CVS

MICROBIOLOGY

Modified NO: 2

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Viral hemorrhagic fevers (VHFs)

Color code
Slides
Doctor
Additional info
Important

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The undrlined text = what doctor mentioned from slides

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 at the first stage it starts under the skin (petechiae ecchymosis), but 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, Filoviridae and Flaviviridae.*
- 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.

Quick Overview: Who are they?

All of them are RNA Viruses

- **Arenaviridae**
  - Lassa Fever
  - Argentine HF (Junin)
  - Bolivian HF (Machupo)
  - Brazilian HF (Sabia)
  - Venezuelan HF (Guanarito)

- **Bunyaviridae**
  - Rift Valley Fever (RVF)
  - Crimean Congo HF (CCHF)
  - Hantavirus (Hemorrhagic Fever with Renal Syndrome (HFRS))
  - Hantavirus Pulmonary Syndrome (HPS)

- **Filoviridae** (the most important type)
  - Marburg (The first isolation was in Marburg which is town in the German).
  - Ebola (The first isolation was in ebola river in africa).
  - Marburg and Ebola have the highest mortality rate (up to 90%), other families are milder, but their mortality rates can reach up to 50%.

- **Flaviviridae**
  - Yellow Fever
  - Dengue Fever

  Their distribution is between Africa and South America

  - Omsk HF (isolated from Russia and its main distribution is in Europe)
  - Kyasanur Forest Diseasee (in India).

- (خلي ببالك) The different names within each family of these viruses are dependent on the first geographic region they were isolated from as they have limited geographic distribution and limited distribution of the host or their natural reservoir. For example, Arenaviridae faimly is divided into West African (Lassa Fever) and South American (The Rest: Argentine Bolivian Brazilian and Venezuelan).

- Hantavirus (from Bunyaviridae family) is divided into 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 (Nombre virus) (doesn't cause hemorrhagic fever).

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, filoviridae

- 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 transmission is an arthropod (such as mosquitoes or ticks). Examples include: Flaviviridae and Bunyaviridae (with the exception of Hantaviruses) .

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.

Common features

- Enveloped Lipid-encapsulated
- Single-strand RNA (some of them are segmented)
- Zoonotic (animal-borne)
- Some can be transmitted through person to person (like in filoviridae (Marburg and Ebola), Yellow Fever and Lassa Fever.
- 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

1. Arenaviridae

- They are enveloped RNA viruses (their RNA is segmented), non-Arboviruses (non-arthropods), 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".

1. Junin virus : Argentine hemorrhagic fever
2. Machupo virus : Bolivian hemorrhagic fever
3. Guanarito virus : Venezuelan hemorrhagic fever
4. Sabia virus : Brazilian hemorrhagic fever

South America

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

✓ Remember, all of them are related to geographic distribution and initial isolation.(الدكتور ركز كثير على هاي المعلومة)

Arenaviridae Transmission

✓ Remember they're non-arthropod (no vector)

- *Virus transmission and amplification occurs in rodents.* They shed 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

- Incubation period 10–14 days (less than 2 weeks) and most of them have an acute onset.
- Fever and malaise 2–4 day
- Hemorrhagic stage
  - Hemorrhage, leukopenia, thrombocytopenia
  - Neurologic signs

See the next slide for further explanation :)

- **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.

In general, Arenaviridae infection is milder than Filoviridae infection.

Arenaviridae: Lassa Fever

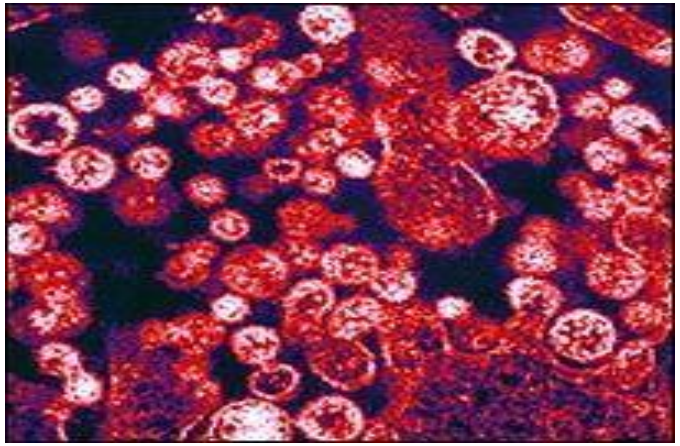
•First seen in Lassa (among missionary nurses who then died by the lassa hemorrhagic fever), Nigeria in 1969.

- Now in all countries of West Africa
  - 5-14% of all hospitalized febrile illness

- 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 or Breast Feeding.



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

Lassa Fever

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

- Distinguishing Features:
  - 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 and hepatitis.
  - Hearing loss in 25% may be persistent
  - Spontaneous abortion
  - Deafness in the fetus after birth if they were infected from their mothers.
- Mortality 1-3% overall in sporadic cases because the transmission cycle is not that active (up to 50% in epidemics)
- Therapy: Ribavirin (antiviral drug, effective documented treatment).

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

- Very important (خلي ببالك) : 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.

2. Bunyaviridae

- All of them are arthropod-borne viruses EXCEPT for Hantaviruses

1. Rift Valley Fever virus (arbovirus, least mortality rates).
2. Crimean-Congo Hemorrhagic Fever virus (arbovirus).
3. Hantavirus (non-arbovirus)

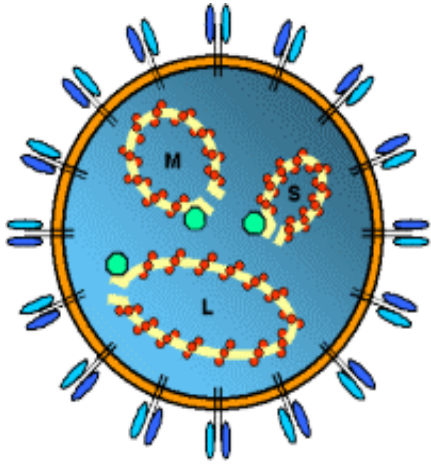
- All of them are zoonotic viruses (they infect animal, and the infection can be transmitted to human).

➢ 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.

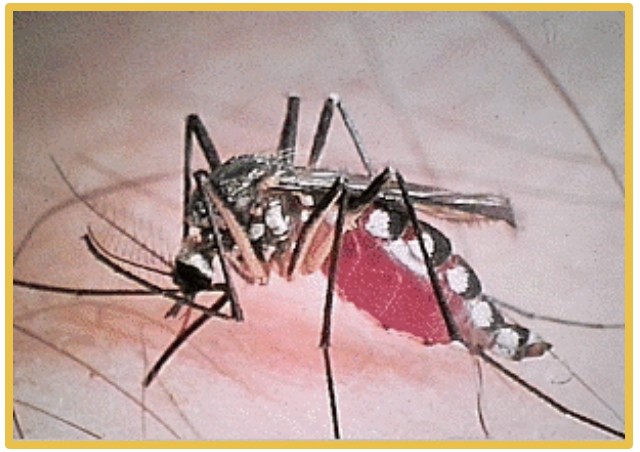
3. S segment (Small) codes for an N-protein (nucleocapsid protein).



Bunyaviridae Transmission

- Arthropod vector Exception >> Hantaviruses
- RVF (Rift Valley Fever) >> *Aedes* aegypti mosquito
- CCHF (Crimean-Congo Hemorrhagic Fever) >> Ixodid tick (*Hyalomma)* in the bottom picture.
- Hantavirus – Rodents
- Less common route of transmission (person to person but it's not a very important route) by:
  - Exposure to Aerosol (mainly in laboratory personnel)
  - Exposure to infected animal tissue from direct contact.

Aedes aegypti mosquito is the vector also for yellow and dengue fever.
So possible question here: All of the following infections are transmitted by aedes aegypti except...



Bunyaviridae

- 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).

Rift Valley Fever

- Asymptomatic or mild illness in humans the simplest virus in this family.

- Distinguishing Characteristics
  - Hemorrhagic complications rare (<5%)
  - Vision loss "blindness" (due to retinal haemorrhage, vasculitis) in 1-10%.
  - The incubation period is less than a week (usually 2-5 days).
  - The lowest overall mortality rate (less than 1%) , but still is a fatal disease in cattle or sheep.

- 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 it in RVF as supportive therapy.

Crimean-Congo Hemorrhagic Fever

• 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. (خلي ببالك).

- Distinguishing features
  - Abrupt (acute) onset
  - Most humans infected will develop hemorrhagic fever
  - Profuse hemorrhage
- 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 types 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).

- Transmission to humans:
  - Exposure to rodent saliva and excreta
    - Inhalation
    - Bites
    - Ingestion in contaminated food/water (?): This route of transmission is still controversial and is not evidence-based yet as a well established route of transmission.
    - Person-to-person (Andes virus in Argentina)

Hemorrhagic Fever with Renal Syndrome (HFRS)

- Distinguishing Features
  - Insidious onset
  - Intense headaches
  - Blurred vision
  - kidney failure (causing severe fluid overload)
- Mortality: 1-15%

3. Flaviviridae

-The third family is also an arthropod borne viruses (**arboviruses**).
-Enveloped, RNA viruses.
-Their replication takes place in the cytoplasm.

- Dengue virus
- Yellow Fever virus
- Omsk Hemorrhagic Fever virus
- Kyassnur Forest Disease virus

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

Flaviviridae Transmission

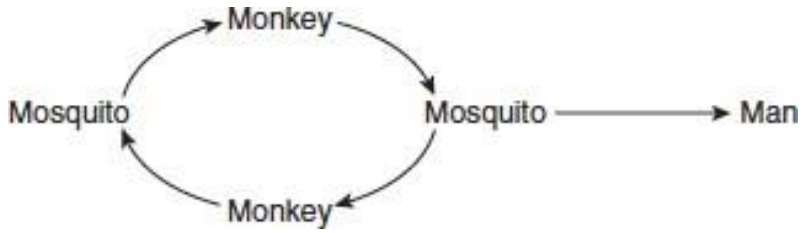
- Arthropod vector (Mosquito/tick is part of their transmission cycle)
- Yellow Fever and Dengue viruses Have three life cycles:
  - ***Aedes aegypti*** **(The mosquito which transmits yellow fever and dengue viruses).**
  - Sylvatic cycle
  - Urban cycle
- Kasanur Forest Virus
  - Ixodid tick
- Omsk Hemorrhagic Fever virus : Fever Lasting sequela
  - Muskrat urine, feces, or blood

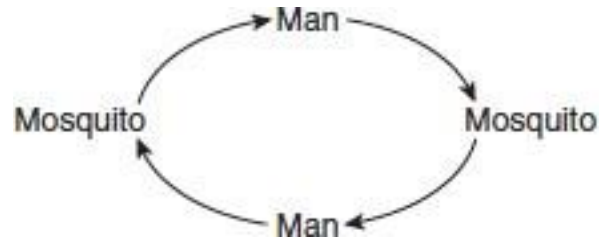
REMEMBER: All viruses in this lecture are zoonotic viruses (their reservoir is an animal).

- 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), before humans become the accidental host. Tree cutters in forests usually get infected through this cycle.

- Urban cycle the vector lives with the normal population, it directly infects humans without an intermediate host (from mosquito to another exposed human) , as you can see in the picture.





Yellow Fever

- Distinguishing features
  - Biphasic infection
  - Common hepatic involvement & jaundice
- Mortality: 15-50%

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 symptoms disappear.

2. **Toxemia phase**: Fever returns along with the constitutional symptoms + Haemorrhagic signs and symptoms appear.

Flaviviridae: Dengue

- Dengue Fever (DF) /Fatality: <1%
- Dengue Hemorrhagic Fever (DHF)/ Fatality: 5-6%
- Dengue Shock Syndrome (DSS) /Fatality 12-44%

  DSS has a higher fatality rate, patients become hypovolemic, and at higher risk for hypovolemic shock followed by death..

- Four distinct serotypes
  - DEN-1, DEN-2, DEN-3, DEN-4
- Distinguishing Features
  - Sudden onset
  - Eye pain
  - Rash
  - Complications/sequelae uncommon
- **Illness is severe in younger children** IMPORTANT!
  - Treatment: supportive management only

Omsk Hemorrhagic Fever

- Distinguishing Features
  - Acute Onset
  - Biphasic infection
  - Complications
    - Hearing loss
    - Hair loss
    - Psycho-behavioral difficulties

      -Neurological deficit
  - Mortality: 0.5 – 3%

    -It's also an arthropod borne infection
    -Muskrat rodent is the natural reservoir host (not the vector)
    -Biphasic (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).

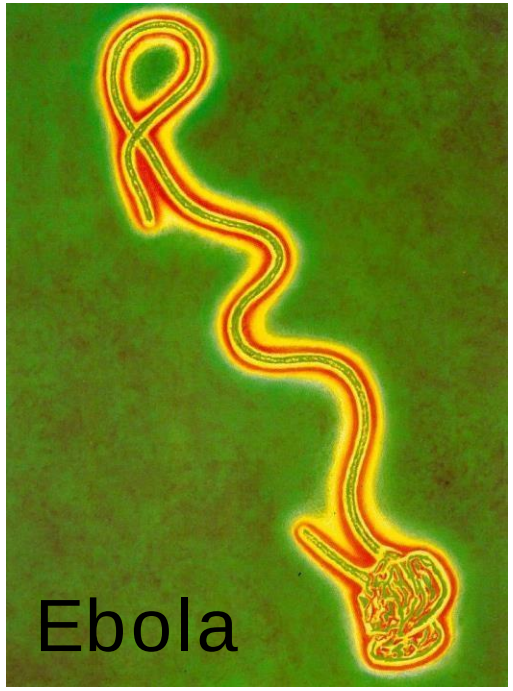
Flaviviridae: Kyanasur Forest

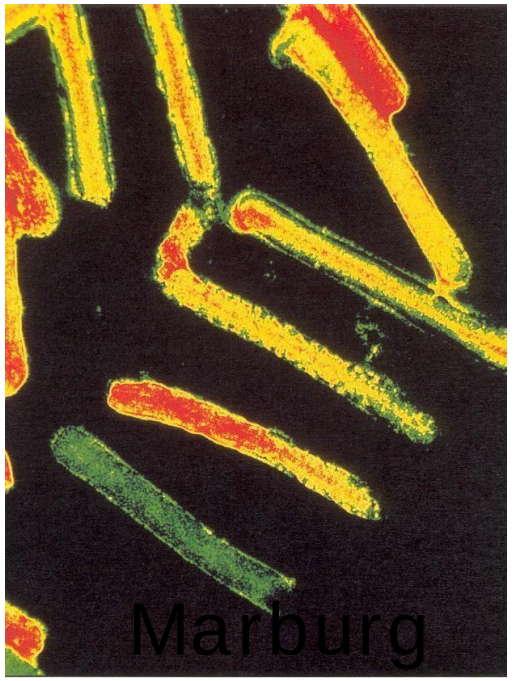
- Distribution: limited to Karnataka State, India ,Pakistan and Bangladesh.
- Haemaphysalis vector
- Distinguishing Features
  - Acute onset
  - Biphasic
- Case-fatality: 3-5% (400-500 cases annually)

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

Filoviridae

- Ebola
  - Ebola-Zaire
  - Ebola-Sudan
  - Ebola-Ivory Coast
  - Ebola-Bundibugyo
  - (Ebola-Reston)
- Marburg





Filoviridae Transmission

REMEMBER: All viruses in this lecture are zoonotic viruses (their reservoir is an animal), but in this group the original host is unknown, some studies state that fruit bats are the reservoir.

- Reservoir is UNKNOWN
  - Bats implicated with Marburg

Filoviridae are non-arthropods (same as arenaviridae)

- Intimate contact
- Nosocomial transmission
  - Reuse of needles and syringes
  - Exposure to infectious tissues, excretions, and hospital wastes
- Aerosol transmission
  - Primates

Filoviridae: Ebola

- Rapidly fatal febrile hemorrhagic illness
- Transmission:
  - bats implicated as reservoir
  - Person-to-person
  - Nosocomial
- Five subtypes According to the location of first isolates.
  - Ebola-Zaire, Ebola-Sudan, Ebola-Ivory Coast, Ebola- Bundibugyo, Ebola-Reston
  - Ebola-Reston imported to US, but only causes illness in non-human primates Though it might infect humans, still it's considered as a cause of non-human infection, while the other four types infect humans causing Ebola hemorrhagic fever.
- Human-infectious subtypes found only in Africa

(continuation for modes of transmission):
-Person-to-person is an effective route of transmission, if someone is exposed to body fluids or excessive contact with an infected patient, they'll be at higher risk to get the infection, that's why it's considered a biosafety level 4 and patients must 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).

-Nosocomial: Includes medical personnel who are in contact with the patient either at hospital or in the lab.

Filoviridae: Ebola

- Distinguishing features:
  - Acute onset
  - GI involvement / Weight loss
  - 25-90% case-fatality

"بهمني تعرف"
Filoviridae group have the highest mortality rate

Filoviridae: Marburg

- Distinguishing features
  - Sudden onset
  - Chest pain
  - Maculopapular rash on trunk
  - Pancreatitis
  - Jaundice
- 21-90% mortality

Filoviridae Humans

- Most severe hemorrhagic fever
- Incubation period: 4–10 days
- Abrupt onset
  - Fever, chills, malaise, and myalgia
- Hemorrhage and DIC (Disseminated Intravascular Coagulopathy) is a marked (well-established) pathophysiology for Filoviruses (Ebola and Marburg) before severe hemorrhage.
- Death around day 7–11
- Painful recovery

Filoviridae have a short incubation period (it might even be 2 days). In the first week symptoms start to appear, and we give the patient supportive treatment. Usually at the second week after exposure most deaths occur so, 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 like getting well, but the lab results say that everything is getting better.

Common Pathophysiology

- Viremia
  - Macrophage involvement
    - Inadequate/delayed immune response

Again, the first phase which is viremia results from the presence of the virus in the blood --> cytokine rush --> constitutional symptoms (fever, fatigue...).

- Small vessel involvement
  - Increased vascular permeability
    - Multiple cytokine activation
  - Cellular damage
  - Abnormal vascular regulation:
    - Early -> mild hypotension
    - Severe/Advanced -> Shock

The other phase, results from immune response --> 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.

Common Clinical Features: Early/Prodromal Symptoms

Not specific (flu-like symptoms) and seen in any infection (viral or bacterial or even fungal infection).

- Fever
- Myalgia
- Malaise
- Fatigue/weakness
- Headache
- Dizziness
- Arthralgia
- Nausea
- Non-bloody diarrhea

Common Clinical Features: Progressive Signs

- Conjunctivitis
- Facial & thoracic flushing
- Pharyngitis
- Exanthems
- Periorbital edema
- Pulmonary edema

- Hemorrhage
  - Subconjunctival hemorrhage
  - Ecchymosis
  - Petechiae
  - But the hemorrhage itself is rarely life-threatening.

Common Clinical Features: Severe/End-stage

- Multisystem compromise
- Profuse bleeding
- Consumptive coagulopathy/DIC
- Encephalopathy
- Shock
- Death

Lab studies

- Complete Blood Count
  - Leucopenia, leucocytosis, thrombocytopenia, hemoconcentration, DIC
- Liver enzymes

-Yellow fever was named so because of the hepatic involvement, these patients suffer from hepatocyte necrosis and jaundice.

-We can perform kidney function test if we suspect Hantavirus with renal syndrome.

- Proteinuria universal
- Serological tests – Ab not detected acute phase; Direct examination blood/tissues for viral Ag enzyme immunoassay.
- Immunohistochemical staining liver tissue
- Virus isolation in cell culture (biosafety level 4 lab).
- RT-PCR sequencing of virus
- Electron microscopy specific and sensitive can be used to visualize the Arenaviridae in Lassa fever sandy cytoplasm.

Treatment

- Supportive care:
  - Fluid and electrolyte management
  - Hemodynamic monitoring
  - Ventilation and/or dialysis support
  - Steroids for adrenal crisis
  - Anticoagulants, IM injections,
  - Treat secondary bacterial infections

Treatment

- Manage severe bleeding complications
  - Cryoprecipitate (concentrated clotting factors)
  - Platelets
  - Fresh Frozen Plasma
  - Heparin for DIC
- Ribavirin in vitro activity vs.
  - Lassa fever
  - New and old World Hemorrhagic fevers
  - Rift Valley Fever
  - No evidence to support use in Filovirus or Flavivirus infections

Prevention

- 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
  - Isolation of infected individuals

• The first step of prevention is by isolation of the patient once diagnosed with one of the 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 it is about controlling the natural host (rodents' control).

Vaccination

Active immunization: When you give the patient bacteria or virus and elicit the immune response without causing infection.
(if we have enough time, active is better than passive).

Passive immunization: When you give the patient already performed antibodies or immunoglobulins from a person who developed immunity against the virus or bacteria. Passive is usually one of the choices for severely ill patients since it's therapeutic more than preventive.

- There is only one active vaccine that is approved for VHF, and it is against the yellow fever as other vaccines are experimental.

- Argentine and Bolivian HF
  - PASSIVE IMMUNIZATION
    - ✓Treat with convalescent serum containing neutralizing antibody or immune globulin
- Yellow Fever
  - ACTIVE IMMUNIZATION
    - ✓Travelers to Africa and South America
- Experimental vaccines under study
  - Argentine HF, Rift Valley Fever, Hantavirus and Dengue HF

Why do VHFs make good Bioweapons?

- Disseminate through aerosols
- Low infectious dose
- High morbidity and mortality
- Cause fear and panic in the public
- No effective vaccine
- Available and can be produced in large quantity
- Research on weaponization has been conducted

NOTE: Slides (46-50) are additional slides

- Important notes :

1. VHFs are enveloped single-strand RNA (some of them are segmented) ,Zoonotic (animal-borne) and some can be transmitted through person to person (like in filoviridae (Marburg and Ebola), Yellow Fever and Lassa Fever.
2. They are Geographically restricted.
3. VHFs are classified according to the involvement of an arthropod vector in their transmission cycle into 2 groups: Arboviruses (Arthropod-borne) and Non-Arboviruses.

4. Bunyaviridae >> their RNA is segmented (genes that encode for certain functions are present on different segments). There are 3 segments: 1. L-segment, 2. M segment 3. S segment
5. Illness of dengue infection is very severe in younger children.
6. Filoviridae are the family with the highest mortality rate and considered a rapidly fatal febrile hemorrhagic illness
7. Ebola-Reston only causes illness in non-human primates.
8. DIC or consumptive coagulation is mainly found in Filoviridae infections.
9. There is only one active vaccine that is approved for VHF and it is against yellow fever.

Virus	Transmission	Incubation period	Distinguishing features
1. Arenaviridae	1. Virus transmission in rodents. They shed virus through urine, feces, and other excreta. 2. Human infection. 3. Person-to-person transmission (with lassa fever).	10–14 days	1.Prodromal phase (viremia phase):constitutional symptoms: (fever, malaise, headache, joints pain, myalgia and photophobia). 2. Hemorrhagic phase (toxemia phase): Hemorrhage, leukopenia, thrombocytopenia and Neurologic signs.
2.Arenaviridae: Lassa Fever	1 . Rodent-borne (the initial route of transmission): direct contact with infected (Mastomys natalensis) rodent. 2. Person to person: ,Sex or Breast Feeding	Gradual onset of the disease with an incubation period	1.Retro-sternal pain 2. Exudative pharyngitis and hepatitis. 3. Hearing loss in 25% may be persistent. 4. Spontaneous abortion. 5. Deafness in the fetus after birth. 6. Mortality 1-3% overall in sporadic cases (up to 50%in epidemics)

Virus	Transmission	Incubation period	Distinguishing fetures
3. Bunyaviridae	1. All of them are arthropod-borne viruses EXCEPT for Hantaviruses. 2. Person to person with CCHF by: Exposure to Aerosol OR Exposure to infected animal tissue from direct contact.	The incubation period is less than a week (usually 2-5 days)	
3.A. RVF (Rift Valley Fever)	arthropod-borne [Aedes aegypti Mosquito]		1. Asymptomatic or mild illness in humans 2. Hemorrhagic complications rare (<5%). 3. Vision loss (due to retinal haemorrhage, vasculitis). 4. The lowest overall mortality rate (less than 1%)
3.B.CCHF (Crimean-Congo Hemorrhagic Fever)	1.Ixodid tick (Hyalomma) 2. Person to person		1. Abrupt (acute) onset 2. Most humans infected will develop hemorrhagic fever. 3. Mortality 15-40% (higher than RVF).
3.C. Hantavirus	1. Rodents 2. Ingestion of contaminated food/water 3. Person-to-person		1. Insidious onset 2. Intense headaches 3. Blurred vision 4. kidney failure 5. Mortality: 1-15%

For Hemorrhagic Fever with Renal Syndrome (HFRS)

Virus	Transmission	Incubation period	Distinguishing fetures
Yellow Fever	-Arthropod-borne [Aedes aegypti Mosquito] -In sylvatic cycle there is non-human primate intermediate -In urban cycle there is no intermediate		-Biphasic infection -common hepatic involvement & jaundice -There is a vaccine against it.
Dengue fever	-Arthropod-borne [Aedes aegypti mosquito]		1. Sudden onset 2. Illness is severe in younger children 3. Has four distinct types 4. Dengue shock syndrome (DSS) has higher fatality rate.
Omsk hemorrhagic fever	-Muskrat is the natural reservoir		1. Acute onset 2. Biphasic infection 3. Hearing loss 4. Neurological deficit
Kyanasur Forest	-Ixodid tick (Hyalomma/Haemaphysalis)		1.Acute onset 2. Biphasic

Virus	Transmission	Incubation period	Distinguishing fetures
Ebola (Filoviridae): has five subtypes	1.Non-arthropod 2. Bats implicated as reservoir 3. Person to person (IMPORTANT) 4. Nosocomial 5. Ebola Reston infects non-human primates	Short incubation period	1. Acute/ abrupt onset 2. Highest mortality rate 3. most severe hemorrhagic fever 4. DIC is a marked pathophysiology 5. Painful recovery 6. Death occurs mostly in the second week
Marburg (Filoviridae):	1.Non-arthropod 2. Bats implicated as reservoir 3. Person to person (IMPORTANT) 4. Nosocomial	Short incubation period	1. Acute/ abrupt onset 2. Highest mortality rate 3. most severe hemorrhagic fever 4. DIC is a marked pathophysiology 5. Painful recovery 6. Death occurs mostly in the second week

The END

@Selda_Sketchy_Bot
Use this telegram bot to find **sketchy** videos and files.

"وَمِنْهُم مَّن يَقُولُ رَبَّنَا آتِنَا فِي الدُّنْيَا حَسَنَةً وَفِي الْآخِرَةِ حَسَنَةً وَقِنَا عَذَابَ النَّارِ"

VERSIONS	SLIDE #	BEFORE CORRECTION	AFTER CORRECTION
V1→ V2			
V2→V3			

امسح الرمز و شاركنا بأفكارك لتحسين أدائنا!!