Chapter 17
Disease and Resistance: The Wars Within

Objectives: After reading Chapter 17, you should understand...
- The concepts relating to infectious diseases, the difference between disease and infection and the disease process.
- The factors that contribute to the infectious relationship between microbes and hosts.

In the late 1960s, the Surgeon General stated that we could “close the book” on infectious disease!

“Because infectious diseases have been largely controlled in the United States, we can now close the book on infectious diseases.” —William Stewart, MD U.S. Surgeon General, 1967

We had effective antibiotics and vaccines that created a sense of optimism.

...why? Look at the trend:

![Graph showing Crude death rate* for infectious diseases in the United States, 1900-1996†](image)

*Per 100,000 population per year.
However, diseases in recent history have appeared to be wildly erratic.

1. Some members of a population would be affected, while others weren’t (e.g. HIV).

2. New diseases emerged (e.g. Ebola virus, HIV, MRSA, SARS).

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**Trends in annual rates of death from leading causes of death among persons 25–44 years old, United States, 1982–1998.**
In 2005, of the 57 million people that died, 25% (15 million) died from infectious diseases.

Second leading cause of death in the world.


Under what kinds of conditions do most of these people live?

We now understand that we live in a precarious equilibrium with the microbes that surround us.

In *most* cases the relationship is harmonious. **Why?**…

1. Microbes might have no disease potential, or

2. We have developed resistance to them.

However, in some cases, this relationship is one-sided and results in a disease or infection. **Why?**

The *host-parasite* relationship.

Your body is constantly living in symbiosis with a community of bacteria and fungi that were acquired during birth and augmented and maintained throughout your life.
Some terminology:

**Contamination** refers to microbes that are found on inanimate objects that are not supposed to be there.

Most living organisms exist in some association with bacteria, viruses, fungi and protists, some of which might be pathogens.

If microbes are able to *survive and reproduce* in a host, we call that **colonization**.

You are all actually *colonized* right now with millions of microbes, but your body has developed a mutual relationship with them.

If the infection causes a *disruption in normal host functions*, then we are faced with an infection or infectious disease.

These are referred to as your **normal microflora**. Where are they located?

Five possible origins of the microbiota in a newborn.

The normal microflora number 100 **trillion** \((100,000,000,000,000)\) microbes that weigh up to 3 pounds.

Some are **transient** – *Streptococcus spp.*, *Staphylococcus spp*.

Some are **permanent** – *E. coli*, *Candida albicans*
The ability of a parasite (bacterial, viral, fungal or protozoal) to gain entry into the host’s tissues and bring about some anatomical or physiological change (disease) is called pathogenicity.

A pathogen is an organism having pathogenicity (examples?).

Most pathogens are opportunistic…they will take advantage of suppressed body defenses (i.e. an unusual situation) to gain access to nutrients (your body).

This is how disease begins.

Example: HIV causes suppression of the host immune system, which allows opportunistic pathogens to infect.

Opportunistic pathogens that take advantage of the suppressed immune system. The opportunistic pathogens actually cause most of the problems associated with HIV infection.

One common first indication of HIV infection is the development of respiratory illness caused by Pneumocystis carinii, a fungus that normally lives in a harmless relationship with your body.

Candida albicans infection (thrush) is another example of an opportunistic infection.
The process of infectious disease.

A) An infectious dose of microorganisms penetrates the host's defensive barrier.
B) Microorganisms enter the sterile environment of the host's tissues.
C) They move into a specific target tissue, such as an organ.
D) Here they cause tissue damage, leading to disease.
E) Microorganisms leave the host through a portal of exit to infect another host.

It is not easy for a microbe to establish disease. Why?

Several factors are at work that attempt to keep the infectious process from occurring.

Disease cycles
1. **The infectious agent must have a place to survive before and after the infection** (why after?). Such a place is termed a pathogen **reservoir**.

The identification of reservoirs is important for efforts to eradicate disease.

Reservoirs can be human (e.g. *Streptococcus pyogenes*), animal (*Salmonella*, hantavirus), insect (*Plasmodium spp.*) or environmental (*Clostridium tetani*)

e.g. smallpox – was eradicated only because the sole reservoir is humans…it cannot survive in animals or the environment.

A **carrier** is a specialized reservoir that has had a disease and recovered from it, but is still shedding infectious agents.

 e.g. people who recovered from typhoid fever became carriers for many weeks after the symptoms of the disease disappeared (contagious).

**Typhoid Mary** (Mary Mallon)

Infected 47 people with *Salmonella enterica sv. typhi* in early 1900s.

She died in 1938 with live *S. enterica* still in her system.
2. **It must be transmitted from the reservoir to the host.**

Two general mechanisms exist: **direct** transmission and **indirect** transmission.

Direct transmission – physical contact with one who has the disease.

STDs such as gonorrhea and herpes are spread by direct contact.

Influenza, measles and strep-throat can be spread in droplets of mucus and saliva expelled from the respiratory tract in aerosols.
**Indirect transmission** – contact with **objects or media** contaminated with an infectious agent.

*Salmonella* infections can result from the consumption of contaminated chicken.

Chicken are often carriers of *Salmonella spp.*

Other infections (e.g. MRSA) can result from contact with **fomites** (e.g. syringes, needles) – surfaces contaminated with microbes.

**Vector transmission** – A form of indirect transmission where arthropods (arachnids and insects) can carry virulent microbes.

Mosquitoes: (West Nile virus, *Plasmodium spp.*), houseflies.

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**Number of mosquito pools collected from Oleander Park (Sylvania, OH) that contained antibiotic resistant bacteria, Summer, 2009.**
3. Invasion of the host’s body/cells must take place...

   A **portal of entry** must be established.

   Respiratory system, digestive system, reproductive system, break in the skin.

   This site varies for differing microbes.

   e.g. *Clostridium tetani* – spores must **enter a wound** and settle in anaerobic pockets within the wound.

   But, spores will **not germinate in the intestines**, so consumption of *C. tetani* with food is not a problem.

4. …and in an appropriate number to sustain an infection.

   The pathogen must initiate the infection at a **minimum infectious dose** (MID).

   Consider two gastrointestinal pathogens…

   *Salmonella enterica sv. typhi* – **hundreds** are necessary to elicit infection.

   *Vibrio cholera* – **millions** are necessary.

   This difference results from conditions in the stomach that favor *Salmonella spp.* over *Vibrio spp.*

   Other notable minimum infectious doses:

<table>
<thead>
<tr>
<th>Infectious agent</th>
<th>Illness origin</th>
<th>MID (infectious units)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Campylobacter jejuni</td>
<td>Food (chicken)</td>
<td>500</td>
</tr>
<tr>
<td>Cryptosporidium spp.</td>
<td>Water</td>
<td>30 cysts</td>
</tr>
<tr>
<td><em>E. coli</em> O157:H7</td>
<td>Food</td>
<td>10-100</td>
</tr>
<tr>
<td><em>Salmonella spp.</em></td>
<td>Food</td>
<td>100</td>
</tr>
<tr>
<td><em>Shigella spp.</em></td>
<td>Food/Water</td>
<td>10</td>
</tr>
<tr>
<td>HIV</td>
<td>Blood</td>
<td>?</td>
</tr>
<tr>
<td>Ebola virus</td>
<td>Aerosols</td>
<td>10</td>
</tr>
</tbody>
</table>

5. The pathogen must be able to multiply in or on the host.

   The initial infection is usually caused by a number of organisms too small to be noticed by the host. As they **multiply**, they make their presence known.
The time between initial exposure and the onset of disease symptoms is called the **incubation period**.

The incubation period is pathogen-specific and important because...

1. It is useful in infectious disease surveillance and control, in which the time of symptom onset may be the only indication of the **time of infection**.

2. Knowing when you were infected (point #1, above) allows epidemiologists to **identify potential sources** of infection.

![Incubation periods of several respiratory viruses (above) and other diseases (below).](image)
Why are pathogens with long incubation periods of particular public health importance?

6. **The pathogen needs to evade the host’s defenses and interfere with normal host functions.**

How do we measure how pathogenic a microbe is?

Pathogenicity can be quantified by assessing a microbe’s **virulence**.

Microbes that invariably cause disease are termed “**highly virulent**”, while those that sometimes cause disease are termed “**moderately virulent**”.

Molecules or structures (e.g. glycocalyx, antibiotic degrading enzymes, toxins) that make an organism pathogenic are known as **virulence factors**. *These can help the pathogen evade host defenses.*

<table>
<thead>
<tr>
<th>DISEASE</th>
<th>INCUBATION PERIOD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chicken Pox</td>
<td>2-5 weeks</td>
</tr>
<tr>
<td>Conjunctivitis</td>
<td>Bacterial 1-3 days, Viral 2-7 days</td>
</tr>
<tr>
<td>Slapped Cheek Syndrome</td>
<td>4-20 days</td>
</tr>
<tr>
<td>Gastroenteritis (Food Poisoning)</td>
<td>2-72 hours according to cause</td>
</tr>
<tr>
<td>Glandular Fever</td>
<td>4-6 weeks</td>
</tr>
<tr>
<td>Hand, foot and mouth</td>
<td>3-5 days</td>
</tr>
<tr>
<td>Hepatitis A (Infectious Jaundice)</td>
<td>2-6 weeks</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>6 weeks - 6 months</td>
</tr>
<tr>
<td>Measles</td>
<td>1-2 weeks</td>
</tr>
<tr>
<td>Meningitis meningococcal/Hib</td>
<td>2-10 days</td>
</tr>
<tr>
<td>Mumps</td>
<td>2-3 weeks</td>
</tr>
</tbody>
</table>
Example: *Staphylococcus aureus* virulence factors

- **Toxin production** – hemolysin, leukocidin
- **Exoenzymes** – lipases, proteases
- **Adherance** – clumping factor, adhesins
- **Antiphagocytosis** – capsule, Protein A

7. **The pathogen must survive to leave the host and reach a new host or reservoir.**

   At the conclusion of the disease cycle, the pathogen must be able to leave the body through a **portal of exit**. Why?

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**Characterizing an infectious disease outbreak**

The outbreak of an infectious agent can be described according to **how prevalent** the disease is within a population.
1. **Endemic** – Disease occurs at a **low level** with a **confined geographic area** (e.g. Measles).
2. **Epidemic** – Disease that breaks out in **explosive proportions** within a population (Influenza, Ebola virus) exceeding the normal, expected occurrence.

Epidemic characteristics of Ebola hemorrhagic fever (Congo and Gabon).

3. **Pandemic** – Disease that occurs worldwide (AIDS).

Worldwide prevalence of HIV. From: CDC

How does an endemic disease become an epidemic or pandemic disease?
Emerging diseases

Emerging infectious diseases are those where incidence in humans has increased within the past two decades or threaten to increase in the near future.

*Emerging Infections Report (2002)*

New diseases are always “emerging”. **Why?**

Human and animal populations throughout history have been afflicted by major outbreaks of infectious disease that swept through the ‘known’ world mostly in the wake of conquering armies or following trade routes.

1. The **black plague** (bubonic plague) in the 14th century decimated the population of Europe and Asia.

   One third of the population from southern to northern Europe were dead within four years of introduction of the disease.

   Bubonic plague is an infection of the lymphatic system by *Yersinia pestis* (a bacterium), usually resulting from the bite of an infected flea.

   The fleas are often found on rodents, such as rats, and seek out other prey when their rodent hosts die.

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**Plague Ecology in the United States**

*Plague in Nature*

Plague occurs naturally in the western U.S., especially in the semi-arid grasslands and scrub woodlands of the southwestern states of Arizona, Colorado, New Mexico and Utah.

*Plague in Humans*

Occasionally, infections among rodents increase dramatically, causing an outbreak, or epizootic. During plague epizootics, many rodents die, causing hungry fleas to seek other sources of blood. Studies suggest that epizootics in the southwestern U.S. are more likely during cooler summers that follow wet winters.

- Humans and domestic animals that are bitten by fleas from dead animals are at risk for contracting plague, especially during an epizootic. Cats usually become very ill from plague and can directly infect humans when they cough infectious droplets into the air. Dogs are less likely to be ill, but they can still bring plague-infected fleas into the home. In addition to flea bites, people can be exposed while handling skins or flesh of infected animals.
2. The Spaniards in their conquest of Central America were aided by the smallpox virus, which was introduced in naïve populations by Spanish troops and decimated the opposing leadership and armies.

3. The first veterinary schools in Europe were founded in the 18th century primarily to study and control recurring epidemics of rinderpest or cattle plague.

Infectious viral disease of cattle, domestic buffalo, and some species of wildlife.

Another outbreak in the 1890s killed 80 to 90 percent of all cattle in Southern Africa.

The black plague killed an estimated 75-100 million in the 14th century: 1/2 of China's population, 1/3 of Europe's and 1/8 of Africa's.

Aztec Indians dying of smallpox. (Aztec drawing transcribed by Fray Sahaguns, “The Florentine Codex”).

The result of a rinderpest outbreak. Photo location and date unknown.
So, what makes these diseases “emerging”?

Emerging diseases can be attributed to either:

1. **True emergence** - a newly appearing disease agent that had not been present previously


2. **Increased recognition** - a disease agent that was always present in a population but became newly recognized due to a significant outbreak or improved diagnostic tests / capabilities.

   Example: Legionnaires disease (*Legionella pneumophila*, in the 70s), gastroenteritis (*Campylobacter jejuni*, now).

3. **Increased incidence of previously recognized disease** – perhaps because of greater human and animal traffic, greater population densities, increased susceptibility of the host population.

   Example: Bubonic plague (*Yersinia pestis*, several times throughout history), West Nile disease, MRSA presently.

**How does emergence occur?**

Disease emergence has been viewed as a two-step procedure.

Step 1. **Introduction** of an agent into a new host group or population.

Step 2. **Establishment** and **dissemination** of the agent in the new host population.

The process by which these agents may be introduced, established and disseminated across populations is called **microbial traffic**.

This can include the movement of infectious agents or genetic elements that facilitate pathogen survival or virulence (like plasmids) among populations.
Several factors lead to the emergence of infectious diseases. (Know how each of these impacts the emergence of disease)

- HIV-AIDS
- Speed and ease of travel
- Global climate change
- Industrial commercial agriculture
- Relocation of animals
- Aging of the population
- Encroachment of human populations on forest habitats
- Population growth
- Dam building
- Increased antibiotic use for humans and animals
- War and social disruption
- Growth of daycare
- Human-animal contact
- Aging of the population
- Human-animal contact
- Encroachment of human populations on forest habitats

Zoonotic (animal-borne) pathogens passed from wildlife to humans. From lowest occurrence (green) to highest (red). Credit: Nature.