The Cardio-VASCULAR System

- ○ Anatomy
- ○ Histology
- ○ Pathology
- ○ Pharmacology
- ○ Physiology
- ● Microbiology

Lec #: 1

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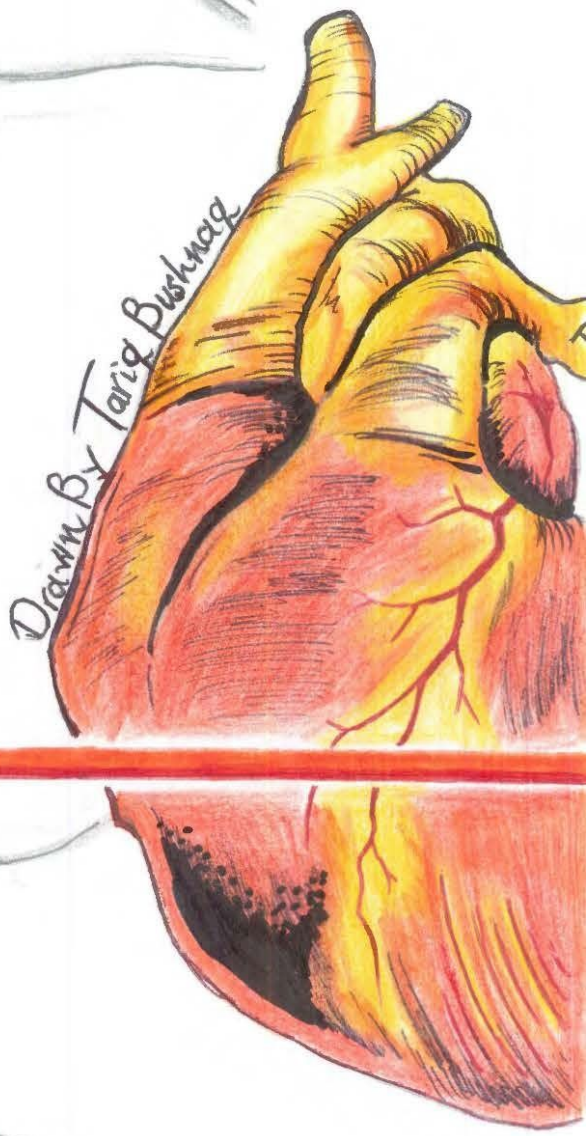
- ○ Handout
- ● Sheet
- ○ Slide



Viral Haemorrhagic Fever

We'll be talking about the viral infections that are associated with both hemorrhage and fever. Hemorrhage and fever are considered severe multisystemic syndromes, in which the damage reaches the vascular system and causes hemorrhage, noticing that hemorrhage itself is rarely the cause of death; the main cause of death is the one associated with multisystemic failure, including conjunctivitis, petechia, and acanthosis (signs of vascular damage).

The severity of the viral infection is determined largely by the viral load, and the immune system responses.

4 main viral families cause hemorrhagic fever, but we won't discuss their genuses specifically;

A. Arenaviridae, B. Bunyaviridae, C. Filoviridae, D. Flaviviridae

All these families share some characteristics:

- Enveloped RNA viruses.
- Have natural reservoirs (Animals: Rodents, or insects and ticks (like mosquito)), it infects human if he gets bitten by the mosquito, or exposed to rodents excreta.
- Human-Human transmission can occur by body fluids exposure. (Only if a human is exposed to the virus from these natural reservoirs.)
- No specific treatment. (Some cases of Arena and Bunya may improve after using Ribavirin, but still it's not approved by FDA.)
- No available vaccine, Except for the yellow fever cases. (experimental vaccines for Argentine virus, Rift valley, and others.)
- Supportive treatment is applied in all cases, depending on the symptoms; anti-pyretics for fever.
  For hemorrhage: platelets infusion; and fluids to maintain his blood pressure.
- Survival depends on the natural reservoir, and this also tells that these infections are localized to certain geographical areas. [Like in Arenaviridae; it has many members, each of which is confined to certain region.] Nevertheless, it starts to be transmitted among different areas due to easy travelling.
- Acquired from either a rodent, mosquito, or tick, and transmissible among humans.
- Target organ: vascular bed.

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- Potential for aerosol transmission (respiratory route); Hantavirus can be transmitted from dry rodents' excreta to air to be inhaled.
- Mortality rate ranges from 1%-90%, depending on the virus.

- These viruses can be categorized to different classes; A and C classes represent those used as biological agents of terrorism. (no vaccine, no treatment, 50% in certain viral hemorrhagic viruses may end in death like in Ebola infections)
  [A: Arenaviridae/Filoviruses, C: Hantaviruses.

- Considered as Zoonotic diseases. (Transmitted from animals to humans.)
- If a rodent transmits the virus to a second rodent (shedding), the second one will probably die. While if the transmission occurs vertically (to offspring), they will survive being carriers of the virus (asymptomatic) but still shedding of the virus can infect us.
- Rift valley fever has the potential to infect domestic animals forming a biological attack.
- Clinical manifestations: Nonspecific, vary according to the causative virus.
- Incubation period: 2 days to three weeks.
- Onset abrupt with Filovirus, Flavivirus, and Rift valley fever <u>suddenly</u>.
- <u>Gradual</u> onset in cases of Arenaviridae.
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  - Initial symptoms: Prodromal illness for one week, high fever, headache, malaise, weakness, exhausation, dizziness, joint and muscle pain, Nausea, Diarrhea.
  - Clinical signs: Flushing, conjunctival injection, rash, pharyngitis, edema, hypotension, shock, mucosal membrane bleeding.

- How to suspect?
  - Consider the geographical area, then look for these signs:

  -Increase in temp for less than 3 weeks.
  -Severe illness and predisposing factors for hemorrhagic illness.
  -Hemorrhage or acanthosis and petechia.
  -And 2 or more of the following: [Epistaxis, hemoptysis, hematemesis, and bloody stool, without known cause], you can find bleeding from the orifices: nose, the ear, the eye and if you did not find any cure then you should suspect viral hemorrhagic viruses.

- Diagnosis can be done by:
  - Serological tests.

- Real Time PC.
- Viral isolation in cellular culture (7-10 days) in biosafety labs level 3 or 4 because we are dealing with full virus, then using electron microscopy to see the structure of the virus.
- Convalescent phase plasma in cases of Argentine hemorrhagic fever and Ebola → It's found that if you exposed ill patients to plasma of patients in recovery state, they might benefit; most probably from the Abs in the recovered patients plasma.

- The fact that there is no available vaccine tells about the highly antigenic variations and antigenic drift; RNA viruses replicate by RNA-dependent RNA polymerase, this enzyme lacks proof reading mechanism, this leads to high rate of mutations (an error every 2000-3000 nucleotides). These mutations affect structural and non-structural proteins of the virus, mainly the most antigenic part of enveloped viruses: the spikes (glycoproteins).
  - The virus will enter your body and be captured by the immune system who will produce specific Abs against the viral Ags. But since the viral RNA is mutated and changed continuously, the spikes structures will change, and the previously formed Abs won't be able to recognize the virus.
- Strict isolation of affected patients is required, especially those with transmissible viruses (among human), also the caregivers should be careful to avoid direct contact with these patients.
- No anti-platelet drugs or injections should be given.
- Prevention and control:
  - Avoid contact with hosts or reservoirs (Rodents, insects).
  - Control rodents populations and their entry to humans populations, and safe cleanup of their excreta.
  - Use insect repellents and window nets.

- Management:
  - For cutaneous and mucco-cutaneous exposure to blood or body fluids → wash with water and saline to decrease the amount of virus entered to the body so the immune system can catch it; because if the amount entering the body is so small, the immune system can take care of it.

➔ Arenaviridae:

- Jenin / Machopu / Lasa / Vonorito / Sabia / etc.
- First isolated in 1933, then in 1958 (Jenin), 1963 (Machopu), 1969 (Lasa), 1989, 1993 (Sabia in south africa).
- [neither the years nor the names are important for exam purposes.]
- Each one is confined to certain area in South America (Lasa is seen in west african Nigeria).
- Reservoir: rodents. [Any contact with their excreta can transmit it.]
- Can be transmitted to humans through aerosol routes, direct contact. Contaminated material can transmit it.
- Human-Human transmission: Yes for Lasa (body fluids), others: No.
- Fatality: up to 35%
- Causes nosocomial outbreaks (Lasa fever).
- Incubation period: 2-3 weeks. [Remember the prodromal stage (1 week) (characterized by fever, malaise and headche), then the hemorrhagic stage and neurological signs (encephalitis); (in most Lasa fever cases: deafness develops).]
- Dx: by ELISA (Enzyme-linked immunosorbent assay), rt-PCR, virus isolation, immunohistochemistry tests from postmortem samples.
- Treatment: supportive care, fluids & electrolytes, oxygenation and BP maintenance, treat complications and infections. Try Ribavirin.
- Prevention: Avoid contacting rodents or infected humans specially in Lasa virus.

➔ Flaviviridae:

- Yellow fever, Denly fever, Omsk hemorrhagic fever, Kyasanurforrest disease.
- In Siberia, tropical areas, India, African americans, etc.
- Transmitted by Arthropods; mosquitoegypti (Yellow+Denly fever), or ticks (Omsk+kyasa..).
- 2 cycles for the mosquito to go through:
  - Sylvatic cycle (Jungle cycle): in forests among rodents and ticks, and once the human comes in contact with these reservoirs, he becomes infected.
  - Urban cycle (City cycle): in cities as a result of mosquito bites.
- Human-Human transmission: Yes for yellow fever, No for others.
- Short incubation period (1week) for Yellow and Denly fevers.

➔ Bunyviridae:

- Rift valley fever, Cranialcingo, Hantavirus (Hanta are types associated with Renal syndrome or associated with Pulmonary syndrome.)
- Transmitted by Arthropods: ticks+mosquitos. Except:Hanta, by rodents specially in pulmonary syndrome (inhalation of Aerosol of excreta).
- The Hantavirus, specially that of the pulmonary syndrome, is transmitted to human by inhalation of rodents excreta.
- Human-Human transmission: Yes for Cranialcongo, no for others.

➔ Filoviridae:

- Ebola, Marburg hemorrhagic fever.
- 3 types of Ebola; 1976: Zaier, Sudan, Restom.
  Then in 1994: Ebola Ku di voar.
  [The biggest outbreak of Ebola in the last year (2014) in Africa, with a 50-55% mortality rate, diagnoised cases were 15,000-17,000 and about 8,000 cases dead]; the outbreak was in Liberia, Guinea, Sierra Leone, and was associated with highest number of cases.
- In Africa.
- Unknown reservoir.
- Associated with nosocomial transmission.
- May be transmitted by fruit bats (Fruit bats are thought as a host but this is still under investigation).
- The most severe hemorrhagic fevers.
- Incubation period: 4-10 days.
- Sudden onset of fever, chills, myalgia, malaise.
- Associated with hemorrhage and DIC.
- Death in 7-11 days. If the patient survives: painful disabilities.
- High mortality rate in animals too.
- Human-Human transmission: Yes for both.

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