Source: [[KBBiologyMasterIndex]]

1 | Overview of Human Diseases

A lecture by the Legendary Dr. Paul Hauser. Slides are here

#flo #disorganized

1.1 | Congenital vs. Acquired disease

- 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

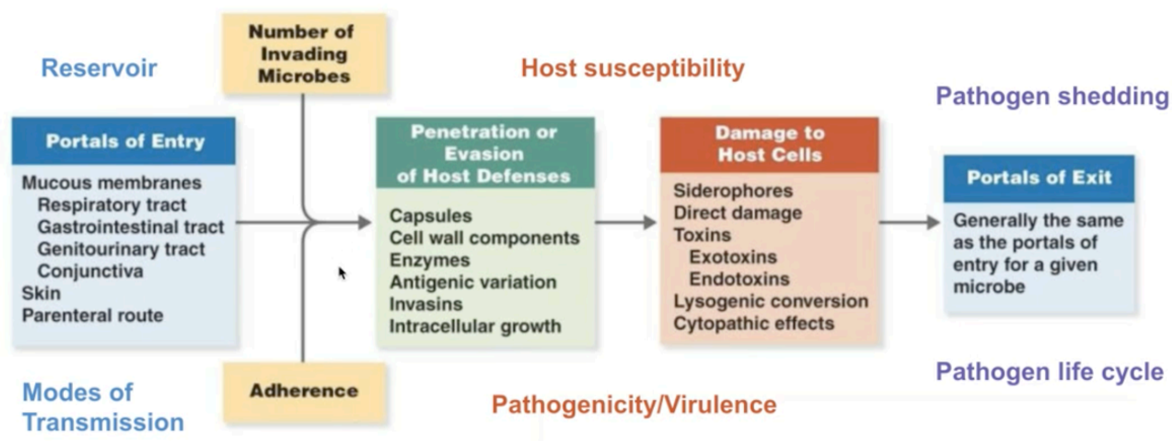

Figure 1: Screen Shot 2020-10-12 at 3.08.53 PM.png

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

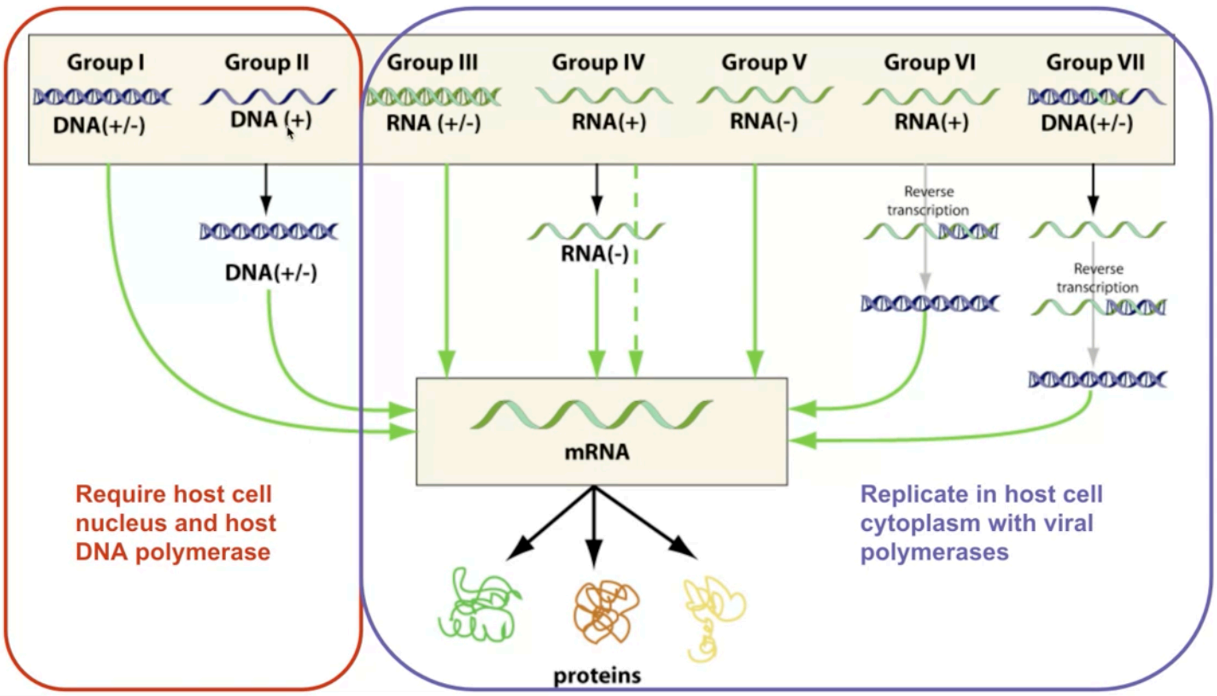

Figure 2: Screen Shot 2020-10-12 at 11.04.53 PM.png

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.

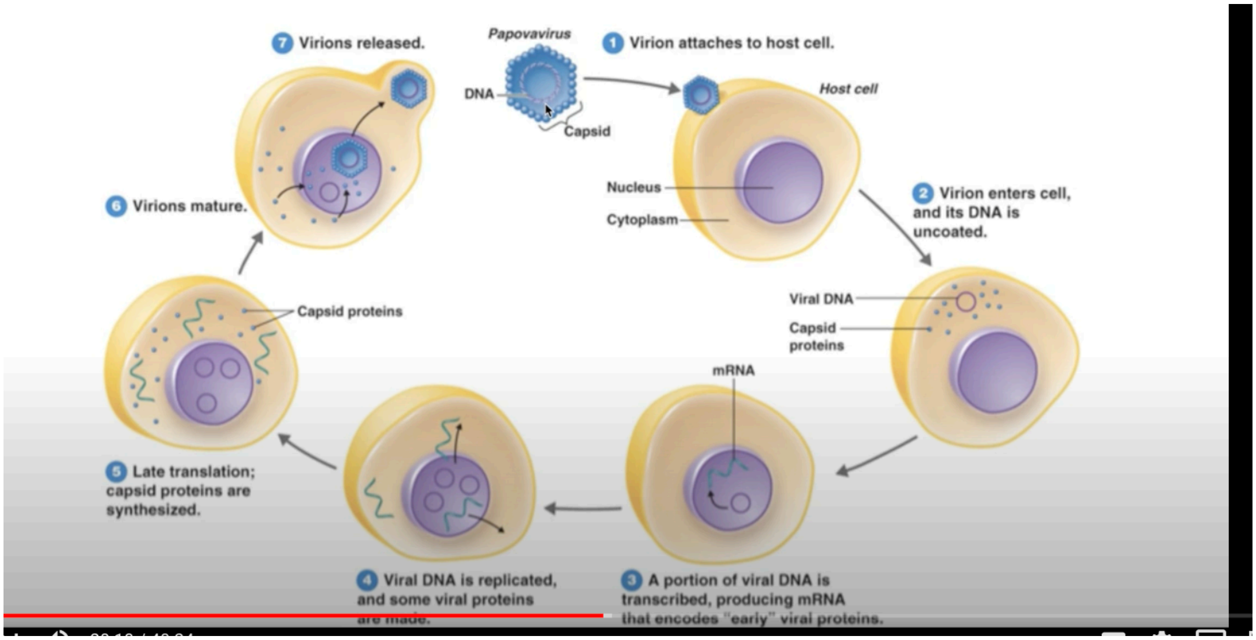

Figure 3: Screen Shot 2020-10-12 at 11.09.46 PM.png

RNA Viruses

How are viral mRNAs produced from the viral genome?

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 | **Viral Genetic Shift + Viral Genetic Drift**

Shift => whole segments of genome exchange abruptly as two flu viruses infect the same cell to create a new strand.

Drift => single/groups of nucleotides flip slowly over time.

The former is an environment-dependent process, where the latter is able to be modeled as it is due to transcription mistake.

1.6.5 | **Retroviruses + How to Stop Them**

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

Early Events

- Viruses is uncoated, and uses an enzyme called reverse transcriptase to turn ssRNA to cDNA, and finally into dsDNA
- Then, the enzyme integrase threads the viral dsDNA into the cell's nucleaus
- HIV protease cuts HIV polyproteins into individual parts ready for budding

Late Events

- Proviral region is transcribed slowly whenever ribosome comes across it by the host DNA polymerase II to make viral proteins + replicate the viral genome
- Components are later exported, assembled, and slowly released through budding

To make this happen, the virus needs…

- **Reverse Transcriptase**
    - Transcript RNA to double-stranded RNA
    - Take double-stranded RNA to turn into DNA
- **Integrase**
    - Force insert the DNA into the genome of the host cell

And because of the fact that viral DNA is now in cellular DNA, these viruses' DNAs are hard to get rid of.

And this is why we can't cure HIV.

Virus, in this case, spread through cell duplication

- Proviral region on the DNA, every time the ribosome comes across it, makes a new viron
- These components are then assembled, sent, etc. as usual
- Because of the fact that the ribosome needs to, well, come across the bit of DNA for this to work, the virons are made slowly by "trickling out.

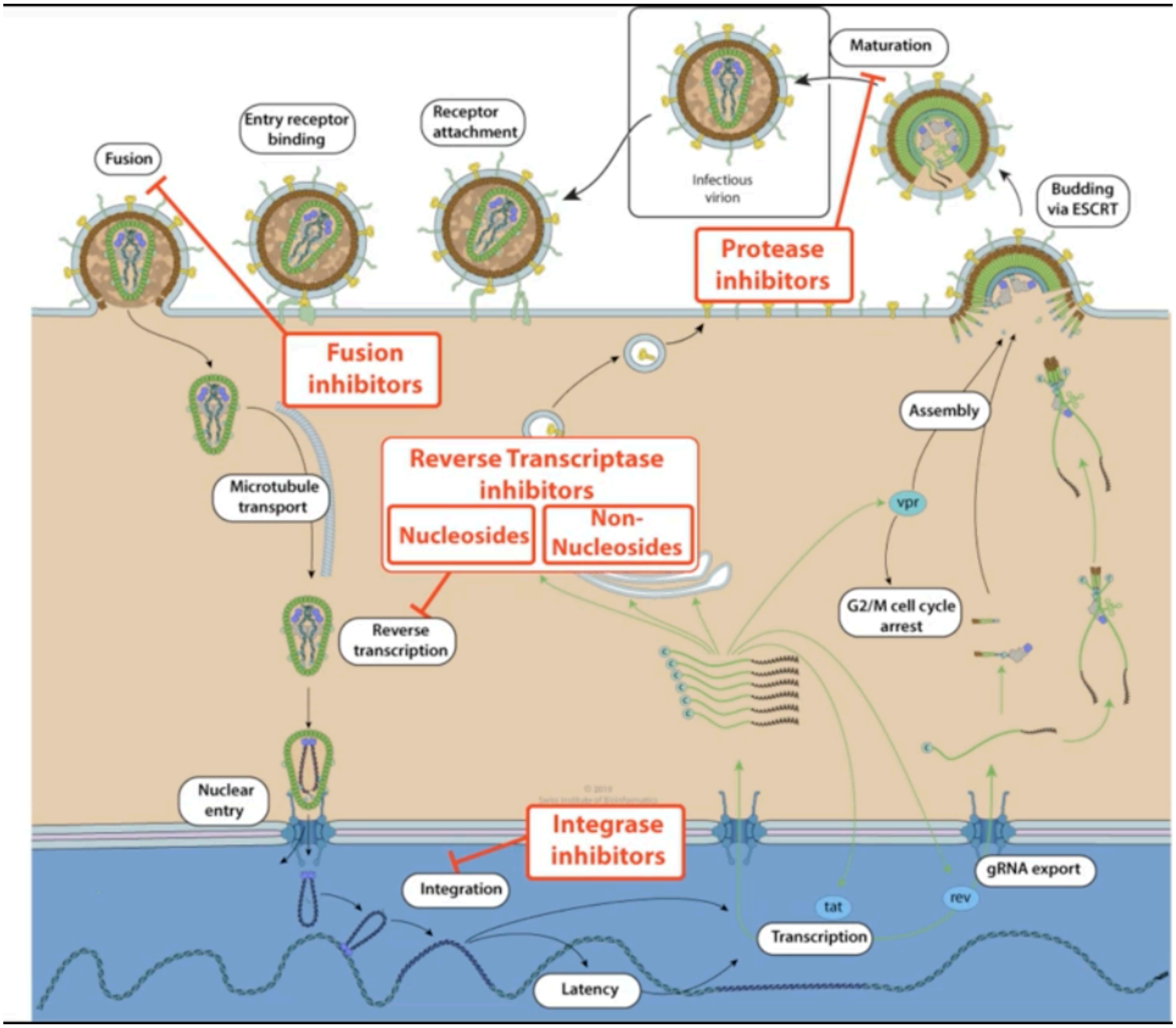

Figure 4: Screen Shot 2020-10-12 at 11.22.35 PM.png

Preventing Retroviruses

- Prevent Fusion `gp120`, `gp41`, `CCR5`
- Prevent reverse transcription `RT`
- Prevent intergration via intergrease `IN`
- Prevent viron maturation `PR`

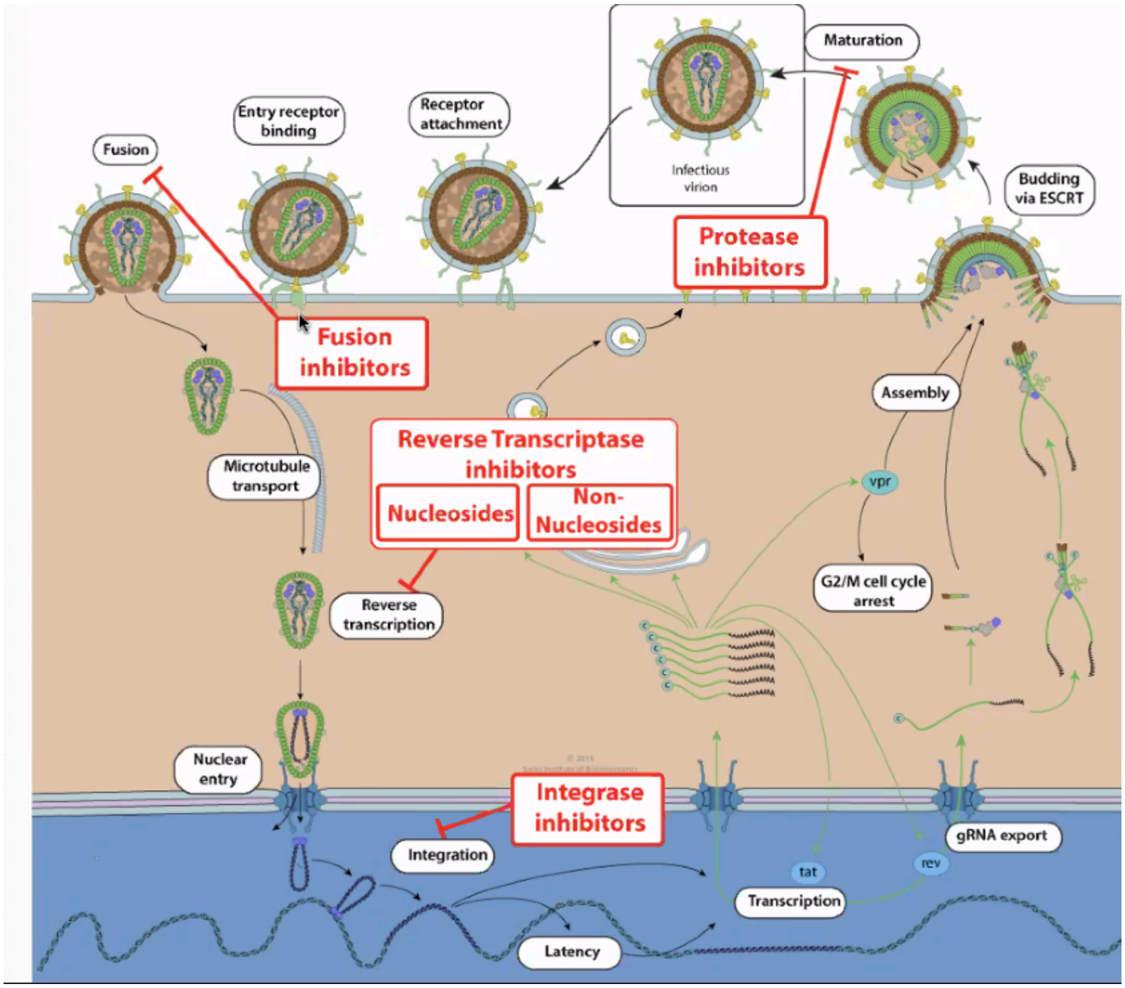

Figure 5: stophiv.png

- Most advanced: HAART (Highly-Active Anti-Retroviral Therapy)
  - Cocktail drug works together for inhibition
  - Two drugs to stop intergration, one to stop protease (viron maturation)
  - Could develop resistance

1.6.6 | **Viral Genome vs Mutation Rate**

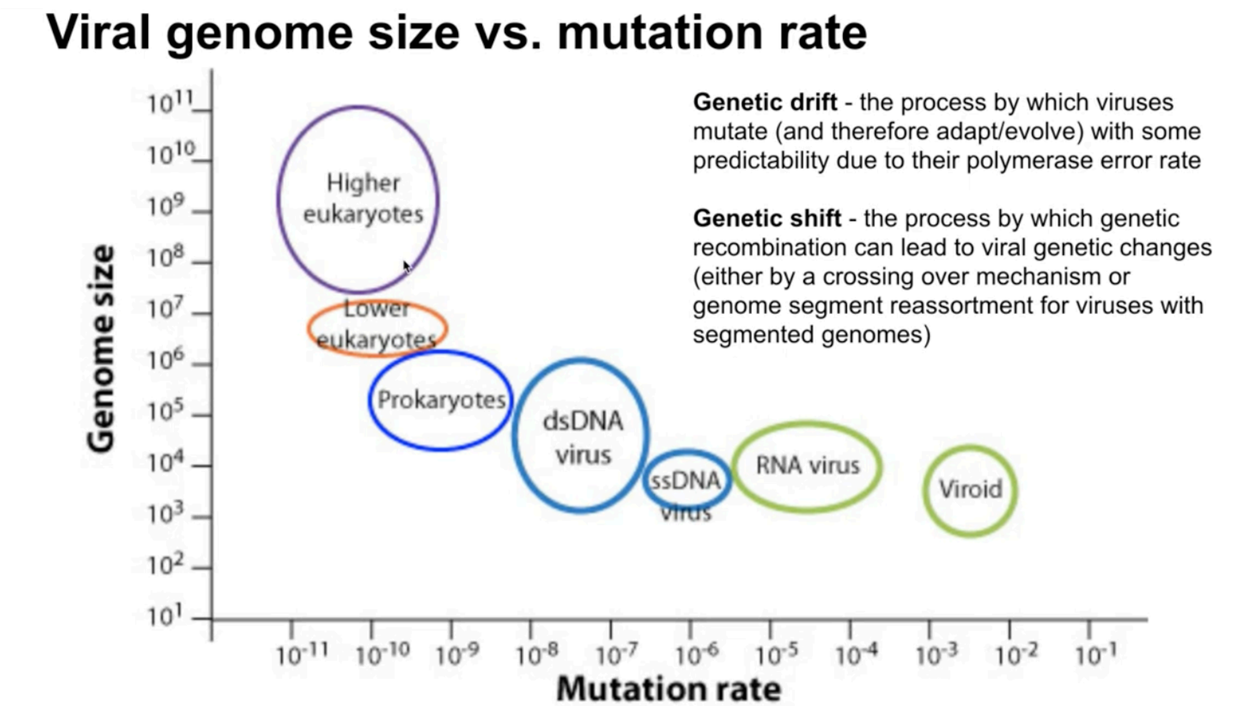

Figure 6: Screen Shot 2020-10-12 at 11.24.39 PM.png

- RNA viruses could mutate more because it does not have checks
- More complex+largest viruses harder to mutate

Genetic drift — viruses mutate due to polymerase error

Genetic shift — viruses recombinate without mutating by crossing-over mechanism or genome segment reassortment. Think! the flu

1.7 | **Why are viruses bad**

Damage host cells/tissues by…

- Reducing gene expression capacity
- Depleting cellular resources
- Causing cell lysis (to explode)
- Promoting tumorigenisis — cancer
- Creating damaging immunological response

1.8 | **Preventing Viruses**

Let's talk about **Remdesivir**! A drug developed by Pfizer that's used to combat Ebola + influenza viral replication.

Modified nucleotide triphosphate which adds onto the RNA strand copied by the RNA-Dependent RNA Polymerase carried by viruses

- Pretends + gets inserted as a nucleotide
- Once added onto the RNA chain, jams further actual nucleotides from being inserted

Could but usually does not jam up normal RNA polymerase which does normal transcription

- Inhibiting transcription in the short term won't kill you immediately
- So, we hurt normal cell transcription a little in order to rid of the virus
- Need hospital treatment for regular and safe dosing for this exact reason
- Viral proteins are usually easy to assemble

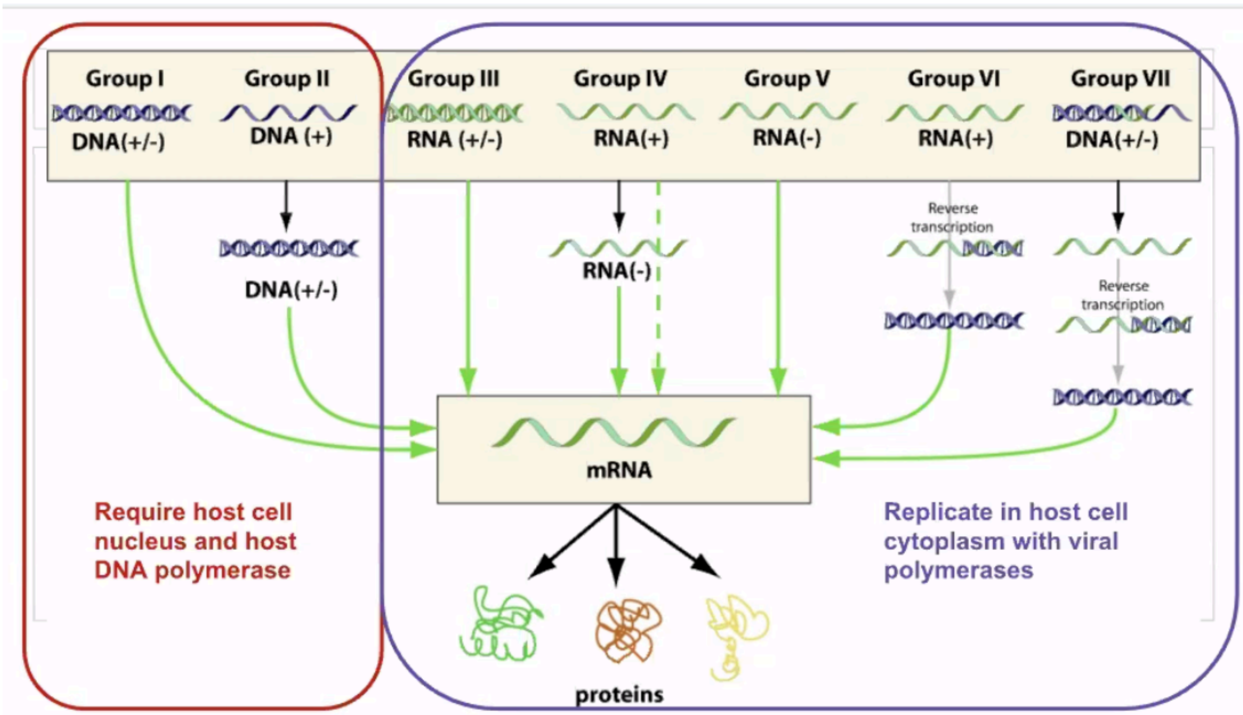

Figure 7: Screen Shot 2020-11-02 at 2.48.22 PM.png

Question: how are proteins made in the viral genome

- No viruses produce ribosomes
- Ribosomes become centrally important for the virus
- What serves as the template to make new virus copies

Viruses attempt to overwhelm the enzyme to entry.

DNA viruses are "less complex", in that as long as they are able to get into the nucleaus, the rest would just be the body's work automatically.