Chapter 14: Principles of Disease

1. Infection
2. Virulence Factors
3. Disease Transmission
4. Epidemiology
1. Infection

Chapter Reading – pp. 415-426
Important Disease Terminology

Pathology
- the study of disease (state of ill health)

Infectious Disease
- disease due to a transmissible microbial agent

Symptoms
- what the patient experiences (subjective)

Signs
- what the health care provider observes (objective)

Syndrome
- a set of multiple signs or symptoms that characterize specific condition or disease
Pathogen
- a disease-causing organism (or virus)

Infection
- growth of a pathogen in host tissue

Virulence
- the degree to which a pathogen causes disease

Portal of Entry/Exit
- tissue through which a pathogen enters or exits a host (i.e., a human body)
Symbiotic Relationships

Symbiosis – “to live together”

**MUTUALISM** (both species benefit)
- e.g., termites and their gut microbes
- many species depend on such relationships for survival

**COMMENSALISM** (one benefits, other unharmed)
- e.g., *Staphylococcus epidermidis* on human skin

**PARASITISM** (one benefits, one is harmed)
- e.g., disease-causing bacteria
- most successful parasites do NOT kill their hosts
Normal Microbiota

The bacteria that live on your exposed surfaces (e.g., skin, mucous membranes) are mostly commensal:

RESIDENT MICROBIOISTA
  • acquired largely at birth, present for entire life

TRANSIENT MICROBIOISTA
  • acquired temporarily, eventually eliminated by immune defenses or outcompeted by other microbes

OPPORTUNISTIC PATHOGENS
  • normal microflora that cause disease when introduced to an atypical area, host is immunocompromised, etc
Reservoirs of Infection

A reservoir of infection is a continual source of pathogen from which it can spread:

- in between “outbreaks” the pathogen must exist somewhere (unless it’s been eradicated entirely)
- common reservoirs of infection include:

  The host species (e.g., humans)
  - some hosts serve as carriers (show no signs of illness)

  Non-host animal species (e.g., insects, rodents)

  Non-living material (e.g., soil or water)
Portals of Entry

Bacteria can enter the body of a human host through several “portals” or types of tissue:

1) Skin
   • the toughest barrier to get through

2) Mucous membranes
   • moist surfaces with mucus coating
   • the linings of the respiratory, digestive & genito-urinary tracts

3) Parenteral entry
   • direct entry into internal tissues
   • i.e., through cuts, punctures or other injuries
The Effect of Numbers

For each pathogen at a particular portal of entry there is a numerical “threshold” required for an infection to occur:

• below the threshold the immune response will control and eliminate the pathogen
• above the threshold growth (infection) occurs
• threshold depends on tissue, individual host

Useful concept:

$ID_{50}$ – infectious dose for 50% of population

• unique for each pathogen, type of host, portal of entry
Preferred Portals

Each type of pathogen has a “preferred” portal of entry, i.e., a tissue through which infection occurs most effectively:

e.g., *Bacillus anthracis* (cause of anthrax)

\[ \text{ID}_{50} \text{ for skin}^* = 10-50 \text{ endospores} \]

\[ \text{ID}_{50} \text{ for respiratory tract} = \sim 10,000 \text{ endospores} \]

\[ \text{ID}_{50} \text{ for gastrointestinal tract} = \sim 500,000 \text{ endospores} \]

***Preferred portal of entry for *B. anthracis* = skin!***
Entry into the host at the preferred portal typically involves adhesion between specific molecules on the surface of the pathogen and certain host cells:

- Complementary interactions between a type of adhesin on the pathogen and “receptor” on specific host cells
- Host cells with appropriate “receptor” are found in preferred portal thus making entry much more likely
Koch’s Postulates

In the late 19th century, Robert Koch established the following principles to identify the microbial source of disease:

1) same pathogen must be present in every case of the disease

2) pathogen must be isolated from diseased host and grown in pure culture

3) pathogen must cause the associated disease following inoculation into healthy test subject

4) pathogen must be isolated from test subject and shown to be identical to the original pathogen
Application of Koch’s Postulates

The following must be shown to “finger” the pathogen:

1) suspect pathogen is isolated from ill subject, identified & cultured

2) test subject is inoculated with pathogen & manifests the same illness

3) same pathogen is isolated from test subject

**If these 3 things are demonstrated, pathogen is guilty!**
Exceptions to Koch’s Postulates

It would be nice if every suspected microbial pathogen was subject to “trial” by this method, however this is not always possible because:

• many pathogens cannot be successfully cultured
  • pure “live” pathogen cannot be produced for inoculation into a test subject

• many pathogens only infect humans
  • it is not OK to use human test subjects!

Does this mean that a pathogen cannot be identified without obtaining a pure culture?

Not necessarily, circumstantial evidence can be enough…
2. Virulence Factors

Chapter Reading – pp. 425-429
Bacterial Toxins

Exotoxins
- proteins produced inside certain bacteria and released into host tissues to inhibit various cellular processes

Endotoxins
- lipid A from the outer membranes of Gram- bacteria
- induce potent physiological responses in host
Types of Exotoxins

Membrane-disrupting toxins

- disrupt the lipid bilayer (e.g., *Staphylococcus aureus*) or create a channel (*Clostridium perfringens*) resulting in lysis of host cell

Superantigens

- trigger intense and dangerous immune response by the non-specific activation of helper T cells

  - **Staphylococcal enterotoxin:** 
    - (*Staphylococcus aureus*)
  
  - **Erythrogenic toxins:**
    - (*Streptococcus pyogenes*, “scarlet fever”)

A-B Exotoxins

- proteins with an “A” part that causes the damage and a “B” part that binds to host “receptor”
A-B Exotoxins

e.g.

**Diphtheria toxin:**
inhibits protein synthesis
(*Corynebacterium diphtheriae*)

**Botulinum toxin:**
inhibits nerve impulses
(*Clostridium botulinum*)

**Tetanus toxin:**
inhibits nerve impulses
(*Clostridium tetani*)

**Cholera toxin:**
disrupts enteric fluid balance
(*Vibrio cholerae*)
Exotoxins, Plasmids & Viruses

In many cases bacteria acquire genes coding exotoxins from viruses or plasmids:

• viruses can transfer exotoxin genes by transduction
  • usually by specialized transduction via lysogenic bacteriophages
  • e.g., diphtheria, cholera, pyrogenic & botulinum toxins

• bacteria can acquire plasmids containing exotoxin genes by transformation or conjugation
  • e.g., tetanus toxin & S. aureus enterotoxins

**transfer of exotoxin genes by these methods can convert benign strains into virulent strains**
Penetration of Host Defenses

Following adhesion, bacteria have a variety of ways to penetrate host tissues avoid destruction by the immune system:

1) Capsules
   • a dense glycocalyx that provides protection from phagocytosis by host immune cells

2) Cell Wall
   • the cells walls of some bacteria also resist phagocytosis (and may have adhesins for attachment)

3) Antigenic Variation
   • some bacteria are able to periodically change the molecules on their surface to avoid immune detection
Penetration of Host Defenses

Following adhesion, bacteria have a variety of ways to penetrate host tissues to avoid the immune system:

1) Capsules
   - a dense glycocalyx that protects from phagocytosis

2) Cell Wall
   - the cell walls of some bacteria also resist phagocytosis
3) Antigenic Variation

- some bacteria are able to periodically change the molecules on their surface to avoid immune detection

(a) Extracellular enzymes

4) Enzymes

- a variety of enzymes are released by bacteria to increase their virulence:
Enzymes that Enhance Virulence

Coagulases – cause blood to clot, isolating bacteria from immune cells

Kinases – phosphorylate fibrin in blood clots causing clot to break down, infection to spread

Hyaluronidase – breaks down hyaluronic acid, an important component of connective tissue, allowing tissue penetration

Collagenase – breaks down collagen in connective tissue

IgA proteases – destroy IgA type antibodies
Siderophores & Iron

Most bacteria secrete proteins referred to as **siderophores** that bind iron:

- iron is a very essential and limiting trace nutrient for all living cells
- siderophores bind and essentially steal extracellular iron from host, damaging it indirectly
- special receptors on the surface of the bacterium bind iron-siderophore complexes and internalize them for bacterial use

**iron supplements can actually worsen a bacterial infection**
3. Disease Transmission

Chapter Reading – pp. 429-434
Stages of Disease Development

- **Incubation period** (no signs or symptoms)
- **Prodromal period** (vague, general symptoms)
- **Illness** (most severe signs and symptoms)
- **Decline** (declining signs and symptoms)
- **Convalescence** (no signs or symptoms)

**Incubation Period**
- from the onset of infection to the first signs or symptoms
- can be short, long, variable
Prodromal Period (“optional”)
• initial appearance of mild symptoms (aches, malaise)
• not seen with every infectious disease

Period of Illness
• when symptoms and signs are most severe
  • e.g., fever, chills, sore throat, swollen lymph nodes

Period of Decline
• when symptoms and signs of illness diminish
  • patient is vulnerable to secondary infections

Period of Convalescence
• recovery of strength, return to pre-disease state
  • disease can still be communicable
Modes of Disease Transmission

Transmission of a pathogen occurs in 3 basic ways:

1) **Contact** Transmission
   • spread of pathogen by direct or indirect casual contact

2) **Vehicle** Transmission
   • spread of pathogen through physical media such as water, air or food

3) **Vector** Transmission
   • animals that spread disease to a different species
Contact Transmission

Direct Contact Transmission
• transmission by direct contact between a source of the pathogen and a susceptible host
• commonly called “person to person” transmission

Indirect Contact Transmission
• transmission to susceptible host through a nonliving object (e.g., cups, utensils, syringes, bedding)
• such “intermediate” materials are called fomites

Droplet Transmission
• transmission over short distances (< 1 meter) through tiny droplets produced by sneezing, coughing, talking
Vehicle Transmission

Waterborne Transmission

• transmission through contact or ingestion of water contaminated with the pathogen
• typically due to contamination with sewage

Foodborne Transmission

• transmission through ingestion of contaminated food
• due to undercooking, improper storage of food

Airborne Transmission

• transmission through airborne particles that travel >1 m
• droplets, dust, airborne spores
Transmission through animal vectors occurs in 2 basic ways:

**Mechanical Transmission**

- physical transport of the pathogen on the external structures of an animal
- e.g., legs of a fly that has landed on fecal matter

**Biological Transmission**

- pathogen survives *within* host animal to be spread by biting, defecation or vomiting
- e.g., mosquitoes that spread *Plasmodium vivax*
Classifying Diseases

Not all diseases are infectious (e.g., cancer, genetic conditions), but those that are can be further classified as follows:

Communicable Diseases

• capable of being spread from one host to another

• a disease that is easily spread is contagious

Non-communicable Diseases

• NOT spread directly from one host to another

• e.g., tetanus
4. Epidemiology

Chapter Reading – pp. 434-440
Epidemiology – the study of when and where diseases occur and their transmission

(a) Endemic disease  (b) Sporadic  (c) Epidemic  (d) Pandemic

= Normal range
= New case of disease
**Endemic**

- disease occurrence in a given area or population is stable

**Sporadic**

- a few scattered cases occur in an area or population

**Epidemic**

- disease occurrence in a given area or population that is greater than usual

**Pandemic**

- an epidemic that occurs *simultaneously* on more than one continent
Incidence vs Prevalence

- Incidence: all cases in a given period (e.g., per year)
- Prevalence: all cases, past & present

Year vs Incidence (thousands) vs Prevalence (thousands)


Graph showing trends in incidence and prevalence over time.
Nosocomial Infections

Infections that occur in a health care environment (e.g., hospital, nursing home):

Nosocomial infections are the 8th leading cause of death in the United States!

So why are hospitals such dangerous reservoirs of infection?
Factors in Nosocomial Infection

Microorganisms in the hospital environment

- most nosocomial pathogens are bacterial
- resistant strains are selected for due to the wide use of antibiotics

Compromised state of hospital patients

- bodily defenses of patients are weakened due to illness, injury, surgery, IVs, catheters (parenteral entry)

Multiple modes of transmission

- direct transmission through hospital personnel, patients
- indirect transmission through fomites (needles, catheters)
- vehicle transmission (through air mainly)
Key Terms for Chapter 14

• symptoms, signs, syndrome, pathogen, virulence
• portals of entry/exit, parenteral
• adhesin, ID$_{50}$, mutualism, commensalism, parasitism
• siderophore, exotoxin, endotoxin, superantigen
• reservoir of infection, antigenic variation
• contact, vehicle & vector transmission
• mechanical vs biological transmission
• epidemiology, prevalence, incidence, nosocomial
• endemic, sporadic, epidemic, pandemic

Relevant Chapter Questions
MC: 1, 3-11, 13, 15     FIB: 1-10     SA: 1-8