Viral Pathogens

1. Ebola Virus
2. Hepatitis B Virus
3. Herpes Simplex Virus 2
4. Human Immunodeficiency Virus
5. Influenza Virus

1. EBOLA
   VIRUS

- Family: Filoviridae
- Genus: Ebolavirus
- Species:
  - (Zaire ebolavirus)
  - (Sudan ebolavirus)
  - (Taï Forest ebolavirus)
  - (Bundibugyo ebolavirus)
  - (Reston ebolavirus)
• Filovirus
• Enveloped
• Single Stranded
• RNA

- Glycoprotein
- Lipid Membrane
- Matrix (VP40)
- Protein (VP24)
- Nucleoprotein
- Transcription Factor (VP30)
- RNA

TRANSMISSION via a Variety of Body Fluids

- Blood
- Saliva
- Tears
- Semen
- Mucus
- Urine
- Breast Milk
- Feces
- Sweat
- Vomit
Infected dendritic cells do not undergo maturation, unable to present antigen material on cell surface. As a result virgin T & B cells are not activated. Many undergo apoptosis.

NK cells fight but are greatly outnumbered due to the lack of immune cell response.

Once infected, macrophages produce proinflammatory cytokines, chemokines and tissue factor. This attracts additional cells which become infected.

**Multi-System Collapse**

- **Skin**: Severe bleeding, itching, redness, spotting
- **Brain**: Fluid accumulation, convulsions
- **Liver**: Fails, internal bleeding
- **Spleen**: Overloaded, broken blood vessels
- **Kidney**: Fails
- **Adrenal Gland**: Damaged, dangerously low blood pressure
- **Pancreas**: Infected, severe abdominal pain
- **Intestines**: Damaged, diarrhea and dehydration

As a last resort the immune system launches a cytokine storm to attack the virus.

- The cytokine storm makes the blood vessel walls more permeable.
- Arteries, veins and capillaries start to leak blood and plasma.
- Also triggers a big release of nitric oxide, which relaxes narrowed blood vessels, increasing oxygen and blood flow. Damages vessels further.

The host dies from multi-organ failure and shock.
## Signs
- FEVER
- INTERNAL BLEEDING
- VOMITING
- COUGHING BLOOD
- DEHYDRATION
- SWEATING
- DIARRHEA
- EYE REDNESS
- RED SPOTS ON SKIN
- EXTERNAL BLEEDING

## Symptoms
- HEADACHE
- DEPRESSION
- CHILLS
- FATIGUE
- NAUSEA
- LOSS OF APPETITE
- MENTAL CONFUSION
- SORE THROAT
- PAIN: ABDOMEN, CHEST, JOINTS, MUSCLES, SKIN

## Diagnosis

**Enzyme-linked immunosorbent assay (ELISA)**
Detects antibodies produced by the body’s immune system in response to the virus.

**Reverse transcriptase polymerase chain reaction (RT-PCR)**
Detects viral RNA by using reverse transcriptase to convert RNA to DNA followed by PCR amplification.

## Treatment
- No FDA approved vaccine or treatment
- No cure
- Stabilize Patient
  - Providing intravenous fluids (IV)
  - Balancing electrolytes (Body Salts)
  - Maintaining Oxygen levels normal
  - Blood transfusions
- Treating infections as they occur
- Experimental drugs
  - ZMapp
    - Contains neutralizing antibodies that provide passive immunity
    - Three monoclonal antibodies that may bind to the virus, if attached the immune system can clear out the virus
- Blood transfusions from those who have survived Ebola
  - The hope is that the survivor’s antibodies will help the recipient’s immune system fight off the virus
HOW IS EBOLA TRANSMITTED TO HUMANS?

PREVENTION

- Health care workers can prevent infection by wearing masks, gloves, and goggles whenever they come into contact with people who may have Ebola.
- People who have Ebola or are suspected of carrying the virus are isolated
- People who came into contact with someone with Ebola are periodically checked on

2. Hepatitis B
Hepatitis B Virus (HBV), a member of the Hepadnaviridae family, is a small DNA virus with unusual features similar to retroviruses.

The nucleocapsid encloses the viral DNA and a DNA polymerase that has reverse transcriptase activity similar to retroviruses.

The infectious HBV virion (Dane particle) has a spherical, double-shelled structure 42 nm in diameter.

Contains a lipid envelope containing HBsAg that surrounds an inner nucleocapsid composed of hepatitis B core antigen (HBcAg) complex with virally encoded polymerase and the viral DNA genome.

HBV leads to the death of many hepatocytes, a cell which composes 70%-85% of the liver and carries out the vital functions of this organ.

Mechanism

1. HBV enters host and attaches to liver cells.
2. HBV enters liver cells (hepatocytes) through endocytosis and begins to rapidly replicate.
3. Cell-mediated immune response is activated.
4. Cytotoxic T cells (CTLs) attack and destroy the infected hepatocytes, causing liver damage.
Mode of Transmission
Hepatitis B is spread when blood, semen, or other bodily fluids infected with the Hepatitis B virus enter the body of an uninfected person.

- Birth (spread from an infected mother to her baby during birth)
- Sex with an infected partner
- Sharing needles, syringes, or other drug-injection equipment
- Sharing items such as razors or toothbrushes with an infected person
- Direct contact with the blood or open sores of an infected person
- Exposure to blood from needles or other sharp instruments

Signs and Symptoms
Range from mild to severe:

- Fever
- Weakness and Fatigue
- Loss of appetite
- Nausea and Vomiting
- Abdominal pain
- Dark urine
- Clay-colored bowel movements
- Joint pain
- Jaundice

Diagnosis
- A doctor will assess patient risk factor.
- Blood tests determine if the virus is present and whether it’s an acute or chronic infection
  - Test for the Hepatitis B surface Antigen (AbbsAg)
  - IgM antibody to Hepatitis B Core Antigen (IgM anti-HBc) Test
  - Hepatitis Viral DNA Test
  - Hepatitis B e Antigen
  - Hepatitis B e Antibody
- Liver biopsy
  - This will determine if there has been damage to the liver, and if so, how severe.
Treatment and Prognosis

Treatment depends on age, condition of patient, viral load levels, biopsy findings, family history, and other aspects:

- **Nucleoside/Nucleotide analogs**: decrease the levels of Hepatitis B DNA in the blood, lowering the viral load.
- **Interferon α-2b**, a synthetic version of interferon: important in alerting other cells to produce anti-viral proteins to inhibit viral replication.
- Complications include: cirrhosis, liver cancer, liver failure, kidney disease, and anemia.
- Liver transplant for those with severely damaged livers.

Prevention and Vaccination

- Since 1982, a vaccine has been available that prevents Hepatitis B infections.
  - Complete vaccine series induces protective antibody levels in more than 95% of infants, kids, and young adults.
  - Protection lasts for at least 20 years and is most likely lifelong.
- If administered within 12 hours of exposure, HBV Immunoglobulin can protect you from developing an infection.
- Decreasing the risk:
  - Use a condom
  - Don’t share needles, razors, or toothbrushes

3. Herpes Simplex Virus Type 2 (HSV-2)
Herpes Simplex Virus

- There are 8 types of herpesviruses that can infect humans.
- Most common types:
  - HSV-1 (oral)
  - HSV-2 (genital)
- Can infect both men and women
- The virus can be dormant and reactivate when it is triggered

The Structure of the Herpes Viruses

- Four-Layered Structure:
  - Capsid: Composed of capsomers, contains the dsDNA
  - Tegument: Surrounds the capsid, protein coated
  - Lipid bilayer envelope: Contains the tegument
  - Glycoprotein "spikes"

HSV-2 Latency

- Virus may be maintained in a latent state hidden in sensory nerve ganglia
- Virus reactivates and is moved by anterograde transport near the original site of entry
- Recurrences can be spontaneous or can be triggered by physical or emotional stress, fever, exposure to UV light, and immune suppression
Transmission

- HSV-2 is very common and highly contagious
- Ways of transmission:
  - Sexual contact
  - Skin-to-skin contact
    - Whether or not the sore is open
- You CANNOT get HSV-2 through:
  - Toilets
  - Towels
  - Any other items used by an infected person

Signs and Symptoms

- Some people have very mild or no symptoms at all
- Symptoms:
  - One or more blisters appear on or around
    - Genitals
    - Rectum
    - Mouth areas
  - Pain or itching
  - Ulcers that form when the blisters rupture and ooze or bleed
  - Scabs (after ulcers heal)
  - Flu-like symptoms (fevers, body aches, or swollen glands)

Damage caused by HSV-2

- HSV-2 may cause complications such as:
  - Higher risk of catching other STDs
  - Bladder problems
    - Sores can cause inflammation around the urethra
  - Rectal inflammation
  - Meningitis (rare)
    - Inflammation of the membranes and cerebrospinal fluid surrounding the brain and spinal cord
  - Newborn infections
    - Infected mothers can expose babies to the virus during the birth
    - This may result in brain damage, blindness or death for the newborn
Diagnosis

- Physical exam
- Viral culture test
  - taking a tissue sample or scraping of the sore for examination in the laboratory
- Polymerase chain reaction (PCR) test
- Blood tests (e.g. ELISA, Biokit or Western Blot)
  - Find the presence of HSV antibodies
  - Distinguish between new or old infections

Treatment for Genital Herpes

No cure for Herpes

Antiviral medication can:
- Reducing the amount of days of the primary episode or outbreak
- Possibly prevent an outbreak
- Help heal faster
- if taking daily, the possibility of infecting a partner becomes less

Prevention

- Abstinence or have your partner tested for the virus before any sexual contact
- If in a relationship with an infected person, get educated on signs and symptoms and know when a person is most infectious
- Use a latex condom to reduce the chances of becoming infected
- Pregnant women who are infected with the virus should notify their OB GYN
- A pregnant woman can be treated with antiviral medication a few weeks before childbirth to reduce the chances of infecting the newborn with neonatal herpes
4. Human Immunodeficiency Virus
H.I.V

What We know/should know

• HIV is a retrovirus that infects our genes in order to weaken and
destroy our Immune system.
• The virus does not actually cause any direct
ilness to its host.
• It infects and destroys T cells or cells that
carry CD4 receptors.
• Acquired immunodeficiency syndrome
  • The loss of CD4+ helper T cells
  • Death by opportunistic infections

HIV Structure
Overview of HIV Function

- When the virus is in the bloodstream it targets specific cells with CD4+ receptors: Dendritic, Macrophages, Helper T Cells
- Once attached to a specific protein on helper T-cells (CCR5), for example, it fuses its envelope with the cell membrane resulting in entry of viral RNA strands and reverse transcriptase.
- The RNA is reverse transcribed into DNA and the new viral DNA enters the nucleus and is integrated into a host chromosome.

Transmission

- HIV is only transmitted through the bloodstream via infected fluids such as: blood, semen, breast milk, vaginal fluid.
- Coitus is said to be responsible for 75% of infected victims.
- Male to male (most common in the US)
- Male to female (universal)
- Female to male (less common) as HIV is present in vaginal, cervical fluid.
- Mother to fetus through the placenta, delivery
- Parenteral entry through shared needles
Symptoms

- Flu like symptoms
- Severe headaches
- Fatigue
- Body rash
- At 200-500 CD4+ T cells/mm³: Swollen lymph nodes, Hairy Leukoplakia (white patch on tongue), Oral Candidiasis (yeast infection in the mouth)
- At <200 helper T cells/mm³, HIV is now AIDS

ACUTE Infection:

- Dendritic cells that are in the Mucosal or Epithelial tissue will capture the HIV virus and take it to the lymph node.
- ALL-YOU-CAN-EAT: Virus goes HAM! Infecting more dendritic cells, macrophages and Helper T-Cells

Diagnosis

- Home Tests — The only home test approved by the U.S. Food and Drug Administration is called the Home Access Express Test, which is sold in pharmacies. (test the blood)
  - Oraquick: Test detects antibodies for HIV, not the virus itself.
- Saliva Tests — A cotton pad is used to obtain saliva from the inside of your cheek. The pad is placed in a vial and submitted to a laboratory for testing. Results are available in three days. Positive results should be confirmed with a blood test.
- RNA tests: detect the virus directly (instead of the antibodies to HIV) and thus can detect HIV at about 10 days after infection—as soon as it appears in the bloodstream, before antibodies develop
Treatment & Prevention

• There is no cure for HIV
• Medicine helps mitigate the spread of the virus.
  • Anti-retroviral drugs block certain enzymes inhibiting replication
  • Anti-retroviral therapy
  • Combination of medications, a HIV regimen.
• Prevention
  • Safe sex
  • Use clean needles
  • PrEP (pre-exposure Prophylaxis): Blocks enzyme reverse transcriptase.

5. Influenza Virus

The Great Influenza Virus

• In the winter of 1918-19 there was a flu pandemic that killed approximately 40 million people
• Influenza is a viral disease of the lower respiratory system capable of mutating making new strains of itself. It has an incubation period of about one day.
DESCRIPTION OF THE PATHOGEN

- **Viral structure:**
  - Envelope: membrane from host cell that surrounds capsid
  - Capsid: helical hollow protein capsule housing genetic material
  - 8 linear pieces of single stranded RNA (-strand) encoding 10 genes

- **Epitopes:**
  - Hemagglutinin (HA): glycoprotein spikes that bind to pulmonary epithelial cells and trigger endocytosis
  - Neuraminidase (NA): glycoprotein spikes that provide the virus access to cell surfaces by hydrolyzing mucus in the lungs

MODE OF TRANSMISSION

Influenza enters the body by inhalation of airborne viruses released by coughing or sneezing OR self-inoculation – transfer of virus from your fingertips to your nose or mouth.

1. Attachment: via HA & NA spikes
2. Entry: epithelial cells lining the lungs take in the viruses via endocytosis
4. Assembly: self-assembly of genetic material into viral particles
5. Release: lysis via budding, exocytosis

MECHANISM OF DISEASE

- Species types A and B cause influenza
- Mutation in the genes coding for the glycoprotein spikes HA and NA produce new strains of influenza virus
- Occurs via
  - **Antigenic drift**: accumulation of HA & NA gene mutations within a single strain of virus in a given geographic area.
  - The slow, gradual change in the viral antigens gives the name drift to the process.
  - **Antigenic shift**: the reassortment of genes among different influenza A viruses infecting the same host cell
SIGN & SYMPTOMS

• Sudden fever between 102-106°F
  • Fever distinguishes flu from a common cold
• Pharyngitis: inflammation of the pharynx
• Congestion, dry cough, headache
• Myalgia: muscle pain due to overuse or overstretching not resulting from physical exercise

DIAGNOSIS, TREATMENT, PROGNOSIS

• Community-wide outbreak of flu signs and symptoms is sufficient for an initial diagnosis of influenza.
• Treatment involves supportive care to relieve symptoms
• Antiviral drugs that inhibit type A and B neuraminidase (NA). These block the release of virions from infected cells. Must be taken during the first 48 hours of infection.
  • Oseltamivir pills
  • Inhalation of Zanamivir mist

PREVENTION & VACCINATION

• Immunization with vaccines that contain several antigens at once. Flu vaccines are at least 70% effective, but only against the viral antigens they contain.
Immune Disorders

1. Systemic Lupus Erythematosus (Lupus)

1. Lupus

What is Lupus?

- Lupus is a chronic inflammatory disease that can affect various parts of the body, specifically the skin, joints, blood, and organs.
- Lupus is considered an autoimmune disease, meaning that not only does the body’s immune system have to fight off outside invaders, it also has to fight against itself.
- Lupus is NOT contagious.
- The Lupus Foundation of America estimates that 1.5 million Americans and at least 5 million people worldwide have a form of Lupus.
Who Does Lupus Affect?

- 90% of people with lupus are women, and most first develop signs and symptoms of the illness between the ages of 15 and 44.

- An estimated 5,000 to 10,000 of the 1.5 million Americans with lupus are diagnosed under the age of 18.

- Lupus is more prevalent in African American, Hispanic, and Native American women.

Signs and Symptoms of Lupus

- Malar rash: a rash that appears across the nose and cheeks in the shape of a butterfly.
- Discoid rash: a rash with round, red, scaly patches that can appear on the face, arms, scalp, or ears.
- Photosensitivity: sensitivity to ultraviolet rays, like sunlight and fluorescent lights.
- Ulcers: in the mouth or nose.
- Arthritis: joint pain, especially in hands and feet.
- Serositis: collection of fluid near linings covering the heart, lungs, or abdomen.
- Kidney problems: this can be mild or severe.
- Neurological problems: issues with the brain and nervous system, such as seizures.
- Blood problems: lower than normal number of red blood cells, white blood cells, or platelets.
- Immune system problems: blood tests may show the immune system is not functioning properly.
Although the cause of lupus is not certain, there are several factors that can possibly increase the likelihood of an individual developing some form of lupus. These factors include genetics, environment, hormones, illness, medications, and a combination of these factors.

Individuals with an inherited predisposition for lupus may come in contact with something that can trigger lupus.

Some potential triggers include...

**Sunlight**: Exposure to the sun may bring on lupus skin lesions or trigger an internal response in susceptible people.

**Infections**: Infections can initiate lupus or cause a relapse in some people.

**Medications**: Lupus can be triggered by certain types of anti-seizure medications, blood pressure medications, and antibiotics.
Pathophysiology

- Lupus is an autoimmune disorder characterized by multisystem inflammation with the generation of autoantibodies.
- Patients with lupus have a complex array of abnormalities involving their immune system.
- Many biochemical studies have revealed abnormalities in genetic-susceptibility factors, environmental triggers, antigen-antibody (Ag-Ab) responses, B-cell and T-cell interactions, and immune clearance processes which all interact to generate and perpetuate autoimmunity.

Diagnosis

- Because many lupus signs and symptoms mimic other illnesses, can be vague, and come and go, lupus can be difficult to diagnose.
- A team of doctors and specialists are generally needed to diagnose a patient with lupus due to the varying degrees of signs and symptoms affecting various parts of the body.
- Doctors will carefully review a person’s entire medical history coupled with an analysis of results obtained in routine laboratory tests, as well as a physical examination.
- A person should see a doctor immediately if they have four or more signs and/or symptoms, or suspect they may have lupus.
Treatment

There is no cure for lupus, HOWEVER a proper treatment plan for lupus can include the use of aspirin or aspirin-like drugs, plaquenil, cortisone drugs, and immunosuppressants with the goals of:

- Reducing inflammation
- Suppressing an overactive immune system
- Preventing flares and treating them when they occur
- Controlling joint pain and fatigue
- Minimizing damage to organs

Prognosis

- Although lupus is not a universally fatal disease, it is sometimes listed as a contributing or underlying cause of mortality in people who had lupus and died of active disease.
- 80-90% of people with lupus can expect to live a normal lifespan.
- This can be achieved through proper management of lupus by following the instruction of their physician, taking their prescribed medication(s), as well as seeking help for unexpected side effects of their medication(s) or a new manifestation of their lupus.