Arboviral infections
(arthropod-borne)
and haemorrhagic fevers

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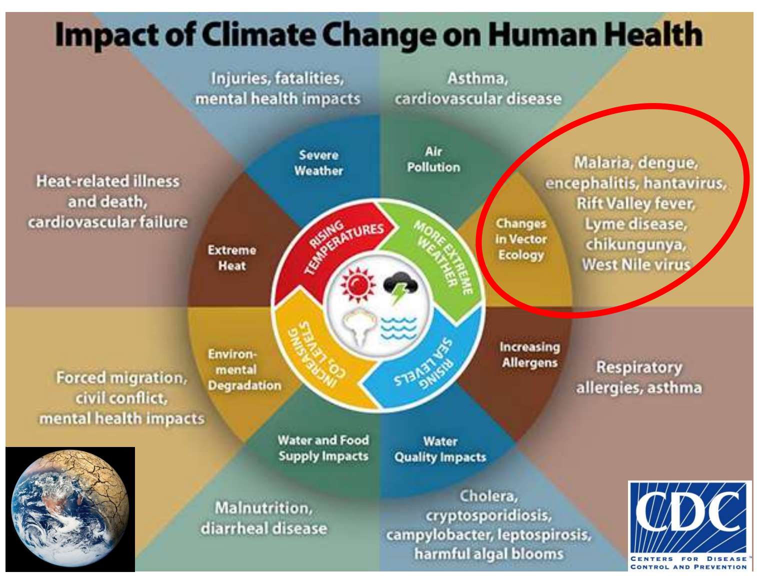
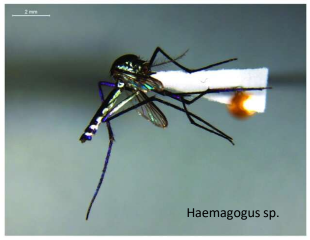
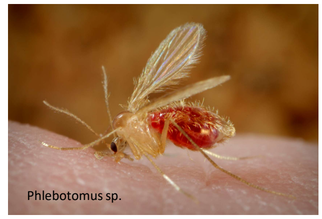
What are arboviral infections (arthropod-borne)?

Arboviruses refer to a diverse group of viruses that are transmitted via mosquitos, ticks, or sandflies and are capable of causing a wide range of diseases. It is important to understand the disease processes caused by these infectious agents, given the increasing frequency of infection and the potential for additional emerging diseases.

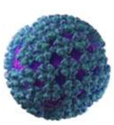




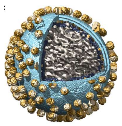
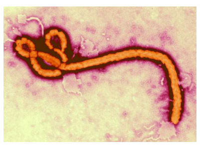


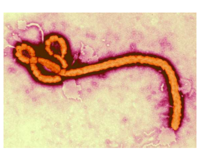
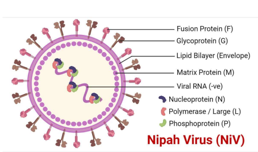
Viral haemorrhagic fever viruses

Virus	Virion	Viral Protein	Receptor/Type/ Function	Virus Tropism	Entry Mode	Immune Evasion
Crimean Congo Virus	Env	Glycoprotein	Nucleolin/Receptor/ Entry	Monocytes, Macrophage, Dendritic Cells, Epithelial Cells, Platelet, Endothelial cells, Hepatocytes	Clathrin Mediated Endocytosis	1. Inhibition of RNA helicase RIG-I stimulation and IFN transcription by processing the viral 5′RNA termini 2. Interfering with activation of interferon regulatory factor –3 (IRF3]
Rift Valley Fever Virus	Env	Envelope Glycoprotein	DC-SIGN/Lectin/ Entry	Macrophage, Dendritic Cells, Granulocytes, Platelet, Splenocytes, Brain?	Clathrin-, Dynamin-, Caveolin – Mediated Endocytosis	1. Targeting INFβ via repressor formation on INFβ Promoter 2. Inhibit the transcription of host type 1 interferon mRNA
Severe Fever with Thrombocytopenia Virus (Now Dabie virus)	Env	Glycoprotein	DC-SIGN/Lectin/ Entry	Dendritic Cells, Monocytes, Macrophage, Platelets, Kidney Cells, Plasmoblast	Clathrin Mediated Endocytosis	1. SFTSV NSs binds and sequesters several host proteins that are important for type I IFN induction, such as TBK1, Iκκepsilon (Iκκε), IRF-3, IRF-7, and tripartite motif 25 (TRIM25), into the NSs-induced "inclusion bodies" or "viroplasm-like structures" 2. SFTSV NSs also inhibits type I IFN signaling pathway by interacting with STAT1 and STAT2 heterodimers, inhibiting their phosphorylation status, and nuclear translocation, which leads to suppression of ISGs expression 3. SFTSV NSs prevents STAT1 homodimerization and reduces STAT1 protein level overall thereby reducing IFN-γ production
Andes Virus	Env	Glycoprotein G	PCDH1/Adhesion Molecule/Entry	Respiratory Tract, Endothelial cells, Platelets, Podocytes	Clathrin-Mediated Endocytosis	1. Z protein directly interacts with cytosolic innate immune sensor protein (RIG-I & MDA-5), thereby inhibiting type 1 IFN 2. Nucleoprotein (NP) serves as an IFN antagonist
Hantaan Virus			Integrin β3/ Adhesion Molecule/ Entry			
Sin Nombre Virus			PCDH1/Adhesion Molecule/Entry			



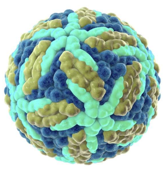
Viral haemorrhagic fever viruses

Lassa Virus 	Env	Glycoprotein Complex Virion Membrane Phosphatidylserine	DC-SIGN/Lectin/Adhesion CLEC4G (LSECtin)/Lectin/Adhesion LAMP1(CD107a)/Glycoprotein/Adhesion A-Dystroglycan/Adhesion Molecule/Entry? HAVCR1 (TIM1)/Receptor/Entry? Tyro3 (TAM Family)/Receptor/Entry AXL (TAM Family)/Receptor/Entry	Dendritic cells, Monocytes, Macrophage in Liver, Kidney, and Brain	Clathrin-Mediated Endocytosis	1. Protect infected epithelial and endothelial from CTL-induced apoptosis via inhibiting the caspase by N protein 2. Hantavirus-induced Program Death Ligand (PD-L1 and PD-L2) upregulation contributes to viral immune escape 3. N protein inhibits NF-κB activation which is required for IFN promotor response. 4. Hantavirus Glycoprotein Cytoplasmic Tail (Gn-T) regulates IFN induction by blocking both IRF3 and NF-κB activation.
Junin Virus		Glycoprotein Complex	TFRC/Receptor/Entry	Macrophage		
Machupo Virus		Glycoprotein Complex	TFRC/Receptor/Entry	Macrophage		
Guanarito Virus		Glycoprotein Complex	TFRC/Receptor/Entry	Vascular System, Multiorgan		
Ebola Virus 	Env	Glycoprotein Virion Membrane Phosphatidylserine	DC-SIGN/Lectin/Adhesion CLEC4G (LSECtin)/Lectin/Adhesion CLEC4M(L-SIGN)/Lectin/Adhesion NPC1/Receptor/Entry in Endosome HAVCR1 (TIM1)/Receptor/Entry Tyro3 (TAM Family)/Receptor/Entry	Dendritic cells, macrophages. Hepatocytes, Kidney cells, Splenocytes, endothelial and epithelial cells	Macropinocytosis	1. Viral protein 35 (VP35) is capable of capping dsRNA and interacts with IRF7 to prevent the detection of the virus by immune cells. 2. VP35 proteins also block signaling through RIG-I-like receptors and prevent the phosphorylation of IRF-3 and IRF-7, thereby short-circuiting the IFN response 3. VP35 also prevent PACT (a protein activator of IFN-induced antiviral kinase) interaction with RIG-I 4. VP35 inhibition of RLR signaling suppresses maturation and function of

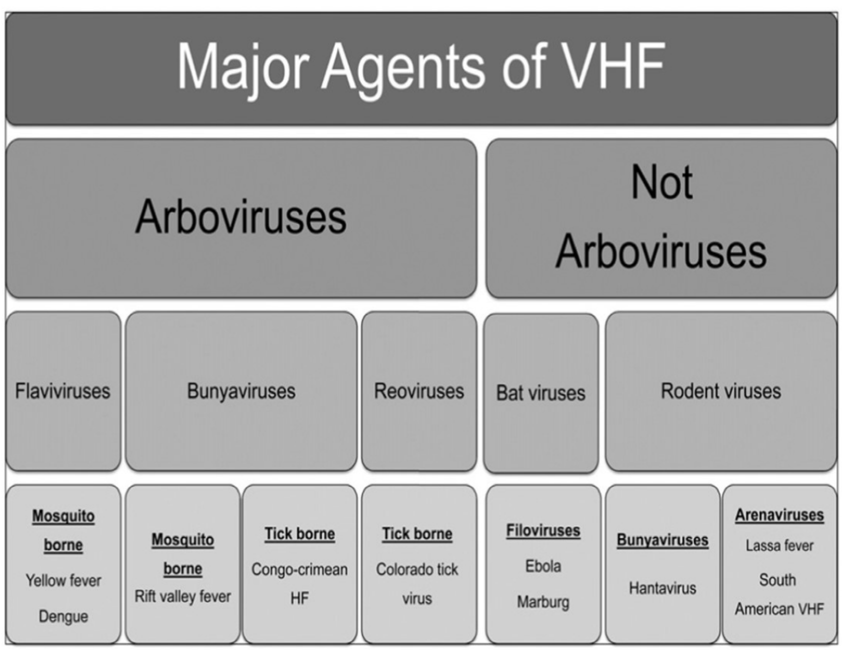
Virus	Virion	Viral Protein	Receptor/Type/Function	Virus Tropism	Entry Mode	Immune Evasion
			AXL (TAM Family)/Receptor/Entry			DCs, thereby inhibiting the innate immune signaling pathway
Marburg Virus 	Env	Glycoprotein Virion Membrane Phosphatidylserine	DC-SIGN/Lectin/Adhesion CLEC4M(L-SIGN)/Lectin/Adhesion HAVCR1 (TIM1)/Receptor/Entry	Macrophage, Dendritic Cells, Endothelial Cells, Epithelial Cells	Macropinocytosis	1. VP35 proteins also block signaling through RIG-I-like receptors and prevent the phosphorylation of IRF-3 and IRF-7, thereby short-circuiting the IFN response 2. VP35 also prevent PACT (a protein activator of IFN-induced antiviral kinase) interaction with RIG-I 3. VP35 inhibition of RLR signaling suppresses maturation and function of DCs, thereby inhibiting the innate immune signaling pathway 4. Marburg virus VP40 blocks the activation and function of Janus kinase 1 (JAK1), inhibiting the type I IFN-induced phosphorylation of STAT1 and STAT2. 5. Marburg virus VP24 can modulate the function of kelch-like ECH-associated protein 1 (KEAP1), enabling activation of antioxidant response elements (AREs) and promoting survival of virus-infected host cells.
Nipah Virus 	Env	Glycoprotein G	EFNB2/Receptor/Entry EFNB3/Receptor/Entry	Endothelial, Type I Pneumocytes, Bronchial respiratory epithelium, Alveolar macrophage, Olfactory epithelial, Epithelial larynx and trachea, Dendritic Cells Brain Cells Neuron Cells	Clathrin-Mediated Endocytosis	1. The phosphoprotein (P), the V protein, the W protein, and the C protein inhibit the activation of interferon (IFN)-α/β response 2. V protein has been shown to interact with the cytoplasmic RNA helicases to prevent downstream signaling and activation of the IFNb promoter 3. The W protein inhibits IFNb promoter activation by disrupting the transcription factor IRF3 in the nucleus 4. The phosphoprotein (P), the V protein, the W protein, and the C protein inhibit the activation of STAT-1 and STAT-2, required for IFN signaling.

Viral haemorrhagic fever viruses

Yellow Fever Virus	Env	Envelope Protein E	Heparan Sulfate/ Carbohydrate/ Adhesion	Macrophage, Dendritic Cells, and Platelets		1. NS1 protein is thought to inhibit the innate antiviral immunity primarily by interfering with the TLR signaling pathway 2. NS2A protein plays an important role in inhibiting the induction of IFNβ promoter-driven transcription 3. NS2B3 can inhibit type I IFN production by cleaving human STING 4. NS2A can Inhibit RIG-I/MAVS signaling by blocking TBK1/IRF3 phosphorylation 5. NS4A can inhibit IFNβ mediated ISRE54 promoter activation 6. NS4B can inhibit RIG-I/MAVS signaling by blocking TBK1/IRF3 phosphorylation 7. NS4B can Inhibit IFN-mediated STAT1 phosphorylation 8. NS4B can Inhibit the activation of ISRE by IFNβ stimulation 9. NS5 can Inhibit IFN-mediated signaling by blocking STAT2 phosphorylation 10. NS5 can Inhibit type I IFN mediated signaling by binding to STAT2
Dengue virus	Env	Envelope Protein E	Mannose Receptor/ Receptor/Adhesion Heparan Sulfate/ Carbohydrate/ Adhesion CLEC5A/Lectin/ Adhesion DC-SIGN/Lectin/ Adhesion Laminin Receptor/ Receptor/Entry	Macrophage, Dendritic Cells, and Platelets	Clathrin-Mediated Endocytosis Macropinocytosis	
		Virion Membrane Phosphatidylserine	HAVCR1 (TIM1)/ Receptor/Entry Tyro3 (TAM Family)/Receptor/ Entry AXL (TAM Family)/ Receptor/Entry			
		Small Protein Envelope M	CLDN1/Adhesion Molecule/Entry			



Current Research in Virological Science 2 (2021) 100009



J. Hidalgo et al. / Journal of Critical Care 42 (2017) 366–372

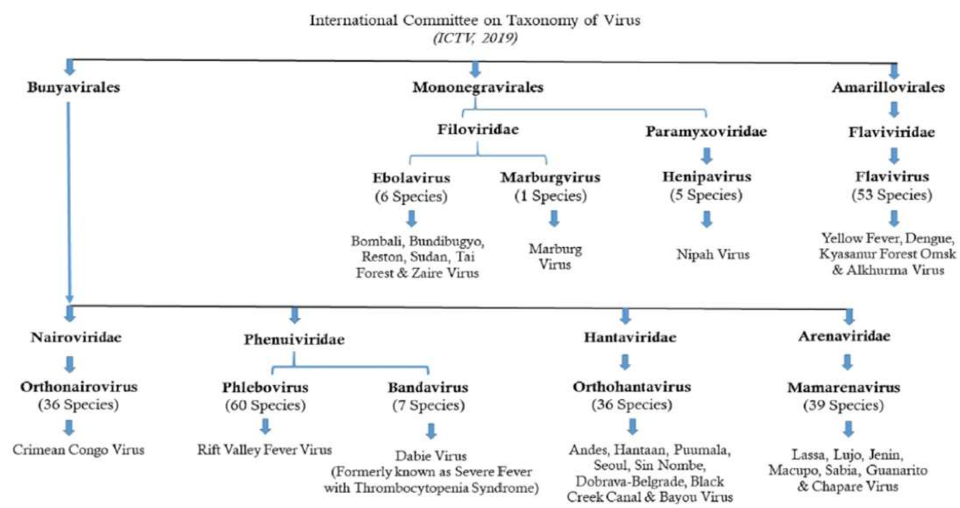


Fig. 1. Overview of VHF causing viruses.

Symptoms of haemorrhagic fevers

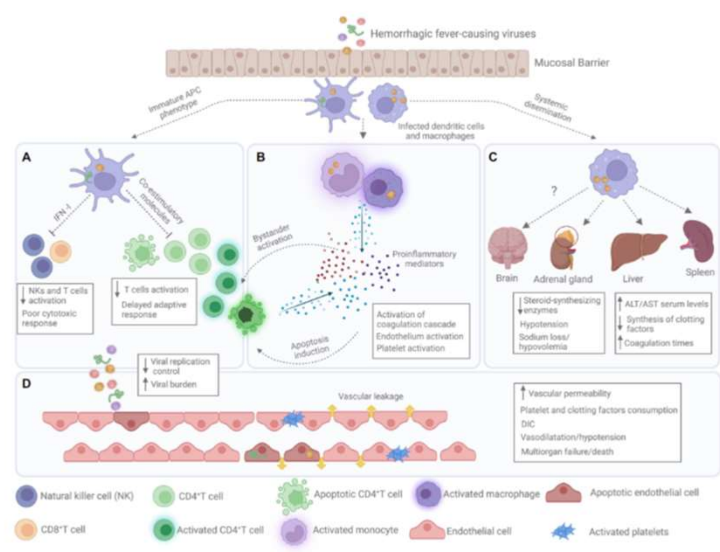
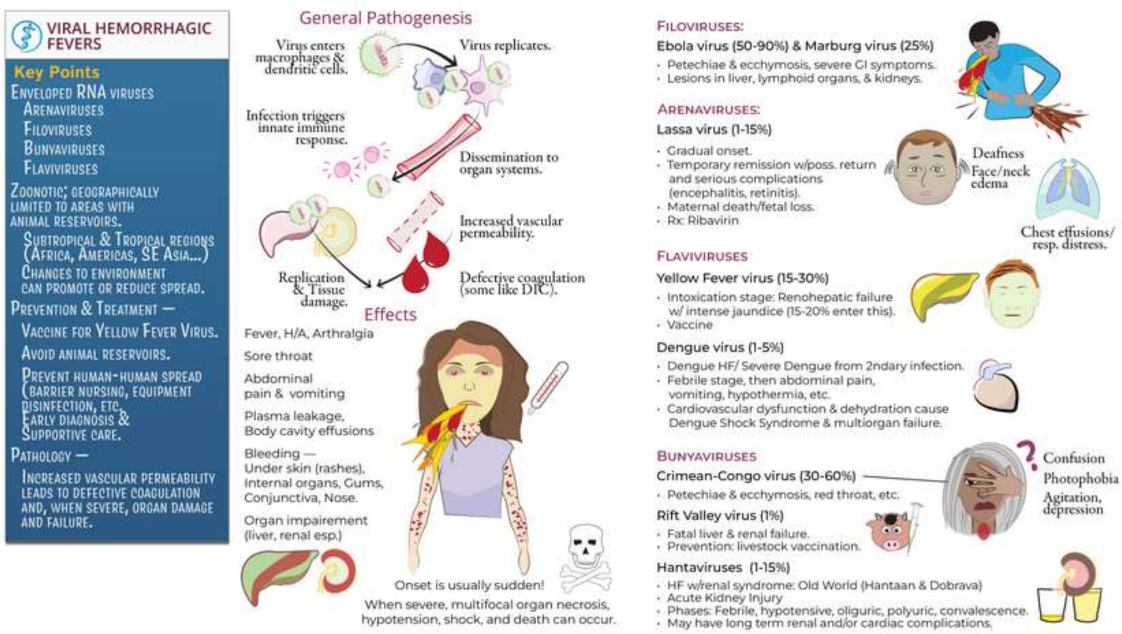
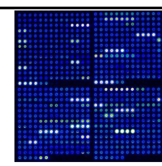


FIGURE 1
Pathogenesis of severe viral hemorrhagic fever. **(A)** Antigen presenting cells (APCs) present an immature phenotype with low expression of co-stimulatory molecules and low type I interferon (IFN-I) production, leading to poor NK and T cells activation causing a generalized immunosuppression, which lead to uncontrolled viral replication and high viral burdens. **(B)** During the infection monocytes and macrophages produced large quantities of proinflammatory mediators causing the phenomenon known as cytokine storm. These proinflammatory mediators cause endothelial and platelet activation and induce bystander activation and apoptosis of T cells. **(C)** Infected APC transport Hemorrhagic fever viruses (HFVs) to lymph nodes and other organs causing a systemic dissemination. Infection of some organs such as liver and adrenal gland results in high serum levels of hepatic enzymes (aspartate amino transferase-AST, and alanine amino transferase-ALT), low production of clotting factors and hypovolemia. **(D)** Sustained proinflammatory state and viral infection of endothelial cells induce abnormal vascular regulation and organ effusion, hemorrhages, and disseminated intravascular coagulation (DIC).



Why we observe emerging viruses?



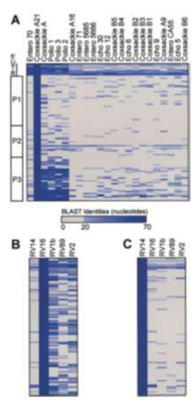
Better detection (even in new) – treatment – resistance

Molecular-biological techniques

Direct and relative cheap detection based on NA

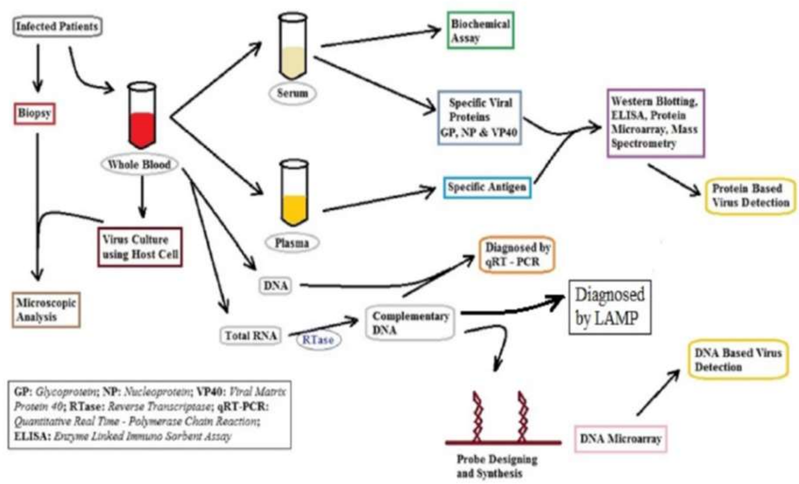
Reasonable time for detection of the agens

Relatively cheap detection of new viruses



CHIP technique was used in new WUV and KIV polyomavirus detection in 2007, which were detected in respiratory tract.

How to diagnose arboviruses and haemorrhagic fever v.?



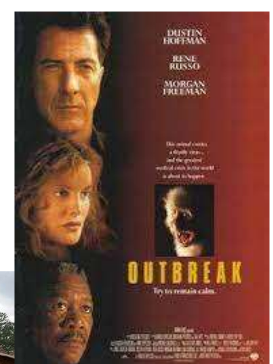
BSL4

Alkhurma hemorrhagic fever
Chapare hemorrhagic fever
Crimean-Congo hemorrhagic fever
Ebola virus disease
Hantaviruses
Kyasanur Forest disease
Lassa fever
Lujo hemorrhagic fever
Marburg virus disease
Omsk hemorrhagic fever
Rift Valley fever…

Zbytek **BSL3**

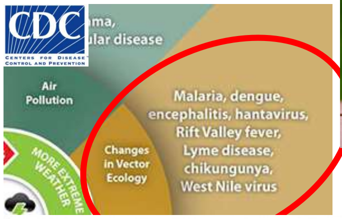
Biosafety level 4

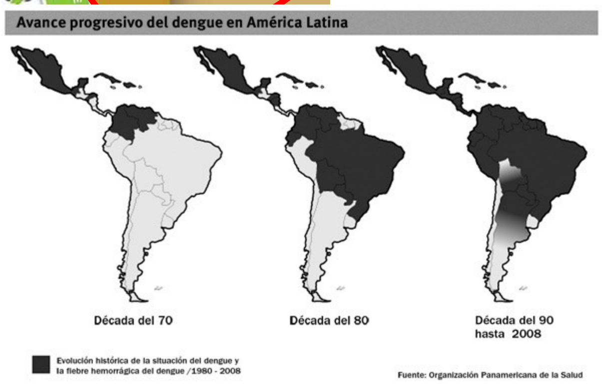
- Double gloves
- Boot covers that are waterproof and go to at least mid-calf or leg covers
- Single use fluid resistant or imperable gown that extends to at least mid-calf or coverall without intergraded hood.
- Respirators, including either N95 respirators or powered air purifying respirator (PAPR)
- Single-use, full-face shield that is disposable
- Surgical hoods to ensure complete coverage of the head and neck
- Apron that is waterproof and covers the torso to the level of the mid-calf should be used if Ebola patients have vomiting or diarrhea



Why we observe emerging viruses?

1. Climate changes





Barmah Forest virus, BFV
Eastern equine encephalitis virus, EEEV
Middelburg virus, MIDV
Ndumu virus, NDUV
Bebaru virus, BEBV[3]
Chikungunya virus, CHIKV[3]
Mayaro virus (–Una virus), MAYV–UNAV[3]
O'nyong'nyong virus, ONNV[3]
Ross River Virus, RRV[3]
Semliki forest virus, SFV[3]
Venezuelan Equine Encephalitis virus, VEEV[4]
Cabassou virus, CABV[4]
Everglades virus, EVEV[4]
Mosso das Pedras virus, MDPV[4]
Mucambo virus, MUCV[4]
Rio Negro virus (RNV)[4]
Western Equine Encephalitis Virus, WEEV[5]
Aura Virus, AURAV[5]
Sindbis Virus ,SINV[5]
Babanki Virus, SINV–B[5]
Kyzylagach virus, SINV–K[5]
Ockelbo Virus, SINV–O[5]
Whataroa virus, WHAV[5]
Highlands J virus, HJV[5]
Buggy Creek Virus, BCV[5]
Fort Morgan Virus, FMV[5]
Tonate virus, TONV

Why we observe emerging viruses?

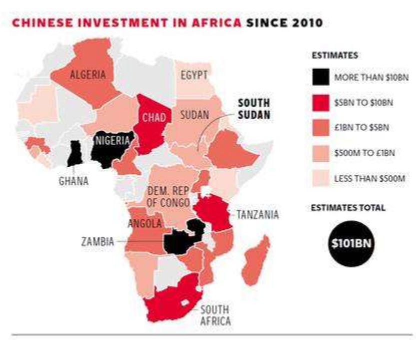
2. Changes in human behaving and travelling

- E.g. expansion of Peoples Republic China activities in Africa

- Fly time

  Amsterdam – Sydney shortest trip 27 hours and 20 minutes – less then 2 days…

- ….

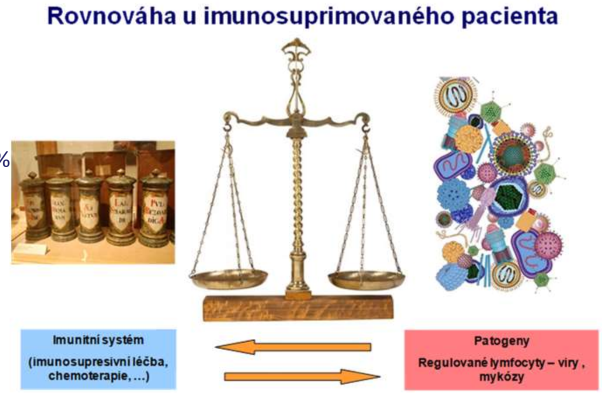


Why we observe emerging viruses?

3. More immunosupression

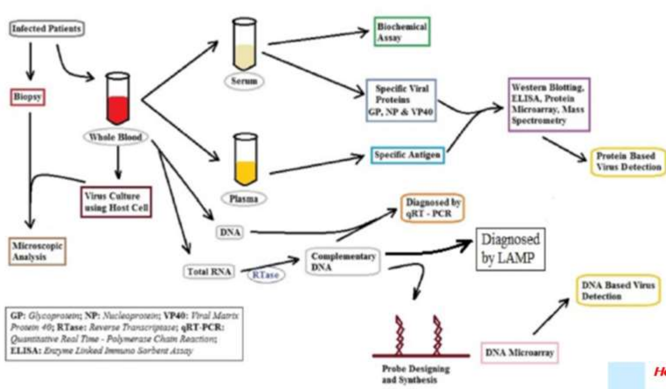
- from 2008 WHO recognized 100 800 solid organ transplants in 104 countries per year (approx. 90% world population).
  - 69 400 kidney (46% from living donors)
  - 20 200 liver (14.6% from living donors)
  - 5 400 heart
  - 3 400 lungs
  - 2400 pancreas

  Approx. 110 000 HSCT per year.
- More monoclonal antibodies (anti-CD20, CD52, TNF-α…) …

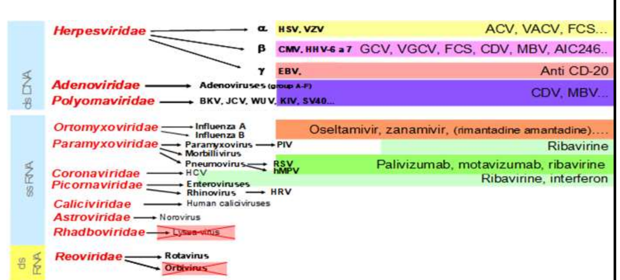


Steroids more then > 2 mg/kg – highly lymphotoxic (used e.g. in NHL, ALL…)

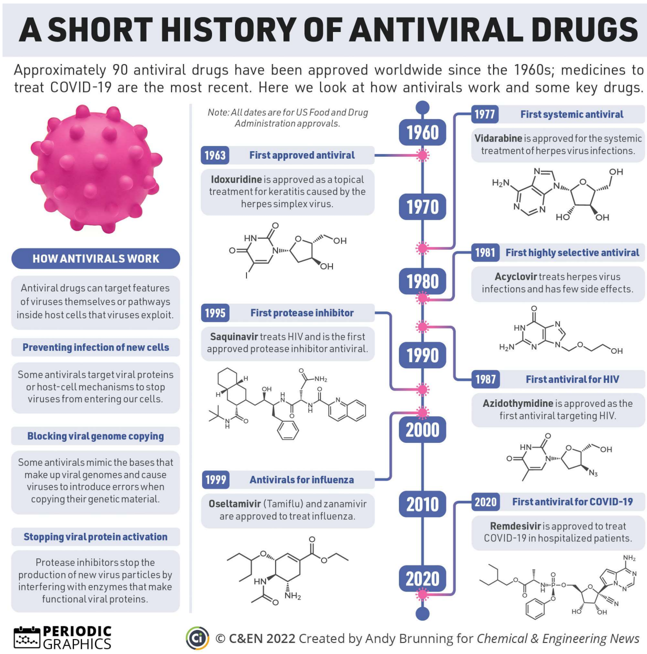
Virostatic therapy



remdesivir
brincidofovir (CMX001)
famciclovir
penciclovir
boceprevir
telaprevir
sofosbuvir
simeprevir
ledipasvir
….. and other



Virostatic therapy



Remdesivir

antibodies (e.g. mAb114 (Ansuvimab; Ebanga) and REGN-EB3 (Inmazeb)

brincidofovir (CMX001)

famciclovir

penciclovir

boceprevir

telaprevir

sofosbuvir

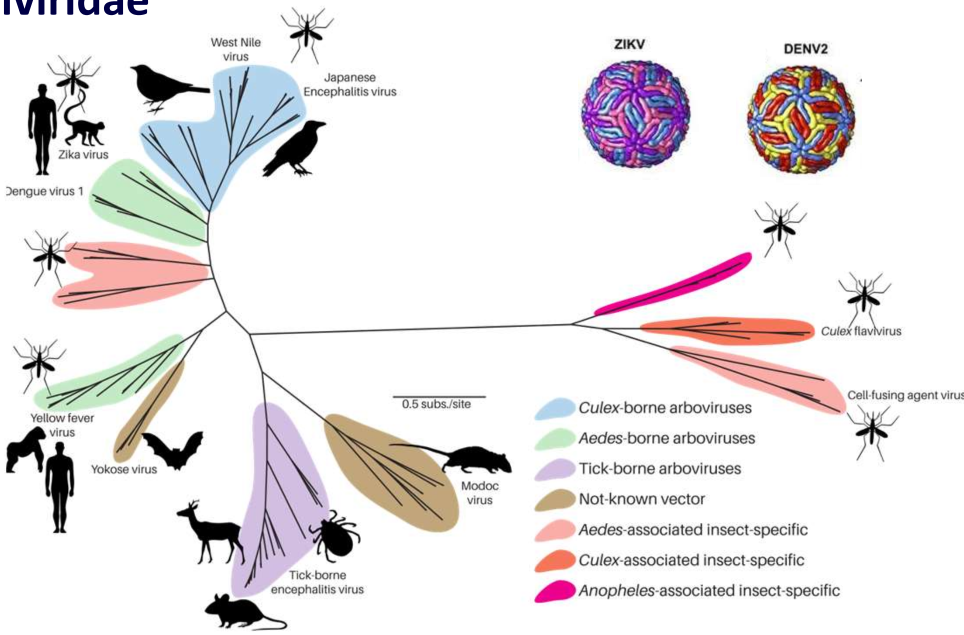
simeprevir

ledipasvir

.....   and others

vaccine

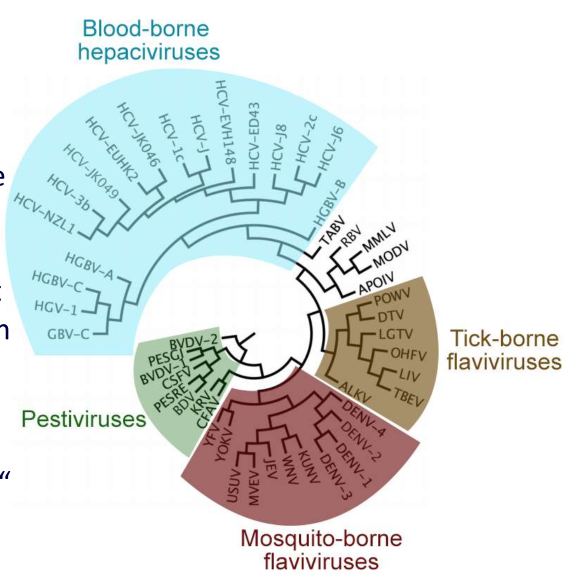
Flaviviridae



https://www.rug.nl/research/gelifes/green/lequime/research?lang=en

Flaviviridae

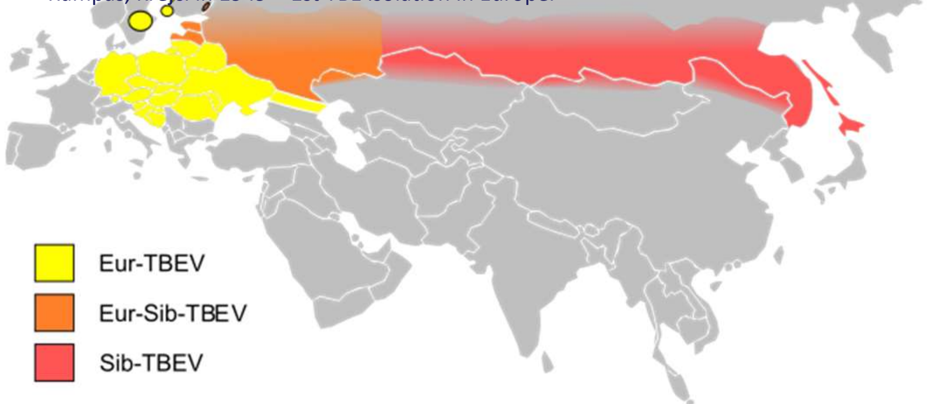
- avr. 40-60 nm
- ss (+)RNA approx. 11 kb
- virions 3 structural proteins – env. gp, core and membrane protein
- replication in cytoplasma, lipid envelope is got during budding from cytoplasmatic vesicules
- disease has often „two“ waves of clinical symptoms



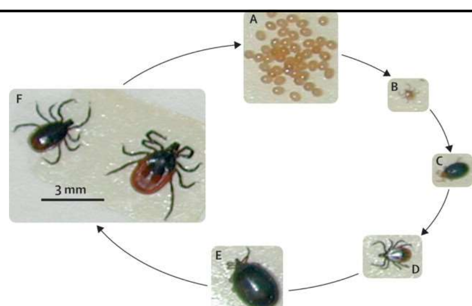
https://www.utmb.edu/discoveringdenguedrugs-together/images/Flaviviridae_adj_LG.jpg

Tick Borne Encephalitis – TBE
geographical distribution

- not west from Austria
- discovered in Austria in 1931
- in Czech Republic (CS) was first isolated independently in two places (dr. Gallia, Rampas, Krejčí in 1949 – 1st TBE isolation in Europe.



http://upload.wikimedia.org/wikipedia/commons/thumb/4/41/EurAsia_TBE-belt.svg/636px-EurAsia_TBE-belt.svg.png

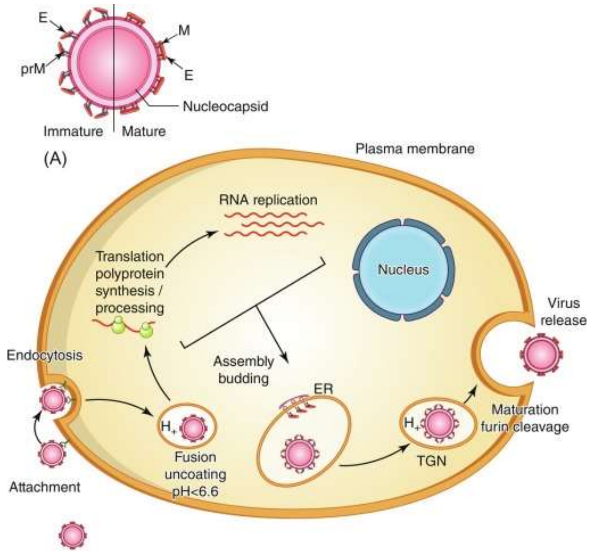


TBE Vector

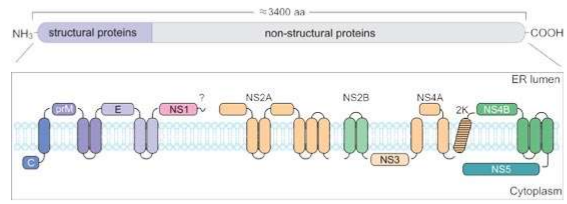
- in 1937 rusian scientest L. A. Zilber proved transmission with tick
  (in russian spring-summer encefalitis)

http://www.tbe-europe.com/?iContentID=66

Tick borne encephalitis – TBE



https://www.sciencedirect.com/topics/immunology-and-microbiology/tick-borne-encephalitis-virus

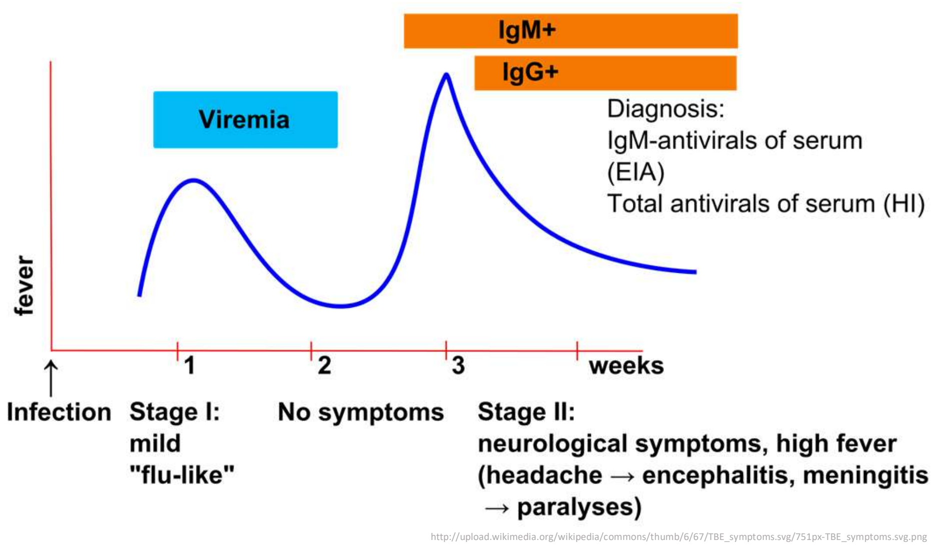


https://www.cusabio.com/infectious-diseases/tick-borne-encephalitis-virus.html

E, C, a PrM (precursor of membrane protein) and seven nonstructural proteins (NS1, NS2A, NS2B, NS3, NS4A, NS4B, and NS5)

Tick Borne Encephalitis – TBE

symptoms and diagnosis



http://upload.wikimedia.org/wikipedia/commons/thumb/6/67/TBE_symptoms.svg/751px-TBE_symptoms.svg.png

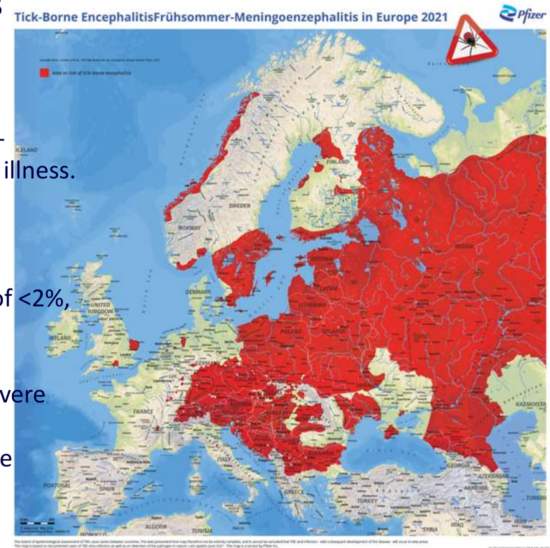
- Vaccination - inactivated virus

Tick Borne Encephalitis – TBE

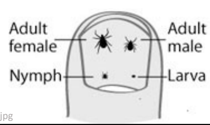
symptoms

- 2/3 of infections asymptomatic
- Incubation period - 8 days (range 4–28 days)
- I: nonspecific febrile illness, headache, myalgia and fatigue. -
  Up to 2/3 of patients may recover without any further illness.
- II: CNS - aseptic meningitis, encephalitis, or myelitis.
  Disease severity increases with age.

- The European subtype - milder disease, a case-fatality ratio of <2%, and neurologic sequelae in up to 30% of patients.
- The Far Eastern subtype – often more severe disease course, a case-fatality ratio of 20%–40% and higher rates of severe neurologic sequelae.
- The Siberian subtype - more frequently chronic or progressive disease and has a case-fatality ratio of 2%–3%.



https://artsen.wanda.be/en/a-z-index/tick-borne-encephalitis-map-of-europe

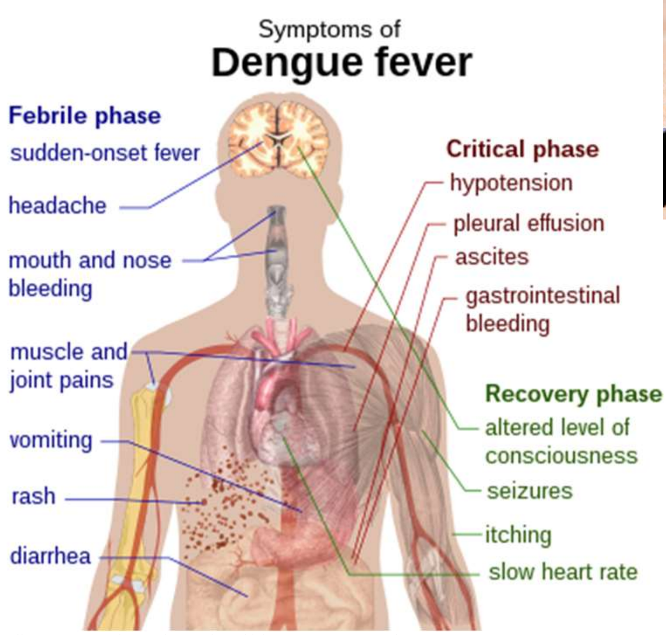


http://www.tickalert.org/img/tickTypes.jpg

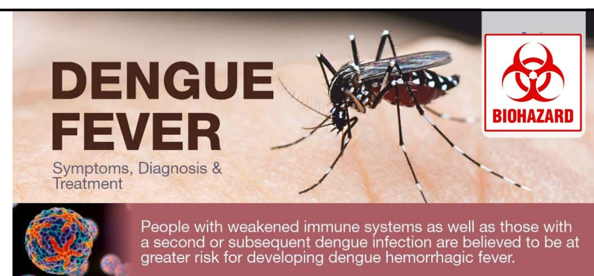
Vaccination - inactivated virus

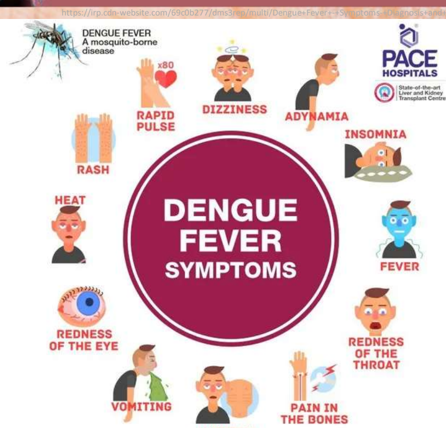
http://www.ha.ax/erik/English/Nursing/Web-tours-05_files/image007.gif

Flaviviridae



https://upload.wikimedia.org/wikipedia/commons/thumb/f/ff/Dengue_fever_symptoms.svg/388px-Dengue_fever_symptoms.svg.png





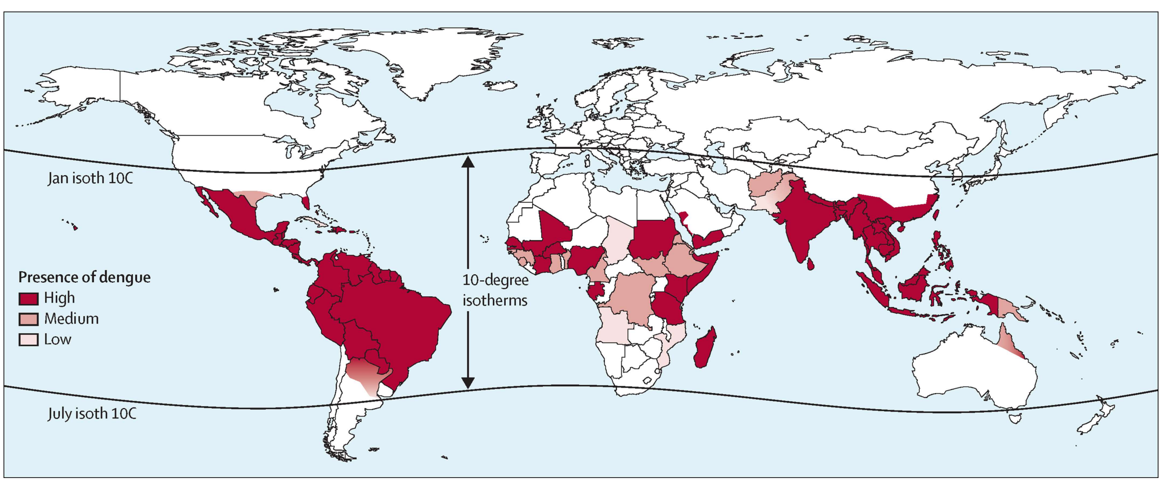
https://lrp.cdn-website.com/69c0b277/dms3rep/multi/opt/Dengue+Fever+Symptoms-640w.jpg

Flaviviridae

https://ckbirlahospitals.com/rbh/uploadedfiles/gallery/1679573852_Dengue-hemorrhagic-fever.webp

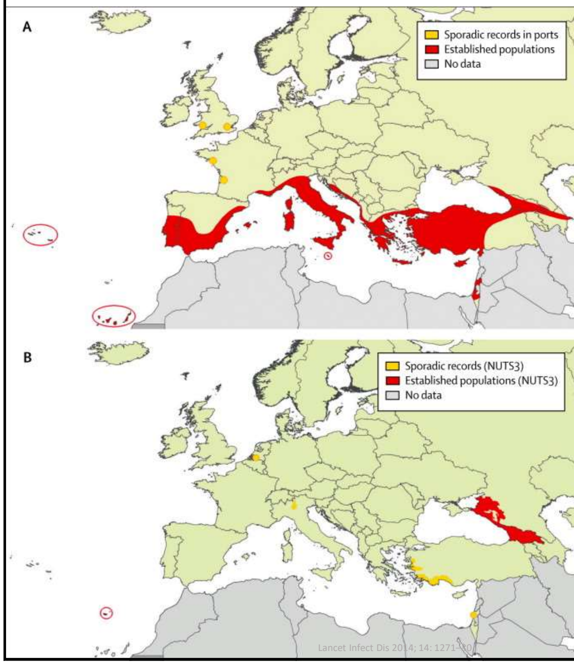
Flaviviridae

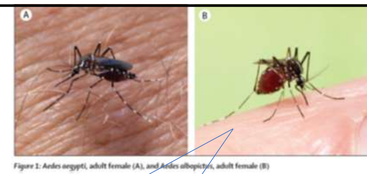
Dengue virus

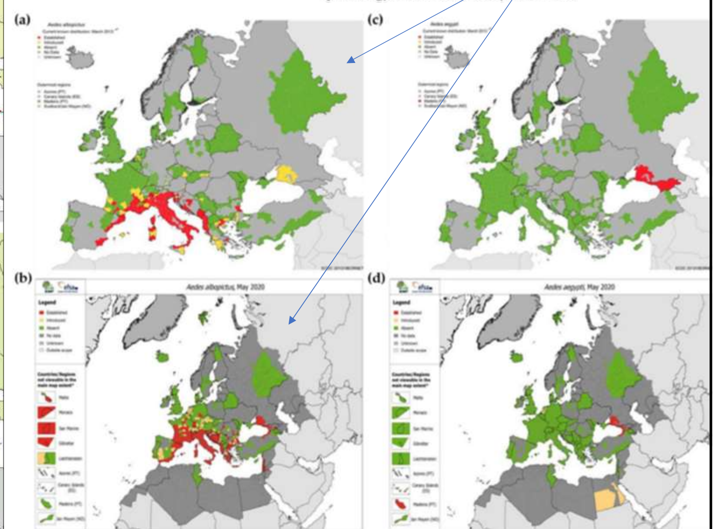


Flaviviridae

Dengue virus



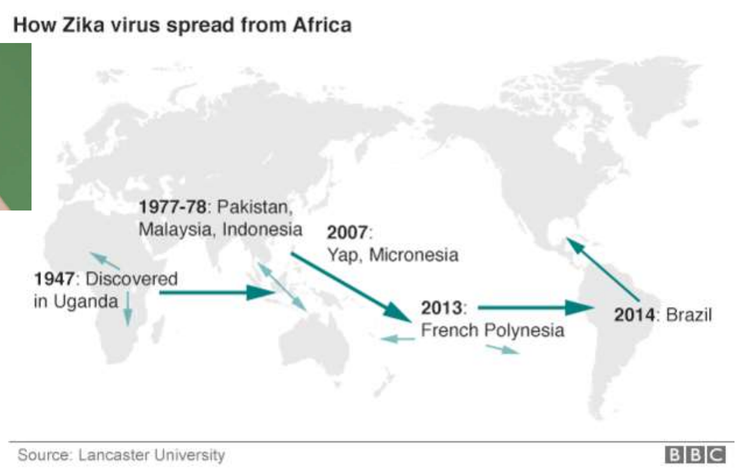




Flaviviridae

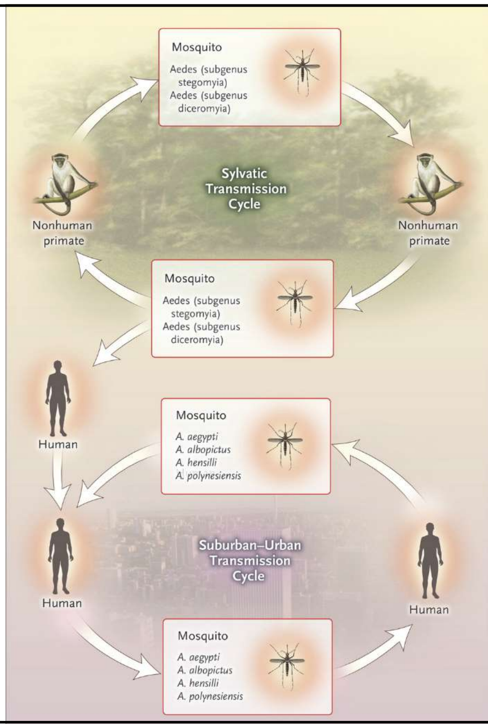
Zika virus

- Described in apes (Makak rhesus) in Uganda during monitoring of the yellow fever in 1947.
- In humans described for the first time in Uganda and Tanzania in 1952 v Ugandě. Subsequently recognised in Africa, Asia, and Pacific (2007-2013) and America (2015 – Brazilia and Columbia).



Flaviviridae

Zika virus



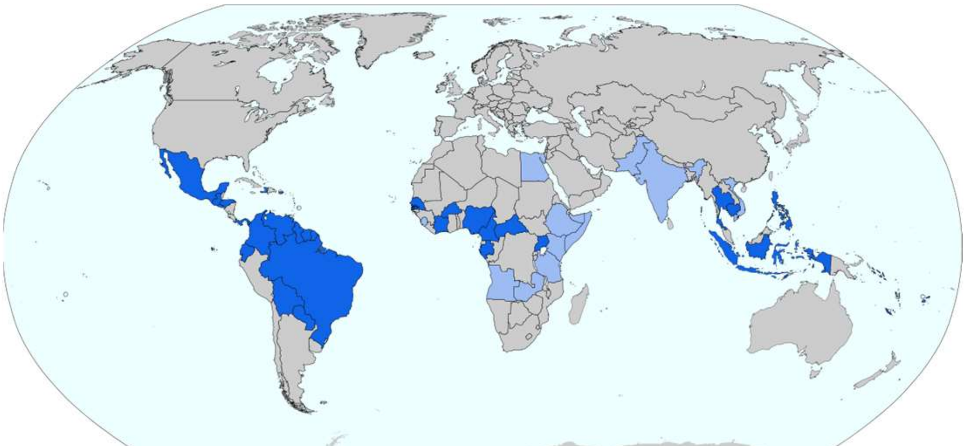
- Transmitted by mosquitos genus Aedes (especially A. aegypti) by blood.
- Transmission is described also by blood directly, perinatal transmission, amnionic fluid, CSF and sperm.

  (However, there are doubts about real presence of the virus in the sperm, or blood contamination).

Flaviviridae

Zika virus

- Incubation period 3-12 days
- Zika fever is presented with fever, conjunctivatis, rash, pain of muscles, joints, and head, malaise lasting for about 2-7 days.

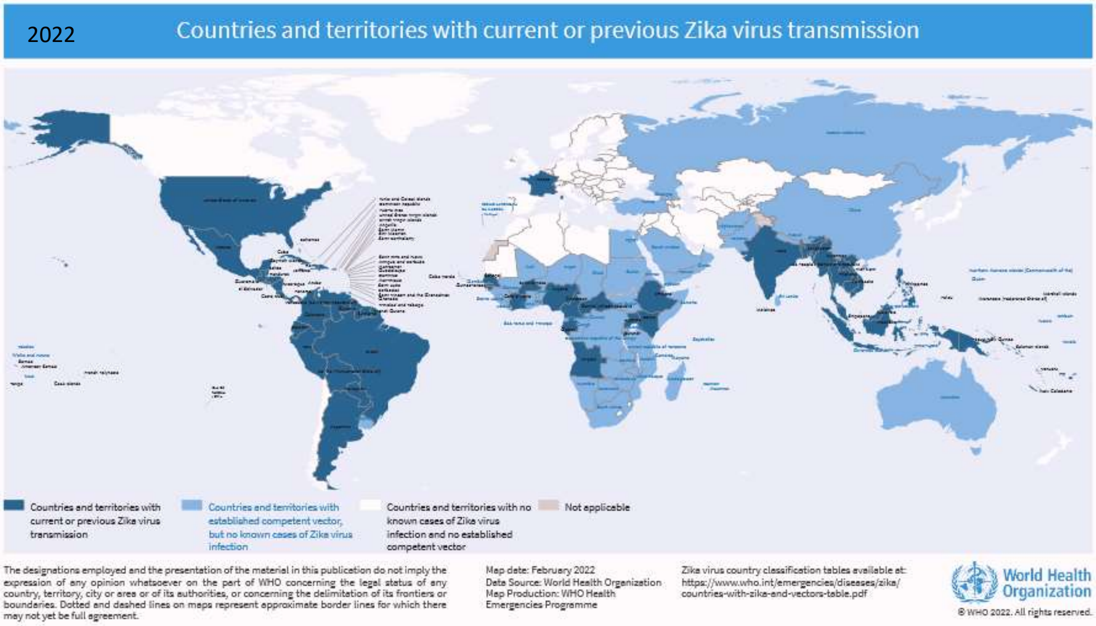


z:BlankMap-World6.svgZika Travel Health Notices, Centers for Disease Control and PreventionZika virus infection – Guyana, Barbados and Ecuador, WHOCountries with local Zika transmission , European Centre for Disease Prevention and ControlVanuatu records first case of rare mosquito-borne zika virus, abcnews.net.auPremier cas autochtone d'infection à virus Zika en Nouvelle-Calédonie, Centre de vaccinations internationales Air France, CC BY-SA 4.0,

Flaviviridae

Zika virus

2022



Flaviviridae

Zika virus

Microcephaly was described in infection during pregnancy during outbreak in Brasil in 2015.

Risk of microcephaly in retrospective study from French polymesia
95 (34–191)/ 10 000 women
+- 0,95%
In Brasil 29%.
(NEJM, Lancet 2016)

Described as causal pathogen in myelitis and Guillain–Barré syndrome.
(NEJM 2016)

Flaviviridae

Dengue virus and Zika virus

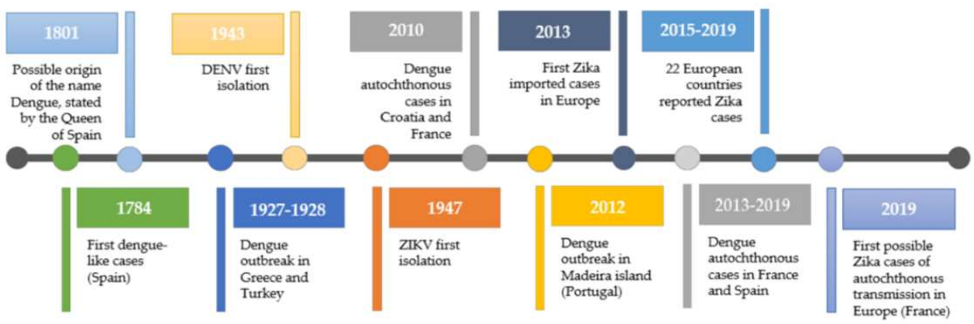


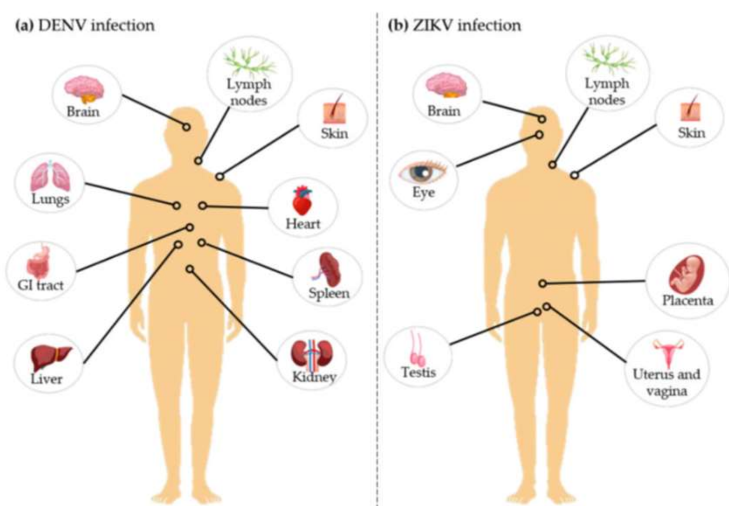
Table 1. Number of reported and travel-associated cases of dengue and Zika in Europe [44].

	Dengue		Zika	
Year	**Reported Cases**	**Travel-Associated Cases**	**Reported Cases**	**Travel-Associated Cases**
2015	2209	1960	29	29
2016	2823	2603	2119	2075
2017	2026	1918	275	264
2018	2191	2062	51	48

Trop. Med. Infect. Dis. **2020**, 5, 150

Flaviviridae

Dengue virus and Zika virus

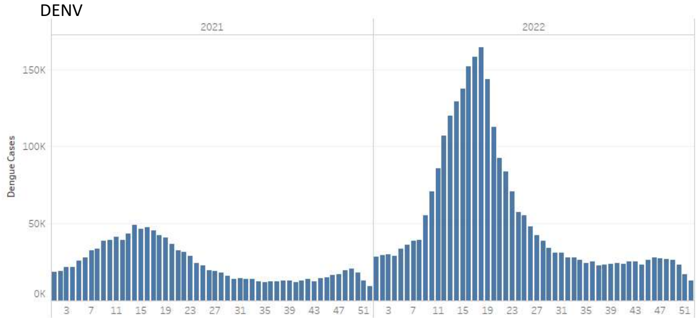


Trop. Med. Infect. Dis. **2020**, 5, 150

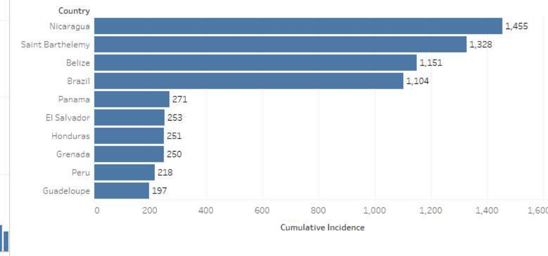
Flaviviridae

Dengue virus and Zika virus

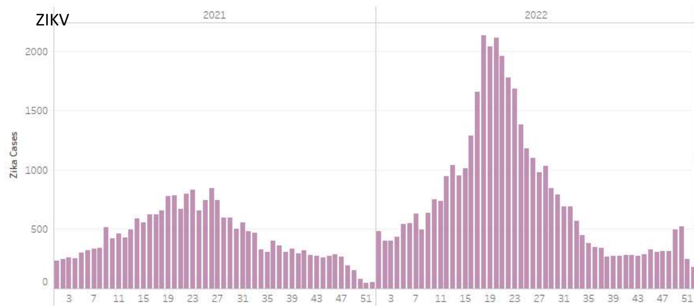
DENV



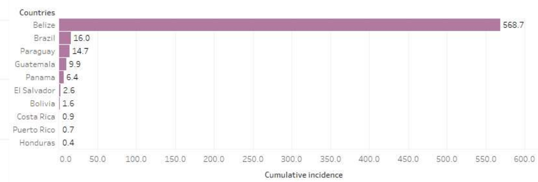
Cumulative incidence of 283.47 cases per 100,000 population.



ZIKV



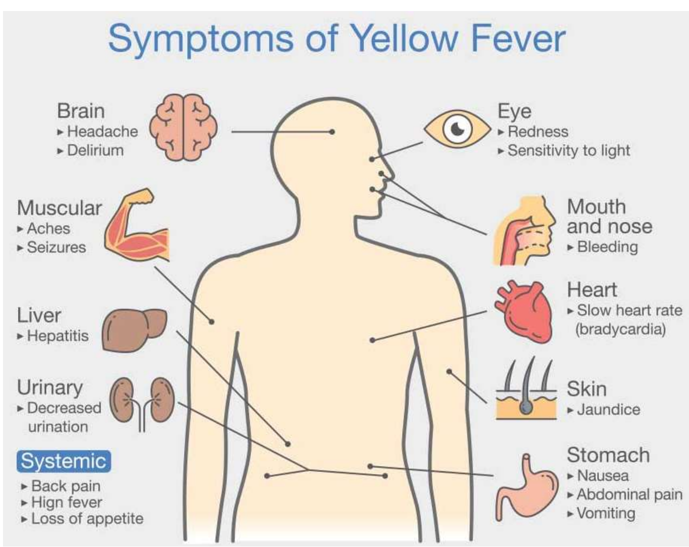
Cumulative incidence 4.08 cases per 100,000 population.



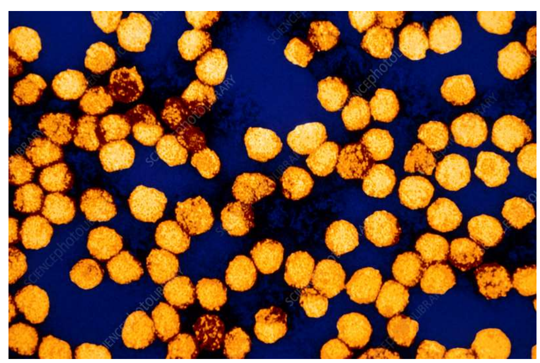
https://ais.paho.org/ha_viz/Arbo/Arbo_Bulletin_2022.asp?env=pri

Flaviviridae

Yellow fever virus



https://www.netmeds.com/images/cms/wysiwyg/blog/2019/11/Yellowfever_big_898.jpg



https://media.sciencephoto.com/image/m0500808/800wm/M0500808-Yellow_fever_virus_particles,_TEM.jpg

Disease described around 1900 by americans physician Walter Reed.

Flaviviridae

Yellow fever virus – Virus žluté zimnice

Tiredness – malaise
Fever
Head ache and retroorbital pain
Muscĺe pain
Conjunctivitis
Vomiting
Stomach pain and diarrhea

Bleeding symptoms

Endothelial dysfunction, capilary leak
Thrombocytopenia and DIC

Subsequent shock, MOF and death.

Highes mortality:
EBOV, MARV, LASV, CCHF and DENV.
Severe liver and kidney failure: YFV, HFRS and HPS.

https://www.cdc.gov/yellowfever/symptoms/index.html

The memory of 20,000 yellow fever deaths in the lower Mississippi valley in 1878 The painful knowledge that during the Spanish-American war of 1898.

A year later, when the US took over the French infrastructure and equipment at the Panama Canal site, Gorgas was sent in to clean up. By then, tens of thousands of workers had died on the site; an estimated 85% fell ill.
In early 1905, hundreds of American labourers fled in fear of the disease. Gorgas' detachment of 4,000 mosquito-fighters got to work. As Agramonte wrote, ten years later, "the work of prevention [is] the only one that may be considered effective when dealing with the epidemic diseases." By December 1905, the workers stopped dying; construction could continue. In 1914, the Panama Canal opened, and a new link between the Atlantic and Pacific oceans was created.

https://www.pbs.org/newshour/world/100-years-panama-canal-10-photos

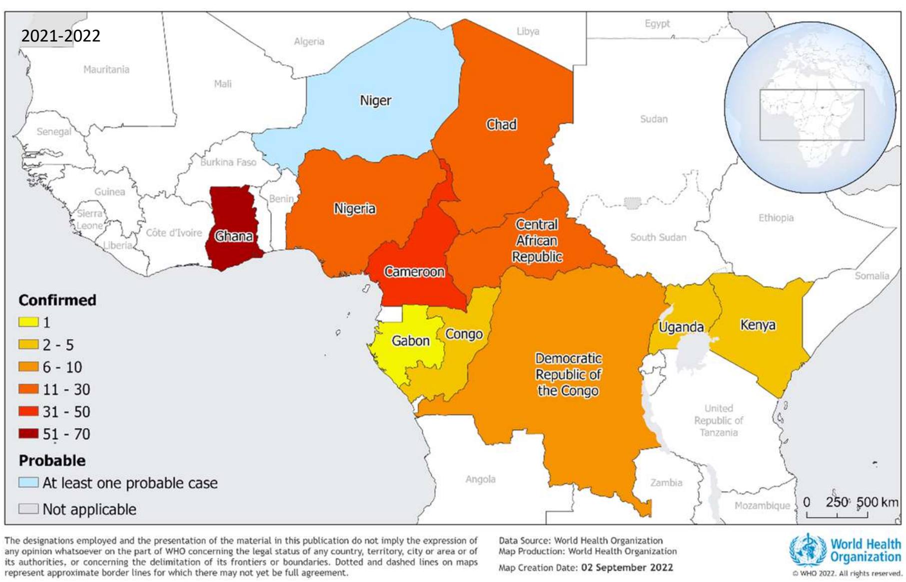
Flaviviridae

Yellow fever virus – Virus žluté zimnice

Yellow fever virus is estimated to cause 200,000 cases of disease and 30,000 deaths each year (90% occurring in Africa).
20% to 50% of infected persons who develop severe disease die.

CDC

From 1 January 2021 to 26 August 2022, a total of 12 countries in the region have reported **184 confirmed cases and 274 probable cases, including 21 deaths**, reflecting ongoing complex viral transmission



Flaviviridae

West Nile virus – Virus západonilské horečky

As of 30 June 2023, European Union (EU) and European Economic Area (EEA) countries have reported **1 133 human cases of West Nile virus (WNV)** infection through The European Surveillance System (TESSy), **including 92 deaths** for 2022, of which **1 113 were locally acquired**, 17 were travel-related, and three had an unknown importation status and unknown place of infection.

Locally acquired cases were reported by Italy (723), Greece (283), Romania (47), Germany (16), Hungary (14), Croatia (8), Austria (6), France (6), Spain (4), and Slovakia (1). Deaths were reported by Italy (51), Greece (33), Romania (5), and Hungary (3).

https://www.ecdc.europa.eu/en/news-events/epidemiological-update-west-nile-virus-transmission-season-europe-2022

Asymptomatic infection in 4 people out of five.
Inkubation period is 3–14 days.

Febrile disease (1/5) – body ache, pain of head, joints, vomiting, diarrhea, or rash. Most of the patients fully recover, but tiredness and weakness can last for weeks and moths.

Severe complications in about 1 of 150 of infected – severe disease affecting CNS (encephalitis), or menigitis (brain, spine). Symptoms are e.g. high fever, headache, neck stiffness, desorientation, coma, tremor, muscle weakness, vision loss and paralysis.

Severe clinical course can be observed in all age groups, however people over 20 yrs and immunosupressed patients are at higher risk…

Recovering may last weeks and months – or CNS damage may last indefinitely.

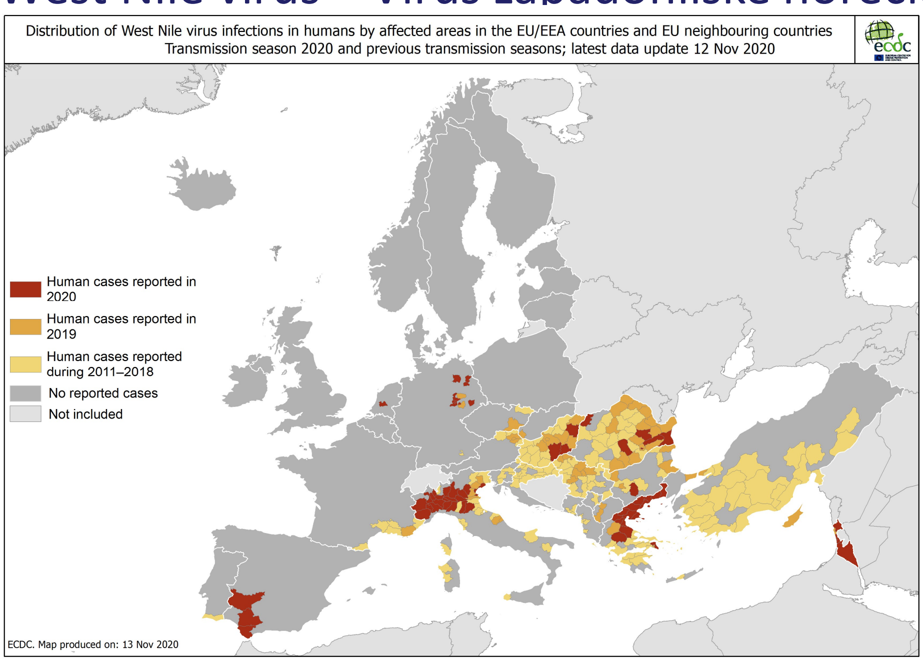
https://www.cdc.gov/westnile/symptoms/index.html

Mortality rate: approx. 1 out of 10 patients with severe disease.

Flaviviridae

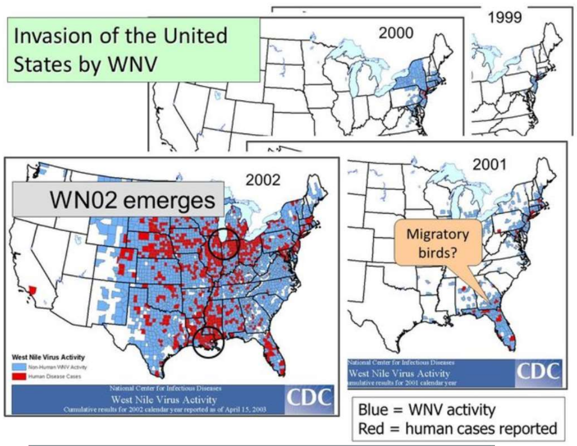
West Nile virus – Virus západonilské horečky

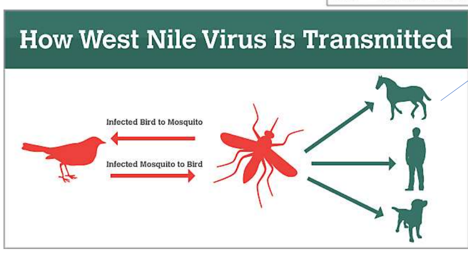
First described in Uganda (West Nile territory) in 1937. Subsequently quickly spread and after WWII it was detected for the first time in Asia. West Nile virus finally appeared also in South and East Europe and Australia. In 1999, WNV spread by ship from Israel to North America.

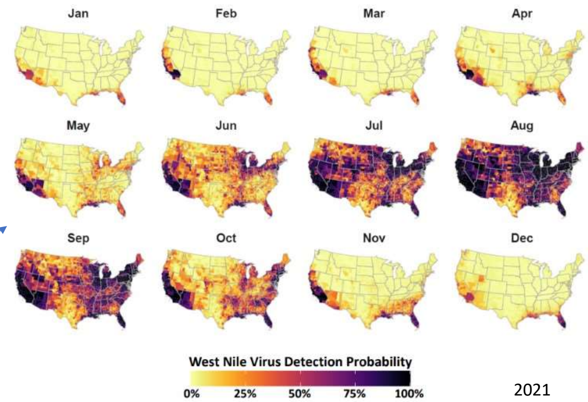


https://www.ecdc.europa.eu/en/publications-data/west-nile-fever-europe-2018-human-cases-compared-previous-seasons-updated-16

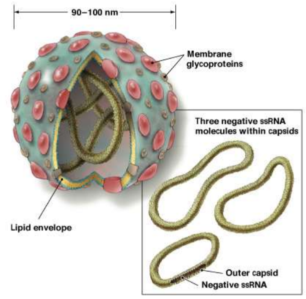
West Nile virus in USA





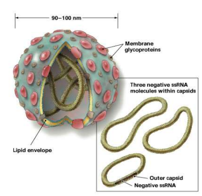


Hantaviruses



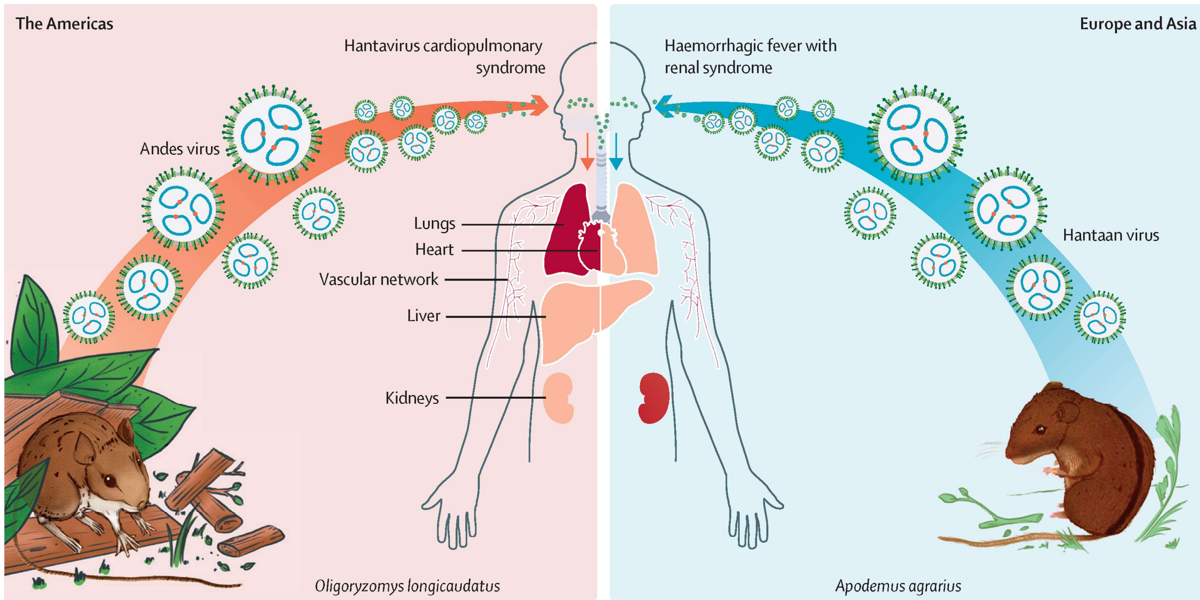
- Bunyaviridae
- ss(-) RNA - 3 segments (small ~ 1.7-2 kb, medium ± 3.7 kb, large ± 6.5 kb)
- enveloped 120-160 nm in diameter
- Incubation period – 2-4 weeks
- The described in 1951, where a hantavirus caused hemorrhagic fever with renal syndrome (HFRS) in North and South Korea.
- Transmitted from rodens, even pet rodens.
- The viruses that caused HFRS in Asia were later grouped as Old World Hantaviruses.
- In 1993 (southwestern USA) was described hantavirus pulmonary syndrome (HPS) - Sin Nombre.
- Hantavirus strains that occur globally – affecting kidneys and lungs mainly.
- Airborne transmission
- Underdiagnosed diseases.

Hantaviruses

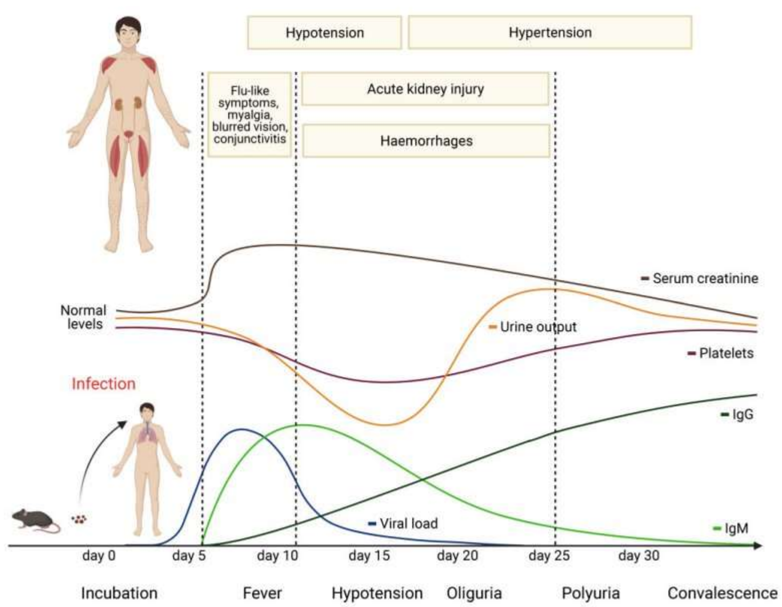


- HFRS – viruses - Dobrava, Hantaan, Puumala a Seoul. Mortality is highest in Hantaan virus – 5–15 %; Puumala and Seoul virus about 1%.
- HPS (Sin Nombre) rare 534 case (1993-2009) – mortality rate 36%; 1-40%.
- List of Hantaviruses: *Andes virus, Amur virus, Asama virus, Azagny virus, Bayou virus, Black Creek Canal virus, Bloodland Lake virus, Blue River virus, Cano Delgadito virus, Calabazo virus, Carrizal virus, Catacamas virus, Choclo virus, Dobrava-Belgrade virus, El Moro Canyon virus, Gou virus, Hantaan River virus, Huitzilac virus, Imjin virus, Isla Vista virus, Khabarovsk virus, Laguna Negra virus, Limestone Canyon virus, Magboi virus, Maripa virus, Monongahela virus, Montano virus, Mouyassue virus, Muleshoe virus, Muju virus, New York virus, Nova virus, Oran virus, Oxbow virus, Playa de Oro virus, Prospect Hill virus, Puumala virus, Rockport virus, Rio Mamore virus, Rio Segundo virus, Sangassou virus, Saaremaa virus, Seoul virus, Serang virus, Sin Nombre virus, Soochong virus, Tanganya virus, Thailand virus, Thottapalayam virus, Topografov virus, Tula virus, Xuan Son virus*

Hantaviruses



https://www.thelancet.com/cms/attachment/c466084c-91d2-4e7e-b9c9-54c0be1ccc1c/gr1_lrg.jpg



Clinical Kidney Journal, 2022, vol. 15, no. 7, 1231–1252

FIGURE 5: The typical disease course in HFRS can be divided into five distinct phases: fever, hypotension, oliguria, polyuria and convalescence. After human infection, viral load peaks after 5–10 days and prodromal symptoms such as flu-like symptoms, myalgia, backache, abdominal pain and blurred vision occur. In parallel, platelets as well as urine output and kidney function decrease, leading to the hallmark triad of AKI, hypotension and hemorrhages in HFRS. With the onset of clinical symptoms, antibodies increase, leading to viral clearance and convalescence. Source: Figure created with Biorender.com and figure concept adapted from Avsic-Zupanc *et al.* [3].

Hantaviruses

FIGURE 1 | Global geographic distribution of hantaviruses as etiological agents of hemorrhagic fever with renal syndrome (HFRS) and hantavirus cardiopulmonary syndrome (HCPS) in humans. The representative hantaviral disease in each continent was marked as different color. Pink color indicates HFRS and blue color indicates HCPS. The gray circle represents the rodent-borne hantaviruses first characterized in nature.

Won-Keun et al. Front. Cell. Infect. Microbiol., 08 January 2021

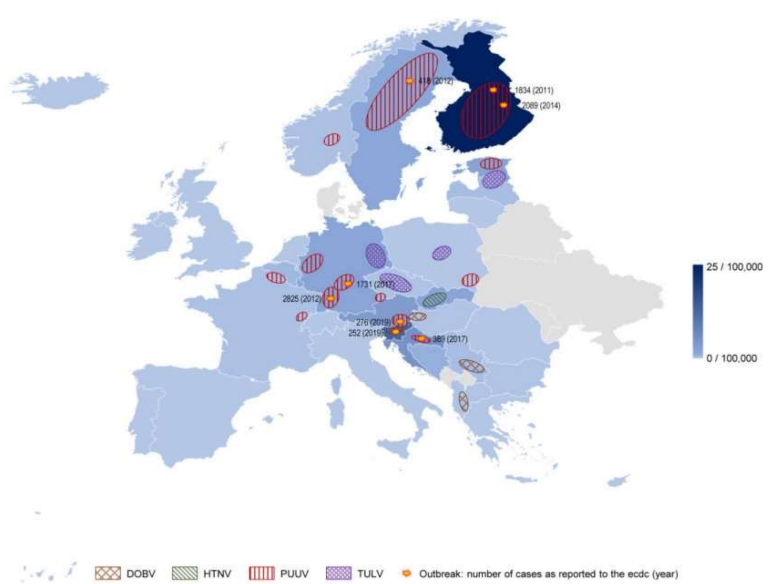
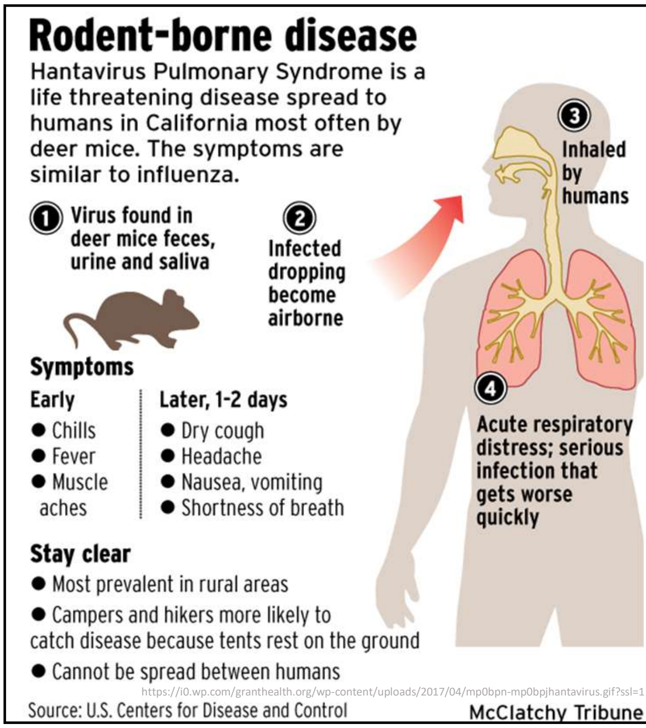


FIGURE 1: Epidemiology of hantavirus infections in Europe. Incidence for hantavirus infection in 2019 as recorded by the European Centre for Disease Prevention and Control (ECDC). More than 4000 cases of hantavirus disease were reported in Europe (0.8 cases per 100,000 population), with detection of PUUV as the causative pathogen in 98% of cases. Finland and Germany accounted for 69% of all reported cases. Distribution of PUUV, Dobrava virus (DOBV), HTNV and Tula virus (TULV) across Europe are depicted by colour. Recent outbreak situations as reported to the ECDC from 2011 to 2021 are indicated with approximately affected cases and year of the outbreak in parenthesis. European countries that do not report hantaviral infections to the ECDC are depicted in grey (Belarus, Denmark, Moldavia, Montenegro, Kosovo, Ukraine).

Clinical Kidney Journal, 2022, vol. 15, no. 7, 1231–1252

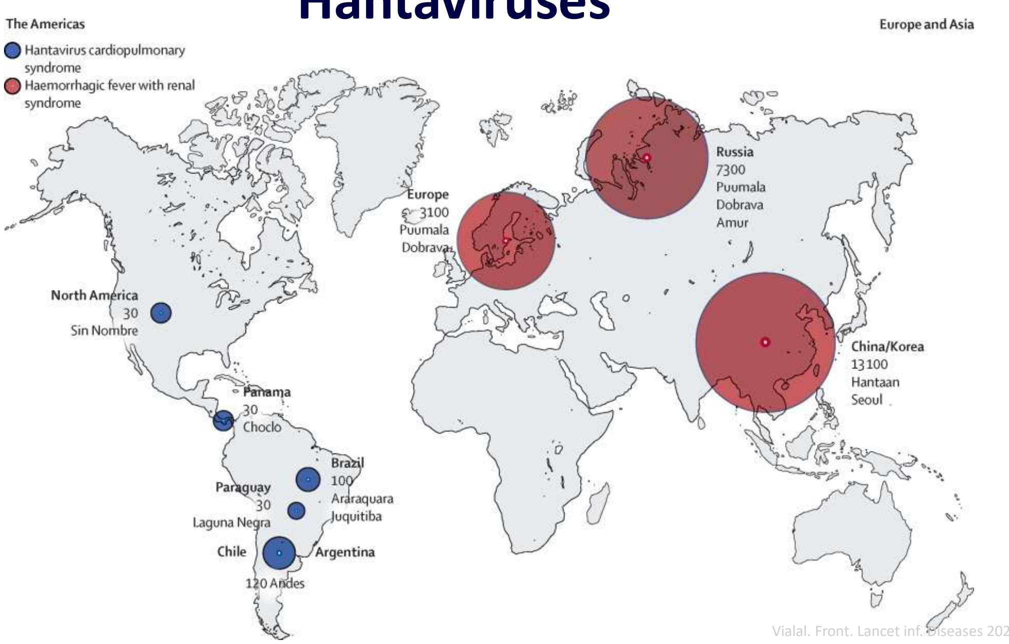
Hantaviruses



https://i0.wp.com/granthealth.org/wp-content/uploads/2017/04/mp0bpn-mp0bpjhantavirus.gif?ssl=1

https://d3i6fh83elv35t.cloudfront.net/static/2019/02/GettyImages-985232088-1024x916.jpg

Hantaviruses

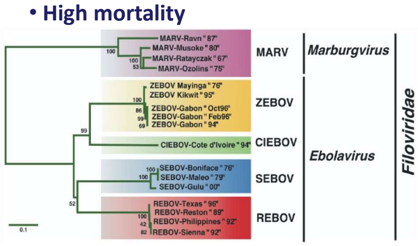


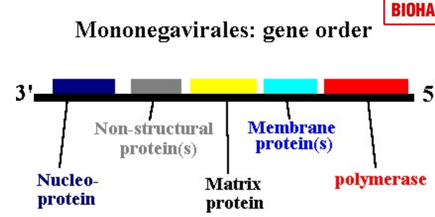
Vialal. Front. Lancet inf. Diseases 2023

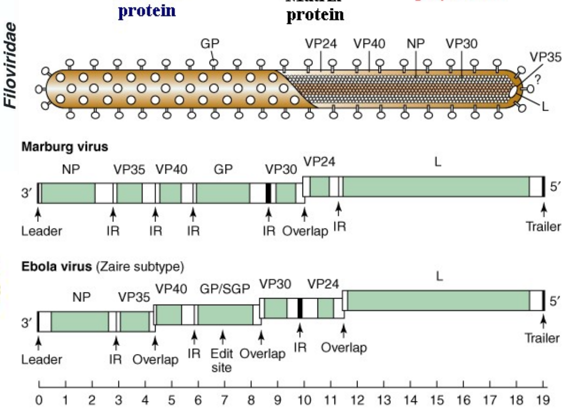
BioSafety Level 4

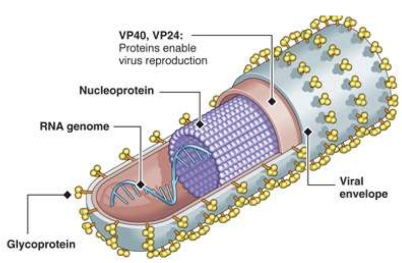
Filoviridae

- ss (-) RNA
- Helical nucleoprotein 13-20 nm wide
- Ebolavirus and Marburg virus
- highly infectious 1-10 virions
- **High mortality**









Source: Brooks GF, Carroll KC, Butel JS, Morse SA, Mietzner TA: *Jawetz, Melnick, & Adelberg's Medical Microbiology, 25th Edition*: http://www.accessmedicine.com

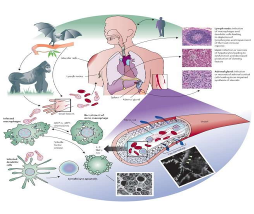
BioSafety Level 4

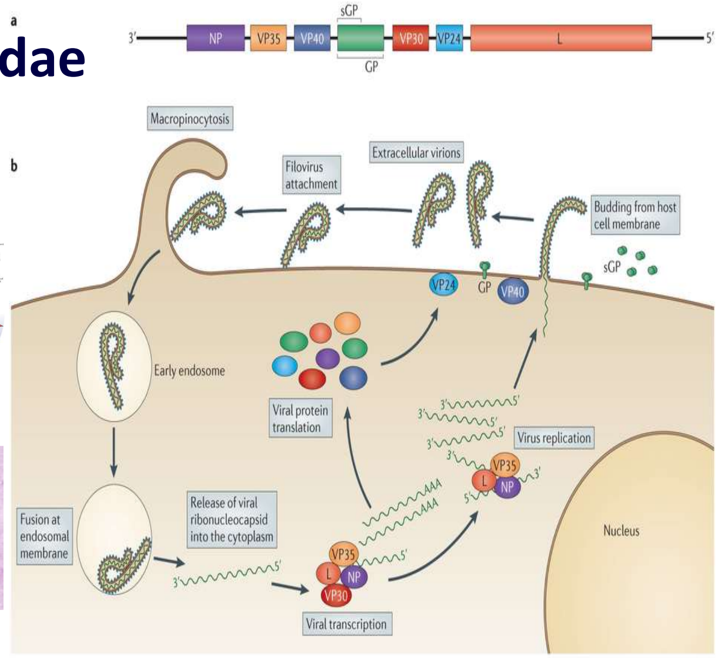
Filoviridae

http://www.nature.com/nrmicro/journal/v13/n11/images/nrmicro3524-f1.jpg

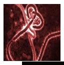
BioSafety Level 4

Filoviridae

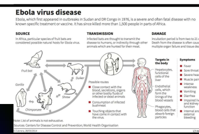


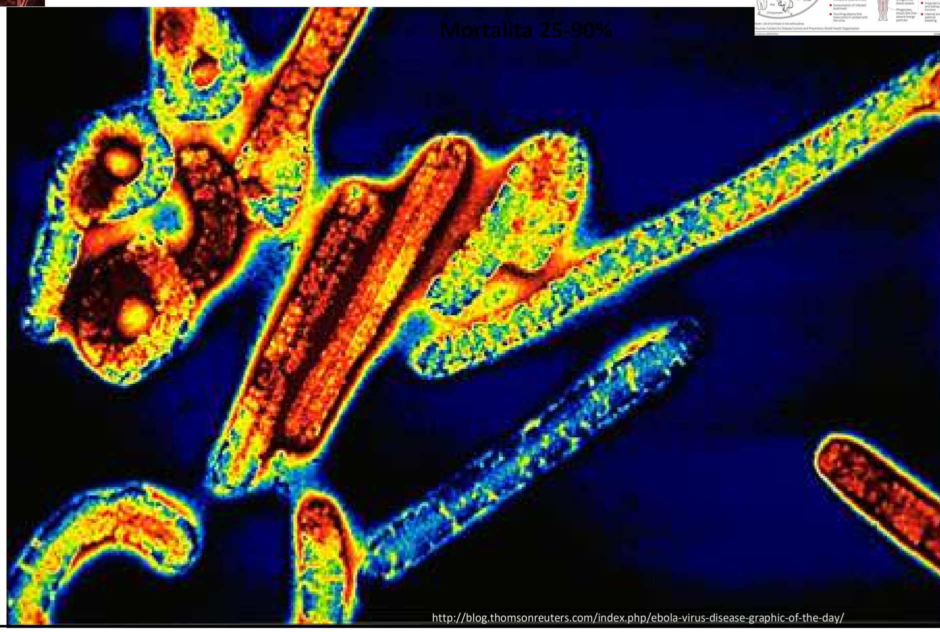


BioSafety Level 4



Filoviridae

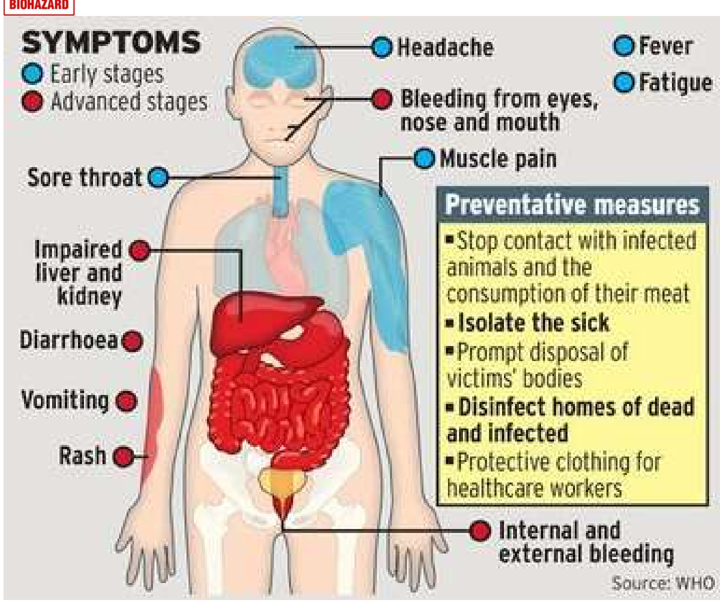




http://blog.thomsonreuters.com/index.php/ebola-virus-disease-graphic-of-the-day/

BioSafety Level 4

Filoviridae



Therapy:

study only

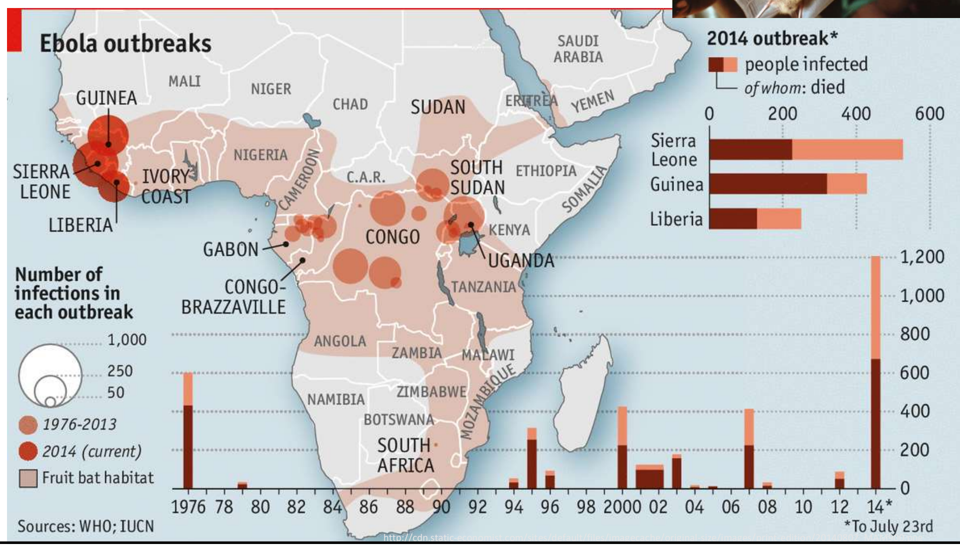
ZMapp – 3 Ab

at the moment

not available!!!!

BioSafety Level 4

Filoviridae



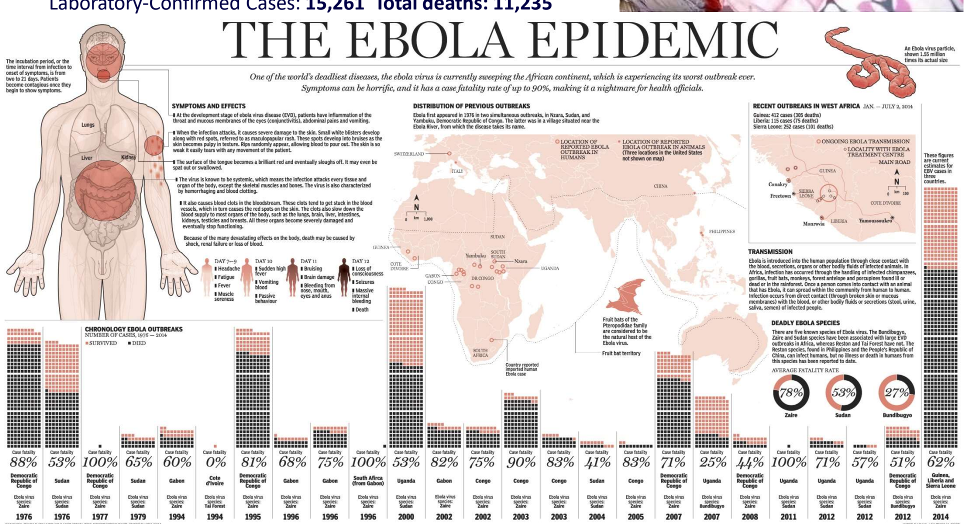
BioSafety Level 4

Filoviridae

2014 EBoV in West Africa (13th April 2016)

-Ebola outbreak: Total Cases: **28,652**

Laboratory-Confirmed Cases: **15,261** **Total deaths: 11,235**



Possible therapy

Virus Family	Virus	Strain	Assay Type	Nuc EC_{50}/EC_{90} (μM)/[SI]	GS-5734 EC_{50}/EC_{90} (μM)/[SI]
Filo-	EBOV	Rec. Mayinga-GFP	REP	1.6/6.7/[31]	0.066/0.203/[151]
		Rec. Mayinga-Gluc	REP	3.1/11/[16]	0.021/0.053/[476]
		Rec. Makona-ZSG	REP	1.3/3.3/[38]	0.014/0.045/[714]
		Makona	VTR	1.0/2.5/[50][#]	0.003/0.019/[666][‡]
	MARV	Rec. Bat371-Gluc	REP	NT	0.019/0.052/[526]
		Rec. Bat371-GFP	REP	1.9/4.6/[26]	0.014/0.047/[714]
Paramyxo-	NiV	Rec. M-Luc2AM	REP	1.5/5.7/[33]	0.045/0.126/[184]
		Rec. M-GFP2AM	REP	2.2/4.0 [22]	0.029/0.053/[286]
		M-1999	VTR	0.49/1.4/[102][#]	0.047/0.083/[180][‡]
		B-2004	VTR/CPE	0.83/2.2/[60][†]	0.032/0.106/[259]
	HeV	1996	VTR/CPE	1.0/1.8/[50][†]	0.055/0.117/[150]
	hPIV3	Rec. JS-GFP	REP	0.51/1.0/[98]	0.018/0.35/[461]
	MV	Rec. rMV^{EZ}GFP(3)	REP	1.0/2.6/[50]	0.037/0.073/[224]
		EZ vaccine	AG	2.0/5.1/[25]	NT
	MuV	IA 2006	AG	9.7/26.3/[5]	0.79/3.4/[10]
Pneumo-	RSV	Rec. rgRSV224 (A2)	REP	0.63/2.2/[79]	0.021/0.059/[395]
	hMPV	Rec. CAN97-83-GFP	REP	0.73/1.7/[NT]	NT
Bunya-	RVFV	Rec. ZH501-GFP	REP	No inhibition	No inhibition
	CCHF	Rec. IbAr 10200	AG	No inhibition	No inhibition
	ANDV	Chile 9717869	AG	NT	7.0/10.1/[1.4]
Arena-	LASV	Josiah	AG	No inhibition	4.5/5.1/[2.2]
Rhabdo-	VSV	New Jersey	CPE	No inhibition	No inhibition
Flavi-	AHFV	200300001	CPE	49.9/ > 150/[NT]	4.2/17.6/[2.4]
	KFDV	P9605	CPE	46.3/ > 350/[NT]	1.8/3.4/[5.6]
	TBEV	Hypr	CPE	51.2/ > 150/[NT]	2.1/3.5/[4.8]
	OHFV	Bogoluvovska	CPE	50.6/ > 350 [NT]	1.2/3.9/[8.3]

GS-5734 = remdesivir

Vakcíny:
mRNA - EBOV

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Co jsou to arbovirové infekce (arthropod-borne)?

- Arboviruses refer to a diverse group of viruses that are transmitted via mosquitos, ticks, or sandflies and are capable of causing a wide range of diseases. It is important to understand the disease processes caused by these infectious agents, given the increasing frequency of infection and the potential for additional emerging diseases.

•Initial symptoms can include sudden onset of fever, chills, severe headache, back pain, general body aches, nausea, vomiting, fatigue (feeling tired), weakness.
•Most people who develop symptoms improve within one week.
•For some people who recover, weakness and fatigue (feeling tired) might last several months.
•A few people will develop a more severe form of the disease.
•For 1 out of 7 people who have the initial symptoms, there will be a brief remission (a time you feel better) that may last only a few hours or for a day, followed by a more severe form of the disease.
•Severe symptoms include high fever, yellow skin or eyes (jaundice), bleeding, shock, and organ failure.
•Among those who develop severe disease, 30-60% die.