	10 (77)
RVF	0 (3)	0 (19)	0 (21)	0 (12)	0 (35)	0 (90)
YF	0 (8)	0 (9)	0 (2)	0 (2)	0 (12)	0 (33)
Total confirmed per year	**1**(21)	**4** (52)	**1**(37)	**2** (26)	**3** (96)	**11 (232)**

EVD=Ebola virus disease; MVD=Marburg virus disease, LF=Lassa fever, CCHF=Crimean-Congo haemorrhagic fever, RVF=Rift Valley fever, YF=yellow fever.

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Table 2. Exposure histories of laboratory-confirmed cases of Lassa fever (LF) and Crimean-Congo haemorrhagic fever (CCHF), South Africa, 2019-2023.

Disease	Source of exposure	Details of exposure	Geographic location of exposure
LF	Not reported	Travel to rural mining areas where exposure to rodents is possible	Various locations in Nigeria
CCHF	Tick	Occupational exposure: veterinarian	Free State Province, South Africa
	Tick	Occupational exposure: livestock farmer	Northern Cape Province, South Africa
	Tick	Occupational exposure: livestock farmer	North West Province, South Africa
	Tick	Occupational exposure: livestock farmer	North West Province, South Africa
	Tick	Occupational exposure: livestock farmer	Free State Province, South Africa
	Tick	Retired, exposed during hiking	Western Cape Province, South Africa
	Not reported	Occupational exposure: Sheep farmer	Western Cape Province, South Africa
	Probably ticks	Occupational exposure: Game culling on farms and nature reserves	Eastern Cape Province, South Africa
	Slaughter	Occupational exposure: Abattoir worker (sheep)	Western Cape Province, South Africa
	Not reported	Occupational exposure: Veterinarian	North West Province, South Africa

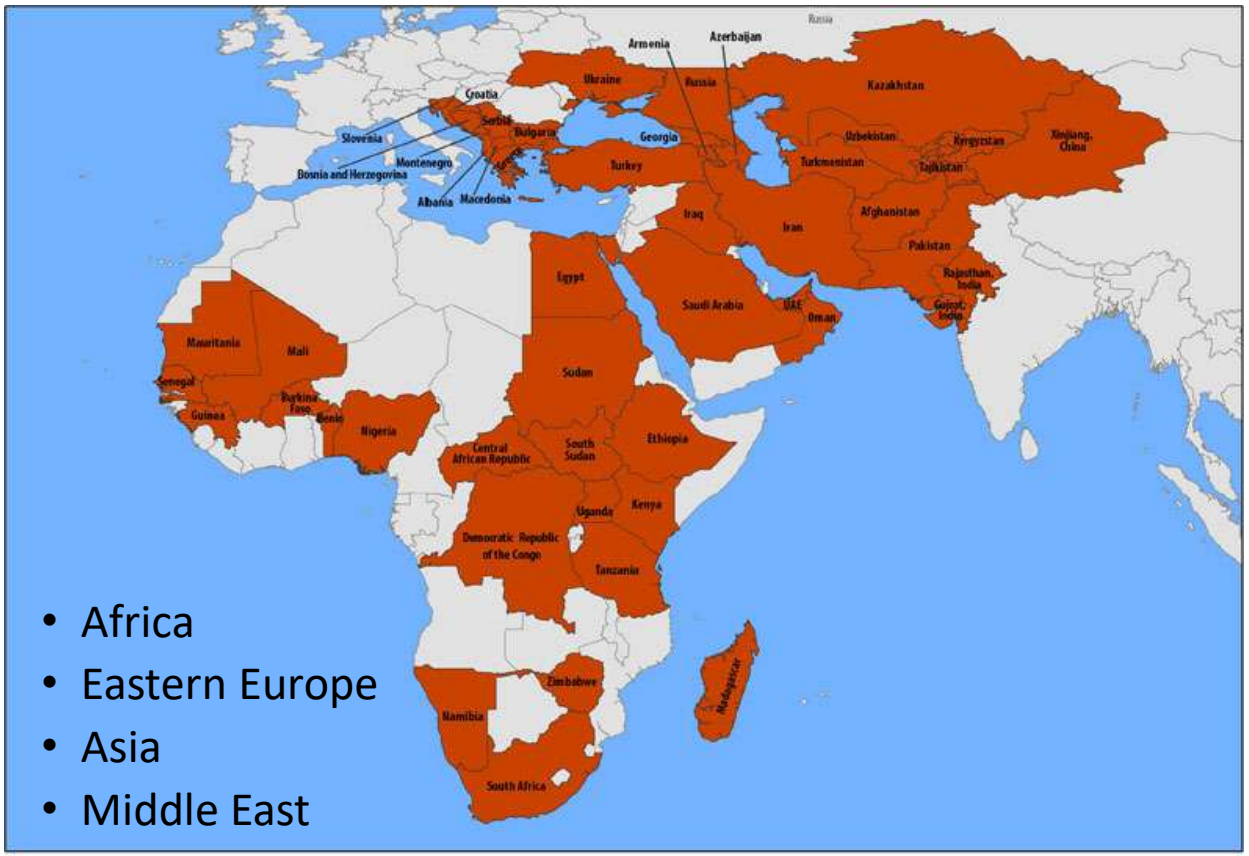
Clinical Criteria	Epidemiological Link	Laboratory
Acute onset of fever >38˚c and one or more of the following: • severe headache • muscle pain • erythematous maculopapular rash on the trunk with fine desquamation 3–4 days after rash onset • vomiting • diarrhoea • abdominal pain • bleeding not related to injury • thrombocytopenia • pharyngitis (Arenaviruses only) • proteinuria (Arenaviruses only) • retrosternal chest pain (Arenaviruses only)	One or more of the following exposures **within the 3 weeks before onset of symptoms**: • Contact with blood or other body fluids of a patient with VHF • Residence in—or travel to—a VHF endemic area or area with active transmission • Work in a laboratory that handles VHF specimens • Work in a laboratory that handles bats, rodents, or primates from a VHF endemic area or area with active transmission • Sexual exposure to semen from a confirmed acute or clinically recovered case of VHF	Any one of the following: • Detection of VHF* viral antigens in blood by enzyme-linked immunosorbent assay (ELISA). • VHF viral isolation in cell culture for blood or tissues. • Detection of VHF-specific genetic sequence by reverse transcription polymerase chain reaction (RT-PCR) from blood or tissues. • Detection of VHF viral antigens in tissues by immunohistochemistry.

Suspected case = Meets clinical criteria AND epidemiologic linkage criteria

Confirmed case = Meets laboratory criteria

https://ndc.services.cdc.gov/case-definitions/viral-hemorrhagic-fever-2022

Epidemiology of Crimean-Congo Haemorrhagic Fever (CCHF)



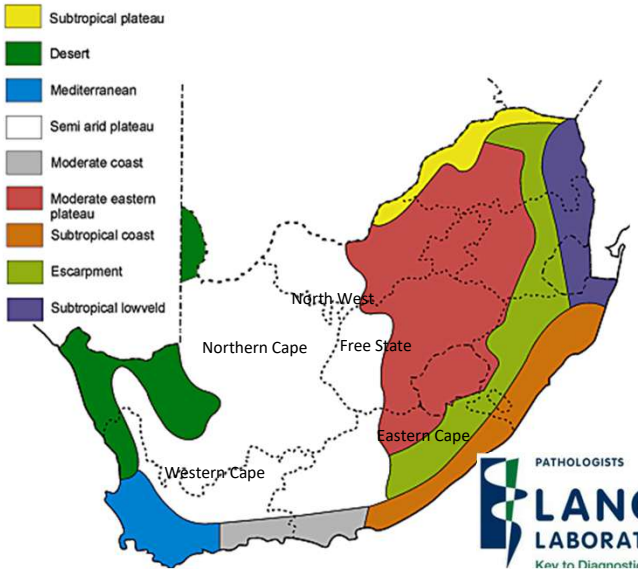
- Africa
- Eastern Europe
- Asia
- Middle East

https://www.cdc.gov/vhf/crimean-congo/outbreaks/distribution-map.html

- Endemic VHF in SA

- Cases in all 9 provinces

- Majority of case from inland central plateau and drier regions mainly the semi-arid areas of the Northern Cape, North West and Free State Provinces



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The laboratory-confirmed CCHF cases were associated with local exposure events. During the reporting period, cases occurred in the North West (n=3), Western Cape (n=3), Free State (n=2), Eastern Cape (n=1) and Northern Cape (n=1) provinces (Figure 2).

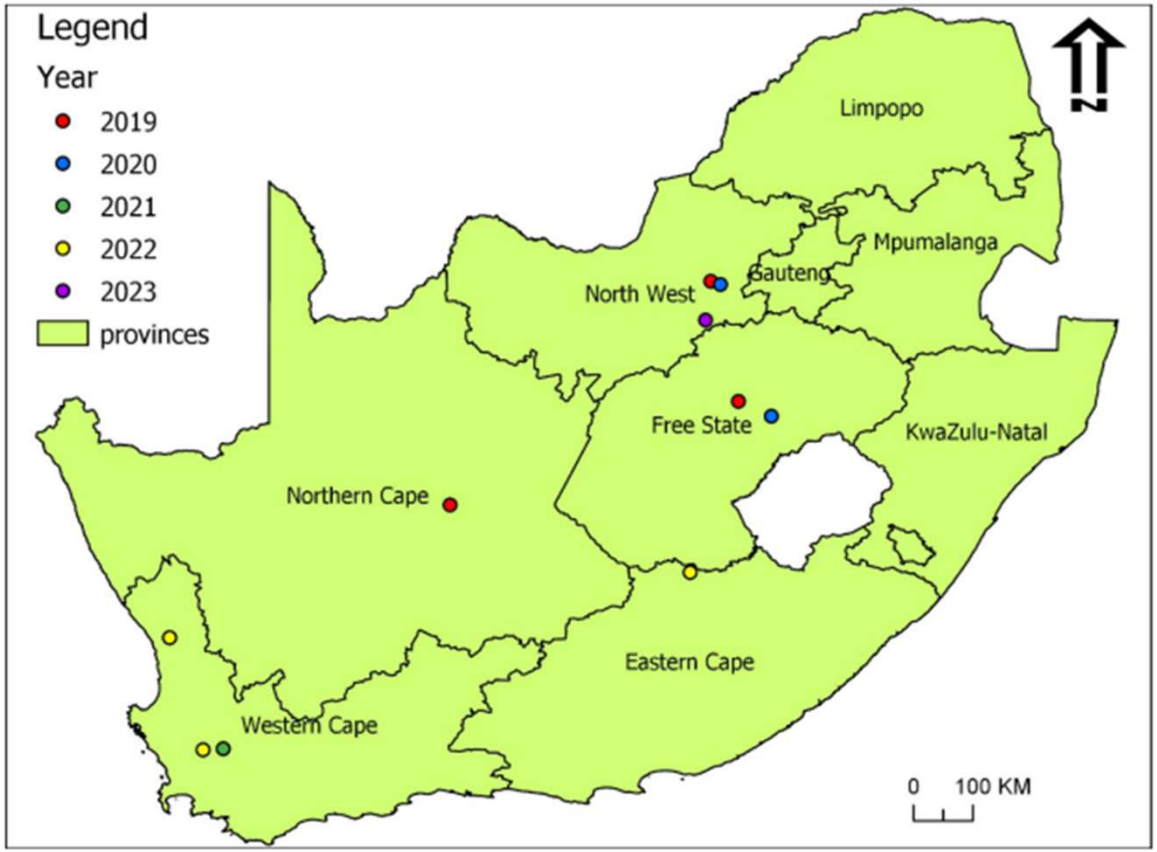


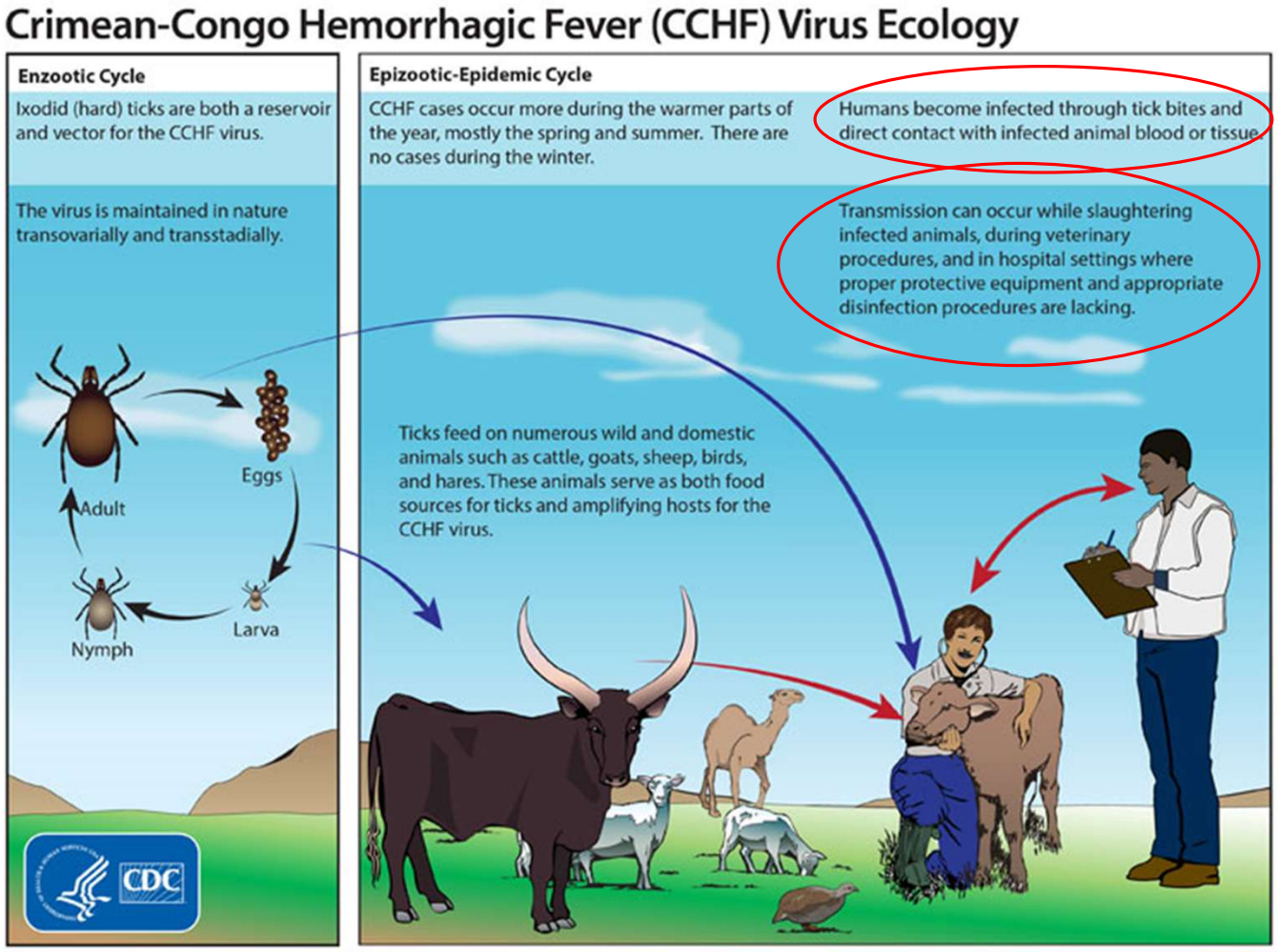
Figure 2. Distribution of human cases of Crimean-Congo haemorrhagic fever (CCHF) by year across South Africa, 2019-2023.

- Zoonotic disease
- CCHF virus is transmitted by ixodid (hard) ticks: Called Hyalomma or ‘Bontpoot’ ticks
- Note the stripped legs

https://en.wikipedia.org/wiki/Hyalomma

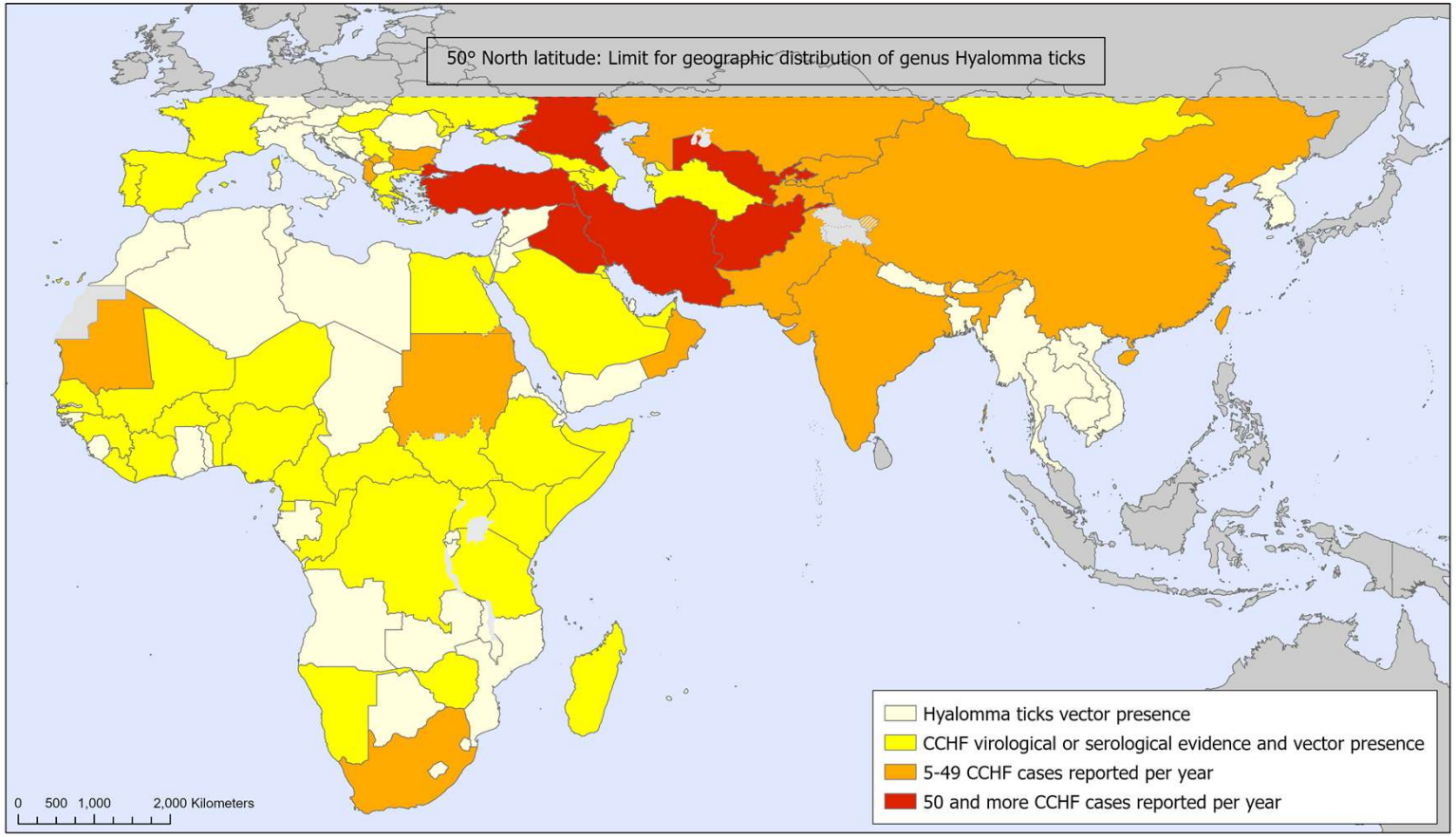
Human to human CCHF transmission?

- Yes, via contact with infectious blood/ body fluids.
- Documented nosocomial transmission spread due to exposure to patient body fluids, contamination & improper sterilization of medical equipment
- Outbreak potential therefore NMC



*Birds are resistant to infection, but ostriches are susceptible

Geographic distribution of Crimean-Congo Haemorrhagic Fever (2022)



Data Source: WHO - Viral Haemorrhagic Fevers (VHF)
Map Production: Jewgeni Bader, EYE Secretariat

Map Creation Date: **01 September 2022**

Clinical presentation of CCHF

Incubation period = 1-3 days

Longest documented incubation period: 13 days

Case definition of a suspected case of CCHF (NICD):

A person with acute onset of fever > 38°C, + least three of the following signs and symptoms:

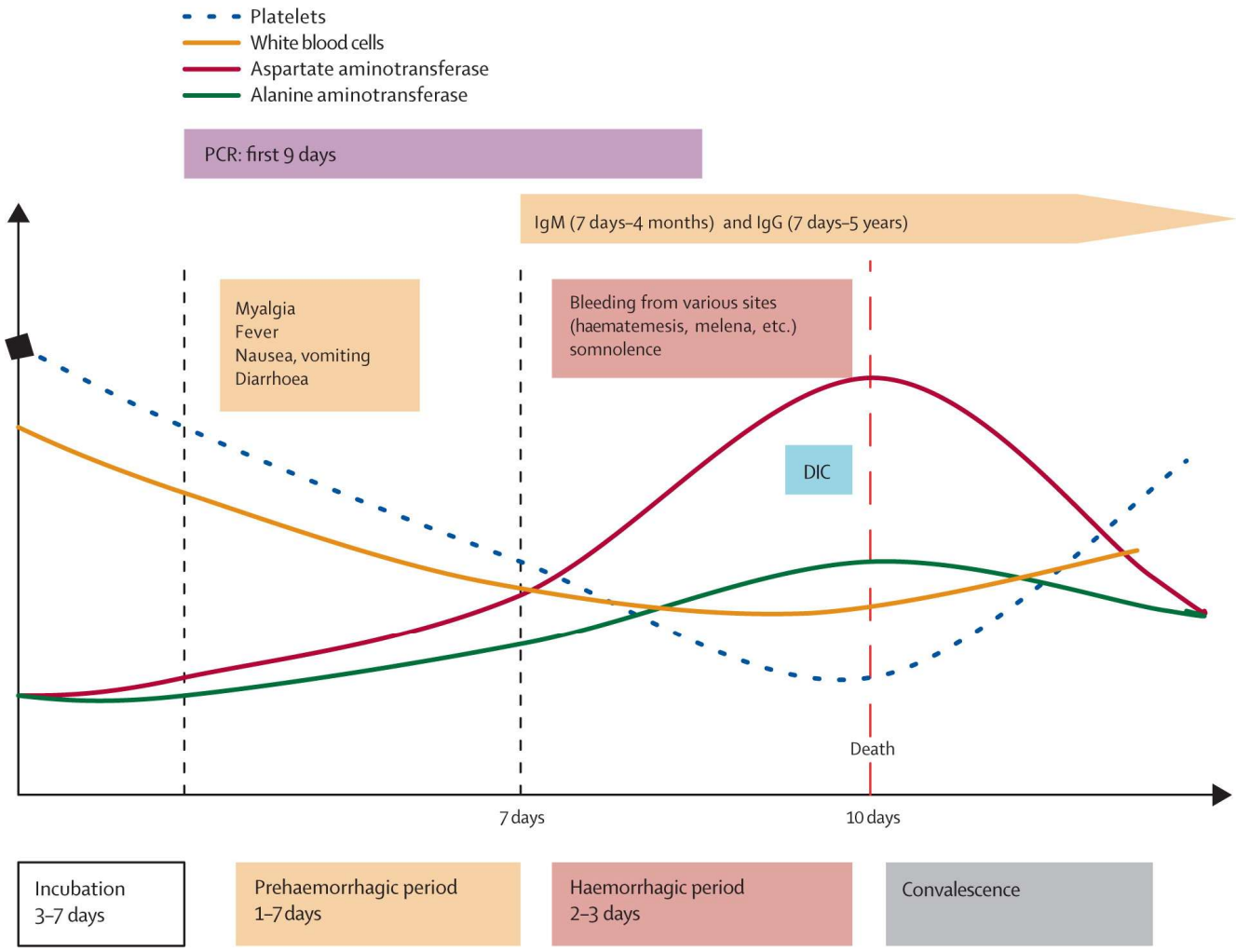
- severe headache, myalgia, prostration, flushing,
- nausea, vomiting, pharyngitis, conjunctival injection,
- petechial rashes, bleeding into skin (ecchymoses), from nose, vomiting of blood, blood in urine or stool, decreased platelets count,
- hypotension and shock, leukopenia or leucocytosis, elevated AST or ALT (> 100 U/L), oedema or neurologic signs.

AND a likely epidemiological exposure including any of the following:

- a history of being bitten by tick/s or crushed tick with bare hands, or
- direct contact with fresh blood or other tissues of hoofed livestock or game or ostriches, or
- direct contact with blood, secretion or excretions of confirmed or suspected CCHF patient (including needle pricks) OR
- resides in or visited a rural environment where contact with livestock or ticks was possible in the past 15 days.

Differential diagnosis include: Tick bite Fever, malaria and leptospirosis (Think CCHF when the patient is unresponsive to doxycycline)

Natural progression of CCHF



Range: 1-14 days

https://doi.org/10.1016/S1473-3099(06)70435-2

Remember: Our CCHF patients bleed. It is a true haemorrhagic fever when platelets are low

- Majority of patients recover (slow)
- Long-term effects of CCHF unknown

- Fatality rate from 3-30%
- End organ complications involving liver, lung and kidney failure

may lead to **death after the 5th day of illness**

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Time to reflect:

- **With regards to CCHF transmission, choose the two best answers?**

A. Bite by Aedes aegypti. mosquito

B. Direct contact with animal blood & tissue

C. Bite by Hyalomma tick

D. Bite by Lone Star tick

E. Eating raw shellfish

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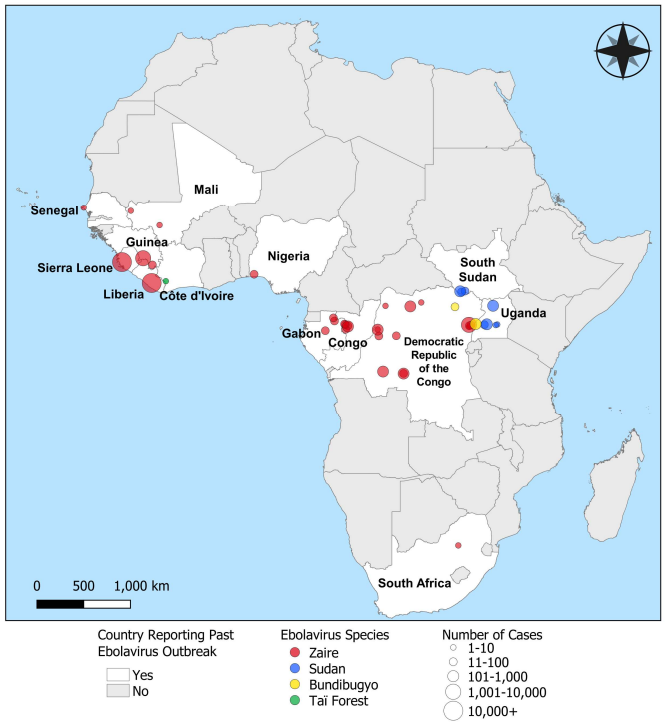
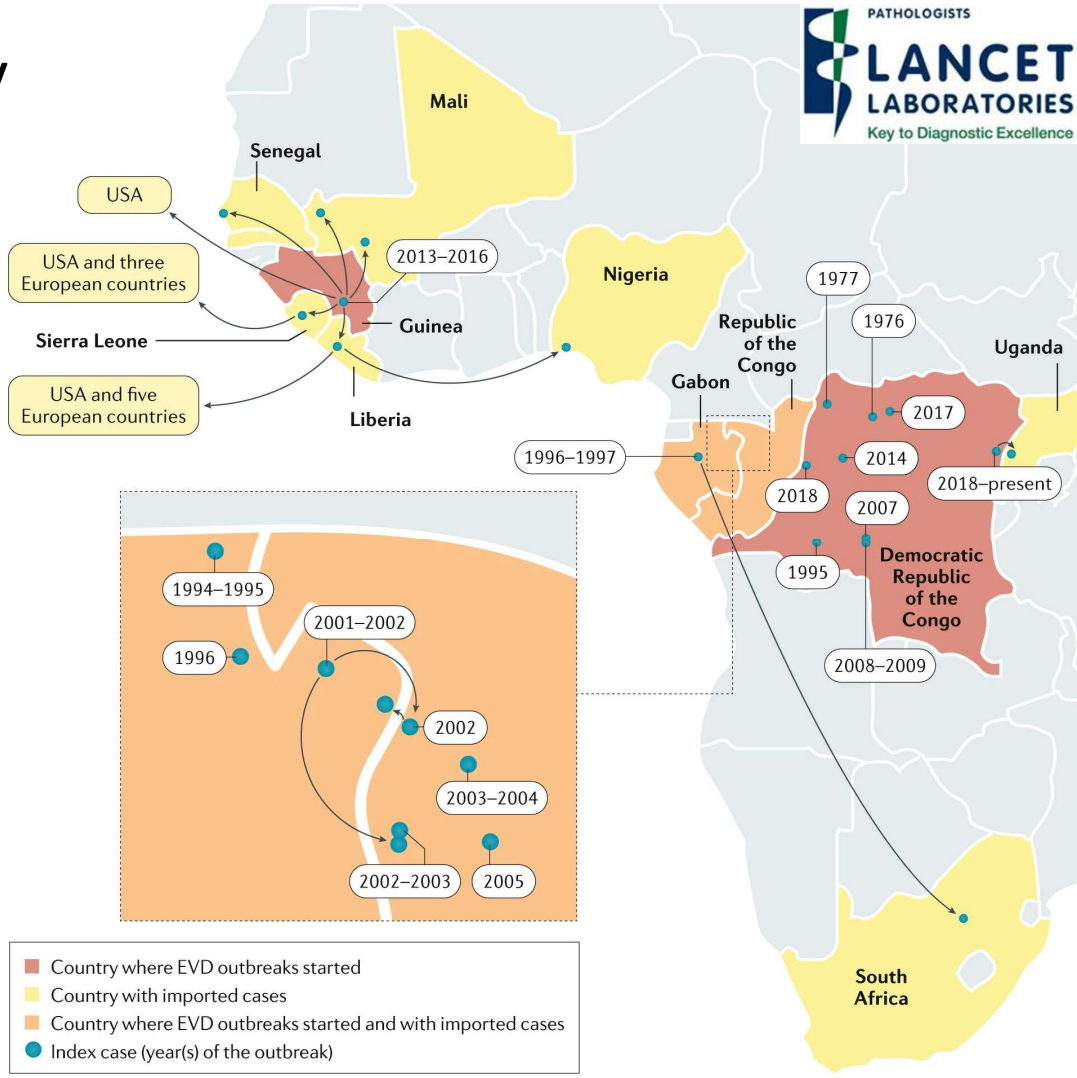
Ebola Virus: Epidemiology

- Six species: Zaire, Sudan, Reston, Tai Forest, Bundibugyo (and Bombali)
- Incubation period: 2-21 days (Av. 1 week)



CDC, Last Reviewed: March 24, 2023



Jacob, S.T., Crozier, I., Fischer, W.A. *et al.* Ebola virus disease. *Nat Rev Dis Primers* **6**, 13 (2020). https://doi.org/10.1038/s41572-020-0147-3

2025 Ebola DRC Outbreak

- 20 August 2025: 34-week pregnant woman (index case) presents to hospital with high fever, bloody diarrhoea, vomiting, extreme weakness → MOF
- 25 August 2025: Patient dies. Two HCWs who had initial contact with this index case also developed similar symptoms and died
- 4 September 2025: Outbreak declared in Kasai Province of DRC (16th outbreak for DRC)
- As of September 17, 2025:
- 48 people with confirmed or probable Ebola
- 31 deaths, including four health workers (>50% CFR)
- Results obtained from whole genome sequencing suggest that the outbreak is a new zoonotic spillover event
- WHO assesses the overall public health risk posed by the ongoing outbreak as high at the national level, moderate at the regional level and low at the global level

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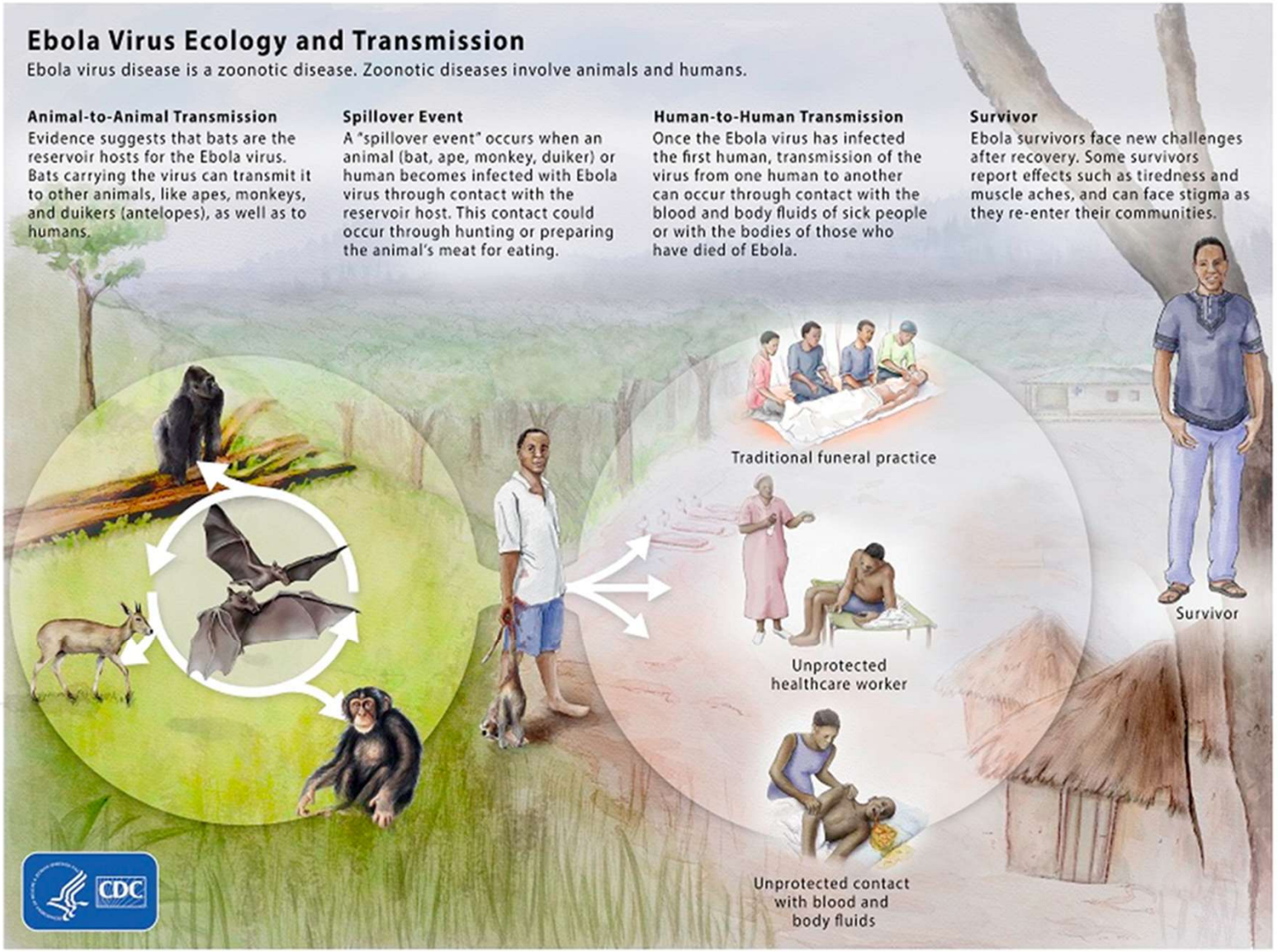

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Basic reproduction number (R0) for Ebola = 1.95
(95 % CI 1.74–2.15)

✚

Persistence of virus in semen: WHO recommends safe sex and hygiene for 12 months from onset of symptoms or until their semen tests negative twice for Ebola virus.

Ebola Virus: Clinical manifestations

Infectivity

Incubation period: 2-21 days
- Asymptomatic
- Not contagious

Dry symptoms: Day 1-3
- Febrile non-specific symptoms

Wet symptoms: > Day 3
- Nausea
- Abdominal pain
- Diarrhea
- Vomiting

Shock & bleeding: > Day 5 to week 2
- Abnormal electrolytes
- Renal dysfunc
- Metabolic acidosis
- Coagulopathy
- Neurological manifestations
- MOF

Death or recovery: Week 2
- Ebola case fatality rate = ± 50% (range of 25% to 90% in past outbreaks)

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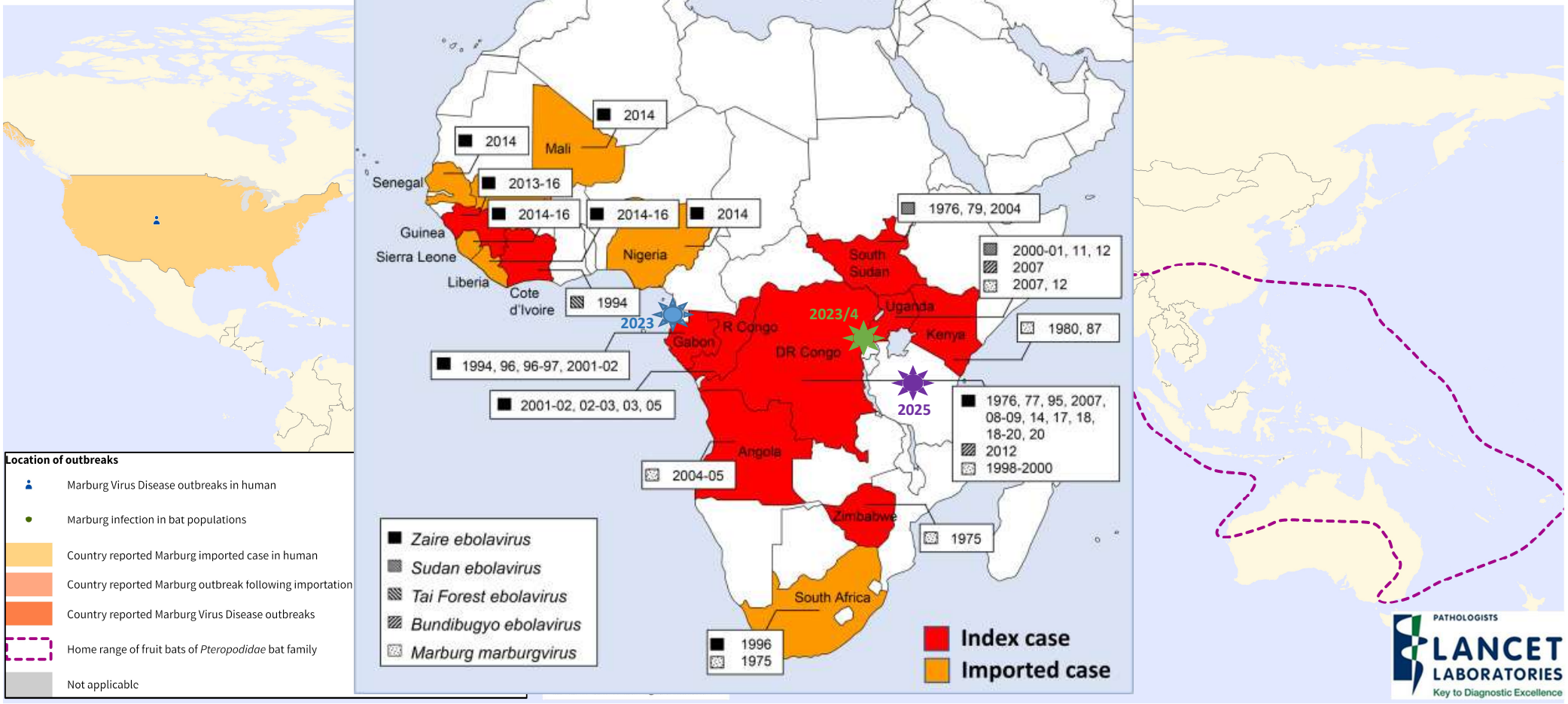
Marburg virus: Epidemiology

Geographic distribution of Marburg Virus Disease outbreaks and bats of *Pteropodidae* family



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Following the initial laboratory outbreaks in Germany and Yugoslavia, outbreaks in other countries have been documented (Fig.1).

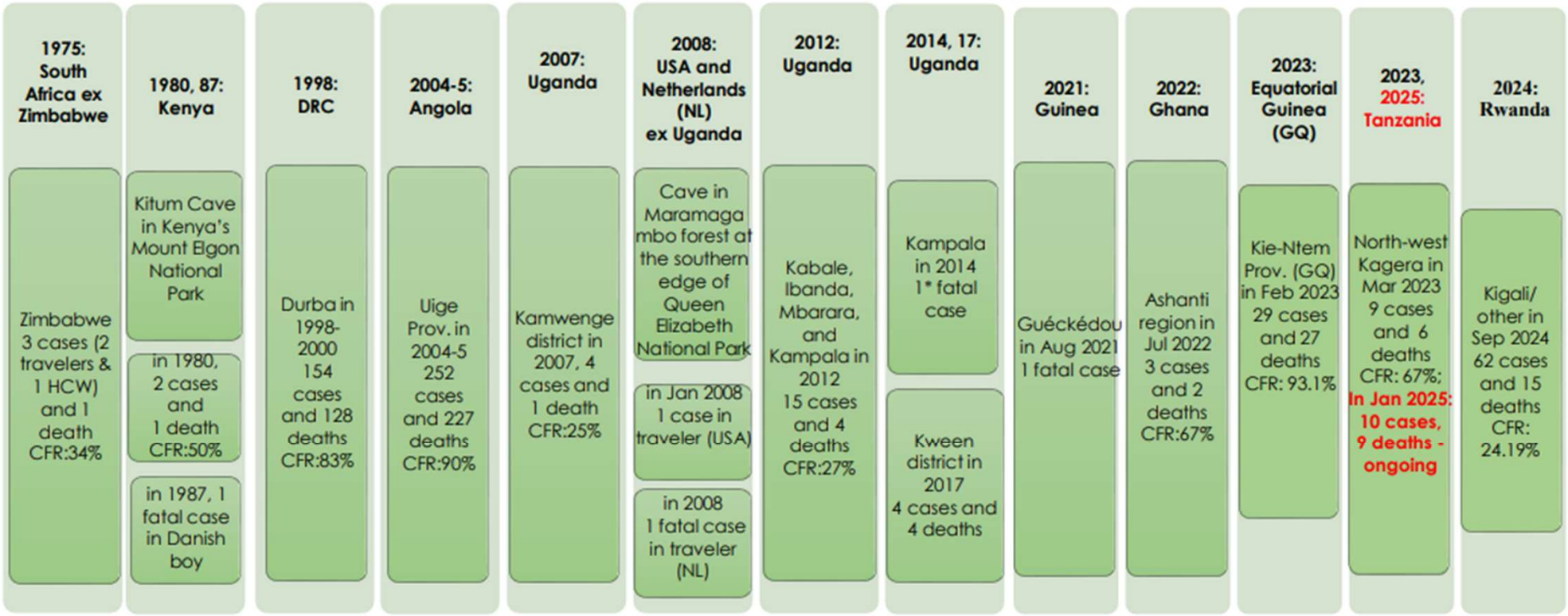


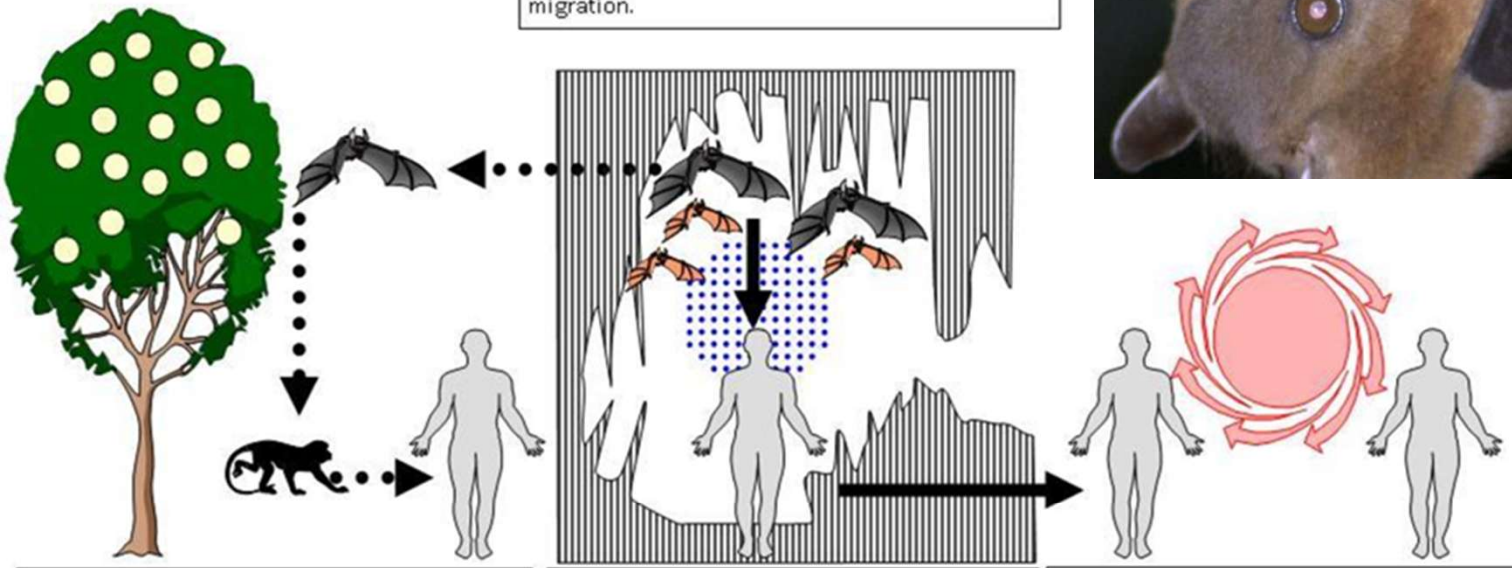
Figure 1. After initial detection, the timeline of MVD outbreaks (*laboratory-confirmed case only) (Russian case of 1990 from laboratory contamination not included.)

https://www.nicd.ac.za/wp-content/uploads/2025/01/MVDFAQS-JAN-2025.pdf

Marburg virus:

1. Virus reservoir : Fruit bats

The virus maintains itself in fruit bats of the *Roussettus* species that sleep during the day in caves or mines. The bats spread the virus during migration.



Epizootic in primates

The *Roussettus* bats leave the caves at night to feed on fruit in the tropical forest. Transmission of the virus to other wild animals, especially monkeys, is possible but rare. Humans may be infected through handling infected monkeys or wild animals.

2. Primary human infection

Most primary cases (index cases) of Marburg infection occurred following an extended stay in mines or caves inhabited by bats of the *Rousettus* species. Transmission may occur through direct or indirect contact with bats or airborne transmission.

3. Secondary transmission

Secondary human-to-human transmission occurs through direct contact with the blood, secretions, organs or other body fluids of infected persons. High transmission risk when providing direct patient care or handling dead bodies (funerals).

Marburg virus disease basic reproduction number (R_0) is 1·59 (95% CI 1·53–1·66)

- Semen from recovered person shown to be infectious up to 7 weeks after recovery (WHO: 12 months safe sex or until 2x neg)
- Contaminated surfaces + materials

Marburg virus: Clinical manifestations

Incubation period: 2-21 days

- Asymptomatic
- Not contagious

Dry symptoms: Day 1-3

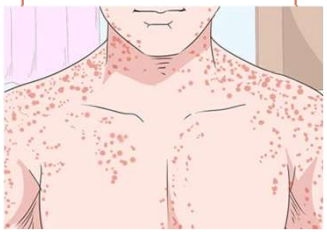
- Abrupt onset high fever
- chills
- non-specific symptoms: severe headache, severe malaise, severe myalgia, conjunctivitis

Wet symptoms: > Day 3

- Severe watery diarrhea
- vomiting,
- nausea, abdominal pain + cramps

Maculopapular rash : ±Day 5

- Non-pruritic, red, blanching maculopapular rash (most prominent on the trunk and limbs)



Severe haemorrhagic manifestations: Day 5-7

- Bleeding is rare in early phase but significant in terminal phase of fatal infection
- Altered CNS
- Death usually due to massive hemorrhage and multi-organ failure at day 8-9
- Case-fatality rate = 50% (Range of **23-88%**)

- Note similarities to Ebola Virus
- Overlap clinically
- Capacity for outbreak with high case-fatality rate

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Time to reflect: Ebola and Marburg virus

- **With regards to pathogenesis of Ebola and Marburg virus, which of the following plays a role:**

A. Reduced production of clotting factors by spleen

B. Fluid loss from diarrhoea and vomiting

C. Leaky capillaries

D. Chronic kidney disease

E. Immune dysregulation

F. High blood pressure

G. Damage to blood vessels

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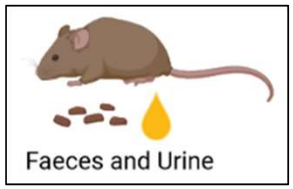
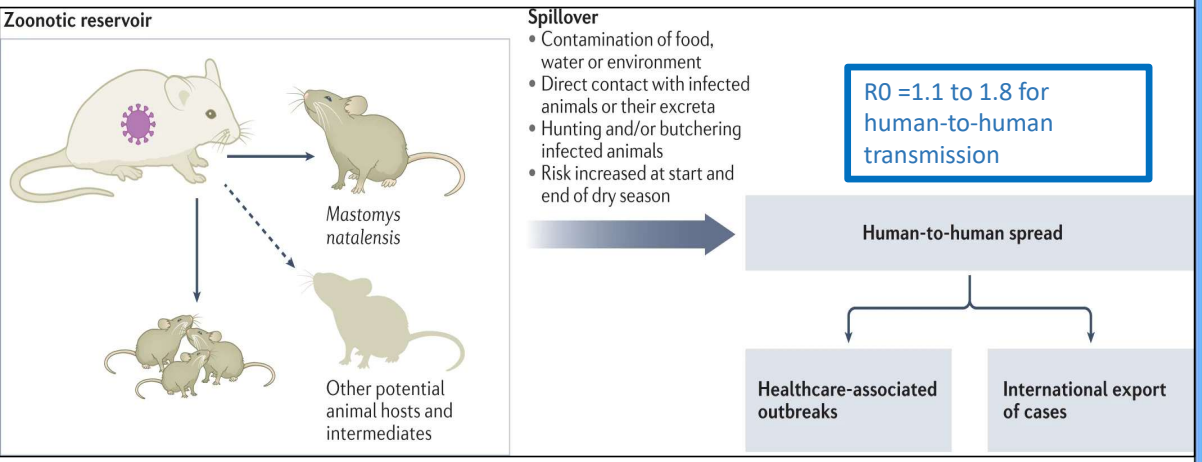
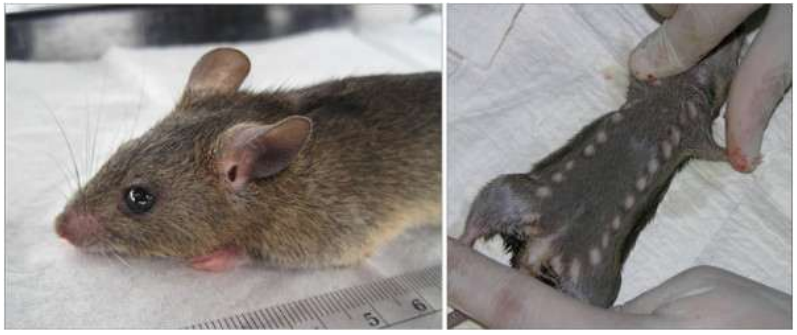
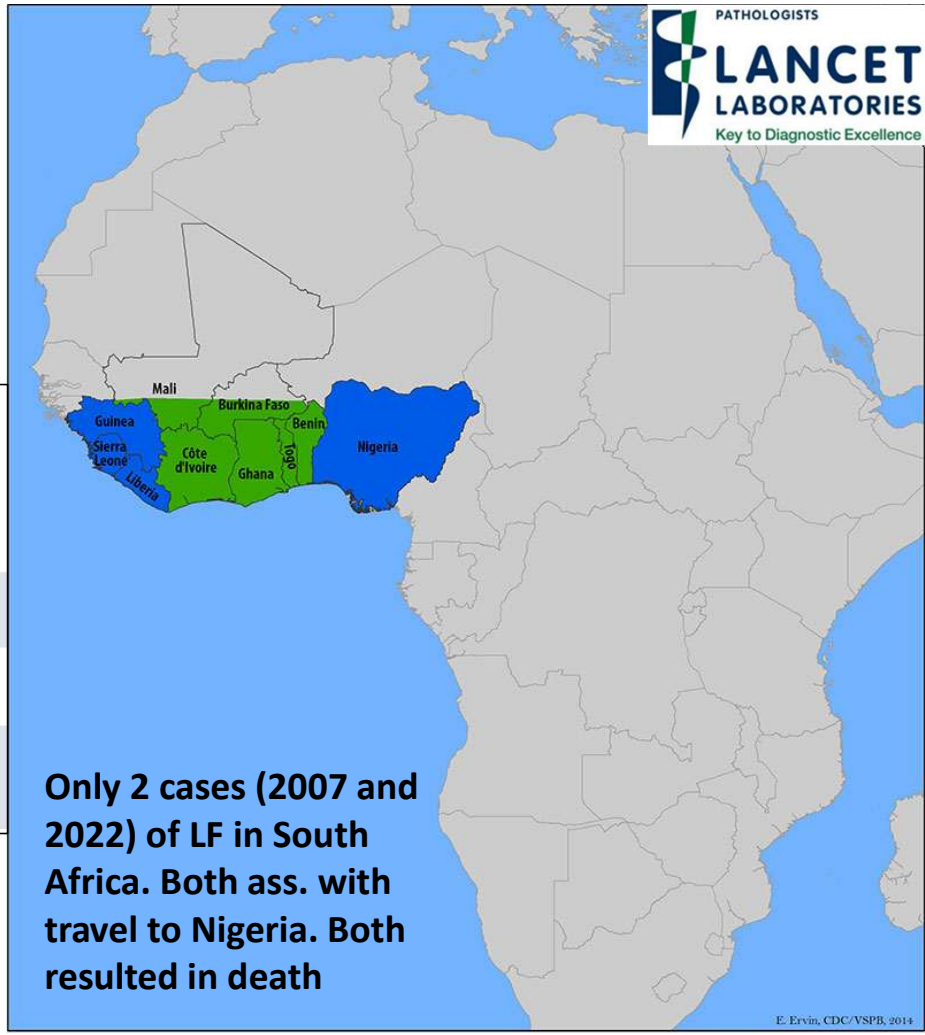
Lassa Virus: Epidemiology







"**multimammate rat**" due to the female's multiple and prominent mammary glands, as seen in the right-hand panel
Photos: L. Moses and D. Bausch.



Lassa Virus: Clinical manifestations

- Incubation period: 2-21 days

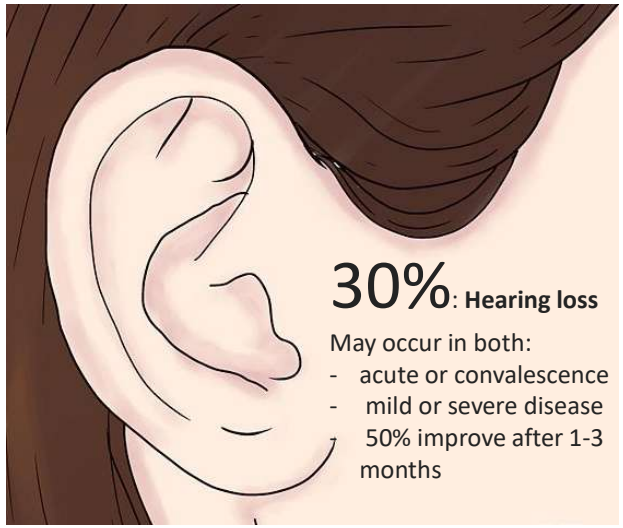
80 %
ASYMPTOMATIC
or MILD
- Low-grade fever
- Malaise
- Mild headache

20% MODEARTE- SEVERE

Headache, **sore throat**, cough, muscle pian, gastro, abdominal pain, chest pain

Severe: **Facial swelling**, pulmonary oedema, proteinuria, bleeding, hypotension, shock, seizures, tremors, disorientated, coma

Infection in **3rd trimester** = Severe disease with **maternal death and/or foetal loss in >80%**



30%: Hearing loss

May occur in both:
- acute or convalescence
- mild or severe disease

50% improve after 1-3 months

Non-specific symptoms
Similar to Ebola and Marburg

Require hospitalisation = 15-30%

Overall case-fatality rate: = 1%

Time to reflect:

- **Which of the following is associated with Lassa virus infection:**

A. Most often caused by rate bites

B. Endemic to Ethiopia

C. Majority of cases are severe

D. Loss of vision

E. Endemic to Nigeria

F. Has very specific early clinical symptoms

G. Infectious cases may be imported to South Africa

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Lujo Hemorrhagic Fever:

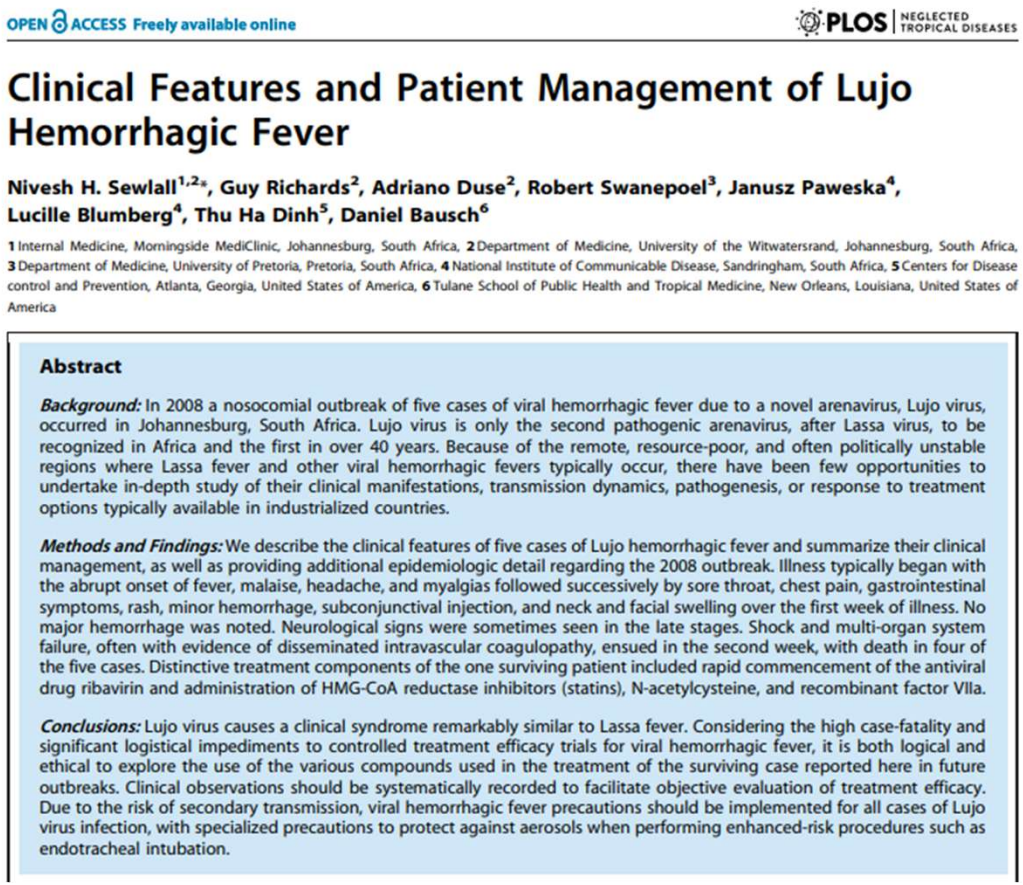
- Arenavirus
- Contact with infected rodents or their urine, droppings, or saliva
- **Nosocomial spread**
- One known outbreak:
- Sept – Oct 2008
- Zambia (Lusaka) & South Africa (Johannesburg)
- 5 cases (1 index and 4 HCW)
- 4 fatalities (80% CFR)

- Incubation : 7 to 13 days
- Symptoms of LUHF resemble those of severe Lassa fever
- Clinical improvement followed by death 10 to 13 days after onset of symptoms in the 4 patient who died
- Only surviving patient: Received IV ribavirin (early)

Sign or symptom	No. of patients manifesting the symptom	Mean day of illness in which sign or symptom first appeared (range)	Comments
Fever	5/5	1 (–)	Range: 38.2°C–40°C
Myalgia	5/5	1.2 (1–2)	
Sore throat or pharyngitis	5/5	3.2 (1–6)	
Nausea and/or vomiting	4/5	4.3 (2–8)	
Diarrhea	4/5	4.5 (2–7)	All diarrhea was nonbloody
Rash	4/5	5.8 (4–8)	Typically maculopapular, starting on the torso and spreading to the limbs
Oliguria	3/5	9.3 (7–11)	
Hemorrhage (excluding subconjunctival hemorrhage)	5/5	5.5 (3–8)	Includes vaginal bleeding (1/5, day 3), pharyngeal ecchymoses (2/5, days 6 and 7) and bleeding at central vein catheter insertion site (2/5, days 7 and 8), injection sites
Subconjunctival injection or hemorrhage	3/5	6.7 (6–7)	
Facial and/or neck swelling	4/5	7.0 (5–9)	
Neurologic signs	2/5	7.5 (5–10)	Includes tremor (1/5, day 5) and seizures (1/5, day 10)

DOI https://doi.org/10.2147/VAAT.S113593

Lujo Hemorrhagic Fever:



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PLOS | NEGLECTED TROPICAL DISEASES

Clinical Features and Patient Management of Lujo Hemorrhagic Fever

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Abstract

Background: In 2008 a nosocomial outbreak of five cases of viral hemorrhagic fever due to a novel arenavirus, Lujo virus, occurred in Johannesburg, South Africa. Lujo virus is only the second pathogenic arenavirus, after Lassa virus, to be recognized in Africa and the first in over 40 years. Because of the remote, resource-poor, and often politically unstable regions where Lassa fever and other viral hemorrhagic fevers typically occur, there have been few opportunities to undertake in-depth study of their clinical manifestations, transmission dynamics, pathogenesis, or response to treatment options typically available in industrialized countries.

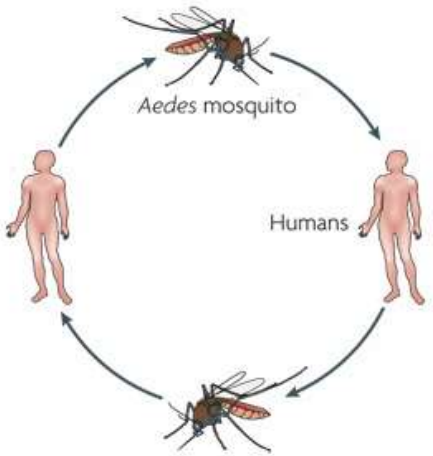
Methods and Findings: We describe the clinical features of five cases of Lujo hemorrhagic fever and summarize their clinical management, as well as providing additional epidemiologic detail regarding the 2008 outbreak. Illness typically began with the abrupt onset of fever, malaise, headache, and myalgias followed successively by sore throat, chest pain, gastrointestinal symptoms, rash, minor hemorrhage, subconjunctival injection, and neck and facial swelling over the first week of illness. No major hemorrhage was noted. Neurological signs were sometimes seen in the late stages. Shock and multi-organ system failure, often with evidence of disseminated intravascular coagulopathy, ensued in the second week, with death in four of the five cases. Distinctive treatment components of the one surviving patient included rapid commencement of the antiviral drug ribavirin and administration of HMG-CoA reductase inhibitors (statins), N-acetylcysteine, and recombinant factor VIIa.

Conclusions: Lujo virus causes a clinical syndrome remarkably similar to Lassa fever. Considering the high case-fatality and significant logistical impediments to controlled treatment efficacy trials for viral hemorrhagic fever, it is both logical and ethical to explore the use of the various compounds used in the treatment of the surviving case reported here in future outbreaks. Clinical observations should be systematically recorded to facilitate objective evaluation of treatment efficacy. Due to the risk of secondary transmission, viral hemorrhagic fever precautions should be implemented for all cases of Lujo virus infection, with specialized precautions to protect against aerosols when performing enhanced-risk procedures such as endotracheal intubation.

https://doi.org/10.1371/journal.pntd.0003233

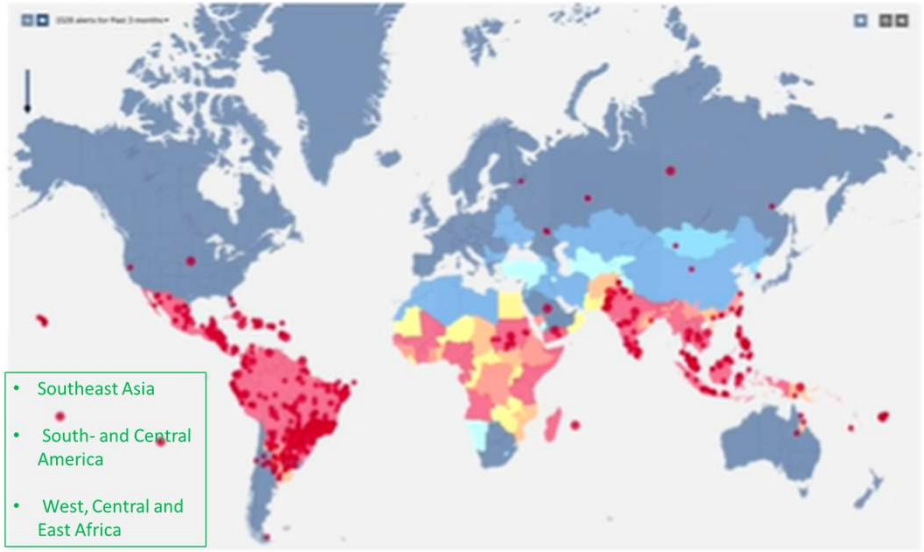
Dengue fever: Epidemiology

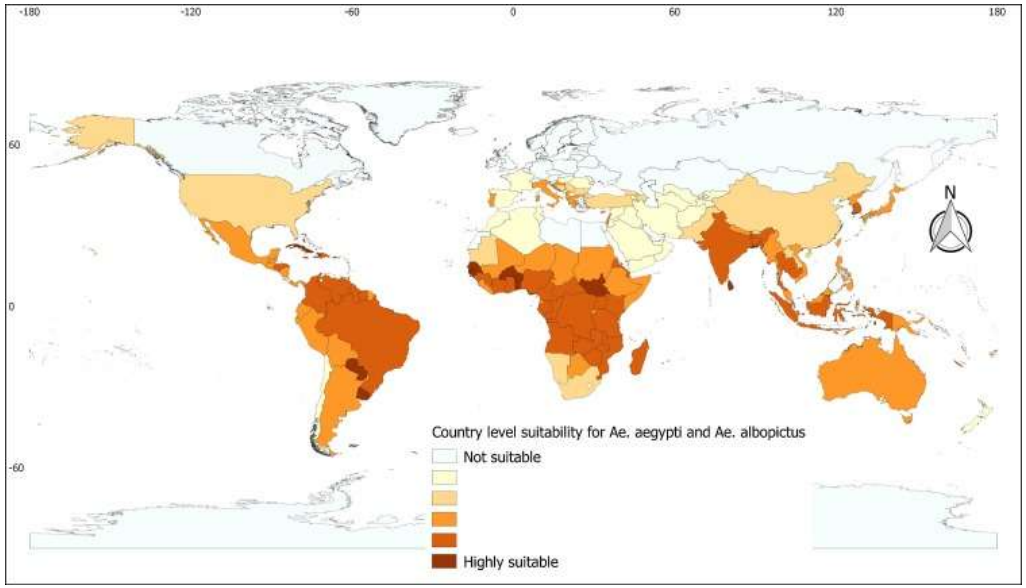
- 4 serotypes: DENV 1-4
- Mosquito-borne pathogen
- Principal vector = *Aedes aegypti*. (also other genera but limited *)*
- Mosquito–human–mosquito life cycle
- Secondary infection → significantly higher risk for severe dengue



Adapted from Whitehead, S. S. et al. Prospects for a dengue virus vaccine. Nature Reviews Microbiology 5, 518–528 (2007).

Cannot be spread directly from one person to another



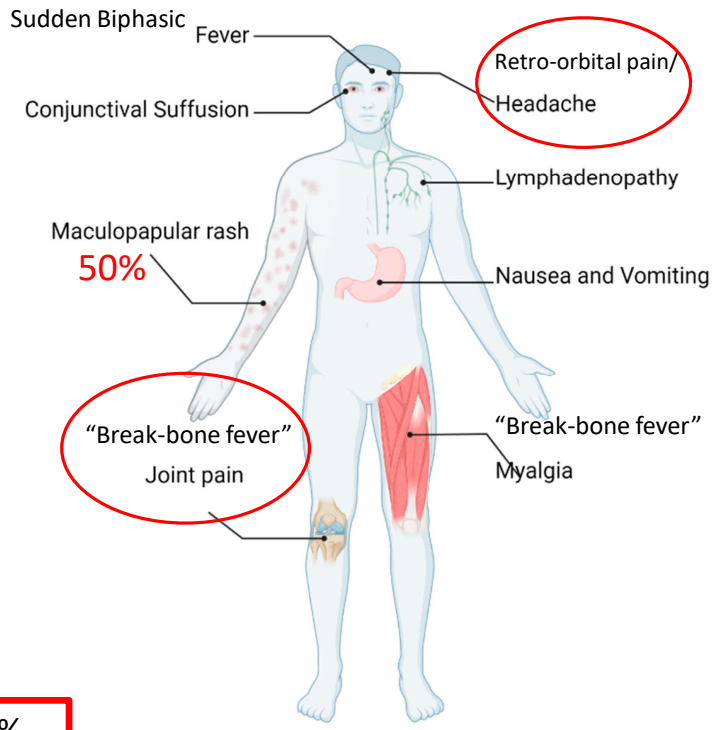


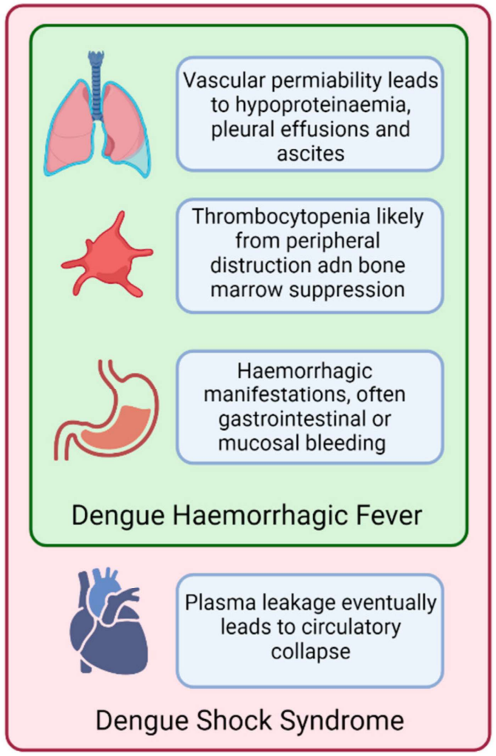
https://doi.org/10.1016/j.ijid.2017.11.026

Dengue Fever: Clinical manifestations

- Asymptomatic (±75%)
- Dengue Fever (non-specific febrile illness)
- Severe Dengue Fever:

- Dengue Haemorrhagic Fever (DHF)
- Dengue Shock Syndrome (DSS)





Dengue fever: self-limiting disease with a mortality rate < 1%

Severe dengue: Treated mortality rate: 2% - 5%
Untreated mortality rate: Can be high as 50%.

Febrile Phase
Onset commonly 5-7 days after bite

Critical Phase
Onset 4-5 days after fever

- Incubation period: 4-7 days (range=3-14 days)

Time to reflect:

- **A risk factor for severe dengue fever infection is:**

A. Previous primary infection with a different serotype
B. Male gender
C. Associated mostly with infection with serotype 1
D. Teenagers
E. Bite by Aedes albopictus instead of Aedes aegypti mosquito

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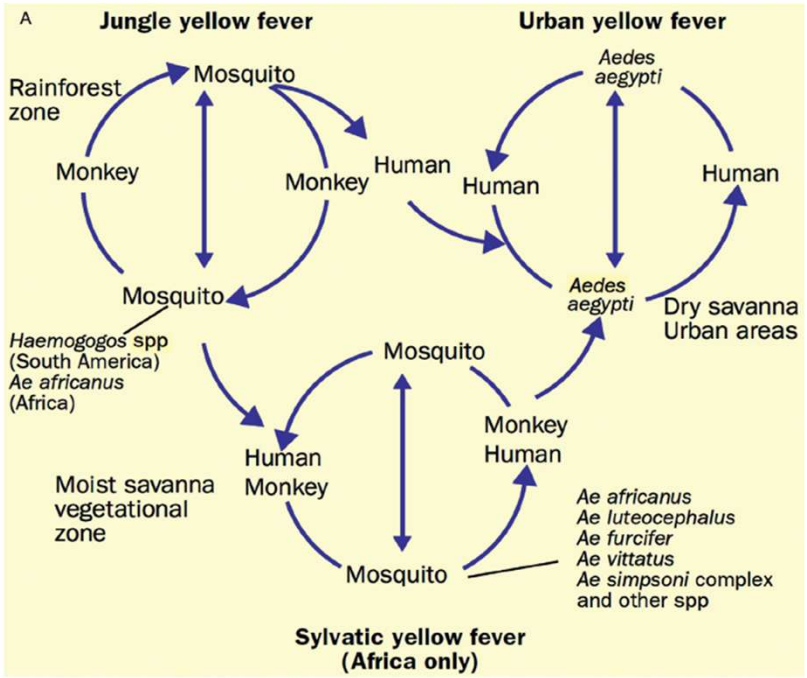
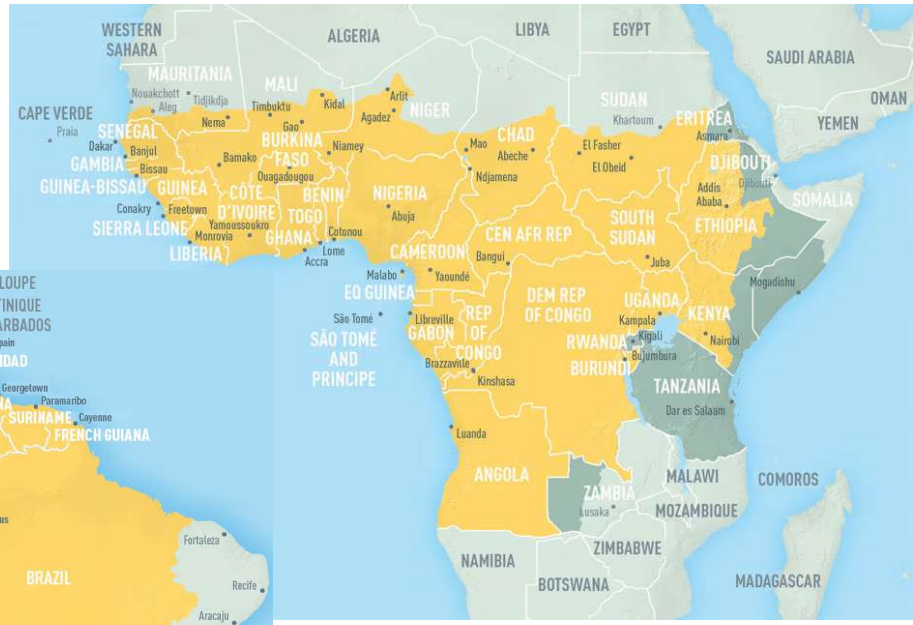
Yellow Fever: Epidemiology

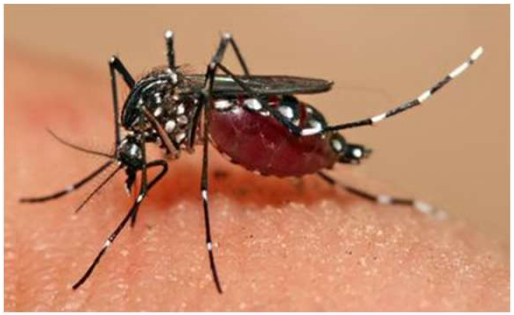
- Vector: Aedes aegypti mosquito
- No direct spread from one person to another documented



Monath, Lancet Infect Dis 2001

Yellow Fever Maps (cdc.gov)





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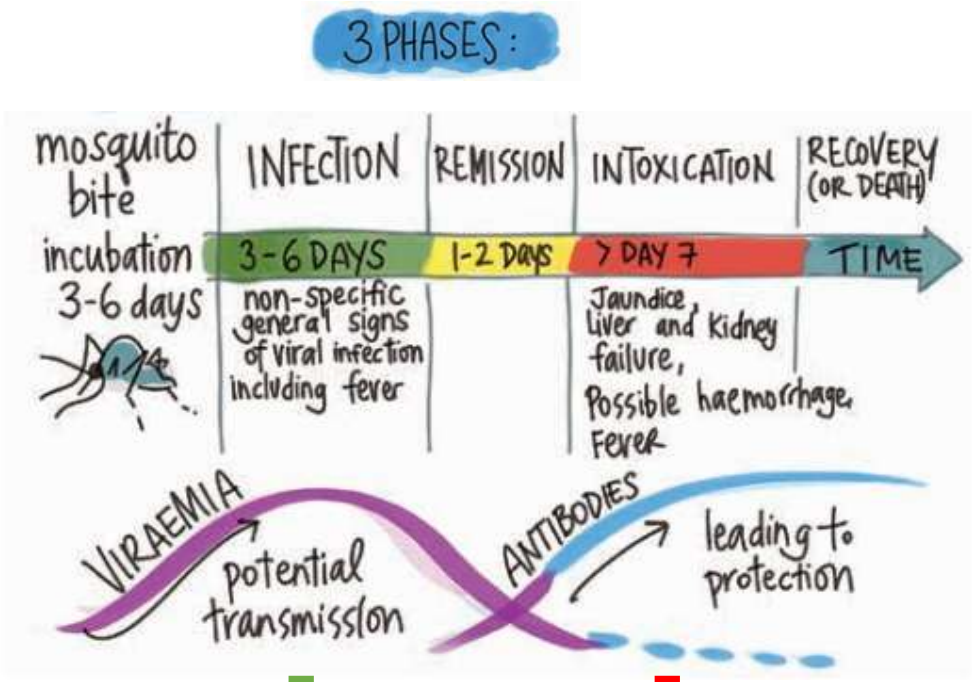
Yellow Fever: Clinical manifestations

Majority asymptomatic (88%)

OR



In most cases symptoms disappear after 3-4 days and patient recovers completely

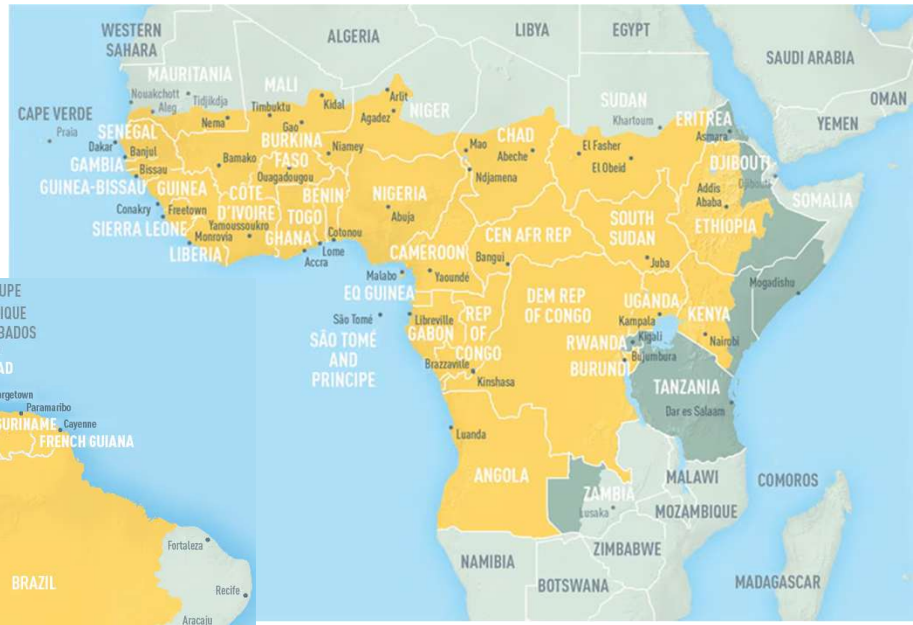
- 2-3% go into second phase
- 50% will die with 7-10 days
- 50% recover without significant organ damage

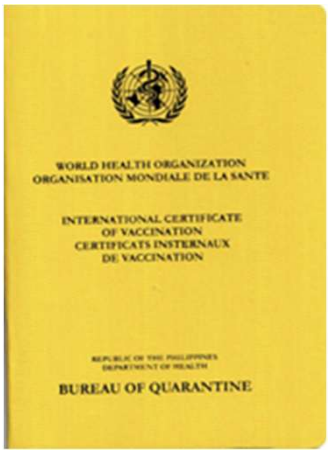
WHO/WHE/IHM/2019.11

Time to reflect:

- A yellow fever vaccine is recommended for a person travelling to the following countries:

A. Morocco
B. Kenya
C. Chile
D. Ghana
E. Mexico
F. Colombia

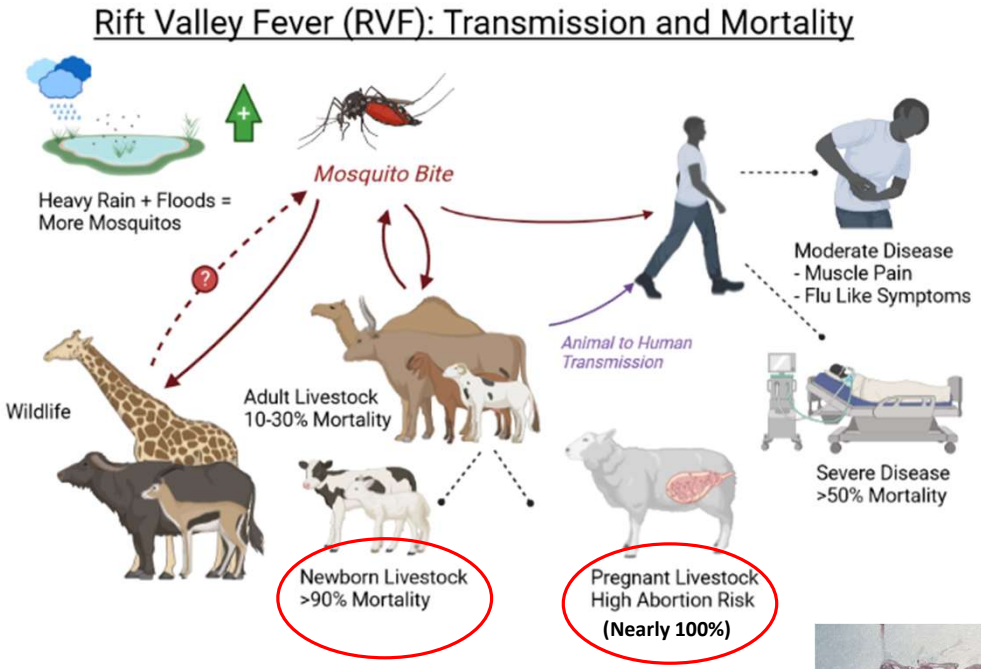




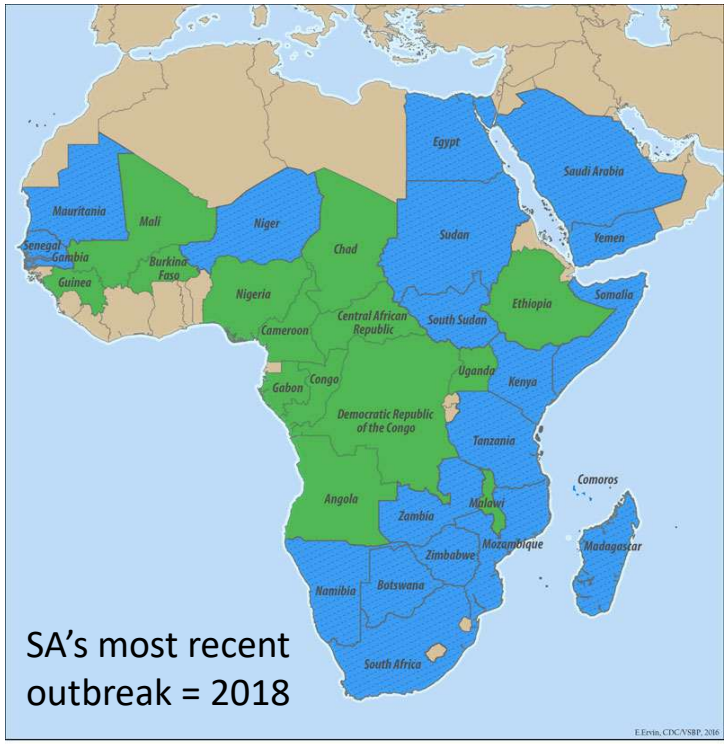
Rift Valley Fever Virus: Epidemiology

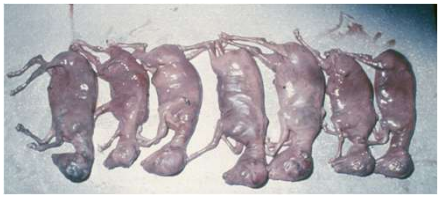
- Vector: Aedes species (and Culex) mosquitoes
- Incubation period: 2-6 days

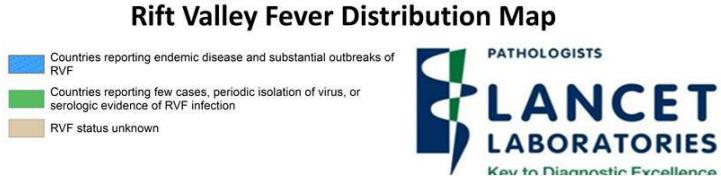
World Rift Valley Fever Distribution



Mode of Transmission:
- Most common is direct and indirect contact with infected animals, carcasses or meat,
- Less often from mosquito bites and unpasteurised milk from infected animals
- No documented person to person spread.







https://www.jenner.ac.uk/research/emerging-pathogens/rift-valley-fever-rvf

Rift Valley Fever Virus: Clinical manifestations

RIFT VALLEY FEVER (HUMAN)

Suspected case definition

A person with acute onset of fever > 38°C with at least one of the following symptoms: headache, loss of appetite, vomiting, diarrhoea, abdominal pain; and any of the following:

- ALT, AST or γ-GT level elevation (3 times above normal), clinical jaundice, hepatitis; OR
- features of encephalitis, such as confusion, disorientation, drowsiness, coma, neck stiffness, hemiparesis, paraparesis, or convulsions; OR
- bleeding into skin (ecchymosis, purpura, petechiae), vomiting of blood, blood in stool, or bleeding from rectum, nose, puncture sites or vagina, decreased platelets count; OR
- retinitis, unexplained acute vision loss or blind spots (scotomas); OR
- unexplicable sudden death with a history of fever, lethargy, diarrhoea, abdominal pain, nausea, vomiting, or headache in the preceding 2 weeks

AND

Any of the following epidemiological exposures:

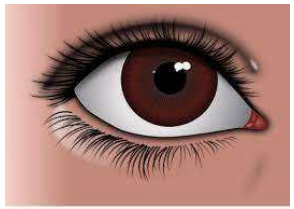
- a recent close contact with hoofed livestock and game animals in or from RVF-affected areas*, including slaughtering and butchering (traditional or commercial), disposal of carcasses and foetuses, assisting with birthing or other animal husbandry activities that resulted in exposure to animal blood and body fluids, or veterinary procedures and necropsies; OR
- History of recent mosquito bites and residing in RVF affected areas*; OR
- consuming unpasteurized milk from RVF-affected areas*.

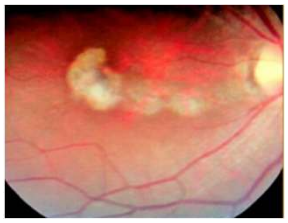
NICD

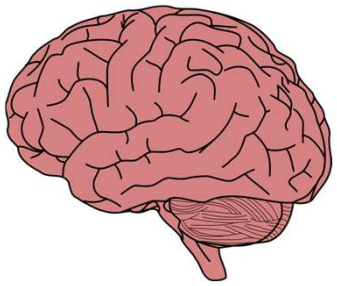
Most common (~90%): Asymptomatic or mild infection: Fever, headache, bleeding, malaise, muscle pain, back pain, vomiting, and joint pain. Recovery within a week.

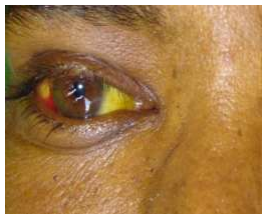
Less common (~10%) :

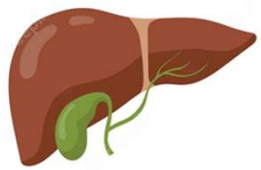
Eye (retinitis, acute vision loss, blind spots)
Meningoencephalitis (1%)
Hepatitis + Bleeding (VHF) (1%)











Mortality rate of patients with haemorrhagic form of RVF is high (up to 65%).

Time to reflect:

- **Which are <u>not</u> epidemiological risk factors for Rift Valley Fever:**

A. History of recent mosquito bites

B. Consuming pasteurized milk from RVF affected areas

C. Close contact with another person with RVF

D. Slaughtering livestock

E. Assisting with birthing livestock

F. Necropsy

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Investigations

- Discuss with NICD
- Alert the local lab
- Notify Category 1 Notifiable Medical Condition (NMC)*

- FBC: Low platelets, low WCC
- LFT: ALT, AST raised
- U&E: ↑ Creatine
- Prolonged INR/PT/aPTT

- Specific investigation to confirm diagnosis:

- Send 1x EDTA **AND** 1x yellow for PCR & serology

PCR	SEROLOGY
RT-PCR on blood (sample within first 5 days)	IgM ELISA (sample within first week)
False negative if tested after 1 week (viraemia declines)	-IgG ELISA (late in disease or convalescence) : Paired acute and convalescent samples show rise in titres
Fast (TAT 24-48 hours)	Cross reactivity within viral families
Specific and sensitive	Severe disease: may not develop Abs

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Sending away samples

DELAYS IN INFORMING NICD + SENDING CIF = DELAYS IN PROCESSING SPECIMENS

ATT: The Centre for Emerging Zoonotic and Parasitic Diseases, Special Viral Pathogens Laboratory, National Institute for Communicable Diseases,
1 Modderfontein Road,
Sandringham, South Africa

Tel: 011 386 6376 or 6338
082 903 9131

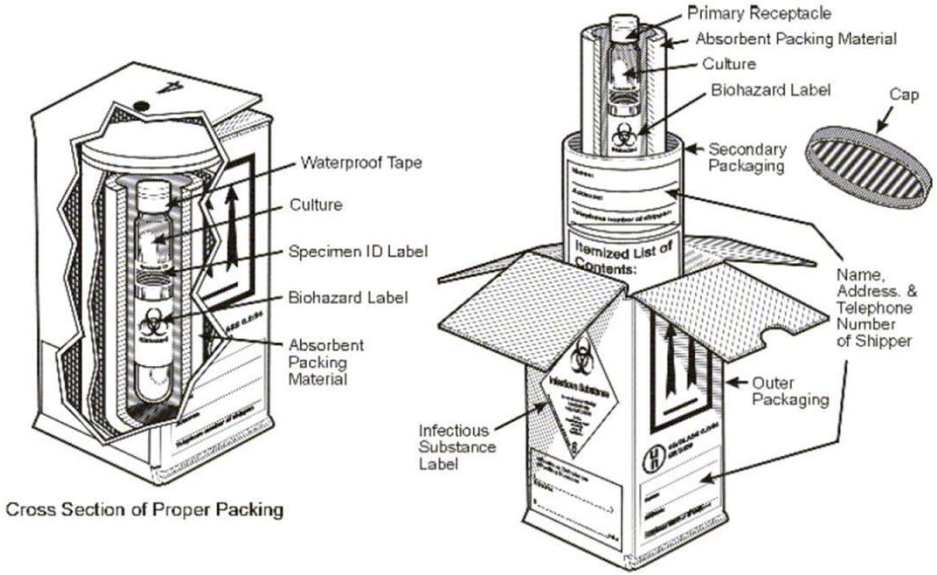

Figure 1: Diagram displaying category A, triple layer packaging.

Figure 2: Commercially available category A packaging that will be available to NHLS Laboratories (Courtesy of World Couriers)

Alert/discuss with NICD + local lab/ courier → Take sample with PPE → Wrap 1◦ tube in absorbent material e.g. paper towel → Place in several layers of sealed plastic bags or rigid screw top container. Tape closed → CIF +sample sealed separately in rigid outer container e.g. polystyrene cold box with ice packs → Address + contact numbers + outer biohazard warning labels

How to notify?

- Category 1: Immediate reporting telephonically and through the NMC app or written within 24hrs of clinically diagnosing a case

- Notify based on clinical suspicion DON'T WAIT FOR laboratory confirmation

- **Who?**

- HCW who suspects infection and requests laboratory testing should notify the case
- Both the public and private health sector

- Failure to report a NMC is a criminal offense

- https://www.nicd.ac.za/nmc-overview/notification-process/

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Management

- Supportive therapy is essential
- **Fluid management**:
- Prevent/treat shock
- Rehydrate: Oral or IV
- Monitor input/output
- **Correct electrolytes**
- **Avoid NSAIDS**
- If needed:
- Give blood products
- Respiratory support e.g. mechanical ventilation
- Antimicrobial therapy
- Hemodialysis
- Vasopressor and inotropic agents

- Specific treatments available :

Virus	Therapy
Ebola	• Two monoclonal Ab for adults, children and neonates against Zaire EV:
	- Ansuvimab/mAb114 (**Ebanga®**) single IV infusion
	- Atoltivimab/maftivimab/odesivimab or Inmazeb (**REGN-EB3®**) single IV infusion
	• Remdesivir (Less effective than mAb)

Virus	Therapy
Lassa	Off-label antivirals: Ribavirin (Most effective when given within the first six days after onset of symptoms), IV (?Oral at higher dose if no IV)
CCHF	Off-label antivirals: Ribavirin

Recovery & discharge from hospital:

- Clinical & RT-PCR to determine readiness for discharge
- WHO: Individuals who no longer have signs and symptoms + two negative PCR tests on whole blood separated by at least 48 hours
- Resource-limited settings: Absence of symptoms for 48 hours rather than PCR testing

- Counseling on safe sexual practices since the virus can persist in semen for up to several months after the plasma tests negative by RT-PCR
- Men who test positive at 3 months, testing should be repeated every month until their semen tests negative. The test should then be repeated with an interval of 1 week between tests. Sexual activity can be resumed if the semen has tested negative twice by RT-PCR
- If semen testing is unavailable, men should practice safe sex for at least 12 months from the onset of illness

- Marburg virus is known to persist in immune-privileged sites in some people who have recovered. These sites include the testicles and the inside of the eye.

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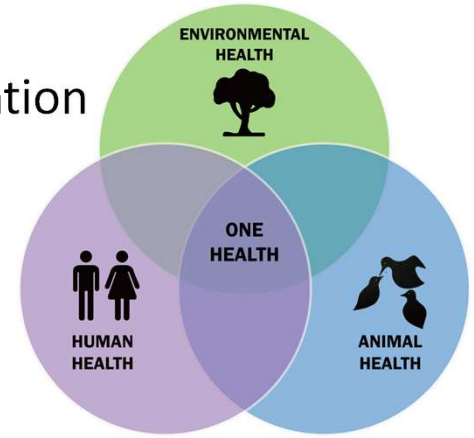
Prevention

- Education on risks & minimizing exposures
- Trace & monitor contacts
- PPE for HCWs/mine workers/tourists
- Safe sex and semen testing
- Chemical + heat inactivation (all enveloped viruses)
- Strict IPC including isolation
- One Health approach



Virus	Vaccines
Yellow Fever	• 17D vaccine • Live attenuated • Single dose • Lifelong immunity • Children and travelers to endemic countries
Ebola	• Two vaccines • Mainly used in outbreak setting • Not approved as PREP for travellers • Except USA: PREP (lab workers, Ebola HCWs) • rVSV-ZEBOV (Ervebo) stat IM, live recombinant, >1 yr, Zaire only • Ad26.ZEBOV (Zabdeno)/MVA-BN-Filo (Mvabea) , <1 yr, prime/boost, 2 months apart
Dengue	• Dengvaxia and Qdenga (TAK-003) - Children and adults living in endemic areas - Not approved as PREP for travellers

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Personal protective equipment
for use in a filovirus disease outbreak

World Health Organization

Rapid advice guideline

https://doi.org/10.1016/j.ajic.2018.08.014.

SUMMARY

Virus	Vector/ reservoir	Incubation period	CFR	H to H transmission	Vaccine	Specific Rx
Ebola	Bats + other mammals	2-21 days	>50%	**YES**	**YES**	**YES**
Marburg				**YES**	NO	NO
Lassa	Rodents		1%	**YES**	NO	**YES**
CCHF	Tick, infected animals	1-14 days	3-30%	**YES**	NO	**YES**
Dengue	Mosquitoes	4-10 days	**DF**: <1% **SD with Rx**: ±5 % **SD without Rx:** Up to 50%	NO	**YES**	NO
Yellow Fever		3-6 days	**Mild:** <1% **Intoxication stage:** 50%	NO	**YES**	NO
Rift Valley	Infected animals, mosquitoes	2-6 days	Up to 65% with haemorrhagic form	Theoretical risk (No documented cases)	NO	NO

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Take home messages for VHF:

- Remember VHF in the returning traveller with fever
- Overlap in clinical symptoms: Epidemiological link is key
- Know geography/consult a map/look up endemic infections/outbreaks
- If in doubt → Call an expert for help
- Identify → Isolate → Inform (majority are **category 1 pathogens**)
- Early diagnosis = Better outcomes
- Don't be caught off-guard: Know what questions to ask, how to protect yourself, who to call, what samples to take, where and how to send samples

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USEFUL CONTACT NUMBERS

REQUIREMENT	CONTACT NUMBER	CONTACT PERSON/S
Reporting of suspected case	0800 212 552	NICD Pathologist on call
Clinical advice regarding suspected cases	0800 212 552	NICD Pathologist on call
Queries regarding laboratory testing	011 386 6376 011 386 6338 jacquelinew@nicd.ac.za naazneenm@nicd.ac.za	Dr Jacqueline Weyer/ Dr Naazneen Moolla
Queries regarding laboratory results	011 386 6376 011 386 6338 jacquelinew@nicd.ac.za naazneenm@nicd.ac.za	Dr Jacqueline Weyer / Dr Naazneen Moolla

Useful resources:

NATIONAL INSTITUTE FOR COMMUNICABLE DISEASES
Division of the National Health Laboratory Service

https://www.nicd.ac.za/

World Health Organization

https://www.who.int/

CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

https://www.cdc.gov/vhf/index.html

ISID ProMED
INTERNATIONAL SOCIETY FOR INFECTIOUS DISEASES

https://promedmail.org/

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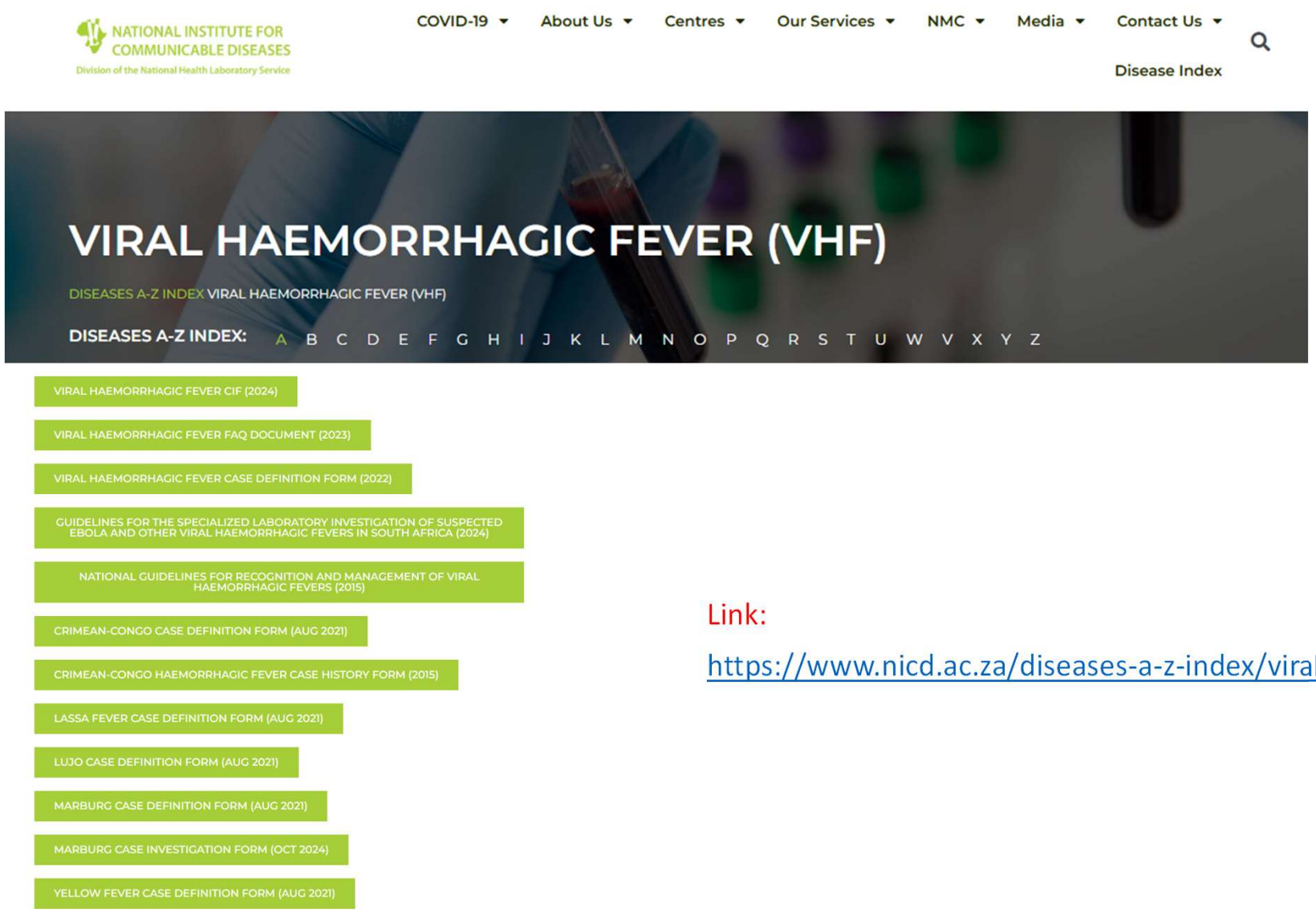

Link:

https://www.nicd.ac.za/diseases-a-z-index/viral-haemorrhagic-fever-vhf/

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THE END