Doctor.021

no. 2

CVS MICROBIOLOGY

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Viral hemorrhagic fevers (VHFs)

Overview:

• As the name implies (viral hemorrhagic) they share the ability to cause viral infections, fever (usually in the viremia phase caused by the cytokine storm), and bleeding (which starts under the skin (petechiae ecchymosis), and at the end stage patients bleed from every orifice in their bodies internally and externally). They are marked by diffuse vascular damage.

• Viral hemorrhagic fevers (VHFs) are a group of illnesses caused by four families of viruses: **Arenaviridae, Bunyaviridae, Flaviviridae, and Filoviridae.**

• **Diffuse Damage to overall vascular system**.

• Symptoms often accompanied by **hemorrhage**.

• **Some VHFs cause mild disease, but some, like Ebola or Marburg,**

cause severe disease and death; caused by Filoviridae and it is the most important type.

• The different names within each family of these viruses are dependent on the firstgeographic region they were isolated from as they have limited geographic distribution and limited distribution of the host or their natural reservoir.

1. **Arenaviridae: Lassa Fever** (West African), **Argentine HF (Junin), Bolivian HF (Machupo), Brazilian HF (Sabia) and Venezuelan HF (Guanarito**) (the last 4 are South African)
2. **Bunyaviridae: Rift Valley Fever (RVF), Crimean Congo HF (CCHF)** and hantavirus which has two types: 1. **Hantavirus (Hemorrhagic Fever with Renal Syndrome (HFRS))**, also known as the old virus (which causes hemorrhagic fever). 2. **Hantavirus Pulmonary Syndrome (HPS)** also known as new world virus (doesn't cause hemorrhagic fever).
3. **Filoviridae: Marburg and Ebola**.

4. **Flaviviridae: Yellow Fever, Dengue Fever** (the first two distribution is between South Africa and America), **Omsk HF** (was first isolated from Russia and its main distribution is in Europe) and **Kyasanur Forest Disease** (in India).

Quick Overview: How do we get infected?

- Rodents & Arthropods, both reservoir & vector:
  - Bites of infected mosquito or tick.
  - Inhalation of rodent excreta.
  - Infected animal product exposure.
- Person-to-Person:
  - Blood/body fluid exposure.
  - Airborne potential for some **arenaviridae (lassa fever and yellow fever)**, **filoviridae (Marburg and Ebola).**

Common features:

- **Enveloped Lipid-encapsulated.**
- **Single-strand RNA.**
- **Zoonotic (animal-borne). Some can be transmitted through person to person (arenaviridae and filoviridae)**
- **Geographically restricted by host.**
- **Persistent in nature (rodents** (most common), bats, mosquitoes, ticks, livestock, monkeys, and primates).
- Survival dependent on an animal or insect host, for the natural reservoir.

- VHFs are classified according to the involvement of an arthropod vector in their transmission cycle into 2 groups:

1. **Arboviruses** (Arthropod-borne): viruses which one of their main routes of transmissionis an arthropod (such as mosquitoes or ticks). Examples include: **Bunyaviridae -with the exception of Hantaviruses- and Flaviviridae.**
2. **Non-Arboviruses**: viruses that are not transmitted by arthropods (don't have a vector), transmitted only through animal to human or human to human. Examples include: **Arenaviridae and Filoviridae.**

1-Arenaviridae

• **Enveloped RNA viruses (their RNA is segmented), non-Arboviruses (non-arthropod**s), their replication takes place in the cytoplasm, and they carry RNA dependent-RNA polymerase.

• They have taken their specific name from the "Arena" (means the place of competition); because these viruses acquire the host's ribosomal subunits in their virion state. Those **ribosomes** appear under the electron microscope as a "**Sandy Cytoplasm**".

• Junin virus: Argentine hemorrhagic fever (South African).

• Machupo virus: Bolivian hemorrhagic fever (South African).

• Guanarito virus: Venezuelan hemorrhagic fever and (South African).

• Lassa virus: Lassa fever- Nigeria (West African, have the highest mortality rate).

• Sabia virus: Brazilian hemorrhagic fever (South African).

Arenaviridae Transmission

• Virus transmission and amplification occurs in **rodents**. Remember they're non-arthropod. They shed the virus through urine, feces, and other excreta.

• Human infection: Contact with excreta, Contaminated materials, Aerosol transmission

• **Person-to-person transmission with lassa fever.**

• Arenaviridae have two types of transmission between the infected rodents:

1. Horizontal transmission: It means the transmission is between two organisms, (NOT between a mother and her progeny). if one rodent got infected by another infected rodent, it will die at the end and the **transmission cycle will not continue.**

2. Vertical transmission: It means the transmission is from a mother to her fetus . Here infected rodents transmit the virus to their fetus' and the **transmission cycle continues**. That is why vertical transmission is **much more dangerous** compared to horizontal transmission.

Arenaviridae in Humans

• The incubation period is 10-14 days (less than 2 weeks) and they have an acute onset.

• Arenaviridae have 2 stages of the disease (Biphasic) according to the severity of the infection:

1. Prodromal phase (viremia phase): the first stage that starts after 2-4 days, it is characterized by a high viral load in the blood. It includes **constitutional symptoms** that are associated with any type of infection; for example: fever, malaise, headache, joints pain, myalgia and photophobia. It is important to know that these signs and symptoms are NOT specific to this family.

2. Hemorrhagic phase (toxemia phase): the second stage in which there is bleeding diathesis (tendency). In this phase, patients are at high risk of **DIC** (Disseminated Intravascular Coagulopathy), also known as Consumptive Coagulopathy; in which there is high consumption of clotting factors and platelets in the body, which increases the bleeding tendency and **leukopenia, thrombocytopenia** (DIC mainly happens in Filoviridae (Marburg and Ebola)) and this explains their high mortality rates. Treatment is supportive, by giving the patient clotting factors, platelets, plasma and blood units.

• **At the end stage** of the Arenaviridae infection, some psycho-behavioral changes (**neurologic signs**) might appear, for example: vision loss and hearing loss.
• Arenaviridae infection is milder than Filoviridae infection.

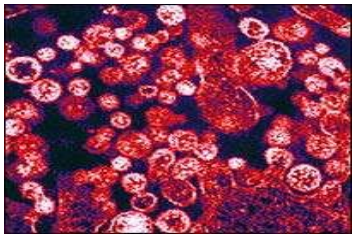
Arenaviridae: Lassa Fever

• First seen in Lassa (among missionary nurses who then died by the lassa hemorrhagic fever), Nigeria in 1969. Now the incidence rate is high in all countries of **West Africa** (5-14% of all hospitalized febrile illnesses).

• Routs of transmission of Arenaviridae (non-arthropod):

1. Rodent-borne (the initial route of transmission): direct contact with infected (Mastomys natalensis) rodent, which is the natural reservoir, or by inhalation of aerosol from the rodent's excreta or urine.

2. Interpersonal transmission (person to person): Direct Contact, Sex, Breast Feeding.



• The figure to the right shows the **sandy cytoplasm** appearance for Lassa virus under EM (looks like the arena of a stadium hence the name).

• **Distinguishing Features** include:
Gradual onset of the disease with an incubation period (opposite to Filoviridae (Marburg and Ebola) which have an acute onset), **retro-sternal pain, exudative pharyngitis, hepatitis, hearing loss** (in 25% may be persistent even after recovery) "**deafness**" in the fetus after birth if they were infected from their mothers and **spontaneous abortion** in pregnant women.

• Stages of lassa fever: gradual, prodromal, progressive and then end stage with marked hemorrhage, organ failure and hypovolemia then it might progress to death.

• Mortality 1-3% overall in sporadic cases because the transmission cycle is not so active (up to 50% in epidemics).

• Lassa fever (and all viruses in this lecture) requires **biosafety level 4**; because they are so dangerous to work with in ordinary laboratories, thus nosocomial infections (infection from hospitals) are so common.

• **Very important:** Lassa fever patients keep shedding the virus from their urine for at least 2 weeks post recovery, so they must be **isolated for 2 weeks.**

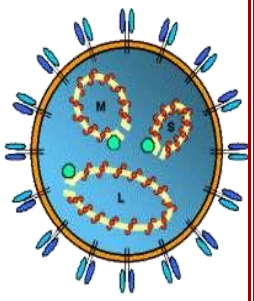
• **Therapy: Ribavirin** (antiviral drug, effective documented treatment).

2-Bunyaviridae

• **Rift Valley Fever virus (RVF) (arbovirus, least mortality rates).**
• **Crimean-Congo Hemorrhagic Fever virus (CCHF) (arbovirus).**
• **Hantavirus (non-arbovirus).**

• They are zoonotic arthropod-borne viruses EXCEPT for Hantaviruses which are non-arboviruses.

• The RNA of this family is **segmented** (genes that encode for certain functions are present on different segments). There are 3 segments:



1. L-segment (Large) codes for an L-protein **(the RNA dependent RNA polymerase).**

2. M-segment (Medium) codes for two surface glycoproteins G1 and G2, which form the **envelope spikes.**

3. S-segment (Small) codes for an **N-protein** (nucleocapsid protein).

Bunyaviridae Transmission

• Arthropod vector. Exception – Hantaviruses, can also be transmitted by person to person but it's not a very important route.

• **RVF** (Rift Valley Fever) – **Aedes aegypti mosquito** (this mosquito transmits yellow and dengue fever).

• **CCHF (Crimean-Congo Hemorrhagic Fever) – Ixodid tick (Hyalomma)**

• **Hantavirus – Rodents**

• Less common: aerosol (mainly in laboratory personnel) and exposure to infected animal tissue from direct contact.

Transmission to humans:

• **Arthropod vector (RVF (Aedes aegypti mosquito), CCHF (Ixodid tick)).**

• Contact with animal blood or products of infected livestock.

• **Rodents (Hantavirus)** (non-arthropod, direct contact with the infected animal).

• Laboratory aerosol.

• **Person-to-person** transmission with **CCHF** (remember **lassa fever** is also transmitted through this route).

Bunyaviridae: Rift Valley Fever

• **asymptomatic or mild illness in humans** as it's the simplest virus in this family with the lowest **overall mortality rate (less than 1%)** It is an, but still is a fatal disease in cattle or sheep.

• Distinguishing Characteristics:

  • it has hemorrhagic complications, but they are rare (<5%).

  • **Vision loss** "**blindness**" (due to **retinal haemorrhage, vasculitis**) in 1-10% of patients.

• Very important: The arthropod vector that transmits RVF is the Aedes aegypti mosquito.

• The incubation period is less than a week (usually 2-5 days).

• **Therapy: Ribavirin** is NOT considered as an effective documented treatment for Rift Valley Fever, it's only documented in Lassa Fever and CCHF, so we mainly use supportive therapy.

Bunyaviridae: Crimean-Congo Hemorrhagic Fever (CCHF)

• The virus causing CCHF is an **arbovirus**, and the vector that transmits the virus is the **Ixodid tick (Hyalomma).**

• **Person to person transmission** is an important mode of transmission for CCHF, in addition to **aerosols inhalation** from laboratories.

• **Distinguishing features: Abrupt (acute) onset, most humans infected will develop hemorrhagic fever, Profuse haemorrhage.**

• **Mortality 15-40% (higher than RVF).**

• **Therapy: Ribavirin (documented effectiveness).**

Bunyaviridae: Hantaviruses

• They are **non-arboviruses (The only exception for Bunyaviridae family).**

We have two serotypes of Hantaviruses:

1. Old-world Hantavirus: which causes Hemorrhagic Fever with Renal Syndrome(HFRS).
2. New-world Hantavirus (Nombre virus): which causes Hantavirus Pulmonary Syndrome (HPS). (Not of our interest for this lecture).

• **Transmission to humans:**

1. **Direct contact or exposure to rodents** through saliva, excreta, inhalation, bites.
2. Ingestion of contaminated food/water: This route of transmission is still controversialand is not evidence-based yet as a well-established route of transmission.
3. **Person-to-person transmission only found in Andes virus in Argentina**.

Hemorrhagic Fever with Renal Syndrome (HFRS)

1. **Distinguishing Features: Insidious (chronic) onset, intense headaches, blurred vision,** acute **kidney failure (causing severe fluid overload).**
2. **Mortality rate: 1-15%.**

3. Flaviviridae

• They are arboviruses, enveloped RNA, and their replication takes place inside the cytoplasm.

• **Dengue virus.**

• **Yellow Fever virus.**

• **Omsk Hemorrhagic Fever virus** (in Russia).

• **Kyassnur Forest Disease virus** (in India).

• This family has a lot of viruses other than the previous four: west nile virus and san carlos virus (which cause encephalitis) and hepatitis virus.

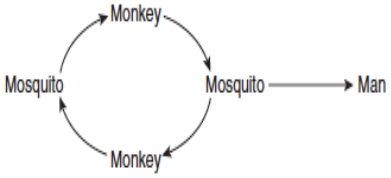
Flaviviridae Transmission

• Arthropod vector

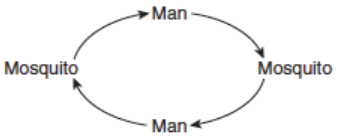
• **Yellow Fever and Dengue viruses** have three life cycles:

  • **Aedes aegypti** (inside the arthropod).

  • **Sylvatic cycle** (mainly in the jungle forest and non-human primates are part of the cycle) as you can see from the picture, the monkeys are a part of the cycle **(intermediate host),** hunters usually get infected through this cycle.



  • **Urban cycle** (the victor lives with the normal population, and it directly infects the human without an intermediate host, as you can see in the picture.



• **Omsk Hemorrhagic Fever virus**: Fever Lasting sequela - **Muskrat** urine, feces, or blood.

• **Kasanur Forest Virus- Ixodid tick.**

• **Very important:** It is important to mention here that the vector for RVF virus is the same as the vector for yellow fever virus and dengue virus, which is the **Aedes aegypti.**

• Yellow and dengue fevers are common in Africa and South America.

Flaviviridae: Yellow Fever

•Distinguishing features: Biphasic infection.

• ALL Flaviviridae are characterized by the **"Biphasic clinical presentation"**:

1. **Viremia phase:** It is characterized by a high viral load in the blood and high secretion of cytokines. It includes **constitutional signs** and symptoms; for example: marked fever.
   In between the 2 phases, there is a **window period**, in which signs and symptomsdisappear.
2. **Toxemia phase: Fever returns along with the constitutional symptoms + Hemorrhagicsigns and symptoms appear.**

• Common hepatic involvement & jaundice

•Mortality: 15-50% (high, but still not comparable with the last family Filoviridae).

Flaviviridae: Dengue

• Dengue fever (DF) Fatality: <1%, has 4 distinct serotypes (DEN 1, DEN 2, DEN 3, DEN 4), all are known to cause diseases in humans (unlike Ebola we will talk about it later).

• There are 2 types of dengue infections:
  1. Dengue Hemorrhagic Fever (DHF): Fatality rate: 5-6%
  2. **Dengue Shock Syndrome (DSS): has a higher fatality rate: (**12-44%), patients become hypovolemic, and at higher risk for hypovolemic shock followed by death.

• **<u>Very important:</u>**

1. **Onset of dengue fever infections is sudden** (acute), Eye pain, Rash, Complications: sequelae uncommon.
2. Remember the vector is **Aedes aegypti**.
3. Illness of dengue infection is **very severe in younger children** (well-documented).

• Treatment: supportive treatment only.

Flaviviridae:Omsk Hemorrhagic Fever

• It's an arbovirus infection, common in Russia and Europe in general.

• Distinguishing Features: Acute Onset, Biphasic infection.

• Biphasic infection: viremia ⟶ window period ⟶ toxemia.

• The hemorrhagic (toxemia) phase starts with hemorrhage under the skin in the form of petechiae and ecchymosis.

•The end-stage is characterized by internal and external bleeding from all the body orifices including upper and lower GI bleeding, mouth, nose. At the end, it can progress to DIC followed by hypovolemic shock and death. That is why Omsk fever has a high fatality rate (but less than Filoviruses).

• The **Muskrat rodent** is the **natural reservoir** (natural host, not the vector).

• Complications: Hearing loss, Hair loss, Psycho-behavioral difficulties (neurological changes).

• Mortality: 0.5 – 3%.

Flaviviridae: Kyanasur Forest

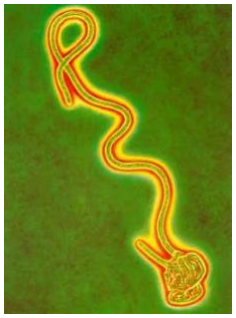
• Distribution: limited Karnataka State, India, Pakistan, and Bangladesh.

• The vector that transmits Kyanasur Forest Fever is the same as the vector for the CCHF, which is the Ixodid tick. (Hyalomma/ Haemaphysalis).

• Kyasanur Fever has an **acute, biphasic onset** of the disease. Case fatality: 3-5% (400-500 cases annually).

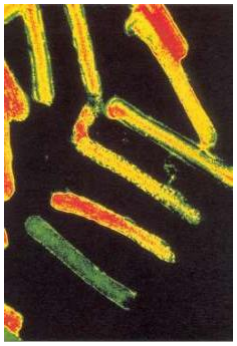
4. Filoviridae

• They are **non-Arboviruses**, that have **abrupt (acute) onset** of the disease with **rapidly fatal febrile hemorrhagic illness.**



• **<u>Very important:</u>** Filoviridae are the family with the **highest mortality rate** (up to 90%), fatality, and morbidity rates, compared to all the previous hemorrhagic fever viruses. It is the most severe hemorrhagic fever.

• Filoviridae include **Ebola and Marburg viruses**.



• Filoviridae have **a short incubation period** (4–10 days). In the second weekafter exposure, patients are at high risk of death (Death around day 7–11). If the patient survives after the **second week**, they are considered to be recovering. However, this **recovery is painful** (for unknown reason), during which the patient does not feel that he is getting well, but the lab results say that everything is getting better.

Filoviridae Transmission:

• **Reservoir is UNKNOWN, fruit bats implicated with Marburg.**

• **Intimate contact:**
  - **Person-to-person** is an effective route of transmission (Very important).
  - **Nosocomial**: Reuse of needles and syringes and exposure to infectious tissues, excretions, and hospital wastes.
  - **Aerosol** transmission: Primates.

• **Biosafety level 4** is required to prevent Filoviridae infections. Patients should be isolated.

• Patients who died from Filoviridae diseases were burnt in certain countries, and some have had a safe burying (approved and applied nowadays in most countries).

Filoviridae: Ebola

• Ebola has **5 subtypes** according to the place from where they were first isolated: **Ebola-Zaire, Ebola-Sudan, Ebola-Ivory Coast, Ebola- Bundibugyo, Ebola-Reston (the last type infects mainly non-human primates** (it can

also establish infection in humans but not as much)**, while the other four types infect humans** (Ebola hemorrhagic fever)).

• Ebola-Reston imported to US, but only causes illness in non-human primates.

• Human-infectious subtypes found only in Africa.

•Distinguishing features: Acute onset and GI involvement / Weight loss.

• 25-90% case-fatality.

Filoviridae: Marburg

• Distinguishing features: Sudden onset, Chest pain, Maculopapular rash on trunk, Pancreatitis and Jaundice

• 21-90% mortality (same as ebola).

• **Marburg virus has a single serotype.**

Common Pathophysiology

• Small vessel involvement.

- Increased vascular permeability.
  - Multiple cytokine activation by the Viremia which causes the constitutional symptoms, Macrophage involvement, Inadequate/delayed immune response and Cellular damage.
- Abnormal vascular regulation:
  - Early -> mild hypotension
  - Severe/Advanced -> Shock

• Again, they have **biphasic clinical presentation**:

A. One in the blood "Viremia phase (Early/Prodromal Symptoms)": high viral overload → cytokine rush → constitutional symptoms (fever, chills, myalgia, malaise, fatigue, headache, dizziness, arthralgia, nausea, non-bloody diarrhea). These are not specific (flu like symptoms).

B. The other is in the immune response "Toxemia phase (Progressive Signs)": endothelial injury → consumption of the clotting factors and platelets; resulting in bleeding under the skin (Ecchymosis, Petechiae), this type of hemorrhage is rarely life-threatening. Severe/End-stage is characterized by DIC, resulting in profuse internal and external bleeding.

2. **Very important**: DIC (Disseminated Intravascular Coagulopathy) is a marked (well-established) pathophysiology for **Filoviruses (Ebola and Marburg) before severe hemorrhage.**

• Common Clinical Features: Progressive Signs: Conjunctivitis, Facial & thoracic flushing, Pharyngitis, Exanthems, Periorbital edema, Pulmonary edema, Hemorrhage, Subconjunctival Hemorrhage, Ecchymosis and Petechiae, But the hemorrhage (under the skin) itself is rarely life-threatening.

• Common Clinical Features: Severe/End-stage: Multisystem compromise, Profuse bleeding (internal and external), Consumptive coagulopathy/DIC, Encephalopathy, Shock and Death.

Lab studies

• In order to diagnose patients with VHF, we can use many tests:

• Complete Blood Count: Leukopenia, leukocytosis, thrombocytopenia, hemoconcentration, DIC.

• **Liver function test: can be used to detect yellow fever** (because of the hepatocytes necrosis and they would have jaundice)

• Kidney function test: can be used to detect HFRS (hantavirus Hemorrhagic Fever with Renal Syndrome).

• Proteinuria universal.

• Serological tests –Abs are not detected during the acute phase: Direct examinationof blood/tissues in viral Ag enzyme immunoassay.

• Immunohistochemical staining for liver tissue.

• Virus isolation in cell culture.

• RT-PCR (real time-polymerase chain reaction) sequencing of the virus.

• Electron microscopy specific and sensitive: can be used to show the Arenaviridae in Lassa fever sandy cytoplasm.

Treatment for VHF in general

• **Supportive care:** Fluid and electrolyte management, Hemodynamic monitoring, Ventilation and/or dialysis support, Steroids for adrenal crisis, Anticoagulants, IM injections and the Treatment of secondary bacterial infections.

• Manage severe bleeding complications: Cryoprecipitate (concentrated clotting factors), Platelets, Fresh Frozen Plasma and Heparin for DIC.

• **Ribavirin shows activity** in vitro (in labs, outside the body) against **Lassa fever, New and OldWorld Hanta-hemorrhagic fevers and the Rift Valley Fever. No evidence to support using Ribavirin in Filovirus or Flavivirus infections.**

Prevention

• The first step of prevention is by isolation of the patient once diagnosed with one ofthe VHFs.

• The second step is dependent on the type of the VHF. If it is an arthropod-borne virus, then this step is about arthropod control (mostly mosquitoes). If it is a non-arthropod-borne, then itis about controlling the natural host (rodents' control).

• Nosocomial: Complete equipment sterilization & protective clothing

• House to house rodent trapping

• Better food storage & hygiene

• Cautious handling of rodent if used as food source

• If human case occurs: Decrease person-to-person transmission and Isolation of infected individuals

Vaccination:

• There is only one **active vaccine** that is approved for VHF, and it is against the **yellow fever** as other vaccines are experimental. It is given for **travellers before visiting Africa and South America.** There are also **passive vaccines** for the **Argentine and Bolivian Hemolytic Fevers.**

• Active immunization is better than passive if there is enough time. However, passive immunization is a good choice for immunocompromised patients for therapeutic purposes not for prevention. (Remember: Active Immunization is the administration of a pathogen to the body in order for the immune system to develop an immune response that forms a long-

• lasting immunity against that pathogen. On the other hand, passive immunization is the administration of preformed antibodies (Treat with convalescent serum containing neutralizing antibody or immune globulin). Because of that, passive immunization doesn't confer a long-lasting immunity, it merely functions as a therapeutic approach not a preventive one).

• Experimental vaccines under study: Argentine HF, Rift Valley Fever, Hantavirus and Dengue HF.

• All VHF viruses can be used as **bioweapons**; because they **disseminate through aerosols, they need a low infectious dose, no effective vaccine, as well as they have high mortality and morbidity rates, available and can be produced in large quantity.** Research on weaponization has been conducted.

Sketchy vedios:
Filovirus: https://mega.nz/folder/VuUFFQrZ#zKktM105APnElLedXIA3Lg/file/wj8kmARZ
Bunyavirus: https://mega.nz/folder/VuUFFQrZ#zKktM105APnElLedXIA3Lg/file/Vrs0magA
Arenavirus: https://mega.nz/folder/VuUFFQrZ#zKktM105APnElLedXIA3Lg/file/Qv9QjIJC

الله يا قاضي الحاجات ويا مجيب الدعوات ويا مفرج الكربات اجعل لغزة وأهلها ومجاهديها من كل ضيق مخرجا ومن كل هم فرجا وكن لهم وليا ونصيرا ووكيلا.

Quick recap of the most important information mentioned throughout this lecture: ˙ᵕ˙

Documented person-to-person route of transmission is found in all of the following:

1) Lassa fever.
2) CCHF.
3) Andes virus in Argentina (the only one from the Hantaviruses).
4) Filoviridae (Ebola + Marburg).

- VHFs that are transmitted by Aedes aegypti vector are:

1) RVF
2) Yellow fever
3) Dengue fever

Ixodid tick (Hyalomma/Haemaphysalis) is the main vector that transmits:

1) CCHF.
2) Kyasanur fever.

Biphasic clinical presentation is found in:

1. Arenaviridae
2. Filoviridae
3. Flaviviridae (mainly).

Ribavirin is considered an effective (well-documented) treatment -in vivo- only for:

1. Lassa fever
2. CCHF

Number of serotypes for:

A. Ebola : five
B. Dengue : four
C. Hantaviruses : two
D. Marburg: one

Lassa fever patients keep shedding the virus from their urine for at least 2 weeks after recovery, so you must isolate the patient for 2 weeks.

Filoviridae (Ebola +Marburg) have the highest mortality, fatality and morbidity rates compared to all other VHFs.

Sandy cytoplasmic appearance under the EM is found in: Arenaviridae (Lassa virus mainly).

DIC or Consumptive Coagulopathy is mainly found in Filoviridae (Ebola +Marburg).

All VHFs are zoonotic.

Lassa fever is transmitted by: (*Mastomys natalensis*).
Omsk fever natural reservoir is Muskrat.

Illness of dengue infection is very severe in younger children (well-documented).

Arboviruses	Non-arboviruses
Bunyaviridae (except Hantaviruses)	Arenaviridae
Flaviviridae	Filoviridae

Hearing loss (deafness)	Vision loss (blindness)
Lassa fever	RVF
Omsk	-

Acute (sudden) onset	Chronic (insidious)/ gradual onset
Filoviridae (Ebola +Marburg)	HFRS, caused by old-world hantavirus
Dengue fever	Lassa fever
Omsk fever	-
Kyasanur fever	-

Past papers:

1. Which of the following doesn't transmit by direct contact between persons?

a. Ebola virus.

b. Lassa virus.

c. Dengue virus.

2. Which of the following Ebola types doesn't cause disease in humans?

a. Ebola Reston.

b. Ebola Ivory Cost.

c. Ebola Sudan.

3. Which of the following is wrong about VHF (Virus Hemorrhagic Fever)?

a. It causes severe hemorrhage.

b. Hanta virus needs vector to be transmitted.

4. The dengue virus, one is correct:

a. The virus is limited to Karnataka State, India.

b. A live attenuated vaccine is available for dengue.

c. Infection with one serotype confers immunity only to the infecting serotype.

d. Dengue virus has five serotypes that cause a variety of clinical manifestations.

e. Is the least prevalent arbovirus in the world.

5. Human-to-human transmission occurs in viral hemorrhagic fevers EXCEPT:

a. Rift Valley virus.

b. Crimean-Congo hemorrhagic fever.

6. All of the following regarding viral hemorrhagic fever are correct EXCEPT:

a. Hantaviruses, Rift Valley fever and Dengue are not associated with person to-person transmission.

b. Arenaviruses are found in South America and Africa andare transmitted by Arthropods.

c. Yellow fever is associated with 2types of infectious cycles.
d. Filoviruses cause the most lethal type of hemorrhagic fever.
e. Bleeding occurs frequently and is a common cause of death.

7. Wrong about hemorrhagic fever:
a. Vaccines are available for most viral infections.
b. Passive immunization is a good choice for immunocompromised patients.

8. Wrong about Dengue fever:
a. The vector is Aedes aegypti.
b. Incubation period is 3 to 4 weeks.
c. Has 4 serotypes.

9. All of the following viruses cause hemorrhagic fever EXCEPT:
a. Hantaviruses.
b. Bunyaviruses.
c. Polio virus.

10. Wrong statement about hemorrhagic fever:
a. Can be caused by arboviruses and non-arboviruses.
b. Most deaths occur due to severe bleeding.

11. Which of the following is associated with nosocomial infection?
a. Hantaviruses.
b. Dengue fever.
c. Yellow fever.
d. Lassa virus.
e. Ebola virus.

12. True about Dengue fever:
a. DNA genomic.
b. non enveloped.
c. very severe in younger children.

ANSWERS: 1.C 2.A 3.B 4.C 5.A 6.B 7.A 8.B 9.C 10.B 11.E 12.C