Source: [KBBiologyMasterIndex]

# 1 | Overview of Human Diseases

A lecture by Paul.

#flo #disorganized

**Disease** is an abnormal condition that causes impairment in/loss of function of an organism (a.k.a. decreased fitness) that is not due to immediate external injury.

- · What causes human disease?
  - · Infectious agents
  - · Deficiency disorders
  - Heritable factors
  - Physiological disorders (immunodeficiency, autoimmune disorders, allergies, etc.)

## 1.1 | Congenital vs. Acquired disease

Congenital diseases => diseases present at birth due to DNA abnormalities / pregnancy pathological issues Acquired diseases => diseases that begin during lifetime, including...

- Microrganism invasion => "infectios diseases"
- Autoimmune reaction
- Nutrient deficiency
- · Mechanical wear
- · Ingestion of noxious chemicals

## Infectious diseases actually smaller on the causes of death in the US

- Heart disease => wear + deficiency
- · Cancer => heritable + DNA
- Unintentional injuries => not a disease
- Chronic respitory disease => wear
- Stroke => not a disease
- Alhetimer disease => wear
- Diabetes => autoimmune, nutrient, wear
- Influenca <= here, finally, an infections disease.</li>

## 1.2 Disease causing agents

- Protozoan => single-celled eukaryotes
- Fungal => single/multi-celled eukarotyes
- **Bacteria** => single-celled prokaryotes
- Viral => acellular parasitic infectious agent
- **Helminuthus** => multicellular worms
- **Prions** => acellular misfolded proteins
- Viroids => infections nucleic acids w/o protein coat to make virus

# 1.3 | Pathogenicity + Virulence

Pathoginecity => relative capacity to cause disease

- Non-pathogenic agents => no diesease
- Primary pathogens => yes disease
- Opportunistic pathogens => yes disease only when it can, for instance, in immunocompromised individuals

**Virulence** => numerical measures for pathonicity

Measured experimentally with LD50 + ED50

# 1.4 | Overview of various diseases

This video

## 1.4.1 | Protozoan

- **Protozoan factors** => direction pathogenisis leading to tissue damage
- Host-mediated factors => immune evation + escape mechnisms + immunalsupression

Adaptable!!

# 1.4.2 | Fungal

- Fungal factors => many shapes and very adaptable, colud produced specialized enzymes to take root in body
- Host-mediated factors => cause immunocomprimzation, acquired though inhalation, etc.

## 1.4.3 | Bacteria

- Bacterial-induced toxicity => produces toxins + has hard capsule cell
- Host-mediated factors => may develop host resistance, could compete for resources, and could be grown introcellularly



Figure 1: Screen Shot 2020-10-12 at 3.08.53 PM.png

# 1.5 | Bacteria causing diseases

#### **Biofilm formation**

- · Communities of bacteria could work together by adhering and exchanging information
- Bacterial could perform quorum sensing => exchange of information with each other + recognize various members of their group

## 1.5.1 | Fighting bacterial infections

**Antibiotics** => drugs with selective toxicity for specific bacterial types Act by...

- Disrupting membrane + cell wall integrity
- Selectively target + impair bacterial ribosomes
- Block bacterial DNA replication/transcription
- · Inhibit bacterial metabolism

## 1.6 | Viruses causing diseases

### Viruses: acellular macromolecular assemblies

- Contain protein coat called capsid
- DNA or RNA, but not both
- · Are obligate parasites that could only replicate within host
- Assembled and mature viral particles => virions, which contain...
  - Capsid
  - · Genetic material

- · Occationally outside lipid layer
- => Viruses exist on the nanometre scale, but they are difference in share and size

## 1.6.1 | Structure of viruses

### · All contain

- Capsid => structural protein coat
- Genome => RNA/DNA; but not both

#### · Some contain

- Membraneous-enclosed capsid => envelope
- Externally-facisg host-cell fusion proteins => spikes
- Viral genome replication enzymes => prlymerases
- Other proteins for fun => enzymes, motor proteins, transcription factors, host-cell interacting proteins, etc.

# 1.6.2 | Two types of virus

### Prokaryotic-infecting viruses

- · Variety of shapes
- Complex and prolate shapes
- · Has, sometimes complex shapes! a la this image

### · Eukarotic-infecting viruses

- · Much more "boring" in terms of shape
- Icosahedral/spherecial outside
- Enveloped constructions => envelope protein layer outside, spherical inside
- Helical/Cylindrical/Bullet shapes, too!
- Often single patterns assemble together to create symmetric shape that creates the whole of the virus

# 1.6.3 | Viral Life Cycle

- 1. Attachment => protein contact between virus and host
- 2. Viral entry/Uncoating => shedding the protein layer
- 3. Biosynthesis => make baby viruses
  - 1. Genome Replication: transcribe DNA/RNA
  - 2. Genome Expression: read DNA/RNA to make proteins
- 4. Viral genome integration => retrovirus only
- 5. Assembly => put it all togethr
- 6. Viral Exit => mature virons leave

## Viral Entry Option 1: Direct Injection/insertion

- Insert genome through the bi-layer
- · Leave the rest behind
- Tada!

## Option 2: Endocytosis

- Trick the host cell into introducing the virus as food
- Endocytosis!
- Bam

#### Option 3: Fusion

- · Virus fuse with cell membrane
- · Shed the protein coat once in
- · Shazam!

### All of these involve attachment first, which usually takes two steps.

This process causes the organism-specific response to viruses:

- 1. Attachment: adhere roughly to random sugar proteins
- 2. Binding: roll over slowly, and bind to the entry receptor it needs

## Uncoating

- · Virus triggers early endosome
  - · Causes pH dependent protein denaturation
  - Causing the capsid to fall apart
  - Triggering late endosome => releasing genome

### Viral Replication Key questions:

- How are viral mRNAs produced from the viral genome? => virus will hijack the ribosomes in the host cells. So, it is more important to ask how the mRNAs are produced to tell ribosomes what to do
- What serves as the template for viral genome replication => replication will need a polymeraese; but the source and mechanism is dependent on viral genome structure/composition

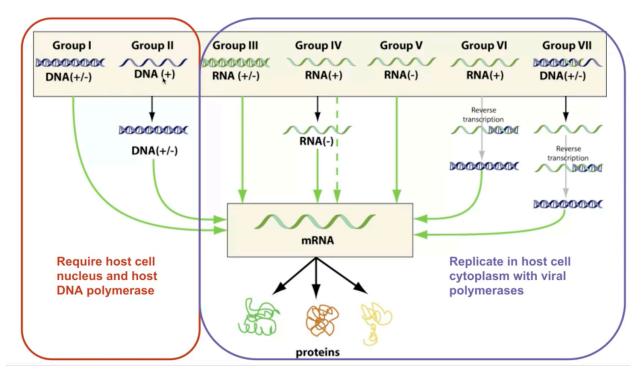


Figure 2: Screen Shot 2020-10-12 at 11.04.53 PM.png

### **DNA Viruses**

How are viral mRNAs produced from the viral genome?

- · Viral DNA enters, through RNA polymerase II in the host cell, mRNA is produced
- · mRNAs then read by ribosomes, and there we go

What serves as the templates for viral genome replication?

- · Viral DNA serves as template for host cell DNA polymerase
- · Viral genome copied repeatedly
- · Virus, then, will be replicated within the nucleus due to it needing the polymerase to copy DNA

Except! Poxvirade carry their own polymerase, so they replicate in the cytoplasm.

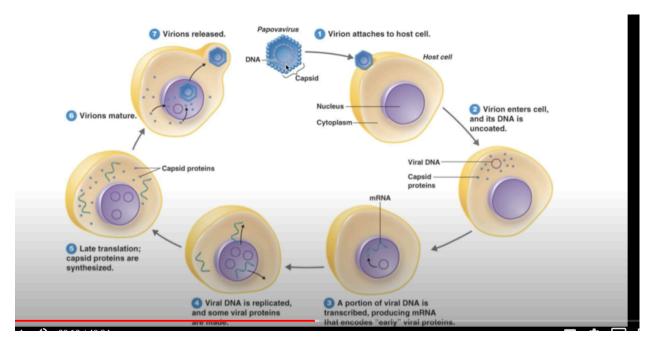


Figure 3: Screen Shot 2020-10-12 at 11.09.46 PM.png

#### **RNA Viruses**

How are viral mRNAs produced from the viral genome?

- double-stranded RNA viron => (+, a.k.a. sense) strand could be translated directly by using as mRNA
- +-stranded RNA => same idea as above
- strand RNA => virus comes with polymerase that convert -ssRNA to +ssRNA. Then, same idea
  as above

What serves as the templates for viral genome replication?

- RNA viruses does not need host-cell polymeraese to copy RNA
- · They come with polymerase that...
  - with dsRNA; takes +ssRNA and makes -ssRMA; combining the two to produce dsRNA
  - · with +ssRNA, takes +ssRNA and makes temporary -ssRNA which makes more +ssRNA
  - with -ssRNA, takes -ssRNA, and makes temporary +ssRNA, which makes -ssRNA

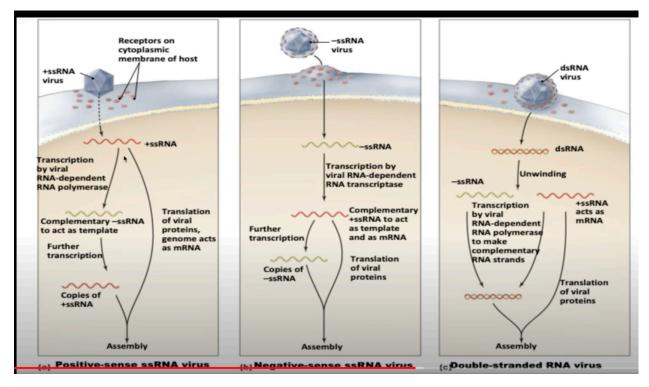


Figure 4: Screen Shot 2020-10-12 at 11.14.30 PM.png

Packaging Does not require ATP. Just sealed in.

## Viral Exis Lysis

Replicate so much that the membrane burst.

# **Budding**

Trigger...

- · Trigger extocytosis
- Meanwhile, send virus's own spikes to the membrane
- · On exit by extocytosis, steal a part of the newly-spikey membrane with it to serve as new casing

## 1.6.4 | Retroviruses

### Viruses that have the ability to intergrate into the chromosomes of the host cell

To make this happen, the virus needs...

- · Reverse Transcriptase
  - · Transcript RNA to double-stranded RNA
  - · Take double-stranded RNA to turn into DNA