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Emerging zoonotic threats:

Ebolavirus and Hantavirus

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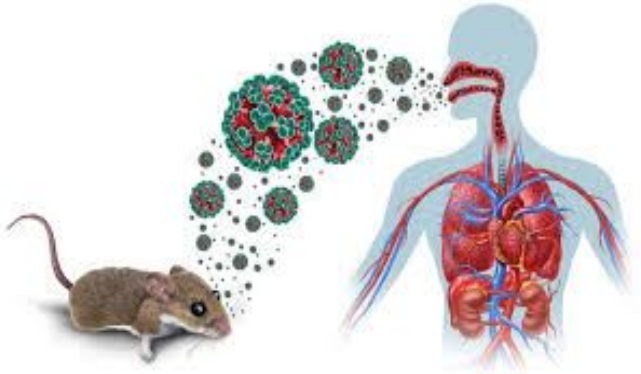


Introduction to Ebola Virus and Hantavirus

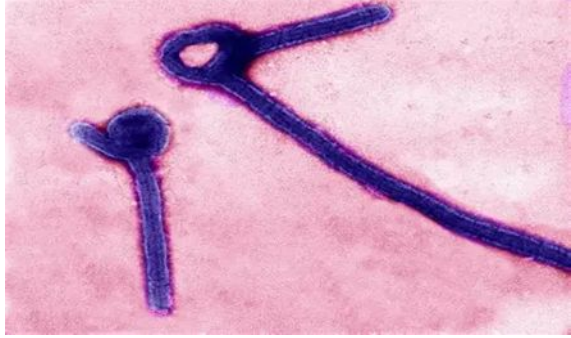
- Ebola virus disease (EVD) and hantavirus infections are important emerging zoonotic viral diseases.
- Ebola outbreaks mainly occur in Central and West Africa, with case fatality rates averaging ~50%.
- Hantaviruses are rodent-borne viruses causing Hemorrhagic Fever with Renal Syndrome (HFRS) and Hantavirus Pulmonary Syndrome (HPS).
- Estimated yearly infections:

✔ Ebola – hundreds to thousands during outbreaks

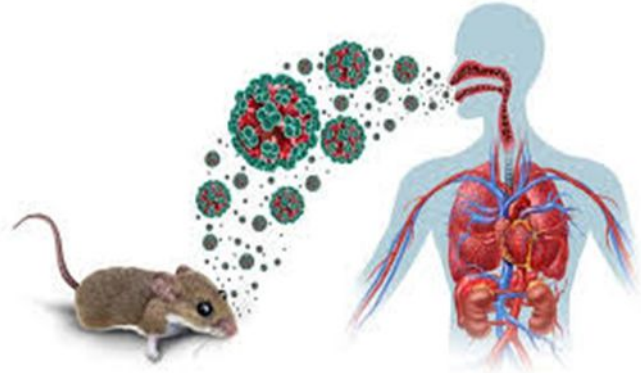
"Emerging zoonotic diseases remain a major global public health challenge."

✔ Hantavirus – approximately 10,000 to >100,000 infections annually worldwide.

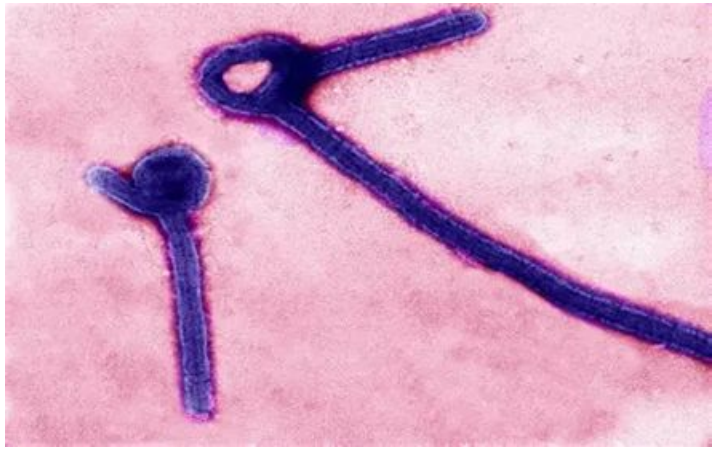
May 2026



- Ebola Virus Disease:
  - ✔ Bundibugyo strain outbreak in DRC & Uganda
  - ✔ Declared a Public Health Emergency of International Concern by WHO
  - ✔ 100 deaths, CFR ~30–50%
- Andes Hantavirus
  - ✔ Outbreak aboard MV Hondius cruise ship
  - ✔ 9 confirmed cases, 3 deathsCFR ~27–30%
  - ✔ Unique: person-to-person transmission possible

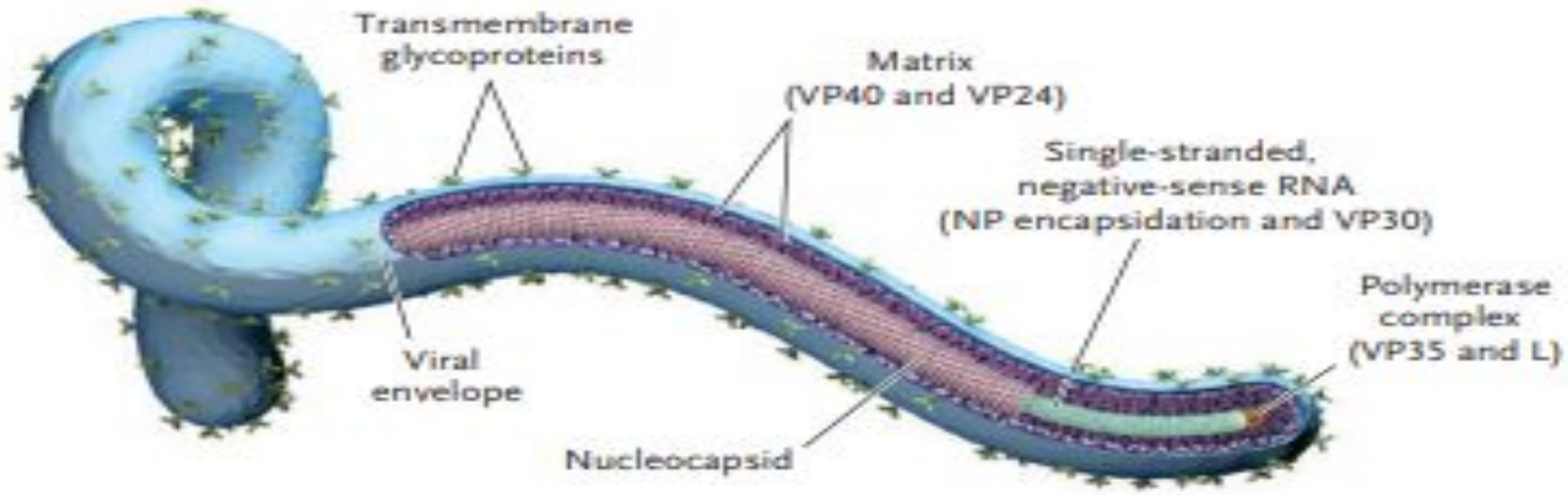


EBOLA VIRUSES



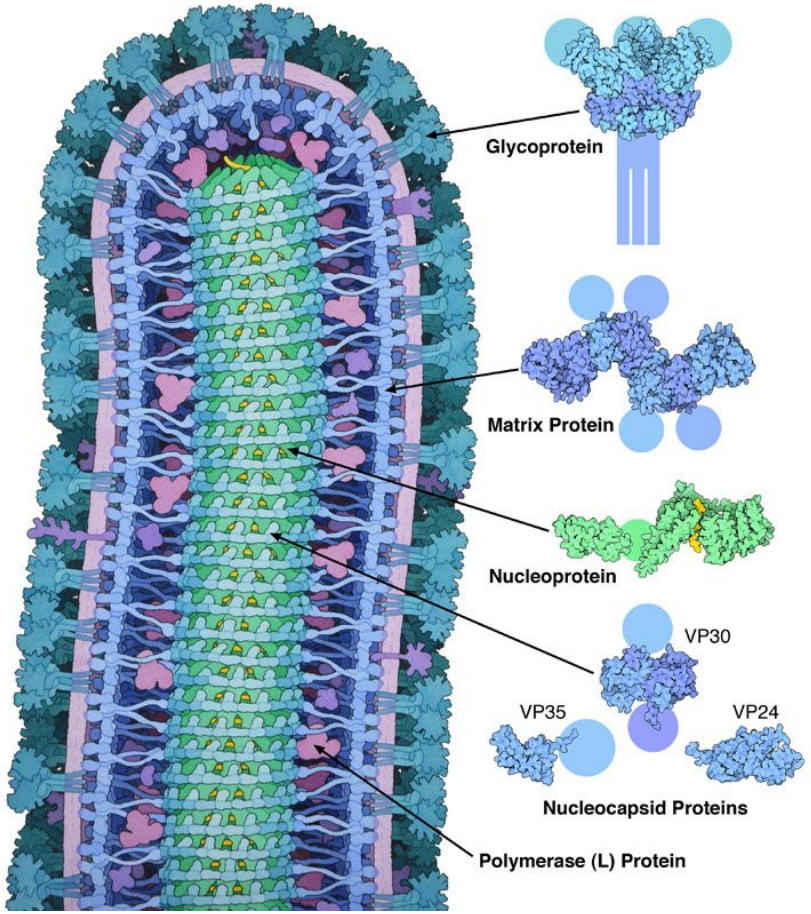
Virology and structure

- Ebolaviruses classified within the *family Filoviridae* , *Genus Ebolavirus*
- Six recognized species, *four* causes disease in humans
- The most lethal is *Zaire ebolavirus*, responsible for the largest outbreaks



Virology and structure

- Enveloped
- Filamentous particles
- Non-segmented ,negative sense RNA genome
- Inactivated by heat, detergents, UV, and disinfectants



Species	Abbreviation	Region of Discovery	Human Disease?	Notes
Zaire ebolavirus	EBOV	DRC (1976)	Yes	Highest mortality rate; caused 2014–2016 West Africa outbreak
Sudan ebolavirus	SUDV	Sudan (1976)	Yes	Lower mortality than EBOV; caused Uganda outbreaks
Bundibugyo ebolavirus	BDBV	Uganda (2007)	Yes	Moderate mortality (~25%)
Taï Forest ebolavirus	TAFV	Côte d'Ivoire (1994)	Yes (rare)	Only one human case documented

Feature	Zaire EBOV	Sudan SUDV	Bundibugyo BDBV
Case Fatality Rate (CFR)	Highest: 70–90%	Moderate: 50–65%	Lowest: ~25%
Human-to-Human Transmission	Very efficient; responsible for largest outbreaks (West Africa 2014–2016)	Efficient, but outbreaks smaller than EBOV	Efficient, but less sustained transmission compared to EBOV
Genetic Diversity	Baseline reference; GP highly adapted for receptor binding	~50% nucleotide identity vs EBOV; moderate divergence	~32% divergence in GP vs EBOV; **weaker receptor binding**
Host/Reservoir	Likely fruit bats (esp. *Hypsignathus monstrosus*, *Epomops franqueti*, *Myonycteris torquata*)	Fruit bats suspected; reservoir not fully confirmed	Fruit bats suspected; discovered in Uganda outbreak (2007)

- **All three viruses use the same receptor set**
- The difference **lies in binding affinity of the glycoprotein (GP) to the receptors**
- Genetic diversity in GP → determines how **well the virus attaches to and enters host cells.**
- EBOV GP binds most strongly, translating into higher viral loads and more severe disease
- BDBV GP binds less efficiently, explaining its lower mortality and smaller outbreaks.

Epidemiology

Transmission

- **Zoonotic** Origin
- Fruit bats are the main reservoir
- Spillover occurs via contact with blood, secretions, or organs of infected animals i.e. Monkeys, chimpanzees, gorillas, porcupines, forest antelopes

Human-to-Human Transmission:

- Direct contact with blood, secretions, organs, or other bodily fluids of infected persons.
- Indirect contact via contaminated materials (bedding, clothing, medical equipment)
- Sexual transmission -Virus persists in semen up to 6 months post-recovery
- Burial ceremonies- Direct contact with corpses drives superspreading
- Healthcare settings- High risk when infection control measures are not followed.

Epidemiology

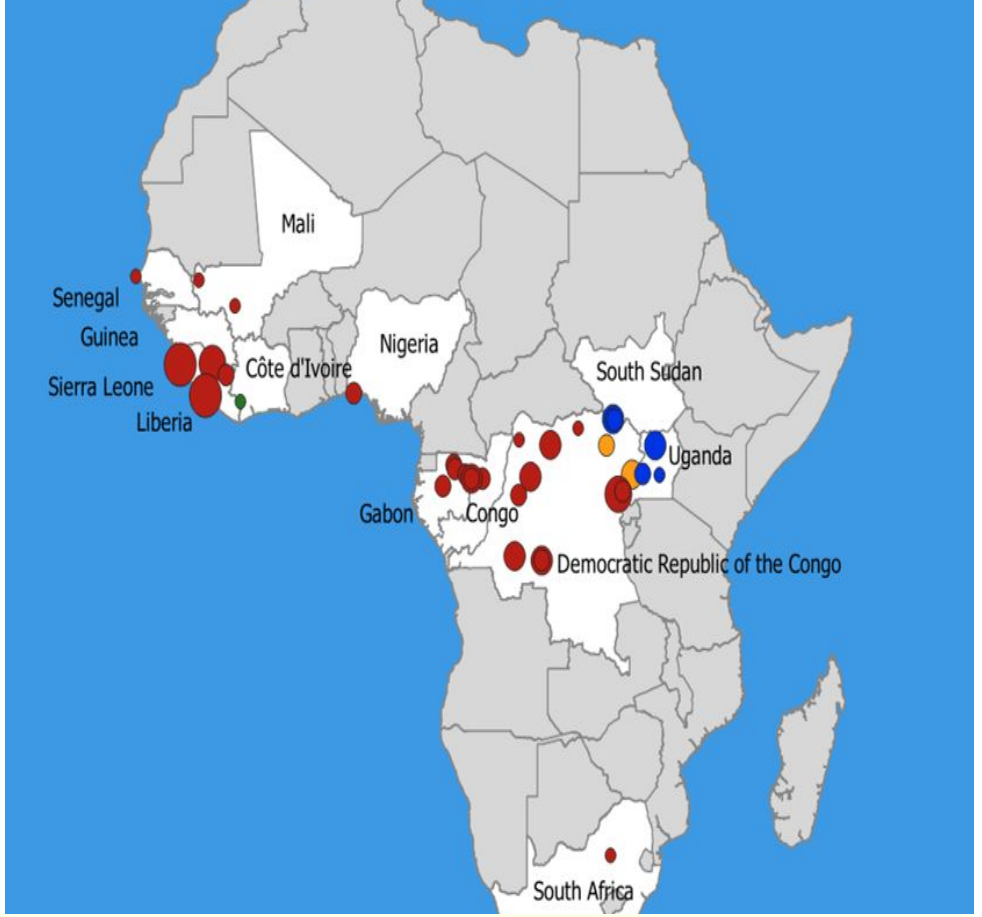
- Reproductive Number (R_o) is the average number of secondary infections caused by one infected individual in a fully susceptible population
- Ebola R_o = 1.2 – 2.5
- SARSCOV-2 R_o = 2.5-3.5
- Measles R_o =12 -18
- Influenza R_o= 0.9-2.1

Virus	**R_o Range**	**Transmission Efficiency**	**CFR**
Zaire EBOV	1.7–2.5	Highest, sustained epidemics	70–90%
Sudan SUDV	1.3–2.0	Moderate outbreaks	50–65%
Bundibugyo BDBV	1.2–1.6	Smaller outbreaks	~25%

Epidemiology

Geographic distribution

- Most outbreaks occur in:
  - ✔ Central Africa
  - ✔ West Africa
- Countries frequently affected:
  - ✔ Democratic Republic of the Congo
  - ✔ Uganda
  - ✔ Sudan
  - ✔ Guinea
  - ✔ Sierra Leone
  - ✔ Liberia



Ebolavirus	*Bundibugyo ebolavirus*	Bundibugyo virus (BDBV)	DRC, Uganda
	Sudan ebolavirus	Sudan virus (SUDV)	DRC, South Sudan
	Taï Forest ebolavirus	Taï Forest virus (TAFV)	Ivory Coast
	Zaire ebolavirus	Ebola virus (EBOV)	DRC, Gabon, Guinea, Liberia, RC, Sierra Leone

Pathogenesis of Ebola Virus

- Entry & Incubation (2–21 days)
  - ✔ Virus enters via mucosa/skin breaks
  - ✔ Early replication in dendritic cells and macrophages
- Immune Evasion
  - ✔ VP35/VP24 proteins block interferon response
  - ✔ Virus suppresses innate immunity.
- Dissemination
  - ✔ Spread to lymphoid tissues → bloodstream
  - ✔ Infects multiple organs (liver, spleen, kidneys)
- Organ Damage
  - ✔ Liver necrosis → ↑ AST/ALT
  - ✔ Immune cell infection → cytokine storm
- Systemic Effects

✔ Uncontrolled replication → vascular leakage

✔ Decreased plasma volume

✔ Coagulation abnormalities → hemorrhage

Disease mechanism:

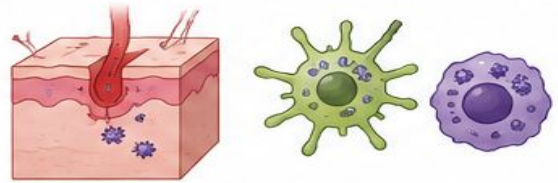
- Driven by **host immune response**
- Excessive production of **cytokines and chemokines** → "cytokine storm"
- **Direct cytopathic effects**:

✔ intracellular inclusion bodies(accumulation of viral proteins and RNA leads to inclusion bodies)

✔ cell lysis(viral particles assemble and bud, the cell's structural integrity is disrupted)

PATHOGENESIS OF EBOLA VIRUS

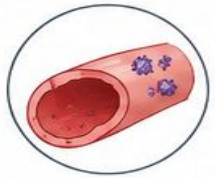
1 ENTRY & INCUBATION (2–21 days)
- Virus enters via mucosa/skin breaks
- Early replication in dendritic cells and macrophages



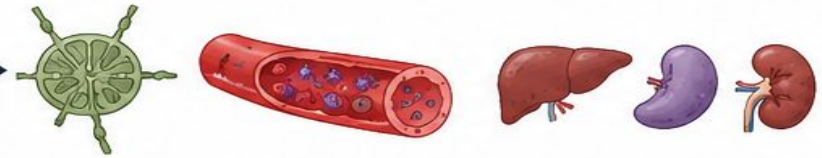
Initial replication in dendritic cells and macrophages

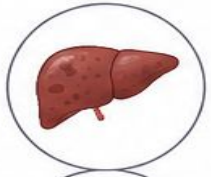
2 IMMUNE EVASION
- VP35/VP24 proteins block interferon response
- Virus suppresses innate immunity

Blocked interferon response → decreased production of cytokines and chemokines = "cytokine storm"



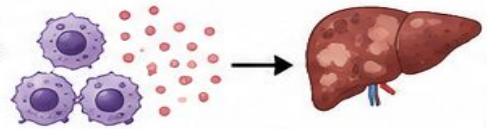
3 DISSEMINATION
- Spread to lymphoid tissues → bloodstream
- Infects multiple organs (liver, spleen, kidneys)





4 ORGAN DAMAGE
- Liver necrosis → ↑ AST/ALT
- Immune cell infection → cytokine storm

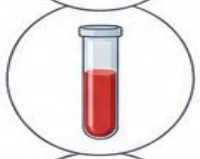
Infected immune cells release large amounts of cytokines



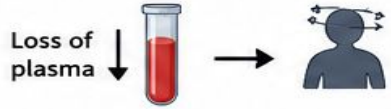
Hepatocyte necrosis → elevated AST/ALT

5 SYSTEMIC EFFECTS
- Uncontrolled replication → vascular leakage

Increased vascular permeability → leakage of plasma and proteins



6 DECREASED PLASMA VOLUME
- Loss of plasma and fluids → hypovolemia



Hypovolemia (shock)

7 COAGULATION ABNORMALITIES
- Coagulation abnormalities → hemorrhage

Impaired clotting + endothelial damage → bleeding (internal and external)

DISEASE MECHANISMS

Dysregulated immune response
Ebola virus evades and overwhelms the immune system.

Excessive production of cytokines and chemokines → "cytokine storm"
Leads to systemic inflammation and tissue damage.

Direct cytopathic effects
Viral replication causes death of infected cells.

Infection and destruction of viral proteins and RNA leads to inclusion bodies
Disrupts normal cell function and contributes to organ failure.

Cell by cell/viral protein assembly and bud, the cell structure integrity is disrupted
Leads to cell death and further viral spread.

Pathogenesis Comparison: Zaire vs Bundibugyo

	Zaire EBOV	Bundibugyo BDBV
Incubation Period	2–21 days (avg. 8–10)	2–21 days (avg. 7–9)
Receptor Binding (GP)	Strong affinity for NPC1, TIM-1, DC-SIGN → high viral entry	Weaker binding → lower viral loads
Immune Evasion (VP35/VP24)	Potent interferon suppression → strong cytokine storm	Less effective suppression → milder cytokine response
Organ Damage	Severe liver necrosis, high AST/ALT	Moderate liver involvement
Systemic Effects	Intense vascular leakage, coagulopathies abnormalities, haemorrhage	Reduced vascular damage, fewer bleeding complications
Case Fatality Rate (CFR)	70–90%	~25%
Outbreak Scale	Large, sustained epidemics (West Africa 2014–2016)	Smaller, localized outbreaks (Uganda 2007)

Clinical Features


Ebola produces a bleeding rash that can start out flat, then form into blisters that fill with blood.

Incubation period

- 3-8 days in index cases & slightly longer in secondary cases ~21days

Signs and symptoms vary by disease

- Early: Non-specific Influenza-like illness (ILI)

i.e fever, headache, fatigue, dizziness, muscle aches ,rash

- Vomiting & diarrhoea are frequent, incl abdominal pain

Severely ill cases

- Multisystem syndrome - multiple organ systems are affected
- Coagulation defects, vasodilation & increased vascular permeability leads to
  - Conjunctival injection with petechial haemorrhage,
  - bleeding under the skin, in internal organs, or from body orifices
  - Oedema, hypotension and shock

VHFs: Diagnostic Testing

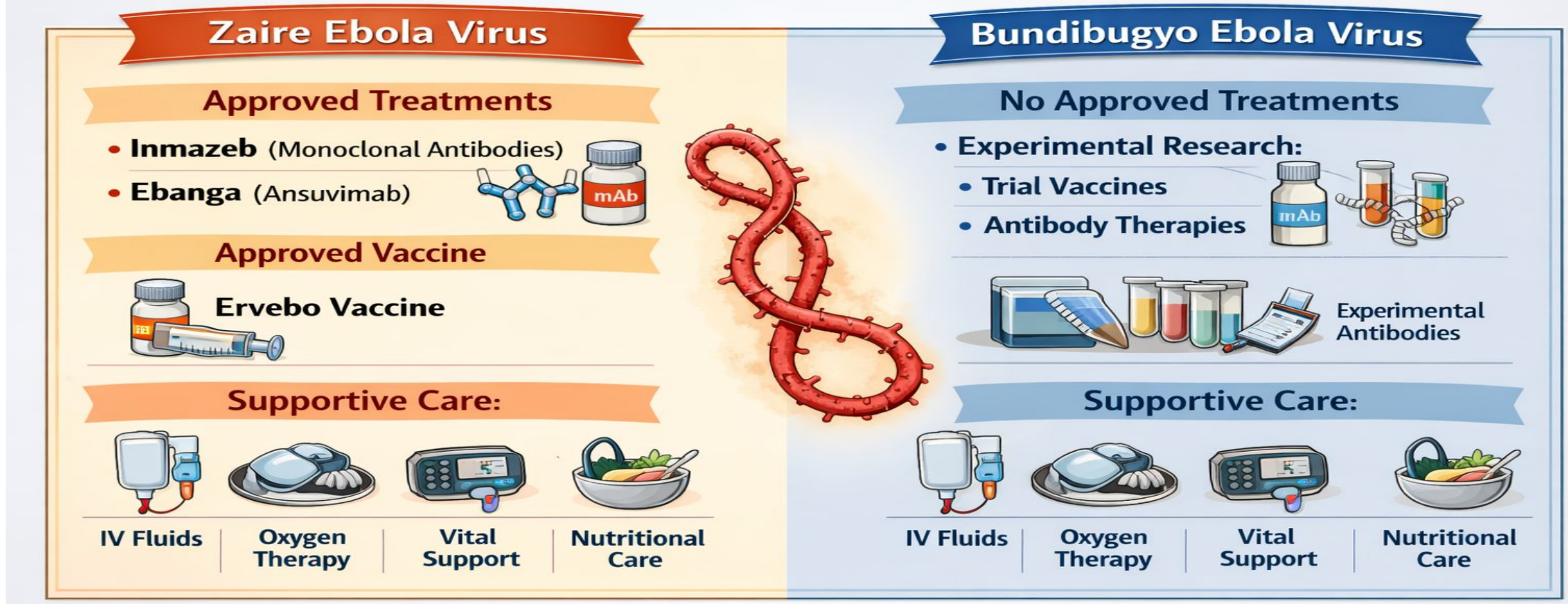
❖ **Routine bloods**

- FBC: Thrombocytopenia and low or normal white cell counts
- LFT: Raised liver enzyme

❖ Specific testing

- Serological screening
  - IgG and IgM antibodies
- Molecular testing
  - **PCR detection of viral genomic material (DNA or RNA)**
- Virus isolation
- **Tests performed under biosafety level 4 conditions (i.e. maximum bio-containment)**

Ebola Treatment & Vaccines



- Ervebo (Merck) — used in ring vaccination strategies.
- Zabdeno/Mvabea (Janssen) — two-dose regimen for preventive use.

- Inmazeb (REGN-EB3): cocktail of three monoclonal antibodies
- Ebanga (ansuvimab): single monoclonal antibody
- Both bind to the viral glycoprotein, preventing entry into host cells.

Bundibugyo Ebolavirus experimental vaccines

- **ChAdOx1 BDBV** :

✔ Chimpanzee adenoviral vector (ChAdOx1)

✔ Phase I

- **IAVI rVSV**

✔ BDBVRecombinant vesicular stomatitis virus (rVSV)

✔ Preclinical

- **Moderna mRNA BDBV**

✔ mRNA (lipid nanoparticle)

✔ Preclinical

- Ervebo is licensed against Zaire ebolavirus; its efficacy against Bundibugyo virus remains unproven and is being evaluated

Preclinical (animals)

↓

Phase I

Safety + antibody + T-cell responses

↓

Phase II

Optimal dose + expanded safety

↓

Phase III

Protection during outbreaks (or using immune correlates when outbreaks are absent)

↓

Regulatory approval

Recommendations for recovered male patients

- Start semen testing 3 months after disease onset
- Repeat testing until 2 consecutive negative PCR tests
- Interval between negative tests ≥1 week apart
- If testing unavailable: Abstain or use condoms consistently for at least 12 months after disease onset or until testing confirms clearance
- Female survivors: No prolonged sexual precautions comparable to those for male survivors are recommended because persistent virus in vaginal secretions has not been demonstrated.

Emerg Microbes Infect. 2024 May 7;13(1):2352520. doi: 10.1080/22221751.2024.2352520

Bundibugyo Ebolavirus Outbreaks & Challenges

Previous Outbreaks

- 2007 – Uganda: 149 cases, 37 deaths – first discovery.
- 2012 – DRC: 36 cases, 13 deaths – spread in Orientale Province.
- 2026 – DRC & Uganda: 30 confirmed, 500 suspected cases – declared a Public Health Emergency of International Concern.

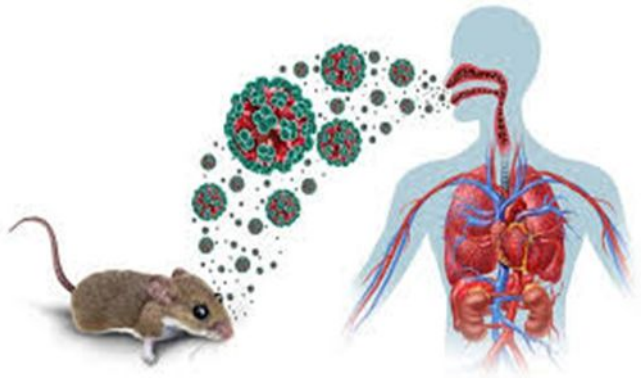
Key Challenges (2026 Outbreak)

- No vaccines or treatments – unlike Zaire strain, only supportive care available.
- Community transmission in conflict zones – insecurity hinders surveillance and response.
- Cross-border spread to major cities – Kampala & Kinshasa at risk of wider transmission.
- Healthcare worker infections – reduces frontline capacity and public trust
- Diagnostic limitations-

✔ Bundibugyo strain is rare and genetically distinct, making early detection difficult

✔ Standard Ebola tests may yield false negatives, delaying isolation and treatment.

HANTAVIRUS



Classification

As of 2017, the Bunyaviridae family was promoted to the order Bunyavirales, and the genera were elevated to family status:

- Orthobunyavirus Peribunyaviridae
- **Hantavirus Hantaviridae**
- Nairovirus Nairoviridae (Crimean Congo hemorrhagic fever virus)
- Phlebovirus Phenuiviridae (Rift Valley virus)

Characteristics of Hantaviruses

- Unique among genera of Bunyaviridae

No arthropod vector established

- Rodent hosts

Each hantavirus is typically associated with a specific rodent reservoir species

- Transmission

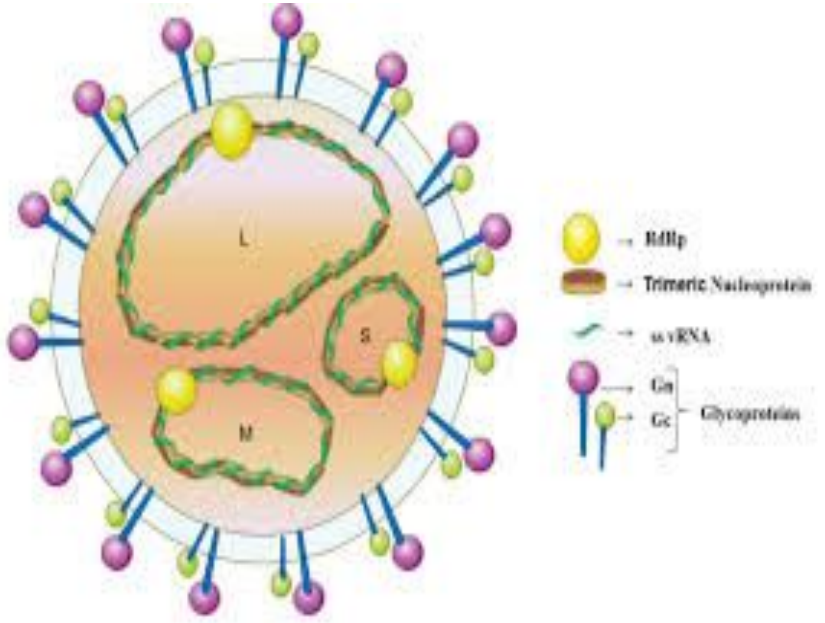
Aerosolization of rodent excret

Virology and structure

- Enveloped,
- Genome: negative-sense, segmented, single-stranded RNA viruses.
- Inactivated by heat, detergents, UV, and disinfectants.
- Genetic divergence

✔ Old World (HFRS-causing) and New World (HPS-causing) hantaviruses is ~25–35% nucleotide difference

✔ Andes virus and related strains (Laguna Negra, Rio Mamoré) show ~20–30% across genome segments



Classification of hanta viruses

Old World Hantaviruses

Europe and Asia

- Hantaan virus
- Seoul virus
- Puumala Virus(mild disease)
- Dobrava virus
- Cause hemorrhagic fever with renal syndrome (HFRS)

New World Hantaviruses

North, Central and South America

- Black Creek Canal
- Andes virus (South America)
- Sin Nombre Virus
- Cause hantavirus pulmonary syndrome (HPS)

Andes virus although extremely rare it can spread from human to human, the only documented one to have spread among humans

Virus	Reservoir	Transmission Mode	Estimated R_0	Notes
Andes virus	Oligoryzomys longicaudatus (pygmy rice rat)	Rodent-to-human + human-to-human	~1.2–2.5	Only hantavirus with sustained person-to-person spread; outbreaks in Argentina and Chile show superspreading events.
Puumala virus	Bank vole (Myodes glareolus)	Rodent-to-human	<1	Causes nephropathia epidemica (mild HFRS); no human-to-human transmission.
Dobrava virus	Field mice (Apodemus spp.)	Rodent-to-human	<1	Severe hemorrhagic fever with renal syndrome (HFRS); localized outbreaks.
Sin Nombre virus	Deer mouse (Peromyscus maniculatus)	Rodent-to-human	<1	Causes hantavirus pulmonary syndrome (HPS) in North America; no human-to-human spread.
Seoul virus	Rats (Rattus norvegicus)	Rodent-to-human	<1	Global distribution; mild to moderate HFRS; spread via pet/trade rats.

Genetic Diversity in Hantaviruses: Andes vs Others

Genetic Diversity & Spread

- Andes virus
  - ✔ Only hantavirus with person-to-person transmission.
  - ✔ Genetic variants (e.g., Epuyén strain) linked to superspreading events.
- Other hantaviruses
  - ✔ Spread only via rodent-to-human exposure (aerosolized urine/feces).
  - ✔ $R_0 < 1$, outbreaks remain sporadic and localized

- **Receptors & Entry**
- Andes virus receptors
  - Uses β3-integrins on endothelial cells.
  - Genetic diversity in glycoproteins (Gn/Gc) **alters binding affinity, potentially enhancing human infection.**
- Other hantaviruses receptors
  - Also target integrins, **but differences in glycoprotein sequences affect tissue tropism and severity**.
  - Example: Puumala virus → kidney involvement; Sin Nombre virus → lung involvement.

Genetic Diversity in Hantaviruses: Andes vs Others

Viral Load & Shedding

- Andes virus viral load
  - ✔ High RNA levels in blood, saliva, urine, and gingival fluid.
  - ✔ Extended shedding increases risk of human-to-human transmission.
- Other hantaviruses viral load
  - ✔ Viral RNA mostly detected in blood during acute phase.
  - ✔ No evidence of sustained shedding in body fluids → explains lack of human-to-human spread.

- **Disease Severity**
- Andes virus disease
  - ✔ Causes **Hantavirus Pulmonary Syndrome (HPS)** with 20–40% fatality.
  - ✔ Rapid progression to respiratory failure; often requires ECMO support.
- Other hantaviruses disease
  - ✔ Puumala virus → mild nephropathia epidemica (low fatality).
  - ✔ Dobrava virus → severe hemorrhagic fever with renal syndrome (higher fatality).
  - ✔ Sin Nombre virus → HPS in North America, ~35% fatality but no human-to-human spread

Epidemiology :Transmission

- Rodents are the primary reservoirs
- Inhalation of virus containing aerosols from rodent excretions such as urine, faeces and saliva
- The risk of infection is highest among people who clean, work, play, or live in spaces with infected dried rodent droppings and urine
- Direct contact with contaminated materials
- Rarely from rodent bite
- Human to human transmission can occur although rare and requires close contact eg people in the same house hold/care giver / intimate patner.

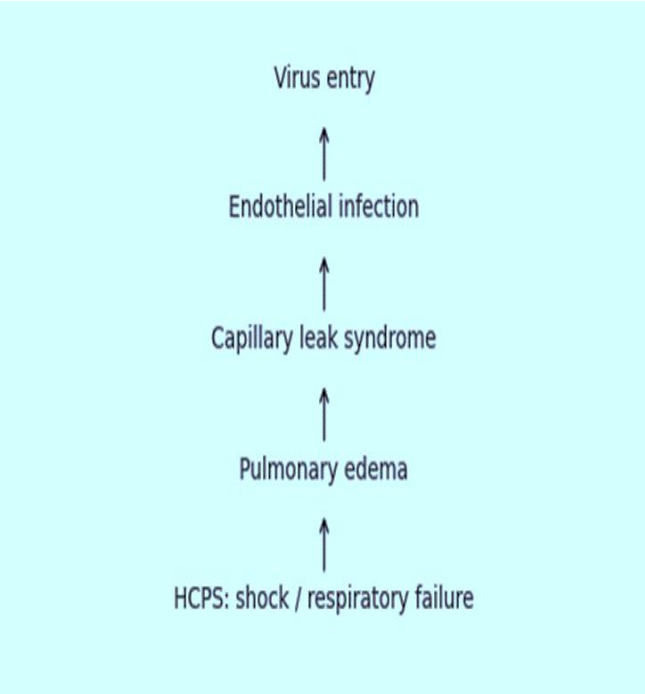
Incubation period

- Overall range 1 to 8 weeks after exposure
- Most commonly: 2 to 4 weeks
- Hantavirus Pulmonary Syndrome (HPS): Often develops 1 to 8 weeks after exposure
- Hemorrhagic Fever with Renal Syndrome (HFRS): Usually has an incubation period of 2 to 3 weeks, but can range from a few days to 6 weeks
- Ussually no transmission during incubation in most cases

Andes virus:
Typically 7–42 days
up to ~6 weeks reported

Pathogenesis

- Virus infects endothelial cells
- Increased vascular permeability
- Capillary leak syndrome
- Pulmonary edema → Hantavirus Cardiopulmonary Syndrome
- Immune response contributes to tissue damage



Clinical Features of HFRS

- Symptoms: fever, headache, abdominal pain, nausea.
- Can progress to kidney failure and hemorrhage.
- Five phases: febrile, hypotensive, oliguric, polyuric, recovery.
- Mortality ranges from <1% to 15%.

Clinical Features of HCPS

- Begins with flu-like symptoms

✔ Fever

✔ Severe myalgia

✔ Headache

✔ Fatigue

- Abdominal Symptoms: Nausea, vomiting, abdominal pains
- Case fatality range 20-40%

<u>Clinical phases of HCPS</u>

- Prodromal phase (1-3 days)
- Cardiopulmonary phase
- Shock phase
- Convalescence if survived

Clinical Features

2nd phase is critical if untreated patient can die

Pulmonary form

- Rapid onset:
- Cough
- Shortness of breath
- Tachypnoea (rapid, shallow breathing >20 breaths per minute in adults)
- Progression to: Pulmonary edema (fluid in lungs)Hypoxia
- Respiratory failure

Diagnosis & Treatment

- Patient History NB!!! Travel history to endemic area or contact with sick person
- Diagnosis: ELISA, immunofluorescence, **RT-PCR.**
- Treatment is mainly supportive care.
- Ribavirin may help in some HFRS cases.
- No FDA-approved specific therapy.

Treatment for Andes Virus

- No specific antiviral universally approved
- Supportive ICU care critical
- Early oxygenation and ventilation
- ECMO in severe cases improves survival

Andes Virus Outbreaks & Challenges

Previous Outbreaks

- **1995 Argentina** First described in humans; linked to rodent exposure.
- **1995 Chile** Identified the long-tailed pygmy rice rat (*Oligoryzomys longicaudatus*) as the reservoir.
- **2018–2019 Epuyén, Argentina** 34 confirmed cases, 11 deaths; superspreading event at a social gathering; clear evidence of human-to-human transmission.
- **2026 – MV Hondius Cruise Ship**-At least 11 confirmed cases and 3 deaths across multiple countries; passengers repatriated to Europe and the U.S.; WHO and CDC monitoring contacts globally.

Key Challenges (2026 Outbreak)

- Person-to-person transmission -Unlike other hantaviruses,especially in close contact settings (families, healthcare, enclosed spaces).
- Diagnostic limitations - Early PCR tests may yield false negatives ,incubation period is longer, complicating monitoring and isolation.
- International spread risk -Passengers disembarked in multiple countries before detection; contacts across Europe, Africa, and the U.S. are under surveillance

PREVENTION/INFECTIOUS CONTRL

Andes Virus: Human-to-Human Prevention

- Strict contact precautions
- Avoid close face-to-face contact
- No sharing of utensils or bedding
- Respiratory **droplet precautions i**n early illness

- **Burial of hantavirus** (including Andes virus) cases requires strict infection control

  - **Ebola:** Very high risk after death → extreme precautions (double bags, chlorine spraying, no family contact).
  - **Andes virus:** Lower risk, but **still requires PPE and sealed handling** because of possible human-to-human transmission.

Healthcare Infection Control

- Standard droplets precautions
- Isolate suspected cases
- Use PPE: N95, gloves, gown, eye protection
- Negative pressure rooms if available
- Safe handling of specimens

How to Handle a VHFs Case

- **NB: Infection control is paramount!**

- Management & infection control officer to be informed
- Isolate the pt
- Pt managed by trained health care staff
- Use standard precautions for infection control
  - PPE – to cover skin & mucous membrane
  - Hand washing
  - Handle sharps safely and dispose by incineration

- Observe universal precaution in handling diagnostic specimen
- Care taken to avoid aerosolized material
- Safe disinfection of spills, equipment & supplies – use hypochlorite
- **Safe handling & burial of corpses**
- **Educate family & community on prevention & control of VHFs**

PPE Donning for VHFs Cases

- **Tyvek oversuit** / surgical scrub suits with impervious gowns &
- Disposable balaclavas
- Double-gloving
- N95 respirators
- Goggles/visors
- Impervious overshoes

Conclusion

- Emerging viruses, zoonotic spillover, and global travel turn local outbreaks into international threats
- Genetic diversity and unique transmission patterns complicate control and increase risk
- Preparedness and surveillance are vital for early detection and containment
- Community education and research strengthen resilience and innovation
- Health system strengthening ensures rapid response and protection of healthcare workers.

Ndo livhuwa. Aa!