

Source: [KBiologyMasterIndex](#)

## 1 | Overview of Human Diseases

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

### 1.1 | Disease causing agents

### 1.2 | Pathogenicity + Virulence

**Pathogenicity** => relative capacity to cause disease

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

**Virulence** => numerical measures for pathogenicity

- Measured experimentally with LD50 + ED50
- 

### 1.3 | Overview of various diseases

This video

#### 1.3.1 | Protozoan

- **Protozoan factors** => direction pathogenesis leading to tissue damage
- **Host-mediated factors** => immune evasion + escape mechanisms + immunosuppression

Adaptable!!

#### 1.3.2 | Fungal

- **Fungal factors** => many shapes and very adaptable, could produce specialized enzymes to take root in body
- **Host-mediated factors** => cause immunocompromise, acquired through inhalation, etc.

#### 1.3.3 | 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 intracellularly

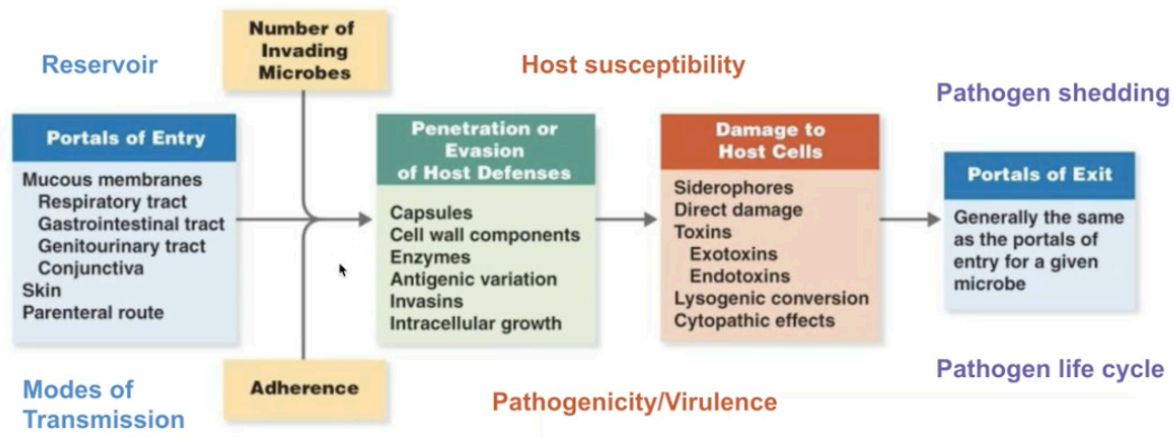


Figure 1: Screen Shot 2020-10-12 at 3.08.53 PM.png

## 1.4 | 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

### 1.4.1 | 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

## 1.5 | 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

- Occasionally outside lipid layer

=> Viruses exist on the nanometre scale, but they are difference in share and size

### 1.5.1 | **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.

### 1.5.2 | **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/sphercial 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

### 1.5.3 | **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 polymerase; but the source and mechanism is dependent on viral genome structure/composition

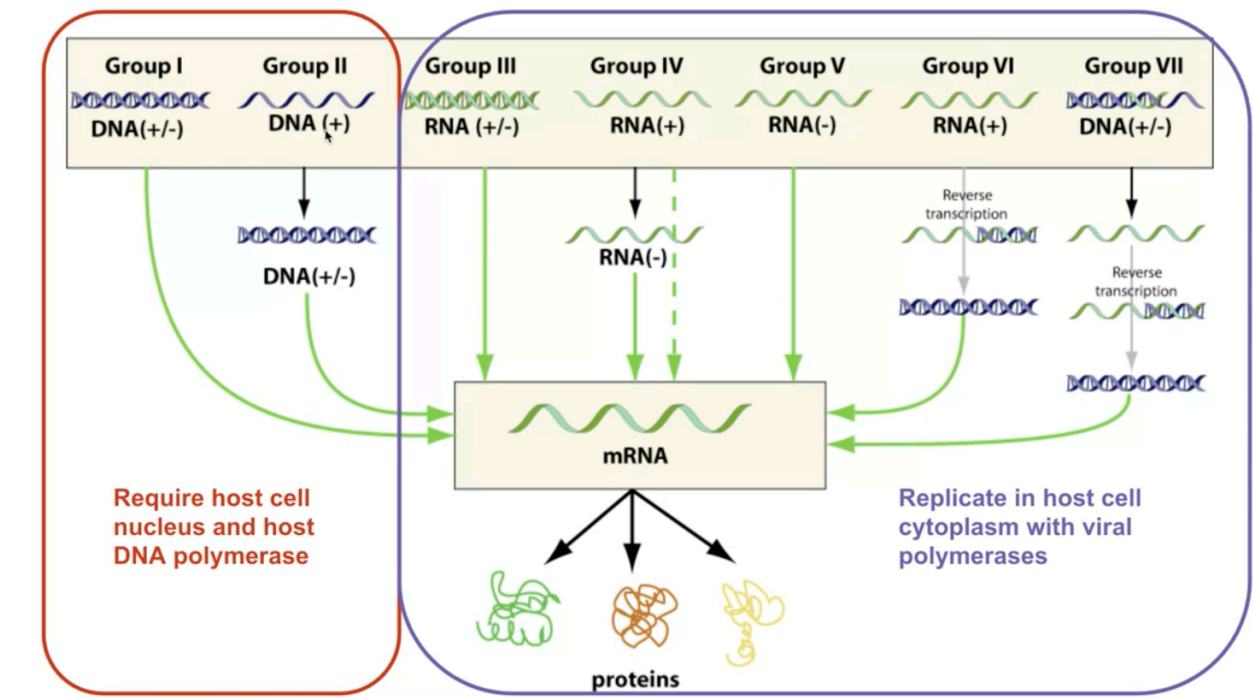


Figure 2: Screen Shot 2020-10-12 at 11.04.53 PM.png

## 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! Poxviridae carry their own polymerase, so they replicate in the cytoplasm.

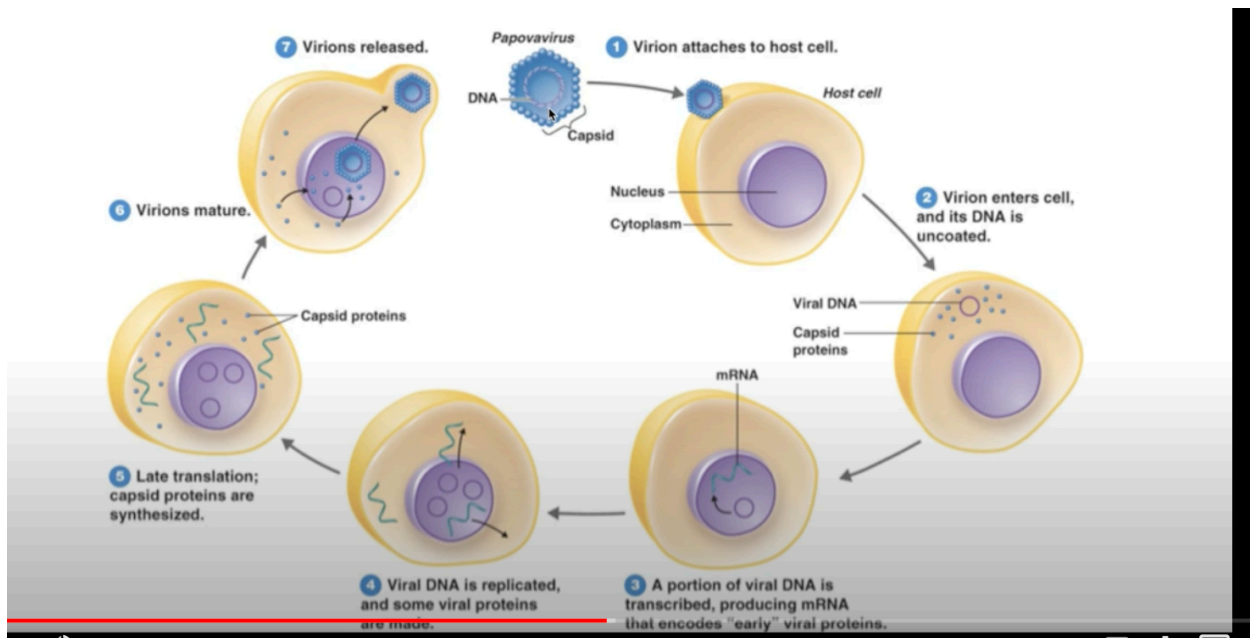


Figure 3: Screen Shot 2020-10-12 at 11.09.46 PM.png

## RNA Viruses

*How are viral mRNAs produced from the viral genome?*

**Packaging** Does not require ATP. Just sealed in.

## Viral Exits Lysis

Replicate so much that the membrane bursts.

## Budding

Trigger...

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

## 1.5.4 | 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.

## 1.5.5 | 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 nucleus
- 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 virions are made slowly by "trickling out."

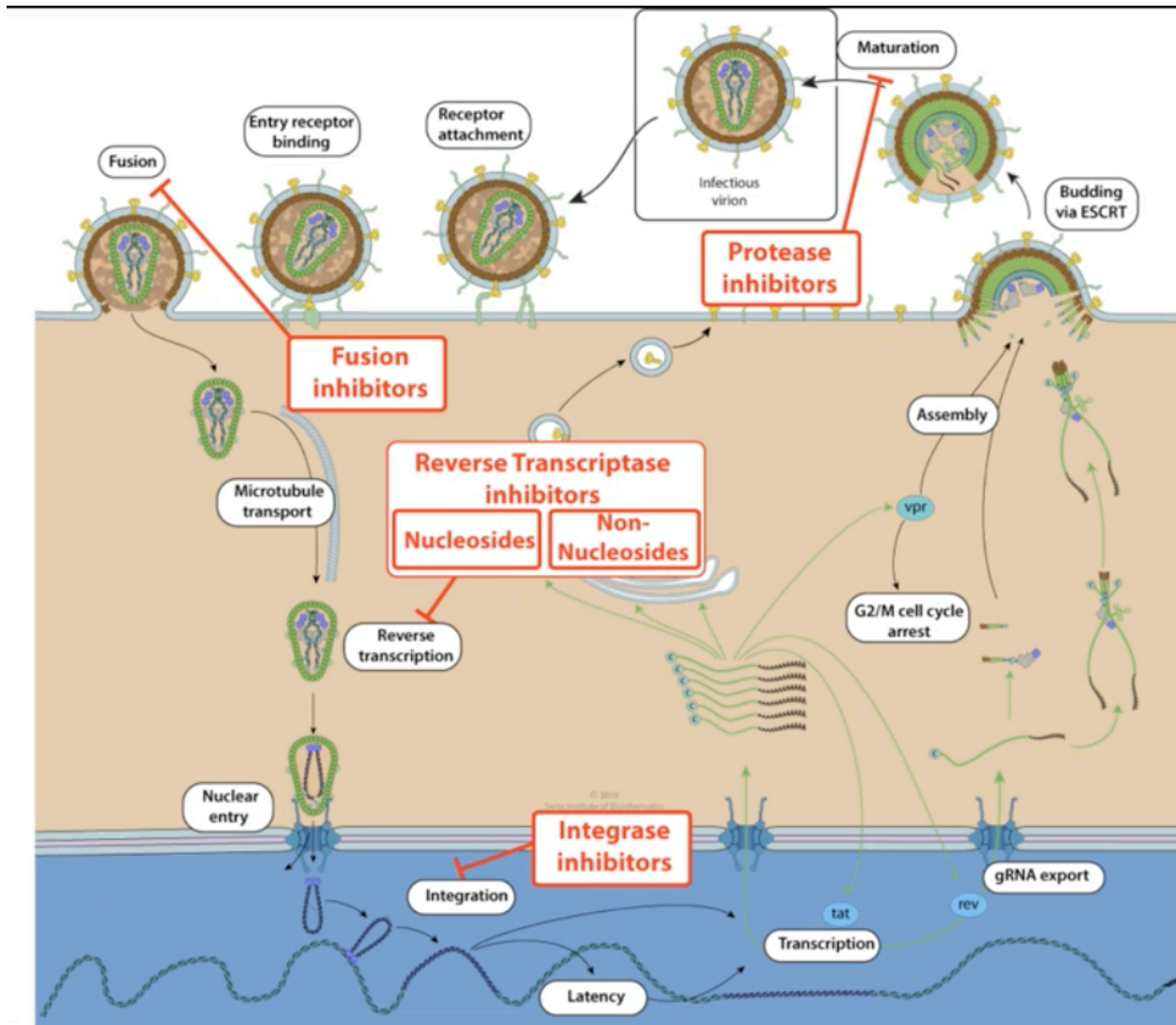


Figure 4: Screen Shot 2020-10-12 at 11.22.35 PM.png

### Preventing Retroviruses

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



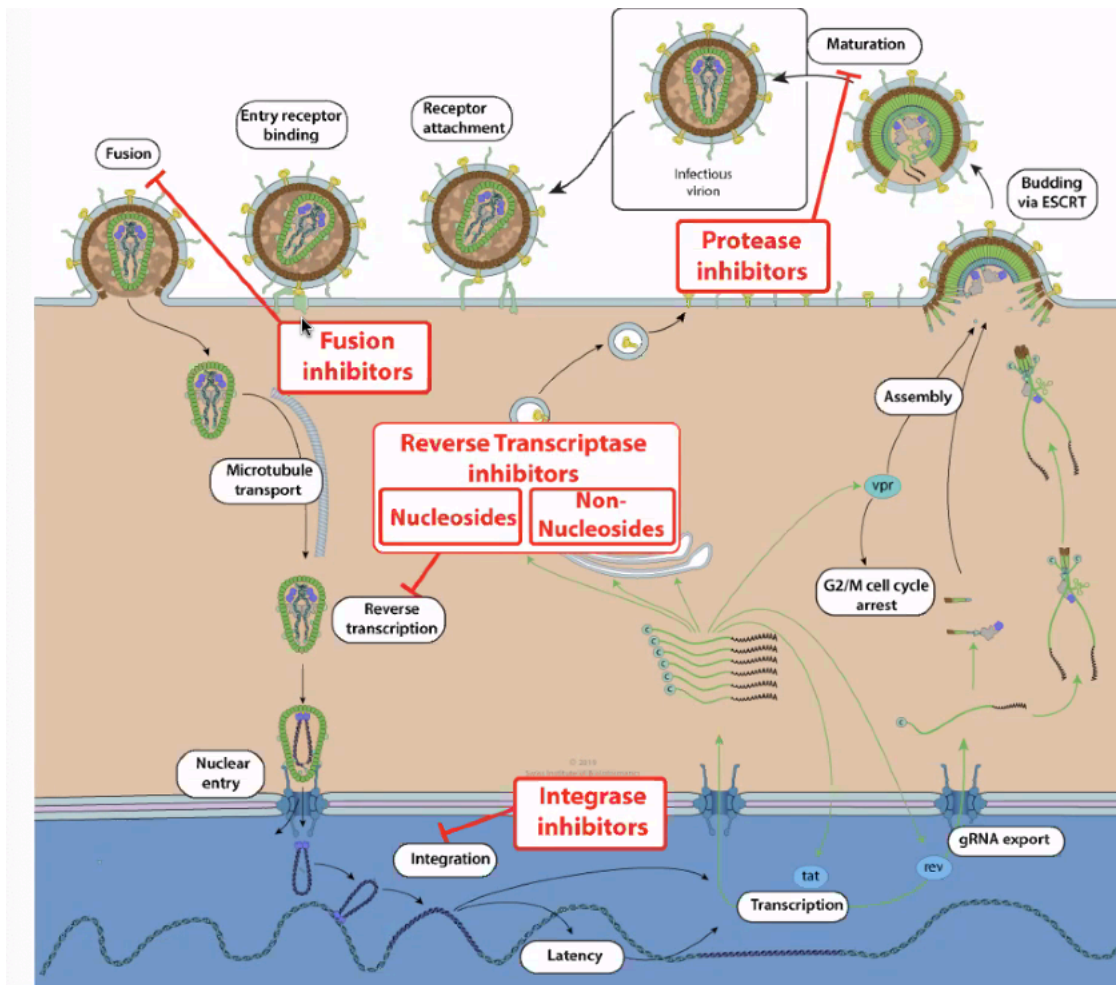


Figure 5: stophiv.png

- 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

## 1.5.6 | Viral Genome vs Mutation Rate

### Viral genome size vs. mutation rate

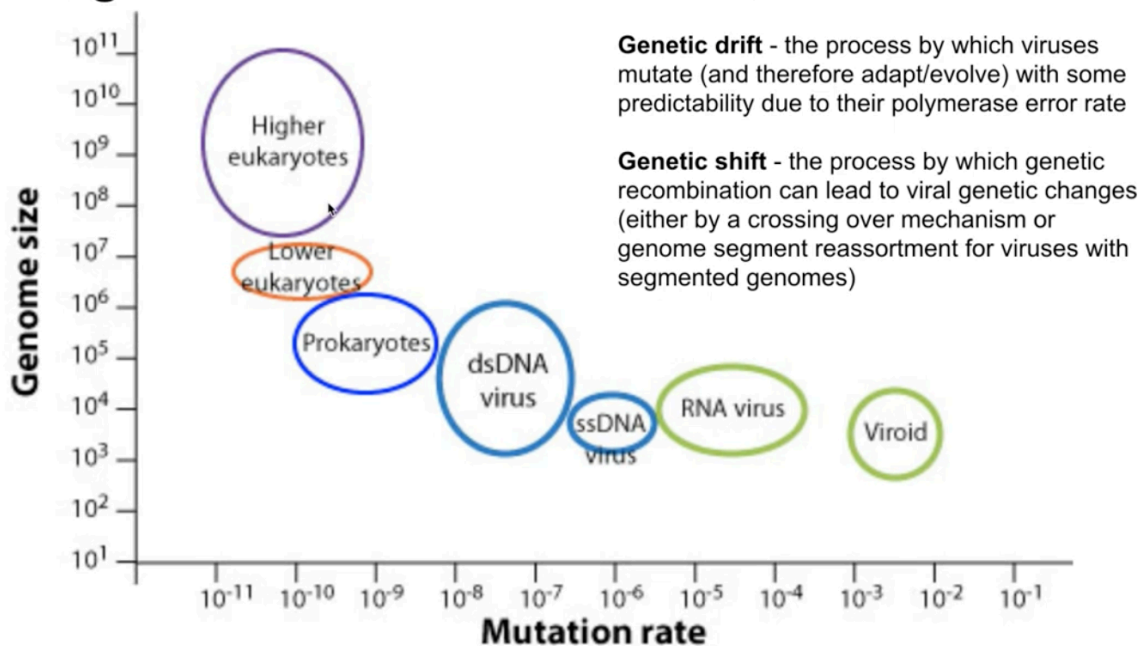


Figure 6: Screen Shot 2020-10-12 at 11.24.39 PM.png

- 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 recombine without mutating by crossing-over mechanism or genome segment reassortment. Think! the flu

## 1.6 | Why are viruses bad

Damage host cells/tissues by...

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

## 1.7 | 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

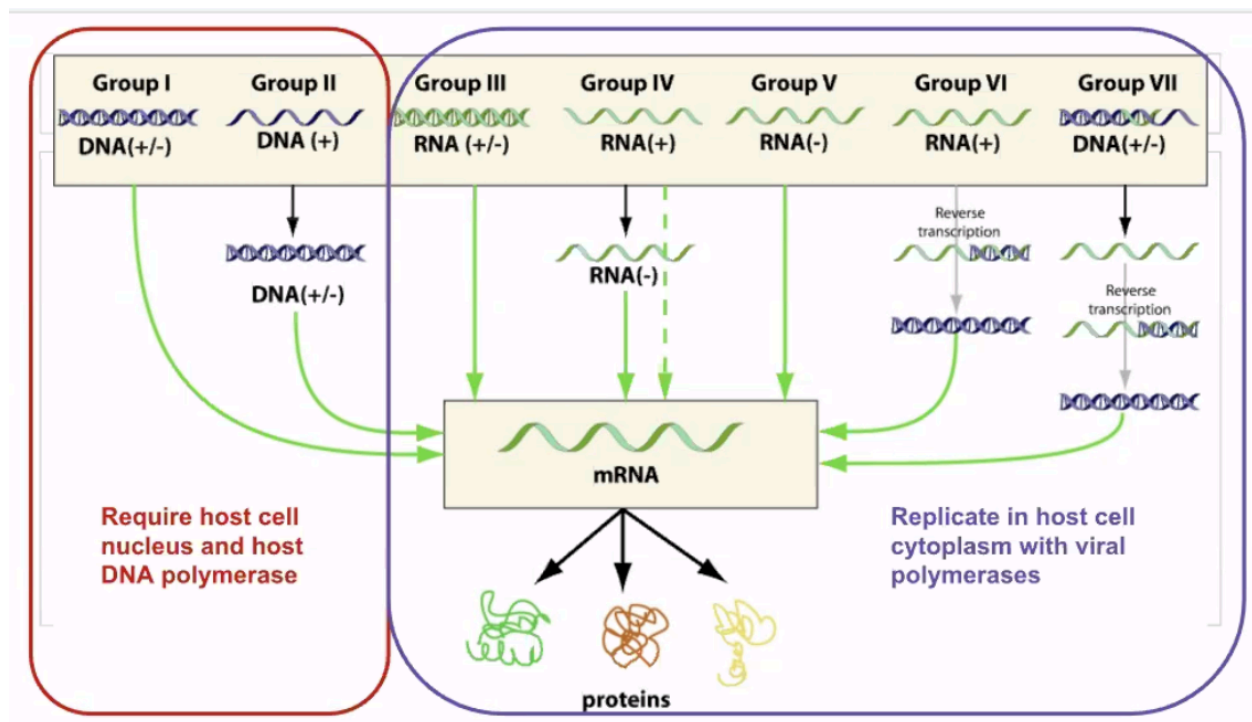


Figure 7: Screen Shot 2020-11-02 at 2.48.22 PM.png

#### 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 nucleus, the rest would just be the body's work automatically.