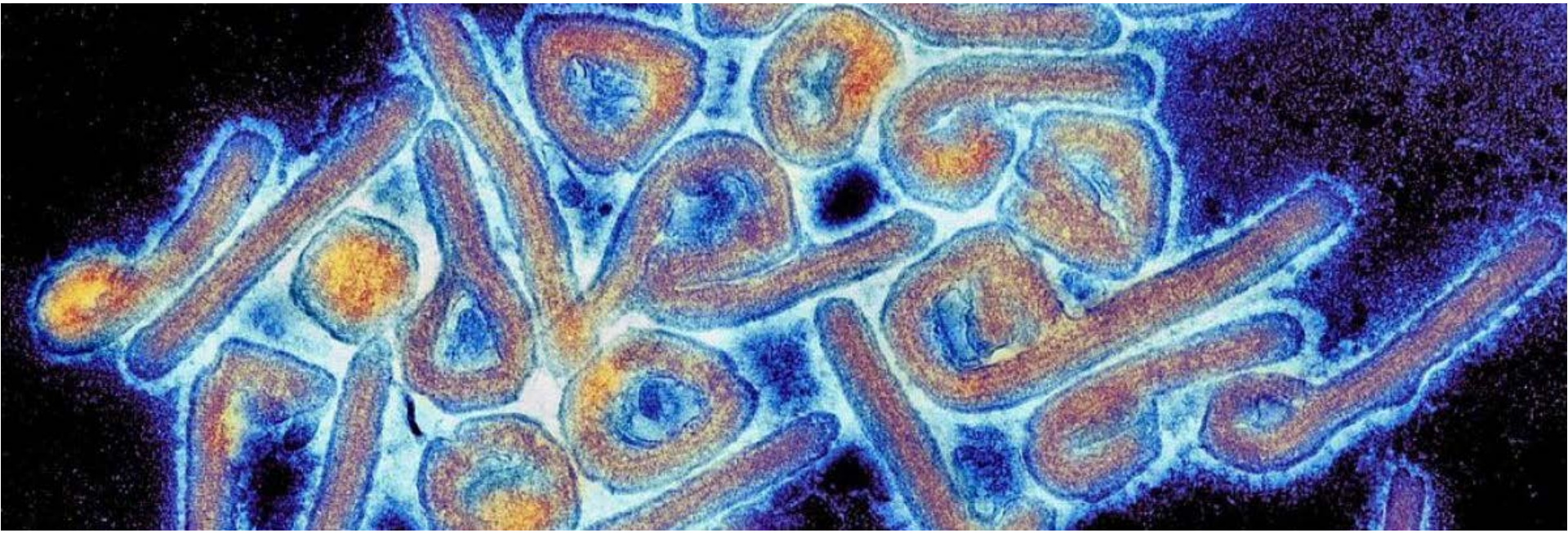


Marburg virus disease: A deadly rare virus is coming.

Fang Zhao , Yun He , Hongzhou Lu, 2022. BioScience Trends (IF: 5.7)
Presented on November 25th, 2024

MSc. Juan Manuel Mendoza Méndez
Dr. CA García-Sepúlveda

Laboratorio de Genómica Viral y Humana
Facultad de Medicina
Universidad Autónoma de San Luis Potosí

Marburg virus (MARV), what is it?

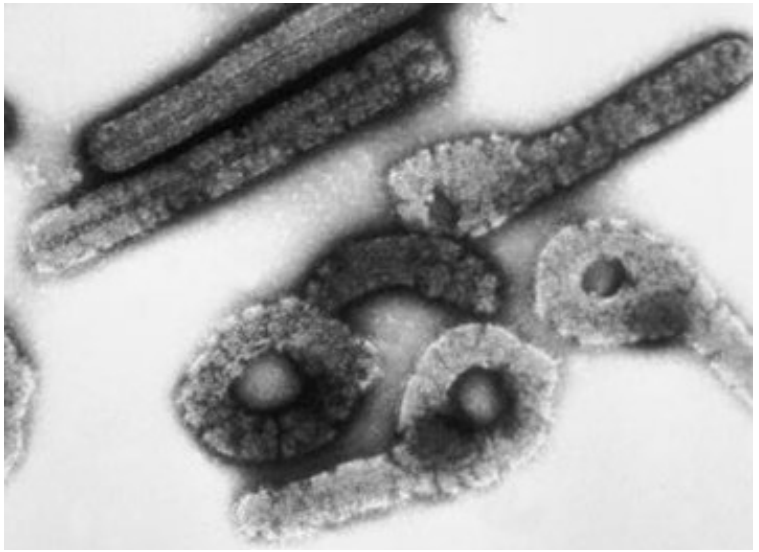
Enveloped, (-)ssRNA virus.

800 – 14,000 nm.

More infectious when 790 nm.

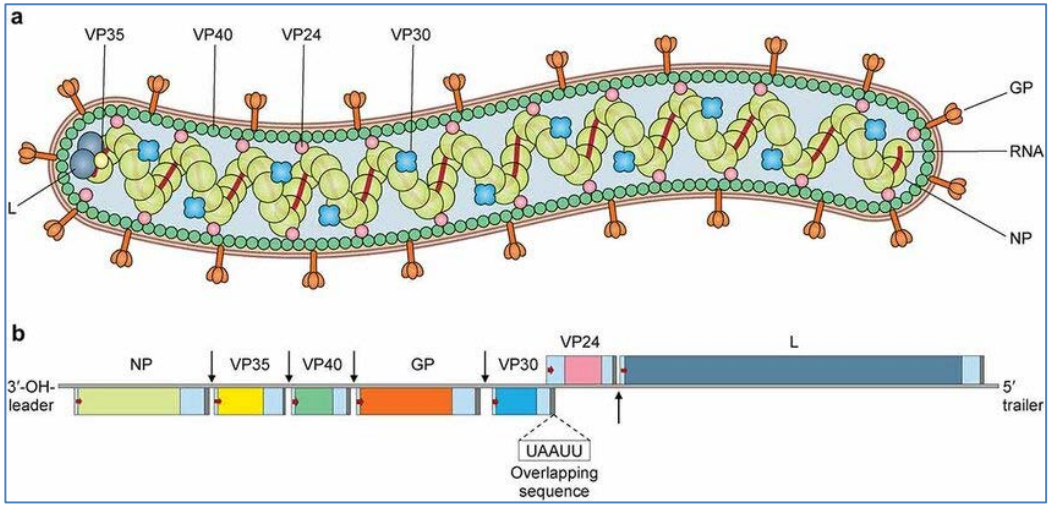
Identical to the Ebola virus in structure

MARV genome encodes 7 structural proteins.



Family: *Filoviridae*
Genus: *Orthomarburgvirus*
Species: Marburg, Ravn

Blue: Non-coding
Red arrows: Transcription start
Grey bars: Transcription stop
Blakc arrows: Intergenic regions



Marburg outbreaks

First reported in 1967 after outbreaks in Marburg, Frankfurt and Belgrade.

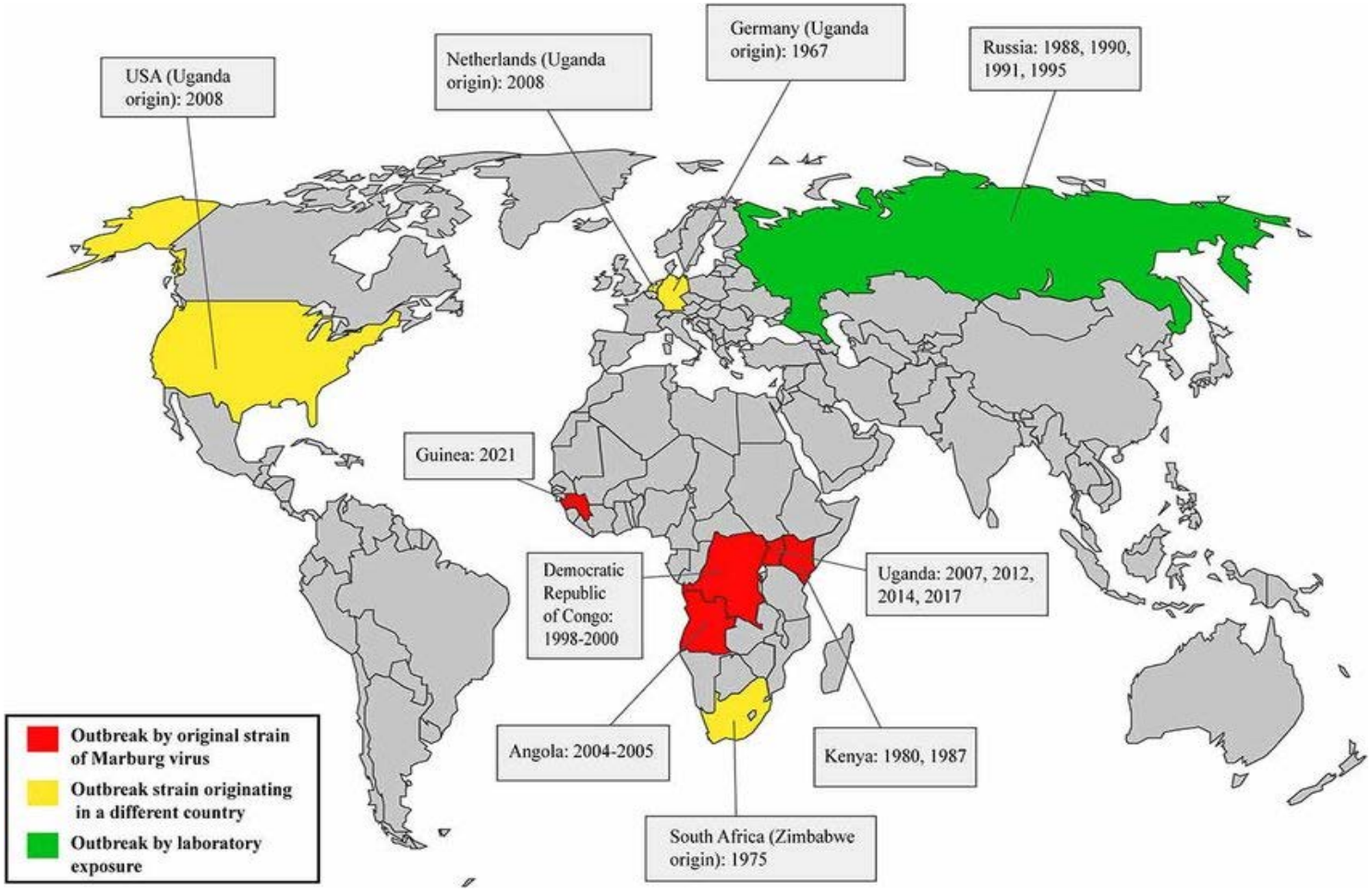
The origin traced to a laboratory using green monkeys imported from Uganda.

Chronology of major Marburg virus disease outbreaks

Year	Country	Suspected origin	Cases	Deaths (mortality rate)	Notes
2022	Ghana	Under investigation	2	2 (100%)	
2021	Guinea	Guinea	1	1 (100%)	
2017	Uganda	Uganda	4	3 (75%)	
2014	Uganda	Uganda	1	1 (100%)	
2012	Uganda	Uganda	15	4 (27%)	
2008	Netherlands	Uganda	1	1 (100%)	Imported
2008	USA	Uganda	1	0 (0)	Imported
2007	Uganda	Uganda	4	1 (25%)	
2004-2005	Angola	Angola	252	227 (90%)	
1998-2000	Democratic Republic of the Congo (DRC)	DRC	154	128 (83%)	
1990	Russia	Russia	1	1 (100%)	Laboratory accident
1987	Kenya	Kenya	1	1 (100%)	
1980	Kenya	Kenya	2	1 (50%)	
1975	South Africa	Zimbabwe	3	1 (33%)	Imported
1967	Germany and Yugoslavia	Uganda	31	7 (23%)	Imported & lab leak

Marburg outbreaks

Most human infections reported in Angola, the Congo, Kenya, South Africa, Uganda and Zimbabwe, along with a laboratory accident in Russia.



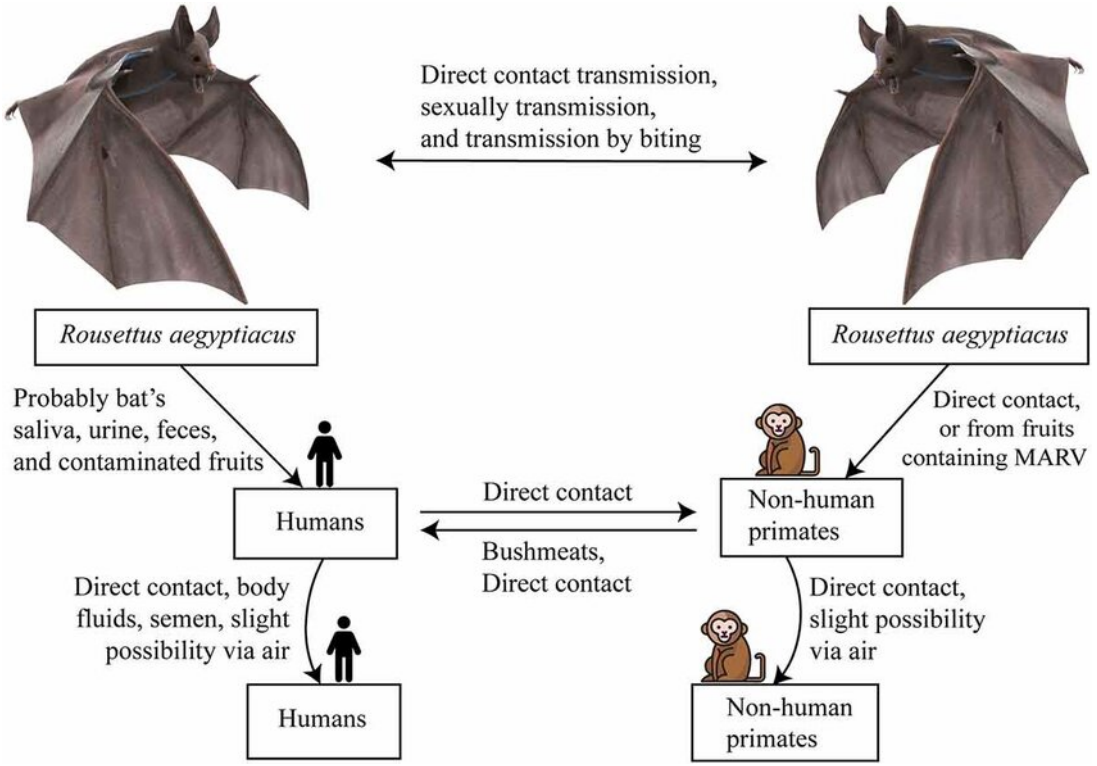
Reservoir and intermediate hosts

Isolated from egyptian fruit bat, in 2009.

Remain chronically infected but free of symptoms (reservoir and natural host).

African green monkeys and pigs play a role as amplifier (intermediate) hosts.


Egyptian fruit bat *(Rousettus aegyptiacus)*



Transmision

Cann be transmitted animal-to-human or human-to-human via direct contact with:

- Blood
- Secretions
- Organs
- Bodily fluids
- Contaminated surfaces
- Placenta
- Amniotic fluid
- Breast milk

Person-to-person transmission occurs in households and health care settings

Through mucous membranes or broken skin.

Needle stick injury in health care settings.

Persist in eyes and testes of convalescent patients.

No evidence that MARV can be transmitted ns by mosquitoes or other arthropods.

Clinical findings in Marburg Virus Disease (MVD)

Incubation period 3–21 days (typically 5–10) and related to infectious dose and route.

Three stage clinical course.

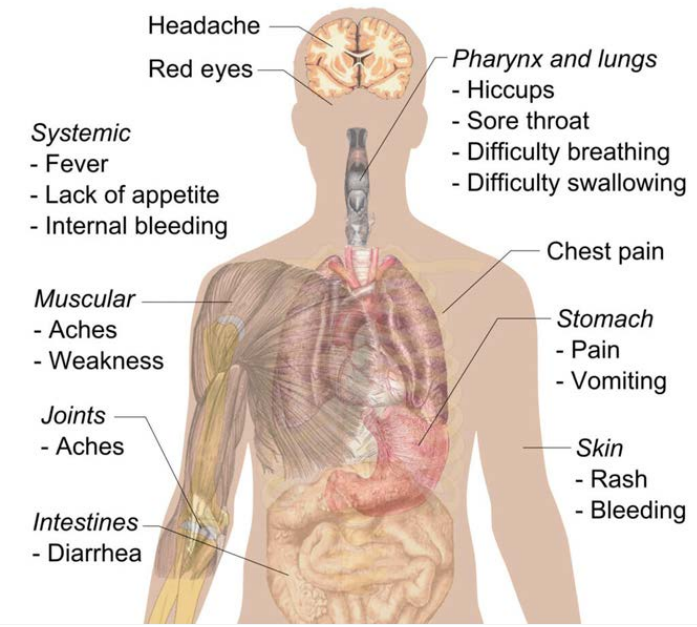
Abrupt start with high fever, severe myalgia and headaches.

By day 3 vomiting, diarrhea, and abdominal pain ensue.

Diarrhea may last for a week, along with severe exhaustion and lethargy.

By day 5 to 7 severe hemorrhagic rash.

Patients who die commonly have fresh blood in vomit, feces, nose, gums or vagina.



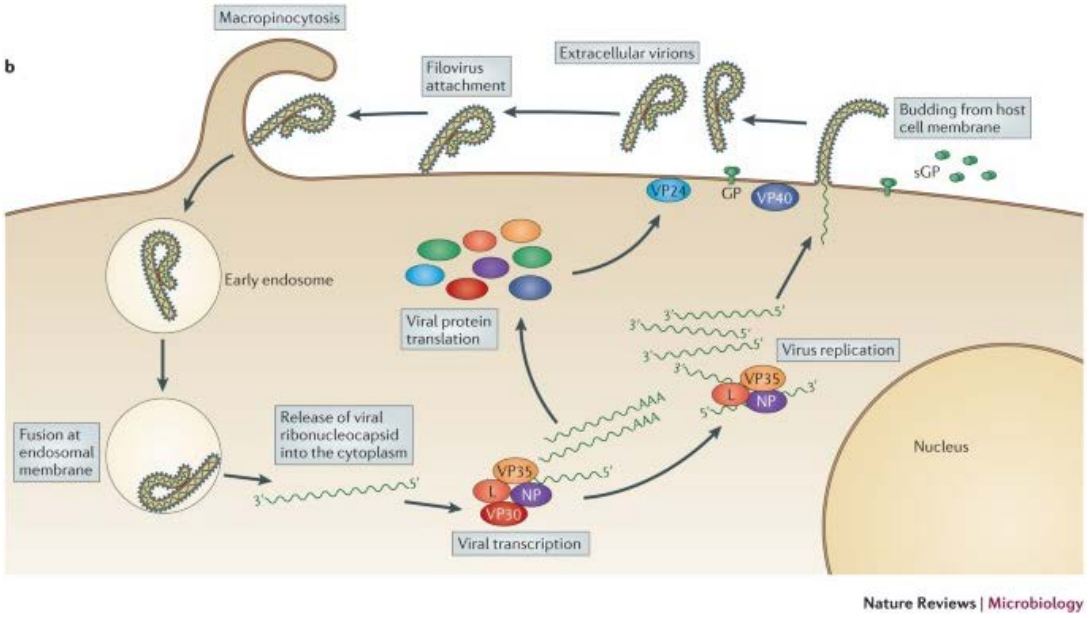
Marburg virus disease signs & symptoms

Pathogenesis

Early replication in monocytes, macrophages and dendritic cells.

Dssemination to hepatocytes, endothelial cells, fibroblasts, and epithelial cells.

GP surface unit (GP1) binds to cellular receptors, and internal fusion loop (GP2) allows cell membrane fusion.



Intra-vesicular cleavage of GP by host cathepsins leads to viral core release into cytoplasm.

Viral replication occurs in target organs (spleen, liver and secondary lymphoid organs).

Cytoplasmic inclusions may be seen in hepatocytes, indicative of viral replication.

Pathogenesis

Massive hepatic necrosis and apoptosis.

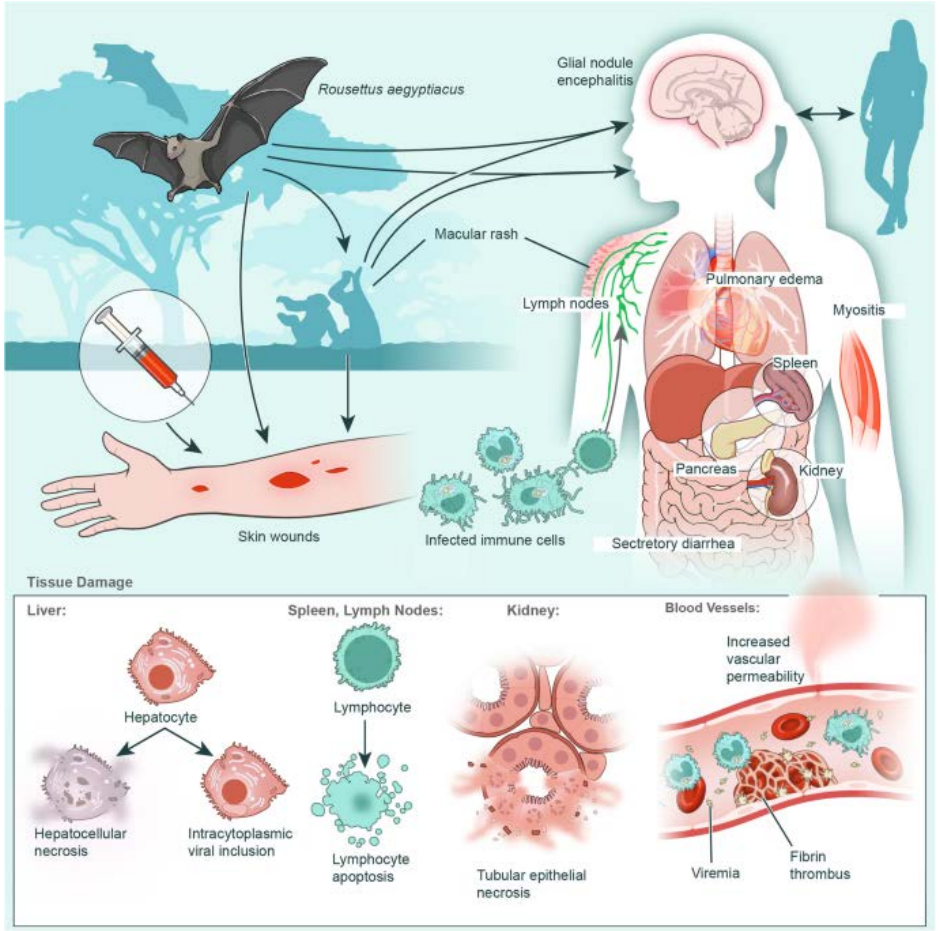
Impaired liver function contributes to coagulopathy & disseminated intravascular coagulation (DIC).

Spleen and lymph node depletion due to lymphocyte apoptosis, haemorrhage and necrosis.

Acute tubular necrosis (ATN) due to infection, hypotension and hypoperfusion.

Pulmonary edema due to vascular leakage caused by endothelial damage.

Interstitial pneumonitis.



MVD Pathogenesis

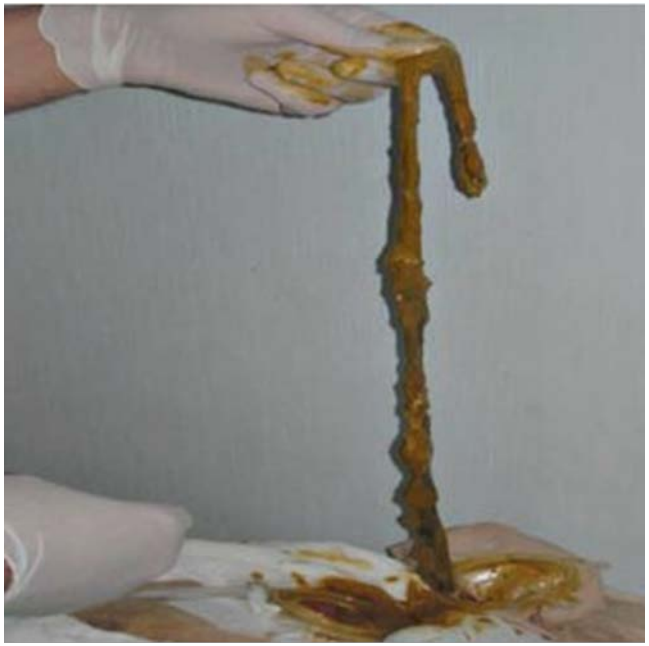
Gastrointestinal tract mucosal erosion and hemorrhage.

Necrosis of mucosal and submucosal layers.

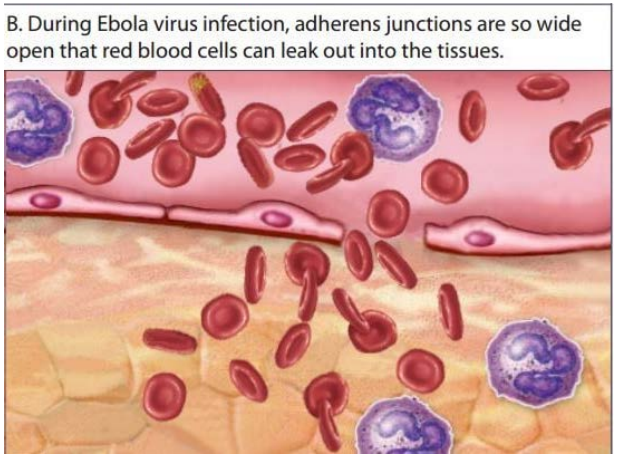
Encephalitis a rare ocurrence involves necrosis and inflammatory infiltration of the brain.

Widespread endothelial damage is a hallmark of filovirus infection, leading to vascular leakage, edema, and hemorrhage.

Bone marrow suppression due to direct infection of progenitor cells.



Gastrointestinal mucosal casts



MVD Diagnosis

MVD analogous to malaria, typhoid fever, meningitis, and the other viral hemorrhagic fevers.

Confirmatory diagnosis through:

Antibody-capture enzymelinked immunosorbent assay (ELISA)

Antigencapture ELISA test

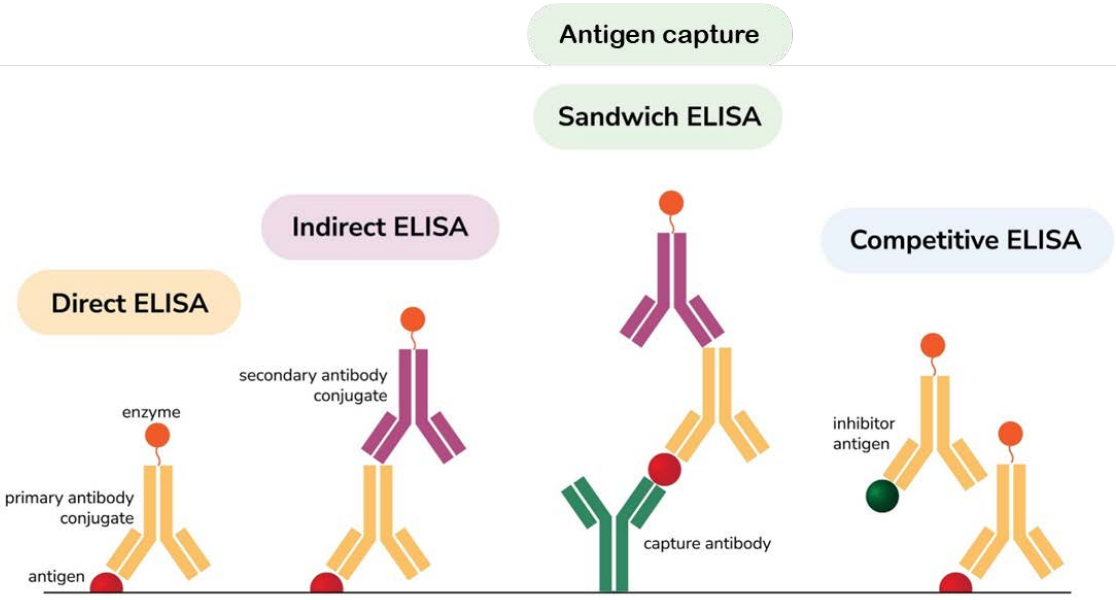
Serum neutralization test

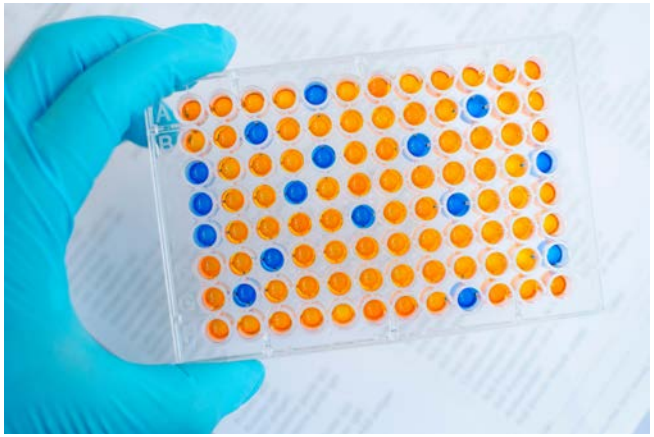
RT-PCR assay

Electron microscopy

Virus isolation by cell culture.

MARV is classified as a Risk Group 4 pathogen (RG-4).





MVD Diagnosis

MVD analogous to malaria, typhoid fever, meningitis, and the other viral hemorrhagic fevers.

Confirmatory diagnosis through:

Antibody-capture enzymelinked immunosorbent assay (ELISA)

tigencapture ELISA test

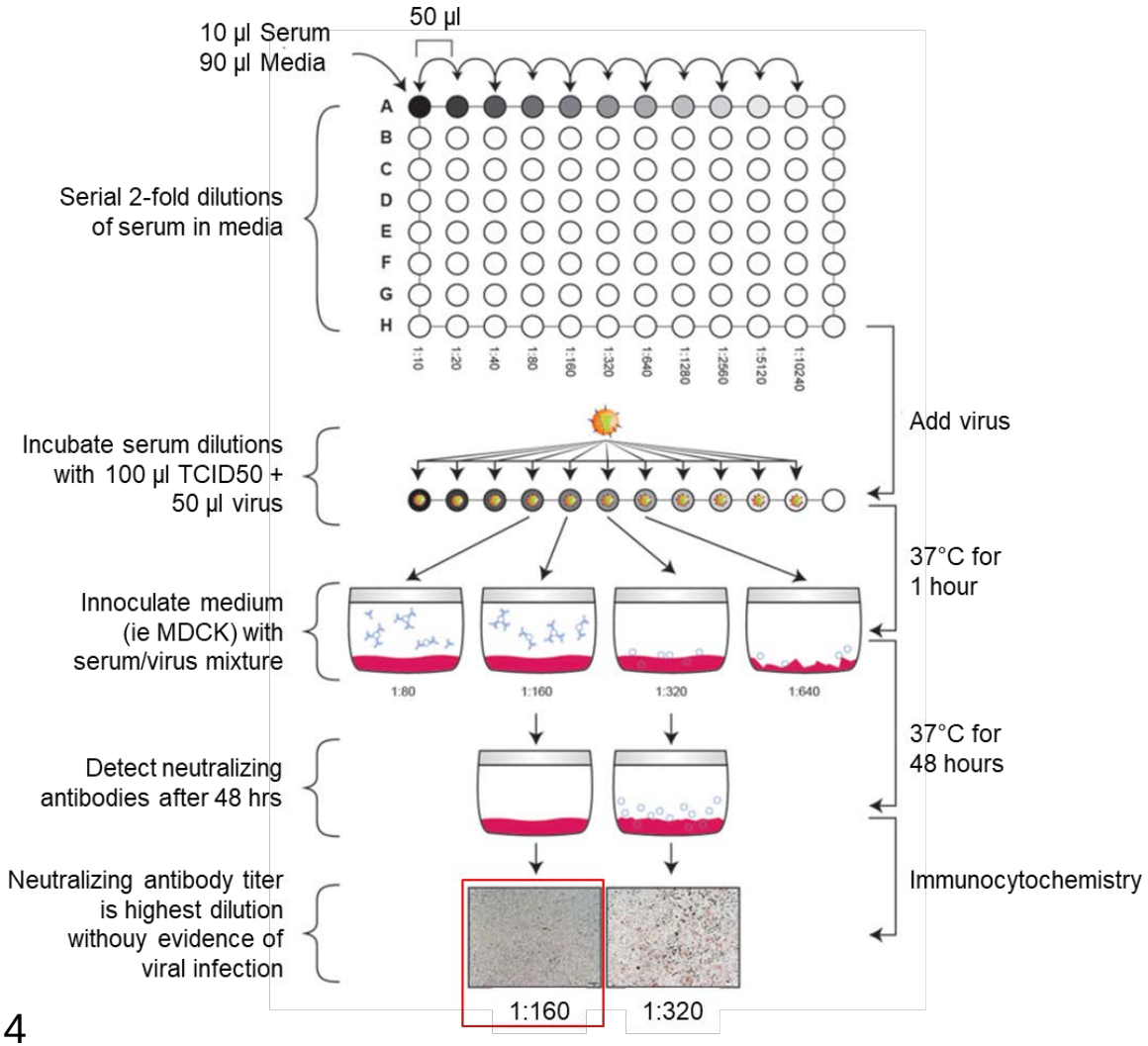
Serum neutralization test

RT-PCR assay

Electron microscopy

Virus isolation by cell culture.

MARV is classified as a Risk Group 4 pathogen (RG-4).



MVD Diagnosis

MVD analogous to malaria, typhoid fever, meningitis, and the other viral hemorrhagic fevers.

Confirmatory diagnosis through:

Antibody-capture enzymelinked immunosorbent assay (ELISA)

tigencapture ELISA test

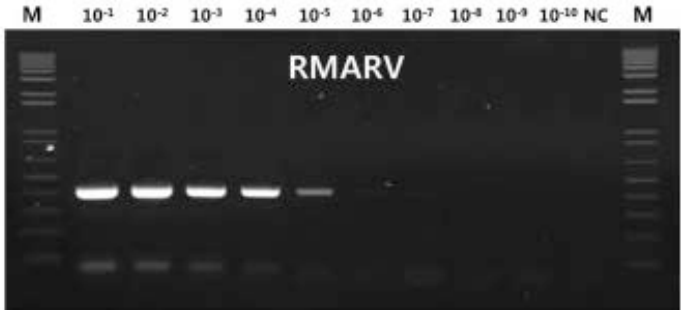
Serum neutralization test

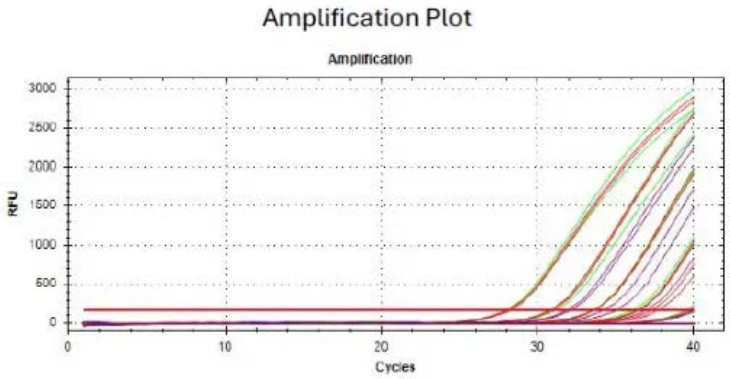
RT-PCR assay

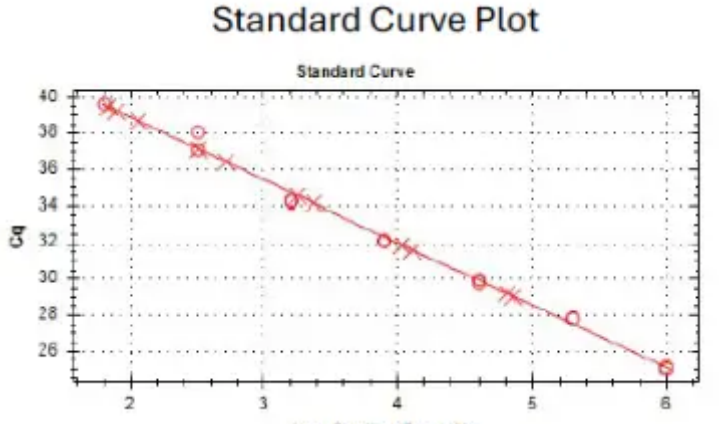
Electron microscopy

Virus isolation by cell culture.

MARV is classified as a Risk Group 4 pathogen (RG-4).







MVD Diagnosis

MVD analogous to malaria, typhoid fever, meningitis, and the other viral hemorrhagic fevers.

Confirmatory diagnosis through:

Antibody-capture enzymelinked immunosorbent assay (ELISA)

tigencapture ELISA test

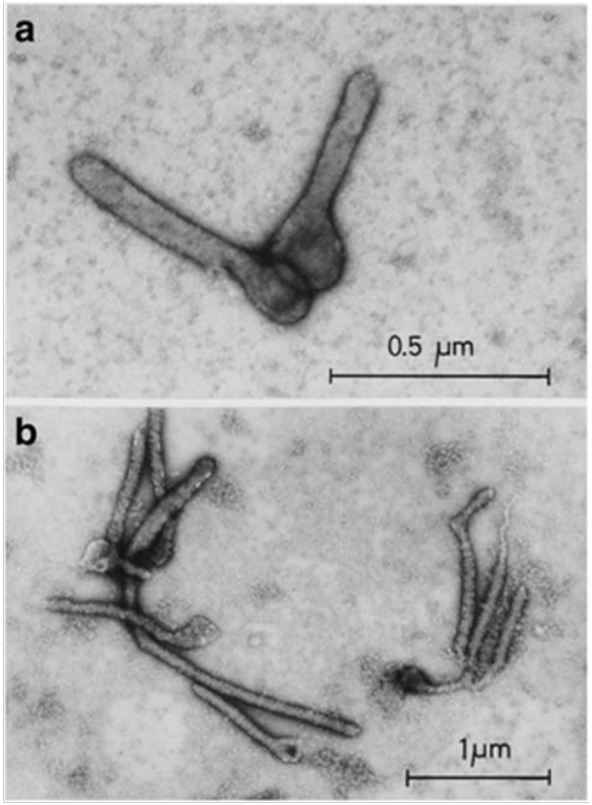
Serum neutralization test

RT-PCR assay

Electron microscopy

Virus isolation by cell culture.

MARV is classified as a Risk Group 4 pathogen (RG-4).



Marburg virus filaments (a) are usually shorter than Ebola virus virions (b). The filaments of both viruses can have loops and branchings

MVD Diagnosis

MVD analogous to malaria, typhoid fever, meningitis, and the other viral hemorrhagic fevers.

Confirmatory diagnosis through:

Antibody-capture enzymelinked immunosorbent assay (ELISA)

tigencapture ELISA test

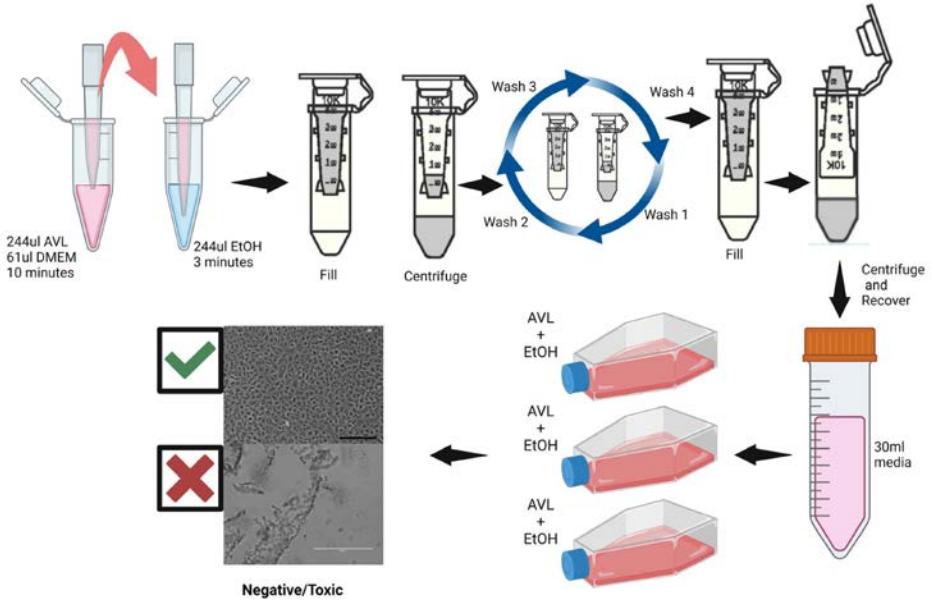
Serum neutralization test

RT-PCR assay

Electron microscopy

Virus isolation by cell culture.

MARV is classified as a Risk Group 4 pathogen (RG-4).



Public health measures

- Risk Group 4
- Bat-borne virus (endemic)
- Social factors may spread virus through land… and air, as well

What do they do?

1. Limit transmission human-to-human
2. Early identification
3. Tracing
4. Monitoring

MVD treatment and prevention

There is no approved vaccine or antiviral treatment for MVD.

Supportive care: Fluid and electrolyte balance, maintaining oxygen levels and blood pressure, and replacing lost blood and clotting factors.

Recombinant vesicular stomatitis virus (VSV)-based vaccine expressing MARV GP (VSV-MARV).

MVA-BN-Filo, containing both Marburg and Ebola virus antigens.

MARV-specific monoclonal antibodies (mAbs) and small-molecule antivirals.

Remdesivir, broad-spectrum antiviral with activity against several RNA viruses.

Public health measures

Once an MVD outbreak is out of hand, it will expand rapidly and cause severe health, social, And economic problems.

Main goal of controlling an MVD outbreak is to interrupt direct human-to-human transmission.

Early identification and rapid solation of case.

Timely tracing and close monitoring of people at risk.

Proper personal protection for health care staff.

Safe burial.

Avoid handling and eating of bush meat.

Take-away, Food for thought

On July 17, 2022, the World Health Organization declared outbreaks of Marburg virus disease (MVD) in Ghana.

The world must be on alert regarding deadly MVD following COVID-19 and mpox.

The Marburg virus (MARV) is a deadly cousin of the Ebola virus.

MARV causes severe viral hemorrhagic fever (VHF) in humans.

MARV is one of the most fatal viruses known, with a mortality rate of 50%.

During the largest MARV outbreak (Angola, 2005) >250 people infected, 90% died.

There is no treatment nor vaccine available for MARV.

Prompt interruption of human to human transmission is the key to outbreak control.

RVPVE

Red de Vigilancia de Patógenos Virales Emergentes

Christian A. García-Sepúlveda — Laboratorio de Genómica Viral & Humana, Facultad de Medicina UASLP
Sandra E. Guerra-Palomares — Laboratorio de Genómica Viral & Humana,Facultad de Medicina UASLP
Juan Carlos Cuevas Tello — Grupo de Bioinformática, Facultad de Ingeniería UASLP
Ignacio Amezcua Osorio — Comité Estatal para el Fomento y Protección Pecuaria de San Luis Potosí (CEFPP)
Guillermo Espinosa Reyes — Centro de Investigación Aplicada en Ambiente y Salud (CIAAS), Facultad de Medicina UASLP
Fernando Díaz-Barriga Martínez — Centro Colaborador OMS/OPS CIAAS, Facultad de Medicina UASLP
Andreu Comas García — Epidemiología y virología molecular, Depto. Microbiología, Fac. de Medicina UASLP

Dulce Ma. Hernández Piña — Lab manager, LGVH UASLP
J. Manuel Mendoza Méndez — Hantavirus americanos en roedores silvestres, LGVH UASLP
Nidya Jurado-Sánchez — Vigilancia de vectores y arbovirus, LGVH UASLP
Mariel Pacheco-Cortez — Hantavirus SEOV en personal biomédico, LGVH UASLP
Samuel Mora-Andrade — Bat collection research, LGVH UASLP
Carolina Escalante Vargas — Bat collection research, CEFPP

www.genomica.uaslp.mx GenomicaUASLP YouTube GenomicaUASLP