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.**

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

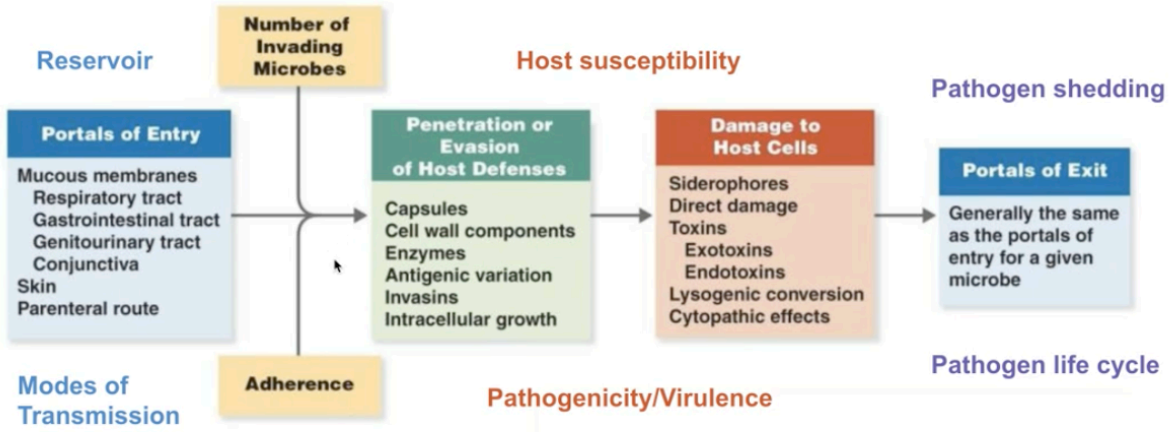

Figure 1: Screen Shot 2020-10-12 at 3.08.53 PM.png

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

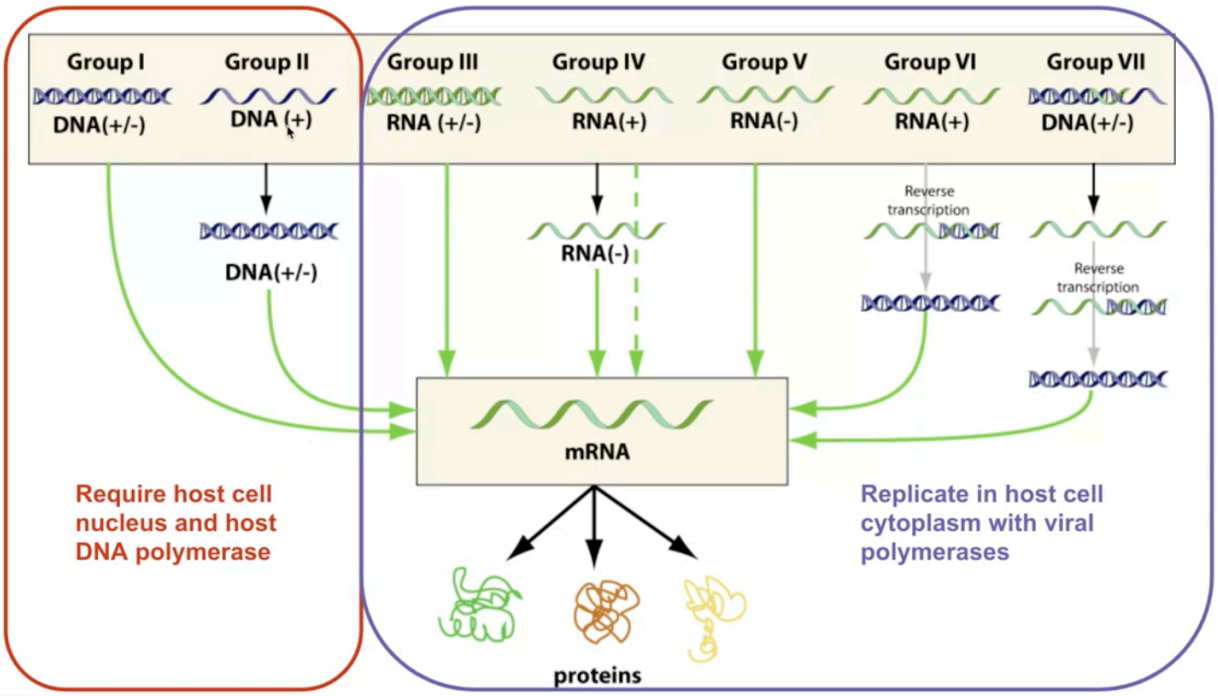

Figure 2: Screen Shot 2020-10-12 at 11.04.53 PM.png

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.

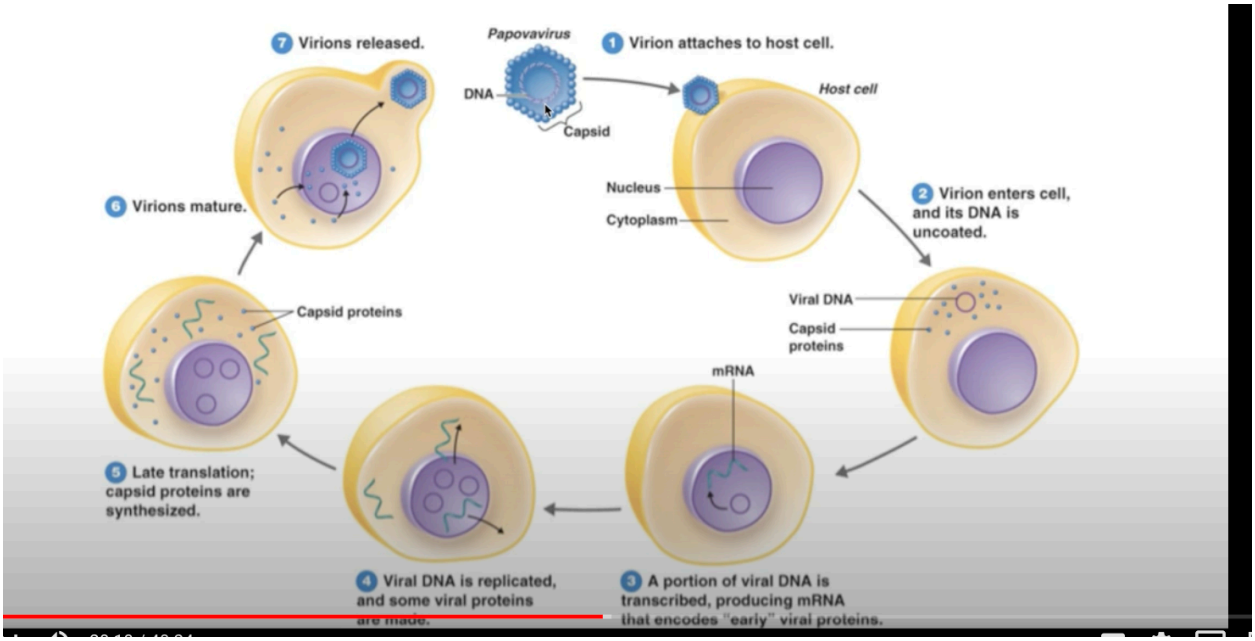

Figure 3: Screen Shot 2020-10-12 at 11.09.46 PM.png

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

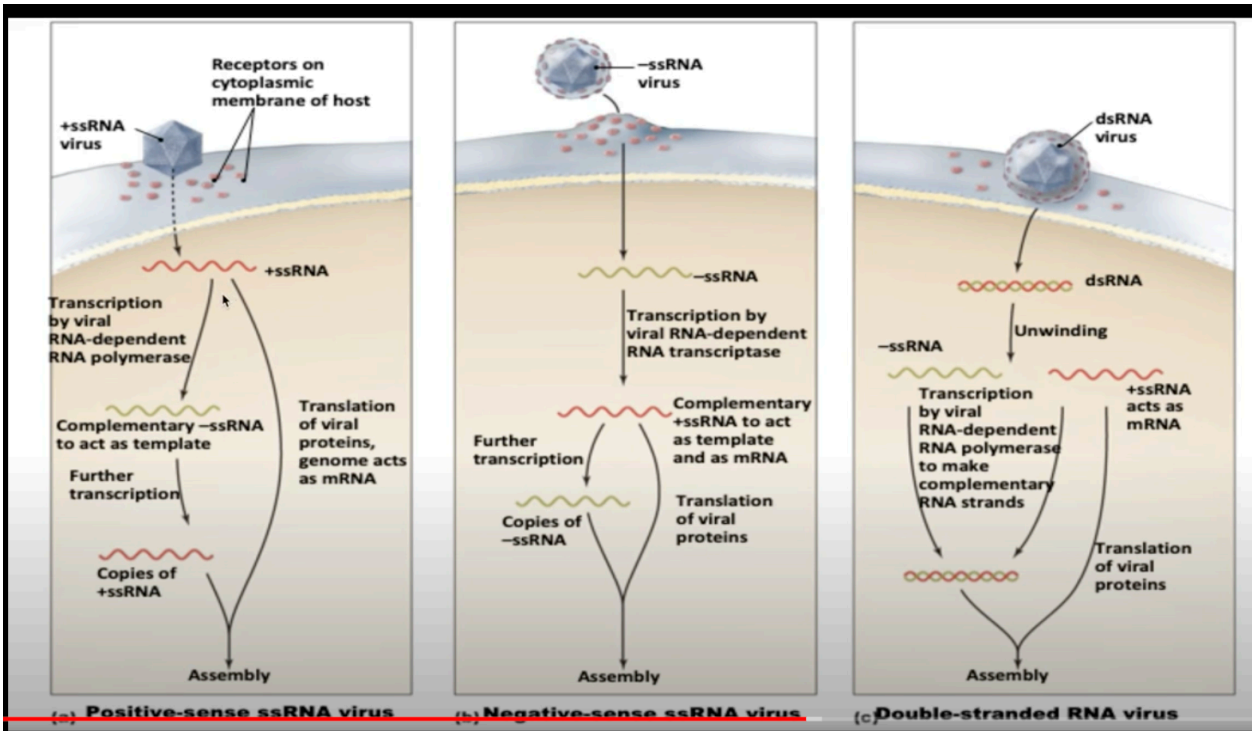

Figure 4: Screen Shot 2020-10-12 at 11.14.30 PM.png

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