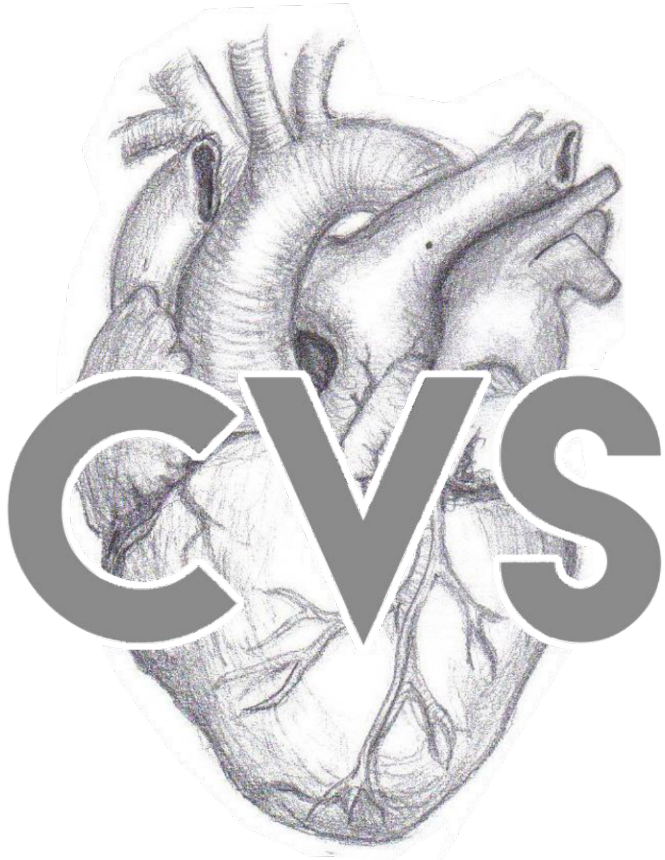

CVS

MICROBIOLOGY

☑ Sheet ○ Slide ○ Handout

Number

1

Subject

Viral hemorrhagic fever

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Date: 00/00/2016

Price:

Before we start …

●This sheet was written according to the recording that belongs to section 2.

●Everything that's required from the slides is included in this sheet.

●Enjoy :p

Introduction ..

●Do you remember Ebola epidemic in 2014?

- The **West African Ebola virus epidemic** (2013–2016) was the most widespread outbreak of Ebola virus disease (EVD) in history—causing loss of life and socioeconomic disruption in the region, majorly in three countries. The first cases were recorded in Guinea in December 2013; later, the disease spread to Liberia andSierra Leone.
- Ebola virus is a part of a large group of viruses that lead to severe multisystem syndrome, characterized by high grade fever and increased tendency for bleeding, known as ***hemorrhagic fever***.
- This syndrome occurs usually as epidemics, and has the potential to be used as a biological weapon.

I. Viral Hemorrhagic Fever

●Today we are going to talk about viral hemorrhagic fever.

- The name tells you a lot about this disease..
- so we can conclude that we have a virus that causes an infection leading to **bleeding**; *by increasing the permeability of the blood vessels* or *affecting blood clotting mechanism*.
- It means also that's this infection is **systemic**, *as it causes fever which is a systemic response*.

●***Viral hemorrhagic fever*** is a multi systemic syndrome, that damages overall vascular system, the symptoms often accompanied by hemorrhage.

- Fever and hemorrhage are rarely life threatening by themselves, as the most common cause of death here is the multisystem failure.

●in this disease, the virus causes endothelial damage by attacking ***VE-Cadherin-catenin complex***.

- ***VE-Cadherin-Catenin complex*** is important for intercellular communication between endothelial cells (cell adhesion), and if present, it closes intercellular gaps between endothelium making it impermeable to blood.
- the virus, by one way or another, changes the arrangement of this complex in a way that increases the intercellular gaps between endothelial cells.
- This well increase vascular permeability, leading to hemorrhage.

●Systemic consequences of this include: conjunctivitis, petechiae, ecchymoses and purpura.

- Remember from hematology that *petechiae, ecchymoses and purpura* all refer to bleeding under the skin which results from problem in the blood vessels.
- The only difference between these lesions is the **size**, petechiae are the smallest.

A. Etiology

●hemorrhagic fever is a diverse group of illnesses caused by RNA viruses from 4 families: (in 2012, a fifth member is added):

- *Arenaviridae, Bunyaviridae, Filoviridae, Flaviridae*.

- In 2012 ,a fifth member is added, which is *rabdoviridea* (Rabies).
- Name also differs by geographic occurrence.
- They differ also by the vector reservoir (mosquitos, ticks or, Rodents).
- But share certain clinical and pathogenic features.

●Virology:

- All RNA viruses.
- All Enveloped in lipid coating.
- Survival dependent on an animal or insect host, for the natural reservoir.
- Potential for aerosol dissemination, with human infection ***via respiratory route (except dengue).***
- Target organ: vascular bed.
- Mortality 0.5 - 90%, depending on agent.

●when you work with these viruses in the lab, the lab must has bio-safety level 3:

- In BSL 3, the lab ventilation must provide ducted, directional air flow by drawing air into the lab from clean areas and with no recirculation.
- All workers must wear positive-pressure, air-supplied full-body suit. (*According to some references, This point is used in BSL 4, but you have to memorize what the doctor said ☹)*

●Transmission:

- **Zoonotic diseases:**
  - ○ Rodents and arthropods main reservoir.
  - ○ Humans infected via bite of infected arthropod (*contaminated animal fluids*), inhalation of rodent excreta (*dried feces*), or contact with infected animal carcasses (*dead bodies*).
- person-to-person transmission(horizontal transmission) is possible with several agents:
  - ○Primarily via blood or body fluid exposure.
  - ○Rare instances of air borne transmission with arenaviruses and filoviruses.
- Rift Valley fever has potential to infect domestic animals following a biological attack.
- all these viruses are candidates to be used in bioterrorism as biological weapons, because these diseases have no treatment or vaccine.

B. Clinical Presentation

● Clinical manifestations nonspecific, vary by agent:

- Incubation period 2-21 days, depending on agent.
- Onset typically abrupt (sudden) with filoviruses, flaviviruses, and Rift Valley fever.
- Onset more insidious (gradual) with arenaviruses.

●Prodromal illness lasting < 1 week may include: (flue like symptoms)

– High fever– Headache– Malaise– Weakness– Exhaustion– Dizziness

– Muscle aches– Joint pain– Nausea– Non-bloody diarrhea

●After prodromal symptoms, **specific signs** and symptoms will appear, as a result of extravasation of the blood out from the blood vessels, these symptoms include:

- Flushing, conjunctival injection ("red eye").
- Pharyngitis.
- Rash.
- Edema *(due to the increase in vascular permeability).*
- Hypotension (*because of the decrease in the blood volume*).
- Shock.
- Mucous membrane Bleeding.
- It may lead to DIC, which is a small blood clot formation that consumes clotting factors, and thus worsening the problem.

C. Clinical Identification of Suspected Cases

● a diagnosis with viral hemorrhagic fever is established when you can identify the ***clinical criteria of this disease, which is a temperature of 101F(38.3 C) for <3 weeks*** and ***2 or more of the following***:

- Hemorrhagic or purple rash.
- Epistaxis (*bleeding from the nose*)
- Hematemesis (*Vomiting of the blood*)
- Hemoptysis (*Coughing up blood*)
- Blood in stools
- Other hemorrhagic symptoms
- No established alternative diagnosis.

●Lab tests include:

- Serology, by looking for seroconversion, which means the formation of specific antibodies "IgG" against the virus.
- PCR(molecular technique).
- IHC (Immunohistochemistry)
- Viral isolation.
- Electron microscopy, as some have specific shape, like Ebola.

D. Treatment and prevention

●Supportive treatment only, as we don't have any specific antiviral drugs

- ***Ribavirin***which as an antiviral prodrug, that works as guanosine analogue may be used.
  - ○ it's Not approved by FDA in USA.
  - ○Effective in some individuals.
  - ○Arenaviridae and Bunyaviridae only.

- Convalescent-phase plasma (serum obtained from one who has recovered from an infectious disease and considered to be especially rich in antibodies).
  - ○Argentine HF, Bolivian HF and Ebola.
- Strict isolation of affected patients is required.
- Report to health authorities.
- Correct coagulopathies as needed.
- No antiplatelet drugs or IM injections.

●Prevention is by avoiding contact with host species:

- ***Rodents*** (القوارض): *Control rodent populations,discourage rodents from entering or living in human populations* and *Safe clean up of rodent nests and droppings.*
- ***Insects***: *Use insect repellents*, *Proper clothing and bed net*, *Window screens and other barriers to insects*.

●There's no vaccine for most species, except the*Yellow fever*.

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

- The problem here that killed virus vaccines failed to stimulate specific antibodies for these viruses, So they are trying now to synthesis live vaccine, either by life-attended vaccine, or by injecting genetic material of these viruses in other viral vectors that are not pathogenic, like adenovirus.

● If human case occurs, we have to decrease person-to-person transmission to break the cycle by:

- isolation of infected individuals.
- Wearing Protective clothing, like: Disposable gowns, gloves, masks and shoe covers, protective eye wear when splashing might occur, or if patient is disoriented or uncooperative.

E.Management of Exposed Persons

●Medical surveillance for all potentially exposed persons,close contacts, and high-risk contacts (i.e., mucousmembrane or percutaneous exposure) x 21 days

- Report hemorrhagic symptoms
- Record fever 2x/day
- Report temperatures (101F/38.3C) to Initiate presumptive ribavirin therapy

●Percutaneous/mucocutaneous exposure to blood or body Fluids of infected:

- Wash thoroughly with soap and water, irrigate mucous membranes with water or saline

●Patients convalescing should refrain from sexual activity for 3 months post-recovery (arenavirus or filovirus infection)

- As person to person transmission may occur by close contact, and the virus shedding with sexual fluids lasts for 3 months.

●by that, we have finished our talking about hemorrhagic fever in general, in next few pages, we are going to have an overview about each family. Memorize underlined viruses only from each family :

II. Arenaviridae

●This family include: Junin virus, Machupo virus, Guanarito virus, **Lassa virus**, Sabia virus, Chapare Lujo.

●**Arenavirus transmission:**

- Virus transmission and amplification occurs in ***rodents.***
- Shed virus through urine, feces, and other excreta.
- Human infection: Contact with excreta, Contaminated materials and Aerosol transmission
- Person-to-person transmission.

●**Clinical manifestations:**

- Incubation period is 10–14 days.
- Fever, malaise and headache for 2–4 days.
- Hemorrhagic stage (gums, eyes, or nose).
- Hemorrhage, leukopenia, thrombocytopenia.
- Neurologic signs (hearing loss, tremors, and encephalitis).

●**Diagnosis:**

- ELISA
- RT-PCR
- Virus isolation in cell culture (7- 10 days)
- Immunohistochemistry, performed on formalin-fixed tissue specimens, can be used to make a post-mortem diagnosis.

●**Treatment:**

- *Supportive care:* Appropriate fluid and electrolyte balance, Oxygenation and blood pressure maintenanceand Treatment of any other complicating infections.
- *Ribavirin*, an antiviral drug, has been used with success in Lassa fever patients.
- *Prevention*: by avoiding contact with rodents.

III. Bunyaviridae

●This family include:**Rift Valley Fever virus**, Crimean-Congo and Hemorrhagic Fever virus, **Hantavirus**

●Bunyaviridae Transmission:

- Arthropod vector, Exception – Hantaviruses.
- RVF – Aedes mosquito
- CCHF – Ixodid tick

- **Hantavirus – Rodents.**
- Less common: Aerosol and Exposure to infected animal tissue.

IV. Filoviridae

●This family include: Marburg virus and **Ebola virus.**

●**transmission:**

- Reservoir is UNKNOWN, but **Bats** implicated with Marburg.
- Intimate contact.
- Nosocomial transmission
- Reuse of needles and syringes
- Exposure to infectious tissues, excretions, and hospital wastes
- Aerosol transmission(from Primates)

●Clinical manifestations:

- **Most severe hemorrhagic fever**
- Incubation period: 4–10 days
- Abrupt onset, with Fever, chills, malaise, and myalgia
- Hemorrhage and DIC
- Death around day 7–11
- Painful recovery.

V. Flaviviridae

●This family include: **Dengue virus, Yellow Fever virus**, Omsk Hemorrhagic Fever virus, Kyassnur Forest Disease virus.

●Flaviviridae Transmission is by **Arthropod vectors**:

- Yellow Fever and Dengue viruses (Aedesa egypti, Sylvatic cycle, Urban cycle)
- Kasanur Forest Virus by Ixodid tick
- Omsk Hemorrhagic Fever virus by Muskrat urine, feces, or blood.

"Don't go where the path may lead. Go instead where there's nopath and leave a trial"

●***Good luck***

●***The end :D :D***