

Source: [KBiologyMasterIndex](#)

## 1 | Overview of Human Diseases

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#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...

- Microorganism invasion => “infectious 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 respiratory disease => wear
- Stroke => not a disease
- Alzheimer disease => wear
- Diabetes => autoimmune, nutrient, wear
- Influenza <= **here, finally, an infectious disease.**

### 1.2 | Disease causing agents

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

### 1.3 | 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
- 

### 1.4 | Overview of various diseases

This video

#### 1.4.1 | Protozoan

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

Adaptable!!

#### 1.4.2 | 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.

#### 1.4.3 | 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 intracellularly



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

- Occasionally 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-facing 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/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

### 1.6.3 | 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 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?*

- double-stranded RNA virion => (+, 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 polymerase to copy RNA
- They come with polymerase that...
  - with dsRNA; takes +ssRNA and makes -ssRNA; 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 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

## 1.6.4 | Retroviruses

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

To make this happen, the virus needs...

- **Reverse Transcriptase**
  - Transcribe 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 5: Screen Shot 2020-10-12 at 11.22.35 PM.png

## Preventing Retroviruses

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

### 1.6.5 | 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

### 1.7 | 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

## 2 | CN10212020

### 2.1 | Making Proteins, a guide

**Genetic Code** => “nucleotide code” found in the DNA that helps make protein. There are two parts of this: translation and transcription.

- The process of **Transcription** involves taking the DNA, separating it, and copying its corresponding pairs to RNA
- The process of **Translation** involves taking the RNA and making proteins.

Occasionally, the RNA is what we want to end up with, so then obviously we no longer need the process of Translation.

### 2.1.1 | **Transcription => converting DNA to mRNA**

- Done by RNA Polymerase Enzyme
- Rip apart hydrogen bonds using DNase enzyme
- Read one side (“template strand”, a.k.a. noncoding strand) of the double helix, recognizing each nucleotide
- Pluck the correct corresponding nucleotide out of the nucleus
  - G->C
  - C->G
  - A->U
  - T->A
- Prokaryotes lack membrane-bound nucleus (or any organelle)

Definition 1 · **Gene** information that successfully encodes a functional protein or a functional catalytic RNA

RNAs could also be catalysts!

- “Promoter” denotes beginning of a gene. “Terminator” denotes the end of gene.

**Starting Transcription** \* RNA polymerase binds to the Sigma Subunit => form a holoenzyme to unwind DNA \* Sigma subunit informs the enzyme where to find a promoter (beginning of binding) \* “Enhancer” gene sequences \* Polymerase Enzyme starts at a promoter and ends at a terminator \*

### 2.1.2 | **Before we continue, two words**

- *Non-coding sequence*: metadata for DNA for the processors
- *Coding sequence*: DNA content for amino-acid production

### 2.1.3 | **mRNA processing => processing mRNA**

Pre-process the mRNA.

**Prokaryotes does not do this!** Prokaryotes’ coding sequence always makes a full protein, so we just start at promoter and end at terminator and make a protein!

In Eukaryotic DNA...

Between Promoter and Terminator, **Exon** and **Intron** alternate. Exon is coding, whereas Intron is non-coding and works as metadata.

After reading the intron, they are spliced out during mRNA processing => done by the “splicesome”. The mRNA, after splicing, is “capped and tailed” to mark pre-processing completion, at which point they leave the nucleus + go to the ribosome.

## 2.1.4 | **Translation => RNA-directed polypeptide synthesis**

Mature mRNA sent to ribosome.

- Ribosome reads the mRNA in groups of 3s (“codons”) by matching with the corresponding nucleotides
- Translates mRNA to tRNA — anti-codon pairs
- Catalyst tRNA combines with rRNA to catalyze amino acid peptide bond
- Each codon (group of 3 units in tRNA), matches a specific [KBhBIO101AminoAcids](#)

After the amino acids are assembled, it's time for [KBe2020bio101refProteinFolding](#). See also [KBhBIO101Proteins](#).