Microbe-Human Interactions:
Contact, Infection and Disease

Host-Microbe Relationships: Symbiosis
- Host
  - Any organism that harbors another organism or particle (virus, prion)
- Symbiosis: An association between 2 species (“living together”)
  - Mutualism
    - Both members benefit from relationship
    - E. coli produce useful products (Vit K) in our large intestine
  - Parasitism
    - One member benefits, one member is harmed
  - Commensalism
    - One member benefits, one member is not benefited nor harmed
    - Microbes on our skin utilize skin products

Microflora
- Resident Microflora
  - Microbes always present on or in the body
- Transient Microflora
  - Microbes present for shorter periods of time (minutes to months)
- Adult human body consists of:
  - 10 trillion (10^{13}) eukaryotic cells-Human cells
  - 100 trillion (10^{14}) prokaryotic cells-Bacteria cells
  - We have 10 times as many prokaryotic cells vs. our own cells!!

Resident Microflora
- Which areas harbor microflora?
- Which body tissues, organs and fluids are usually microbe-free?

The Absence of Resident Microflora can have Harmful Effects
- Cattle Studies:
  - Enlargement of cecum
  - Vitamin deficiency
  - Underdeveloped immune system

Resident Microbial Compete with Possible Pathogens
Microbial Antagonism:
- Normal biota are unlikely to be displaced by incoming microbes
- Limited number of attachment sites
- Chemical or physiological environment created by resident biota is hostile to other microbes

- Normal biota is beneficial, or at worst, commensal to the host in good health with a functioning immune system

First Acquiring Resident Microflora
- Mother’s birth canal
- Mother’s breast milk
- Bottle-feeding
- People
- Air
- Surfaces

- The only time that humans are sterile is when they are in the womb (in utero)
Areas of the Body that are usually Sterile

- Circulatory system
- Organs
- Glands
- Lungs
- Sinuses
- Middle and inner ear
- Brain
- Internal eye
- Muscles

- Blood
- Urine in the kidneys, ureters, and bladder
- Cerebrospinal fluid
- Saliva before oral cavity
- Semen before the urethra

Contact to Disease

1. Contact: Microbes are present
2. Colonization: The presence of bacteria on body surface (skin, mouth, intestines, airway) without causing disease
3. Infection (Infestation-larger parasites)
   Multiplication of microbes (Microbes penetrate host defenses, enter tissue and multiply)
4. Disease
   Disturbance in normal homeostasis

   1. doesn’t usually lead to 3. and 4.

True vs. Opportunistic Pathogen

True pathogen
- Causes disease in healthy individuals
- Associated with a specific and recognizable disease

Opportunistic pathogen
- Causes disease in immune compromised host
- Gain access (injury) to sterile regions

Opportunistic Microbes

Opportunists usually do not cause disease unless the “opportunity” arises.

Conditions that opportunists can flourish:
- Failure of the host’s normal defenses
  - Immunocompromised populations
- Intro of the organism into unusual body sites
  - E. coli normal in gut but not urinary tract
- Disturbances in normal microflora
  - Yeast infection after antibiotic use. Why?

Pathogens, Pathogenicity and Virulence

- Pathogen: Disease causing agent
- Pathogenicity: The ability to cause disease
- Virulence: The degree of pathogenicity
- Virulence of a microbe is determined by its ability to
  - establish itself in a host
  - cause damage

- Virulence factor: any characteristic or structure of the microbe contributes to its ability to establish itself in the host and cause damage

The Progress of an Infection

Pathogen needs to become established by being successful at the following:
1. Portals of entry
2. Attachment
3. Surviving host defenses
4. Causing disease
5. Portals of exit

If you stop a pathogen from being able to do any of these steps they will not be able to infect the host
The Progress of an Infection:
1. Portal of Entry

- Portal of entry: the route that a microbe takes to enter the tissues of the body to initiate an infection
- Exogenous: microbe originating from a source outside the body from the environment or another person or animal
- Endogenous: microbe already existing on or in the body from normal biota or a previously silent infection

The Progress of an Infection:
1. Portals of Entry

- Occasionally, an infectious agent can enter by more than one portal
- Mycobacterium tuberculosis can enter through both the respiratory and gastrointestinal tracts
- Streptococcus and Staphylococcus can enter through the skin, urogenital tract, and the respiratory tract

The Progress of an Infection:
2. Attachment/Adhesion

- Gain a stable foothold on host tissues
- Dependent on binding between specific molecules on both the host and pathogen
- Pathogen is limited to only those cells (and organisms) to which it can bind
- Firm attachment is almost always a prerequisite for causing disease since the body has so many mechanisms for flushing microbes from tissues

The Progress of an Infection:
1. Portals of Entry

- The majority of pathogens have adapted to a specific portal of entry
- Usually if pathogens enter the "wrong" portal, they will not be infectious
- Inoculation of the nasal mucosa with the influenza virus will result in infection, but if the virus contacts the skin, no infection occurs

Infectious dose (ID)

- The minimum number of microbes necessary to cause an infection to proceed
- Microorganisms with smaller infectious doses have greater virulence
  - ID for rickettsia is a single cell
  - ID for tuberculosis and beaver fever is about 10 cells
  - ID for gonorrhea is 1,000 cells
  - ID for typhoid fever is 10,000 cells
  - ID for cholera is 1,000,000,000 cells

The Progress of an Infection:
2. Attachment/Adhesion

- Capsules
- Pili or fimbriae
- Hooks
- Spikes
The Progress of an Infection: 3. Surviving Host Defenses

- Microbes not established as normal biota will likely encounter the host immune defenses when first entering.
- Phagocytes: cells that engulf and destroy host pathogens by means of enzymes and antimicrobial chemicals.

![WBC engulfing S. cerevisiae](attachment:image)

The Progress of an Infection: 3. Surviving Host Defenses

- Antiphagocytic factors:
  - Virulence factors that help pathogens avoid phagocytes
  - Leukocidins: kill phagocytes; *Streptococcus* and *Staphylococcus*
  - Slime or capsule: makes it difficult for the phagocyte to engulf the pathogen; *Streptococcus pneumoniae* and *Salmonella typhi*
- Some bacteria survive inside the phagocyte; *Legionella, Mycobacterium*

The Progress of an Infection: 4. Causing Disease

- Virulence factors are adaptations a microbe uses to establish itself in a host.
- Three ways that microorganisms cause damage to their host:
  A. directly through the action of enzymes
  B. directly through the action of toxins (both endotoxins and exotoxins)
  C. indirectly by inducing the host’s defenses to respond excessively or inappropriately

The Progress of an Infection: 4. Causing Disease-Enzymes

- Exoenzymes
  - enzymes secreted by microbes that break down and inflict damage on tissues
  - Often dissolve the host’s defense barriers to promote the spread of disease to other tissues
- Examples of exoenzymes
  - hyaluronidase: digests the ground substance that cements animal cells together
  - coagulase: causes clotting of blood or plasma

The Progress of an Infection: 4. Causing Disease-Exoenzymes

- Toxin: a specific chemical product of microbes, plants, and some animals that causes cellular damage in other organisms
- Toxins are named according to their target:
  - neurotoxins act on the nervous system
  - enterotoxins act on the intestines
  - hemotoxins lyse red blood cells
  - nephrotoxins damage the kidneys
- Two types of toxins in pathogenic bacteria
  - Exotoxin
  - Endotoxin
Exotoxins
• proteins that targets a specific cell type
• affect cells by damaging the cell membrane and initiating lysis
• Don’t confuse with exoenzymes!
• Ex: Hemolysins
  - disrupt the membrane of red blood cells to release hemoglobin
  - Ex. Streptococcus pyogenes and Staphylococcus aureus

Endotoxin
- lipopolysaccharide (LPS), part of the outer membrane of gram-negative cell walls
- Released when cells die
- has a variety of systemic effects on tissues and organs
- causes fever, inflammation, hemorrhage, and diarrhea

Some endotoxins are pyrogenic

Endotoxin
- Enables pathogen to spread to other hosts
  - Respiratory
  - Salivary
  - Skin
  - Fecal
  - Urogenital
  - Blood

Pathogenicity:
The ability to cause disease

Depends on a pathogen’s ability to:

1. Enter
2. Attach
3. Survive host defenses
4. Cause disease
5. Exit

Look familiar?
Virulence: The degree of pathogenicity

- Intensity of disease produced
- Virulence can be decreased as a pathogen is sub-cultured time after time
- Many virulence factors (weapons) exist to increase a pathogen's ability to:
  1. Enter
  2. Attach
  3. Survive host defenses
  4. Cause disease
  5. Exit

Establishment of Infections

- Localized infection: An infection that is limited to a specific part of the body and has local symptoms
- Systemic infection: Pathogen is distributed throughout the body

Establishment of Infections

- Focal infection: A bacterial infection localized in a specific part of the body that spreads to other parts of the body
- Mixed infection: Bacterial infection composed of different species of bacteria

Establishment of Infections

- Primary and secondary infections: Illness caused by new microbe becoming established in the wake of an initial (primary) infection
- Acute: rapid onset of infection, short course of infection
- Chronic: Long duration of infection
- Asymptomatic or subclinical: Not noticed by host

Signs, Symptoms and Syndromes

- Signs
  - Objective/measurable (i.e., fever, inflammation)
- Symptoms
  - Subjective (pain, tummy ache)
- Syndromes
  - Combo of signs and symptoms that occur together
  - How would you classify a sore throat? A red throat? A fever?

Stages of an Infectious Disease

- Incubation period (no signs or symptoms)
- Prodromal phase (early symptoms)
- Illness phase (severe signs and symptoms)
- Declining phase (recovery)
- Convalescence period

Number of infectious agents

Time
Incubation periods vary

The Persistence of Microbes and Pathologic Conditions

• Recovery of the host does not always mean the microbe has been removed or destroyed by host defenses
• **Latency**: a dormant state of microbes in certain chronic infectious diseases
  - viral latency: herpes simplex, herpes zoster, hepatitis B, AIDS, Epstein-Barr
  - bacterial/protozoan latency: syphilis, typhoid fever, tuberculosis, malaria
• **Sequela**: long-term or permanent damage to tissues or organs caused by infectious disease
  - meningitis: deafness
  - strep throat: rheumatic heart disease
  - Lyme disease: arthritis
  - polio: paralysis

Epidemiology

• Epidemiology: The study of disease within populations (human, plant, etc.)

• Epidemiology helps us investigate the factors regarding a specific disease:
  - what causes a disease
  - how is it transmitted
  - how do we prevent and treat it
  - how many people are afflicted.

Epidemiology Terminology

• Epidemiologists
  • “disease detectives”, scientists who study epidemiology

• Etiologic agent
  • The cause of a disease

• Morbidity
  • Illness

• Mortality
  • Death

Epidemiology Terminology

• Incidence
  • Number of NEW cases within a period of time

• Prevalence
  • TOTAL number of cases within a period of time

• Which one informs us if we have taken proper measures to halt disease transmission?
Epidemiology Terminology

Tracking Disease in the Population

- Reportable or notifiable diseases
  - Certain diseases must be reported to authorities
  - Other diseases are reported on a voluntary basis

- A network of agencies at the local, district, state, national, and international levels keeps track of infectious diseases

Commonly reported diseases that are tracked in the United States

<table>
<thead>
<tr>
<th>Disease</th>
<th>Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acquired immunodeficiency syndrome (AIDS)</td>
<td>Reportable</td>
</tr>
<tr>
<td>Anemia</td>
<td>Reportable</td>
</tr>
<tr>
<td>Bacterial meningitis</td>
<td>Reportable</td>
</tr>
<tr>
<td>Cholera</td>
<td>Reportable</td>
</tr>
<tr>
<td>Dengue fever</td>
<td>Reportable</td>
</tr>
<tr>
<td>Hepatitis A</td>
<td>Reportable</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>Reportable</td>
</tr>
<tr>
<td>Hepatitis C</td>
<td>Reportable</td>
</tr>
<tr>
<td>Legionnaires disease</td>
<td>Reportable</td>
</tr>
<tr>
<td>Malaria</td>
<td>Reportable</td>
</tr>
<tr>
<td>Polio</td>
<td>Reportable</td>
</tr>
<tr>
<td>Rabies</td>
<td>Reportable</td>
</tr>
<tr>
<td>Typhoid fever</td>
<td>Reportable</td>
</tr>
<tr>
<td>Yellow fever</td>
<td>Reportable</td>
</tr>
<tr>
<td>Severe acute respiratory syndrome coronavirus (SARS-CoV)</td>
<td>Pandemic</td>
</tr>
<tr>
<td>Influenza A (H1N1)</td>
<td>Pandemic</td>
</tr>
<tr>
<td>Influenza A (H5N1)</td>
<td>Pandemic</td>
</tr>
<tr>
<td>Influenza B</td>
<td>Pandemic</td>
</tr>
<tr>
<td>Measles</td>
<td>Pandemic</td>
</tr>
<tr>
<td>SARS-CoV-2</td>
<td>Pandemic</td>
</tr>
</tbody>
</table>

Epidemiological Terminology

- Endemic: Pathogen is continually present in population
- Sporadic: Occasional cases are reported at irregular intervals at random locales
- Epidemic: An "outbreak" or higher than normal number of cases. I.e. prevalence of an endemic or sporadic disease is increasing beyond what is expected for a population
- Pandemic: Spread of an epidemic across continents

Diphtheria cases after the break up of the former Soviet Union.

Is this disease endemic, epidemic, pandemic or sporadic?

Statistical data can be represented graphically, and can be used to predict trends

We can analyze the data according to year, age, affected, and geographic location to help us predict what diseases we need to watch out for and identify precautions to prevent them. (Similar to Influenza H5N1)
Epidemiologic Studies

- Epidemiologists collect data on diseases to help prevent outbreaks in the future.

- Three Types of Epidemiologic Studies:
  - Descriptive
  - Analytical
  - Experimental

Descriptive Studies

- Concerned with the physical aspects of an existing disease and disease spread.
- Provides the what, who, when and where
- Records as many details as possible:
  - Number of cases
  - Populations affected
  - Locations and time
  - Age, gender, race, socioeconomic status, etc.

Examples of Data from Descriptive Studies

Analytical Studies

- Provides the why and how
- Studies determine causes and factors that influence the rate of disease. These factors include demographic, biological, behavioral, and environmental influences.
- Disease groups are compared to control groups and data is analyzed for similarities and differences.

Example analytical question: in the hanta virus epidemic, did people get sick if they had been outside near mice habitats or if they had been cooped up in office buildings?

Experimental Studies

- Designs experiments to test a hypothesis.
- These are the “cleanest” types of studies and often considered the gold-standard.
- Many experimental studies are performed for pharmaceutical (“clinical trials”) or other treatments.

Disease Transmission

- Disease transmission is affected by:
  - Reservoirs of infection
  - Portals of Entry and Exit
  - Mechanisms of Transmission

  We will investigate all three in order to understand how to break the chain of disease transmission. You can break it at just one site to stop transmission.
Disease Transmission: Source of Infection

- **Reservoir**
  - The natural host or habitat (living or nonliving) of a pathogen

- **Source**
  - The person or item from which an infection is DIRECTLY acquired

- **Carrier vs. Asymptomatic Carrier**
  - An organism that harbors infections and can spread them to others. They may show symptoms or not.

- **Biological vector**
  - An organism which not only transports a pathogen but also plays a role in the life cycle of the pathogen (virus inside of mosquito, bacteria inside of tick)

- **Mechanical vector**
  - An organism which only transports a pathogen (fly)

**Zoonosis**
- An infectious disease humans can acquire from animals (Ex. rabies)
- 70% of all new emerging diseases worldwide
- Impossible to eradicate without also eradicating the animal reservoir
- Attempts have been made to eradicate mosquitoes and certain rodents

**Common Zoonotic Infections**

<table>
<thead>
<tr>
<th>Disease</th>
<th>Primary Animal Reservoir</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rabies</td>
<td>All mammals</td>
</tr>
<tr>
<td>Yellow fever</td>
<td>Wild birds, mammals, mosquitoes</td>
</tr>
<tr>
<td>Yellow fever</td>
<td>Wild mammals</td>
</tr>
<tr>
<td>Leptospirosis</td>
<td>Domestic animals</td>
</tr>
<tr>
<td>Anthrax</td>
<td>Domestic animals</td>
</tr>
<tr>
<td>Brucellosis</td>
<td>Cattle, sheep, pigs</td>
</tr>
<tr>
<td>Plague</td>
<td>Rodents, felines</td>
</tr>
<tr>
<td>Salmonellosis</td>
<td>Variety of mammals, birds, and rodents</td>
</tr>
<tr>
<td>Tularemia</td>
<td>Rodents, birds, arthropods</td>
</tr>
<tr>
<td>Malaria</td>
<td>Anophelesaeceae, birds, mammals</td>
</tr>
<tr>
<td>Typhus</td>
<td>Cattle, sheep, pigs</td>
</tr>
<tr>
<td>Echinococci</td>
<td>Swine, boars</td>
</tr>
<tr>
<td>Erysipotes</td>
<td>Cattle, swine, bats</td>
</tr>
<tr>
<td>Rabies</td>
<td>Domestic animals</td>
</tr>
</tbody>
</table>

**Zoonotic infections are caused by vectors and animal reservoirs spreading their own infections to humans**

**Some diseases are communicable but others are not**
- Communicable
  - Infected host transmits an infectious agent to another host
  - Receiving host must become infected
- Non-communicable
  - Host acquires infectious agent but can’t transmit it to another
    - From self (compromised individual): microflora
    - Nonliving reservoir – soil (tetanus)
Disease Transmission: Source of Infection

- Communicable
  - Disease spread from one host to another
    - I.e., cold, meningitis

- Contagious
  - Easily communicable
    - I.e. measles, influenza

  - Are all communicable diseases contagious?
  - Are all contagious disease communicable?

Disease Transmission: Patterns of Transmission

- Horizontal transmission
  - Disease is spread through a population from one infected person to another
    - Kissing, sneezing

- Vertical transmission
  - The disease is transmitted from parent to offspring
    - Ovum, sperm, placenta, milk

Disease Transmission: Patterns of Transmission

- Direct (contact)
  - Kissing, sex
  - Droplets (sneezing, coughing directly upon a person within 3 feet)
    - Vertical
    - Vector

- Indirect
  - Contaminated materials
    - Vehicles: Food, water, biological products (blood, serum, tissue), fomite (door knobs, toilet seats, etc.)
    - Fecal-oral (aka oral-fecal)
  - Air (greater than 3 feet away)
    - Droplet nuclei (dried microscopic residue)
    - Aerosols (dust or moisture particles)

A sneeze can release enormous amounts of moist droplets, and the dry droplets form droplet nuclei. (so cover your mouth with your elbow 🙃)

Disease Transmission: Prevention

- Sanitation
  - What is the #1 way to stop disease?

- Immunization

- Isolation

- Quarantine

- Control vectors

- Education about prevention and treatment

Disease Transmission: Prevention

- Herd immunity is the proportion of people immune to a certain disease. Is it easier or more difficult to transmit disease when herd immunity is low? How do we acquire herd immunity?
Nosocomial Infections: The Hospital as the Source of Disease

- Nosocomial Infection: An infection acquired in a hospital
- About 2-4 million (5-20 percent) of admitted patients acquire a nosocomial infection
- 90,000 die of nosocomial infections
- $5-10 billion per year to treat nosocomial infections

The most common nosocomial infections

Common nosocomial pathogens

Nosocomial Infections

- Healthcare processes that lead to nosocomial infections:
  - treatments using reusable instruments such as respirators and thermometers
  - indwelling devices such as catheters, prosthetic heart valves, grafts, drainage tubes, and tracheostomy tubes form ready portals of entry
  - high proportion of the hospital population receives antimicrobial therapy, drug-resistant microbes are selected for at a much higher rate

Nosocomial Infections: Contributing Factors

- compromised patients
- collection point for pathogens
- lowered defenses permit normal biota to enter the body
- infections acquired directly or indirectly from fomites, medical equipment, other patients, medical personnel, visitors, air, and water

Nosocomial Infections: Prevention and Control

- Recent evidence suggests that more than 1/3 of nosocomial infections could be avoided by consistent and rigorous infection control methods
- Use Universal Precautions (aka Standard Precautions)
- Assume all patients and fomites may harbor pathogens