1 Ebola Virus

1. Filoviridae Family
2. RNA virus but has an unusual structure and genetic sequence
3. Virions are variable in length (1000 nm average)

5 species of Ebola are known so far

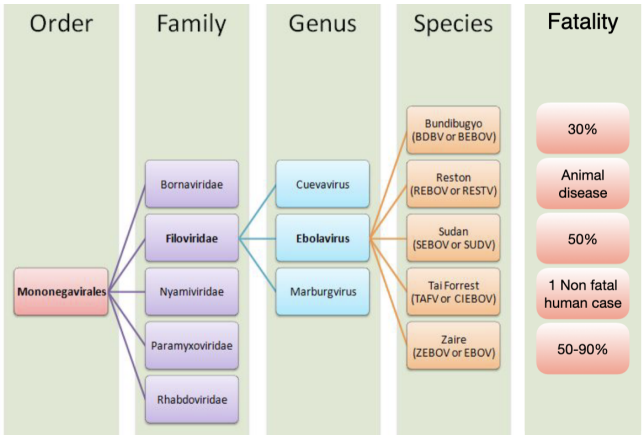

Figure 1: Ebola statistics

Ebola virus is in BSL-4 because it can be extremely lethal

Biosafety Level (BSL)	Characteristics	Pathogens/Disease
BSL-4	Infectious aerosol transmission that may cause serious or lethal infections with no treatment available	Ebola virus, Variola virus (smallpox), Marburg virus
BSL-3	Infectious aerosol transmission that may cause serious or lethal infections	Coronavirus, Mycobacterium tuberculosis, Yersinia pestis (plague), malaria
BSL-2	Infectious agents of moderate risk with ingestion or mucous membrane transmission	Influenza, Lyme disease, salmonella, measles, mumps
BSL-1	Low-risk agents that are not known to cause human disease	E. coli

Risk

Figure 2: Biosafety Levels

1.1 Predicted Distribution

3 species of Megachiroptera (bats) *suspected* to reservoir Ebola virus in West / Central Africa

While direct evidence of Ebola in bats is limited, they are thought to play a significant role in the virus' ecology and transmission

Ebola has also been detected in the carcasses of chimpanzees, gorillas, and antelopes

Infections in humans have been documented as occuring through the handling of bats, infected primates, and forest antelopes (dead or alive)

2 Disease

2.1 First Ebola Outbreaks

First outbreak of Ebola virus disease was reported in the DRC (in the village of Yambuku) in 1976

318 cases and 218 deaths (88% fatality rate)

Village had no running water, electricity, radio, phone, etc.

2.1.1 Naming

Yambuku village didn't want to be namesake

Congo already had disease named after it

Named after nearby river (Rio Ebola)

2.2 Ebola Virus Disease (EVD)

Symptoms typically appear 2-21 days after exposure to the virus, with an average onset of 8-10 days

Symptoms generally progress from 'dry' to 'wet' as the disease advances

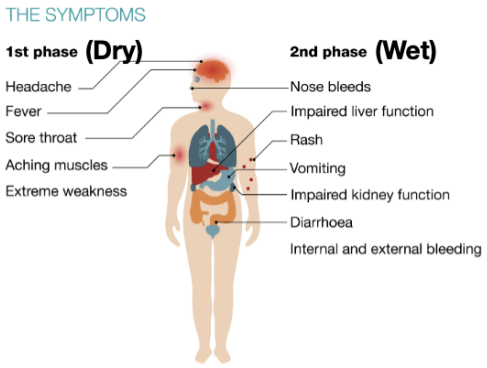

Figure 3: Ebola Virus Disease Symptoms

Previously named Ebola Hemorrhagic Fever

Primarily infects macrophages in the liver

→ Infection in liver may be important due to fluid loss or hemorrhaging, leading to liver dysfunction

Reduced blood clotting factors

Low blood pressure (hypotension)

2.2.1 Mortality

Pathogenesis of the virus is closely tied to triggering vigorous inflammation

Does the high amount of virus replication cause the disease symptoms (systemic inflammation) directly

OR

Is there a potential role for immune initiated inflammation triggering hemorrhagic disease

2.3 Course of Disease

1. Exposure
2. 2-21 days incubation period (8-10 days average)
3. Symptoms begin (virus become transmissible)
4. Weakness, fever (1-3 days)
5. Vomiting, diarrhea, hypotension (4-7 days)
6. Confusion, bleeding, shock (7-10 days)
7. Recovery or death

Ebola outbreaks determined as concluded after 42 days of negative tests

Clearance of the virus may be delayed in a few immunologically protected body compartments and fluids (ear, testis, eye, brain, uterus, joint)

2.4 Transmission

Ebola virus is transmitted by direct contact with

1. Blood
2. Organs
3. Bodily fluids (Saliva, urine, feces, vomit, sperm, sweat)
4. Contaminated Objects (fomites)
5. Infected animals

2.4.1 Human-to-Human Transmission

1. Close family contacts or caregivers
2. Burial ceremonies with direct contact
3. Hospital settings (Nosocomial transmissions)

2.4.2 Nosocomial Infections

Healthcare workers are primarily infected through inadequate protection

Outbreak may spread to other patients in a hospital

Nosocomial infections of Ebola are higher than with most pathogens

3 Outbreaks

From 1976 to 2020, over 28 outbreaks of Ebola virus occurred in Africa

Usually 1 to a few hundred people infected

25-90% fatality, most often with Ebola Zaire

3.1 2014 Epidemic

The Guinea outbreak strain was Ebola-Zaire virus but a distinct strain from those in prior outbreaks

Seemed to be resolving after the first 8 weeks, but the outbreak of less than 100 increased exponentially, spreading to other countries

Why was this outbreak so much larger?

Through rural spread, there were 1,850 cases from 1974-2014 with 1200 deaths

Through urban spread the 2014 epidemic had 28,616 cases with 11,310 deaths

Although there was only 40% mortality

3.1.1 Challenges

1. Never had Ebola outbreaks in so many countries at the same time
2. It took 6 months for government and aid organizations to get involved
3. Nonspecific treatment
4. Very big structures had to be built, scaring patients and families

   Some governments turned to authoritarian tactics to force patients into compliance, scaring them further
5. Most aid organizations were inexperienced with ebola
6. Coordinating organizations in multiple places was extremely challenging

4 Immune Response

Adaptive immune response is activated and hels resolve infection in those who survive

Those who survive infection are thoguht to be protected from re-infection

IgG antibodies seem to be the key to protection

Passive transfer of antibodies was also beneficial to people with active infection

4.1 VSV Vaccine

Vesticular Stomatitis Virus (VSV), which affects cattle, is weakened and acts as a vector

Infected humans may be asymptomatic or have a mild fever for 2-5 days

The VSV displayed the surface proteins of Ebola virus, mounting an immune response without the dangers of infecting the Ebola Virus

4.1.1 Vaccine Trial During 2014-2016 Outbreak

Ring vaccination method

$>$ 3500 individuals were recruited

One group was vaccinated immediately, whereas the other group was vaccinated after 21 days

No cases were observed in the immediate cluster compared with 10 cases of EVD in the delayed group

Vaccine was improved in 2019

4.1.2 Outbreak Monitoring

Small outbreaks must be followed up with treatment and contact tracing

Easier and cheaper than vaccinating the entire African population

March 2016

1. 8 cases reported in Guinea
2. 1000 contacts identified
3. 800 vaccinated

June 2016

1. WHO declared end of Ebola virus in Guinea and Liberia

5 Treatment

Symptoms of Ebola virus disease (EVD) are treated as they appear

1. Fluids

2. Electrolytes
3. Oxygen
4. Medication (Blood pressure, vomiting, diarrhea, fever, pain)
5. Treating other infections

5.1 Antiviral Drugs

Several drugs have been developed and approved for EVD, particularly for Zaire ebolavirus

Monoclonal antibodies are now used successfully to treat patients with confirmed Ebola (90% when administered soon after infection)

Remdevisir was being developed to stop ebolavirus from making copies of itself but was shown to be effective against SARS-CoV-2

5.2 Better Global Handling of Outbreaks

1. Ebola vaccine
2. Rapid diagnostic tests
3. Ebola treatment centers
4. Monoclonal antibody therapies
5. Public health education
6. Contact tracing
7. Quarantine measures