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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...

- 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
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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
- Bacteria 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-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/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