Antimicrobial Drugs
Chapter 20
BIO 220

Vocabulary

• **Pathogen** – disease-causing microorganism
• **Pathology** – study of disease  
  * Etiology, pathogenesis, structural and functional changes
• **Pathogenesis** – manner in which a disease develops  
• **Infection** – colonization of body by pathogenic microbes  
• **Disease** – results when infection causes changes in the body, such that the body or some body part no longer functions normally

Normal microbiota

• Mammals begin to be colonized with microbes at birth  
  • Lactobacilli from mother’s vagina  
  • Additional microbes enter from the environment via breathing and feeding  
• A typical human body contains $1 \times 10^{13}$ eukaryotic cells and $1 \times 10^{14}$ bacterial cells  
• The goal of the Human Microbiome Project is to analyze microbial communities (microbiomes) in and on the body  
  • What is the relationship between the microbiome and health and disease?

Human microbiota

• **Normal microbiota** (normal flora) – microbes that establish more or less permanent residence in/on the body but do not cause disease under normal circumstances  
• **Transient microbiota** – microbes that take up a temporary residence (days, weeks, or months)  
• Microbes are not found throughout the body, rather they are localized to certain regions
What determines the distribution/composition of the normal microbiota?

• Nutrient availability
• Temperature
• pH
• Oxygen and carbon dioxide
• Salinity
• Light
• Host’s defenses
• Mechanical forces (i.e. urine flow, respiratory and digestive secretions)
• Host’s age, diet, health status, stress, personal hygiene, environment, etc.

Could you live without your microbiota?

• Yes, but . . .

• Germ-free mammals can be obtained by breeding them in a sterile environment

• These germ-free animals tend to have undeveloped immune systems and are unusually susceptible to infection and serious disease

• Germ-free animals also require more calories and vitamins
Relationships between the normal microbiota and host

- Microbial antagonism (competitive exclusion)
  - Normal microbiota protect the host against colonization by pathogenic microbes by competing for nutrients, producing substances harmful to pathogenic microbes, and altering $[\text{H}^+]$ and oxygen levels
  - Normal microbiota maintain a vaginal pH @ 4, but if those microbes are eliminated pH increases and Candida albicans can proliferate
  - *Escherichia coli* produces bacteriocins, which inhibit the growth of closely-related bacteria, like *Salmonella* and *Shigella*
  - Normal colon microbiota inhibits *Clostridium difficile*, but if those normal microbes are removed then *Clostridium* can become an issue
  - *C. diff*-associated diarrhea has been successfully treated with fecal transplants

Opportunistic microbes

- Do not cause disease in their normal habitat, but can in a different environment.
  - *E. coli*
  - *Pneumocystis jirovecii*
  - *Neisseria meningitidis*
  - *Streptococcus pneumoniae*

The relationship between the normal microbiota and the host is called symbiosis

Symbiotic relationships are those in which at least one organism is dependent on the other.

Koch’s postulates
Koch's postulates

1. The same pathogen must be present in every case of the disease.
2. The pathogen must be isolated from the diseased host and grown in pure culture.
3. The pathogen from the pure culture must cause the disease when it's inoculated into a healthy, susceptible laboratory animal.
4. The pathogen must be isolated from the inoculated animal and must be shown to be the original organism.

Exceptions to Koch's postulates

- Some pathogens can not be grown on artificial media
- Treponema pallidum, Mycobacterium leprae
- i.e. Legionnaire's disease (Legionella)
  - Scientists could not isolate pathogen from humans, so injected lung tissue into guinea pigs
  - Guinea pigs injected with infected tissue became sick, those injected with normal tissue did not
  - Tissue samples from sick guinea pigs were cultured in the yolk sacs of chicken embryos
  - Electron microscopy revealed bacilli bacteria in the embryos
  - Ultimately, a variety of scientific techniques showed that the bacteria isolated from the embryos was the same as the bacteria in sick humans and guinea pigs

Exceptions to Koch's postulates

- Human host exhibits certain symptoms and signs that are associated only with a certain pathogen and its disease
  - Diphtheria – swollen neck glands, pseudomembrane formation
  - Tetanus – muscle stiffness, "lockjaw"
- Other infectious diseases many involve one of several different pathogens
- Some pathogens can cause several disease conditions
- Ethical considerations

Classifying infectious diseases

- Symptoms – subjective changes
- Signs – objective changes
- Syndrome – a specific group of symptoms or signs may always accompany a particular disease
- Communicable disease – a disease that can be transmitted from person to person
- Contagious disease – disease that is communicable and capable of spreading quickly
- Noncommunicable disease – not spread from one host to another
  - May be caused by microbes already in body
  - Other microbes that gain entrance into the body
Occurrence of a disease

- Incidence of a disease – the rate of new (newly diagnosed) cases of a disease
  - Reported as # new cases occurring within a specified time period
- Prevalence of a disease – actual number of cases within a certain time period or on a specific date number, regardless of when the disease first appeared
  - Takes into account both old and new cases
- Knowing the incidence and the prevalence of a disease in different populations enables scientists to estimate the range of the disease's occurrence and its tendency to affect some groups more than others

Frequency of occurrence

- Sporadic disease – occurs only every now and then
- Endemic disease – a disease that is constantly present in the population
- Epidemic disease – a disease that is acquired by many people in a given area in a relatively short period
- Pandemic disease – an epidemic disease that occurs world-wide

Fig. 14.4

Severity/duration of disease

- Acute disease – a disease that develops rapidly but only lasts a short time
- Chronic disease – a disease that develops more slowly but is likely to persist or recur for long periods
- Subacute disease – a disease that is intermediate between acute and chronic
- Latent disease – etiological agent of disease remains inactive for a time but later becomes active and produces symptoms of the disease
- Herd immunity – when a portion of a community is immunized against a contagious disease, most members of the community are protected because of the reduced chance of an outbreak

Extend of host involvement

- Local infection – invading microbes are limited to a relatively small area of the body
- Systemic (generalized) infection – microbes or their products have spread throughout the body via blood or lymph
- Focal infection – agents of a local infection gain access to blood or lymph and spread through the body
- Sepsis – a toxic inflammatory condition arising from the spread of microbes or their toxins from a focus of infection
- Septicemia – a systemic infection arising from the multiplication of pathogens in the blood
Extend of host involvement

- **Bacteremia** – presence of bacteria in the blood
- **Toxemia** – presence of toxins in the blood
- **Viremia** – presence of viruses in the blood
- **Primary infection** – acute infection that causes the initial illness
- **Secondary infection** – caused by an opportunistic pathogen after the primary infection has weakened the body's defenses
- **Subclinical (inapparent) infection** – one that does not cause any noticeable illness
  - Patients may never develop the illness

Patterns of disease

- **Predisposing factors**
  - Gender
  - Genetic background
  - Climate and weather
  - Nutrition
  - Fatigue
  - Age
  - Environment
  - Habits
  - Lifestyle
  - Occupation
  - Preexisting illness
  - Medical treatment

Development of disease

- **Incubation period**
  - Interval between infection and the first appearance of any signs or symptoms
  - Depends on specific organism, its virulence, number of infecting organisms, resistance of the host

- **Prodromal period**
  - Characterized by early, mild symptoms of the disease

- **Period of illness**
  - Symptoms are most severe

- **Period of decline**
  - Signs and symptoms decline

- **Period of convalescence**

Stages of disease
Reservoirs of infection

For a disease to perpetuate itself, there must be a continual source of the disease organisms. This reservoir of infection can either be living or an inanimate object that provides conditions in which the pathogen can survive, multiply, and has the opportunity for transmission.

- **Humans**
  - Some may be asymptomatic but still harbor pathogens (carriers)
- **Animals**
- **Nonliving**
  - Soil and water

**Transmission of disease**

- **Direct contact transmission** – person-to-person
  - Touching, kissing, sexual contact
- **Indirect contact transmission** – agent of a disease is transmitted from its reservoir to a susceptible host by means of a nonliving object (fomite)
- **Droplet transmission** – microbes are spread in droplet nuclei (mucus droplets) that travel only short distances (<1 m from reservoir)
Transmission of disease

- **Vehicle transmission** – transmission of disease agents by a medium such as food, water, air, bodily fluids, drugs, and IV fluids

![Transmission of disease images](a) Water (b) Food (c) Air)

Fig. 14.7

Transmission of disease

- Arthropod vectors transmit disease by either mechanical transmission or biological transmission
  - **Mechanical transmission** involves the passive transport of pathogens on the arthropod’s feet or other body parts
  - **Biological transmission** is an active process (i.e., arthropod bites infected person or animal and later transfers pathogen to another host)

Fig. 14.8

<table>
<thead>
<tr>
<th>Table 14.3 Representative Arthropod Vectors and the Diseases They Transmit</th>
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<tbody>
<tr>
<td>Disease</td>
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<tr>
<td>African trypanosomiasis</td>
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<td>Chagas disease</td>
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<td>Yellow fever</td>
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<td>Dengue</td>
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<td>Arthropod-borne encephalitis</td>
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<td>Tick-borne encephalitis</td>
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<td>Epidemic typhus</td>
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<td>Rocky Mountain spotted fever</td>
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<td>Relapsing fever</td>
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<td>Lyme disease</td>
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Fig. 14.9

Healthcare-associated infections (HAIs)

- These are infections that patients acquire while receiving care in health care facilities, like hospitals, nursing homes, and outpatient clinics.

- Result from the interaction of three factors:
Compromised host

- An individual whose resistance to infection is impaired by disease, therapy, or burns

- Broken skin or mucous membranes and a suppressed immune system can compromise the host

Chain of Transmission

- Direct contact transmission from hospital staff to patient and from patient to patient

- Indirect contact transmission through fomites and the hospital's ventilation system (airborne transmission)
Control of HAI

- Wash hands!
- Disinfect tubs between patients
- Respirators and humidifiers must be cleaned and disinfected
- Bandages and tubes (for intubation) should be single-use or sterilized
- Reducing use of antibiotics when unnecessary
- Avoiding invasive procedures if possible
- Minimizing use of immunosuppressive medications
- Health care facilities should have infection control staff/epidemiologist

Emerging infectious diseases

Diseases that are new or changing, showing an increase in incidence in the recent past, or a potential to increase in the near future

- About 75% of emerging infectious diseases are zoonotic, mainly of viral origin, and are likely to be vector-borne
- Factors that contribute to the emergence of new infectious diseases
  - New strains of bacteria and viruses, perhaps as a result of recombination
  - Indiscriminate use of antibiotics and pesticides encourages resistance
  - Global warming and changes in weather patterns
  - Diseases may spread to new locations via travel
  - Animal control measures
  - Failures in public health measures

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### Table 14.6 Emerging Infectious Diseases

<table>
<thead>
<tr>
<th>Microorganism</th>
<th>Year of Emergence</th>
<th>Disease Caused</th>
<th>Chapter Reference</th>
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<tr>
<td><strong>BACTERIA</strong></td>
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<td>Clostridium difficile</td>
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<td>Bovine tuberculosis</td>
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<td>Pneumocystis jirovecii</td>
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<td>Plasmodium falciparum</td>
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<td>Trypanosoma brucei</td>
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### Table 14.6 Emerging Infectious Diseases (Continued)

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<td><em>Babesia</em></td>
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<td>Toxoplasma gondii</td>
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### Additional Information

- Vector-borne diseases
- zoonotic diseases
- Re-emerging diseases
- Occupational diseases
- Staphylococcus aureus
- Streptococcus pyogenes
- Bacillus anthracis
- Yersinia pestis
- Brucella melitensis
- Leptospira interrogans
- Babesia microti
- *Rickettsia* species
- *Ehrlichia* species
- *Anaplasma* species
- *Neorickettsia* species
- *Toxoplasma* gondii

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#### Footnotes

- *Toxoplasma gondii* encephalitis: 1985
- *Babesia* species: 1985
- *Rickettsia* species: 1985
- *Ehrlichia* species: 1985
- *Anaplasma* species: 1985
- *Neorickettsia* species: 1985
- *Toxoplasma* gondii: 1985

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#### References

- World Health Organization
- Centers for Disease Control and Prevention
- National Institutes of Health

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10
Epidemiology

• The study of when and where diseases occur and how they are transmitted in populations
  • Etiological agent of disease
  • Analyzing data concerning age, sex, occupation, personal habits, socioeconomic status, history of immunization, presence of other diseases, common history of affected individuals, time of year

Descriptive epidemiology

• Collection of all data that describe the occurrence of the disease under study
  • Retrospective
  • Epidemiologist backtracks to the cause and source of the disease

Analytical epidemiology

• Analyzes a particular disease to determine its probable cause
  • Case control method – looks for factors that may have preceded the disease
    • Individuals who have the disease are compared against those that do not
  • Cohort method – two populations are studied; one that has had contact with the agent causing a disease and another that has not
Experimental epidemiology

- Begins with a hypothesis about a particular disease, involves experiments to test the hypothesis conducted with a group of people
- i.e. effectiveness of drug
  - If group taking drug recover more rapidly than group taking the placebo, it can be concluded that the drug was the experimental factor that made the difference

Case reporting

- An effective way to establish chain of transmission
- Requires health care workers to report specified diseases to local, state, and national health officials