

Viral hemorrhagic fevers (VHFs)

Caused by 4 families of viruses: Arenaviridae, Bunyaviridae, Filoviridae, Flaviviridae
 Cause diffuse damage to overall vascular system
 Good bioweapons
Ebola and Marburg have the highest mortality rate

| Common features | How do we get infected? | Common pathophysiology + common clinical features | Lab studies | Treatment | Prevention + vaccination |
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| <p>-Enveloped lipid-encapsulated</p> <p>-single stranded RNA (replication in cytoplasm)</p> <p>-zoonotic (animal-borne)</p> <p>-geographically restricted by host</p> <p>-present in nature (rodents, bats, mosquitoes, ticks)</p> | <p>1-rodents & Arthropods, both reservoir & vector</p> <p>2-person to person: airborne potential for some arenaviridae and filoviridae</p> <p>Two types of viruses:</p> <p>Arboviruses: transmitted by arthropod vectors bunyaviridae (expect Hantavirus) + Flaviviridae</p> <p>non-arboviruses: arenaviridae, filoviridae</p> | <p>Viremia – cytokine storm -> constitutional symptoms</p> <p>Immune response -- endothelial injury, consumption of clotting factors and platelets, bleeding internally and externally through orifices</p> <p>Early/ prodromal symptoms: fever, myalgia, malaise, headache, arthralgia ...</p> <p>Progressive signs : hemorrhage starts as ecchymosis, petechiae ...</p> <p>End-stage: profuse bleeding (internally and externally), consumptive coagulopathy/ DIC</p> | <ul style="list-style-type: none"> ✓ CBC ✓ Liver enzymes (yellow fever) ✓ Kidney test ✓ Serological test: RT- PCR ✓ Electron microscopy (arenaviridae) | <ul style="list-style-type: none"> ➤ supportive care: fluid and electrolyte management, anticoagulants ➤ mange severe bleeding complications: platelets, fresh frozen plasma ➤ ribavirin (in vitro activity): Lassa fever, New world HF, Rift valley fever, <i>no evidence to support use in Filovirus or Flavivirus infections</i> | <p>-Vector control in arboviruses</p> <p>-Rodents control in non-arboviruses</p> <p>-Isolation of infected individuals</p> <p>-Biosafety level4</p> <p>Passive immunization: Argentine and Bolivian HF</p> <p>Active immunization: Yellow fever</p> |

Arenaviridae

Argentine HF, Bolivian HF, Venezuelan HF, Lassa fever (**highest mortality rate in this group**), Brazilian HF

Under the EM the cytoplasm appears sandy

| Transmission | Clinical features | Example(s) | Distinguishing features for the example(s) | treatment |
|---|---|---|---|---|
| <p><i>Non-arboviruses</i> Virus transmission and amplification occurs in rodents -> shed virus through urine, feces, and other excreta -> human infection (contact with excreta, contaminated materials, aerosol transmission) Person to person transmission</p> | <p>Incubation period (10-14 days) fever and malaise (2-4 days) Hemorrhagic stage: hemorrhage, leukopenia, thrombocytopenia, neurological signs</p> | <p>Lassa fever: (west Africa) ✓ Rodent-borne (mastomys natalensis) ✓ interpersonal transmission (direct contact, sex, breast feeding) Patients still shed the virus in their urine at least 2 weeks after recovery / isolation</p> | <ul style="list-style-type: none"> ○ <u>Gradual onset</u> ○ Retro-sternal pain ○ Exudate pharyngitis ○ Hearing loss in 25% <u>may be persistent</u> ○ Spontaneous abortion <p>Mortality 1-3% overall (up to 50% in epidemics)</p> | <p>supportive treatment, ribavirin</p> |

Bunyaviridae

Rift Valley Fever virus, Crimean-Congo Hemorrhagic Fever virus, Hantavirus

L segment — codes for an L- protein (the RNA dependent RNA polymerase)

M segment — codes for two surface glycoproteins G1 and G2 which form the envelope spikes

S segment — codes for an N- protein (nucleocapsid protein)

| Transmission | Clinical features | Example(s) | Distinguishing features for the example(s) | Treatment |
|---|-------------------|---|---|---|
| <p><i>Arthropod vector except for Hantaviruses</i> RVF — <u>Aedes mosquito</u> CCHF — <u>Ixodid tick (Hyalomma)</u> Hantavirus — Rodents Less common= Aerosol, Exposure to infected animal tissue</p> <p><u>Transmission to humans</u></p> <ul style="list-style-type: none"> ✚ Arthropod vector (RVF, CCHF) ✚ Contact with animal blood or products of infected livestock ✚ Rodents (Hantavirus) ✚ Laboratory aerosol ✚ Person to person transmission with CCHF | | <ul style="list-style-type: none"> ✓ Rift valley fever Asymptomatic or mild illness in humans ✓ Crimean-Congo Hemorrhagic Fever ✓ Hantaviruses Transmission to humans: Exposure to rodent saliva and excreta, inhalation, bites, Ingestion contaminated food/water (?), Person-to-person (Andes virus in Argentina) 1- Hantavirus (Hemorrhagic Fever with Renal Syndrome (HFRS)) 2- Hantavirus Pulmonary Syndrome (HPS) | <ul style="list-style-type: none"> ○ Hemorrhagic complications rare (<5%) ○ Vision loss (retinal hemorrhage, vasculitis) in 1-10% <p>Overall mortality 1%</p> <ul style="list-style-type: none"> ○ Abrupt onset ○ Most humans infected will develop hemorrhagic fever ○ Profuse hemorrhage <p>Mortality 15-40%</p> <ul style="list-style-type: none"> ○ <u>Insidious onset</u> ○ Intense headaches ○ Blurred vision ○ kidney failure (causing severe fluid overload) <p>Mortality: 1-15%</p> | <p>supportive treatment, Ribavirin?</p> <p>Ribavirin</p> |

Flaviviridae

Dengue virus, Yellow fever virus, Omsk hemorrhagic fever virus, Kyassnur forest disease virus

| Transmission | Clinical features | Example(s) | Distinguishing features for the example(s) | treatment |
|--|-------------------|---|---|-----------|
| <p>Arthropod vector</p> <ul style="list-style-type: none"> Yellow Fever and Dengue viruses (<u>Aedes aegypti</u>) Kasanur Forest Virus (<u>Ixodid tick/ Haemaphysalis vector</u>) Omsk Hemorrhagic Fever virus: Muskrat urine, feces, or blood <p>Sylvatic cycle [mosquito, man and monkey] – humans are accidental hosts</p> <p>Urban cycle [mosquito and man]</p> | | <ul style="list-style-type: none"> ✓ Yellow fever ✓ Dengue fever: Dengue Fever (DF)/ Fatality: <1% Dengue Hemorrhagic Fever (DHF)/ Fatality: 5-6% Dengue Shock Syndrome (DSS)/ Fatality 12-44% Four distinct serotypes (cause human disease): DEN-1, DEN-2, DEN-3, DEN-4 ✓ Omsk Hemorrhagic Fever: Fever Lasting sequela ✓ Kyanasur Forest: (India) | <ul style="list-style-type: none"> ○ Biphasic infection (viremia → window → toxemia) ○ Common hepatic involvement & jaundice Mortality 15-50% ○ Sudden onset ○ Eye pain ○ Rash ○ Complication/ sequelae uncommon Illness is severe in younger children ○ Acute onset ○ Biphasic infection ○ Complication: hearing loss, hair loss, psycho-behavioral difficulties Mortality 0.5-3% ○ Acute onset ○ Biphasic Case-fatality: 3-5% (400-500 cases annually) | |

Filoviridae

Ebola: Ebola-Zaire, Ebola-Sudan, Ebola-Ivory Coast, Ebola-Bundibugyo, (Ebola-Reston) + Marburg

Ebola-Reston doesn't cause a human disease

| Transmission | Clinical features | Example(s) | Distinguishing features for the example(s) | treatment |
|---|---|---|---|-----------|
| <p>Non-arboviruses</p> <p>Reservoir is UNKNOWN = Bats implicated with Marburg</p> <ul style="list-style-type: none"> Intimate contact | <p>Most severe hemorrhagic fever</p> <p>Incubation period: 4-10 days</p> | <ul style="list-style-type: none"> ✓ Ebola Rapidly fatal febrile hemorrhagic illness | <ul style="list-style-type: none"> ○ Acute onset ○ GI involvement / Weight loss 25-90% case-fatality | |

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| <ul style="list-style-type: none"> + Nosocomial transmission -- Reuse of needles and syringes, Exposure to infectious tissues, excretions, and hospital wastes + Aerosol transmission | <p>Abrupt onset (Fever, chills, malaise, and myalgia) Hemorrhage and DIC Death around day7-11 Painful recovery</p> | <p>Transmission: bats implicated as reservoir, Person-to-person, Nosocomial</p> <p>✓ Marburg</p> | <ul style="list-style-type: none"> ○ Sudden onset ○ Chest pain ○ Maculopapular rash on trunk ○ Pancreatitis ○ Jaundice <p>21-90% mortality</p> | |
|---|--|--|--|--|