Topic 6 (Ch13,12): Microbe-Human Interactions: Infection and Disease

Topics
- Human Host
- Progress of an Infection
- Epidemiology

Symbiosis
- “to live together”
- symbiotic relationships with microorganisms
- Main kinds of symbiosis:
  – Mutualism
  – Commensalism
  – Parasitism

3 Kinds?

<table>
<thead>
<tr>
<th>The Three Types of Symbiotic Relationships</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Organism 1</strong></td>
</tr>
<tr>
<td>----------------</td>
</tr>
<tr>
<td>Mutualism</td>
</tr>
<tr>
<td>Commensalism</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Parasitism</td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>
Normal Flora
– Also termed indigenous microbiota
– Organisms colonize body without normally causing disease
– Two types
  • **Resident**, normal, mostly commensal
  • **Transient**, short time, usually cannot persist due to competition, immune cells, body changes

Examples

Human Host
• Acquire resident flora
• New born exposure
Acquire resident flora

- The human body supports a wide range of habitats
  - temperature, pH, nutrient, oxygen tension
- Wide range of microbes can inhabit
- Resident flora or microflora
  - Microbes that inhabit but do not harm the host

Acquire resident flora

- Beneficial outcome
  - Removed by immune system
  - Microbial antagonism
- Adverse effects
  - Escape immune system
  - Multiply and disrupt tissue

Benefits and adverse effects of microbial contact
**TABLE 13.1 Sites That Harbor a Normal Flora**

- Skin and its contiguous mucous membranes
- Upper respiratory tract
- Gastrointestinal tract (various parts)
- Outer opening of urethra
- External genitalia
- Vagina
- External ear canal
- External eye (lids, conjunctiva)

**Microbes and the anatomic sites they occupy**

<table>
<thead>
<tr>
<th>Anatomic Site</th>
<th>Normal Flora</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin</td>
<td>Bacteria, Actinomyces, Micrococcus, Coagulans, Propionibacterium, Staphylococcus, Corynebacterium, Acinetobacter, Enterococcus, Escherichia, Enterobacter, Pseudomonas, Serratia, Stenotrophomonas, Mycobacterium, Staphylococcus epidermidis, Staphylococcus aureus, Enterococcus faecalis, Enterococcus faecium, Lactobacillus, and various fungi.</td>
</tr>
<tr>
<td>Upper respiratory tract</td>
<td>Bacteria, Yeasts, Histoplasma, Cryptococcus, Candida, Aspergillus, and various fungi.</td>
</tr>
<tr>
<td>Gastrointestinal tract</td>
<td>Bacteria, Yeasts, Cryptococcus, Enterococcus, Escherichia, Enterobacter, and various fungi.</td>
</tr>
<tr>
<td>Urogenital tract</td>
<td>Bacteria, Yeasts, Cryptococcus, Enterococcus, Escherichia, Enterobacter, and various fungi.</td>
</tr>
</tbody>
</table>

**Normally sterile regions of the body**

- All internal Tissues and Organs
  - Heart and circulatory system
  - Liver
  - Kidneys and bladder
  - Brain and spinal cord
  - Muscles
  - Bones
  - Ovaries/hosies
  - Glands (pancreas, salivary, thyroid)
  - Sinuses
  - Middle and inner ear
  - Internal eye
- Fluids Within an Organ or Tissue
  - Blood
  - Urine in kidneys, bladders
  - Cerebrospinal fluid
  - Saliva prior to entering the oral cavity
  - Spermatozoa entering the urethra
  - Amniotic fluid surrounding the embryo and fetus
The absence of normal flora can have harmful effects.

New born exposure

Newborns are exposed to different types of microbes depending on the source and their stage of development.

- Mother’s birth canal
- Mother’s breast milk
- Bottle-feeding
- People

Overview: general disease stage progression

1. Pathogens (bacteria, virus, fungi, etc.)
2. Germ x begins to grow (germination)
3. Multiplying (growing)
4. Eruption with signs and symptoms
5. Recovery from illness with or without immunity

<table>
<thead>
<tr>
<th>Germ-Free Animals Display</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mice, guinea pigs, hamsters</td>
<td>Mice are essential for normal intestinal development</td>
</tr>
<tr>
<td>Rats, rabbits, chickens</td>
<td>Mice are a significant nutritional source of vitamins</td>
</tr>
<tr>
<td>Horses</td>
<td>Mice are needed to stimulate development of certain host defenses</td>
</tr>
<tr>
<td>Pigs</td>
<td>Mice are essential in cancer formation and granuloma disease</td>
</tr>
<tr>
<td>Sheep, goats</td>
<td>Normal flora are antagonistic against pathogens</td>
</tr>
<tr>
<td>Newborns</td>
<td>Normal flora facilitate the completion of the life cycle of the amoeba in the gut</td>
</tr>
</tbody>
</table>
Progress of an Infection

- Pathogenicity
- Portals of entry
- Attachment
- Surviving host defenses
- Causing disease
- Process of infections and disease
- Portals of exit

Infection time line

Pathogenicity

- True pathogens:
  - Cause disease in healthy individuals
  - Associated with a specific and recognizable disease
- Opportunistic pathogens:
  - Cause disease in immune compromised host
  - Gain access (injury) to sterile regions
- Virulence:
  - Ability to establish itself in the host
  - Cause damage
How do Some Become Pathogenic?

- Opportunistic pathogens
  - Some normal flora can cause disease under certain circumstances
- Conditions provide opportunities for pathogens
  - Introduction of normal flora into unusual site in body
  - Immune suppression
  - Changes in the normal flora
    - Changes in relative abundance can allow opportunity for a member to thrive and cause disease

What Reservoirs?

- Animal reservoir - zoonotic
- Human carriers – infected, asymptomatic or healthy carriers
- Nonliving reservoir – soil, water, food

Infection predisposition factors

TABLE 13.4 Factors That Weaken Host Defenses and Increase Susceptibility to Infection

- Old age and extreme youth (infancy, prematurity)
- Genetic defects in immunity and acquired defects in immunity (AIDS)
- Surgery and organ transplants
- Organic disease: cancer, liver malfunction, diabetes
- Chemotherapy/immunosuppressive drugs
- Physical and mental stress
- Other infections

*These conditions compromise defense barriers or immune responses.
So How do they get in?

Portals of Entry!
(Sites where pathogens enter body)
Four major pathways:
- Skin
- Mucous membranes
- Placenta
- Parenteral route (non-oral)

Portals of entry
- Most pathogens have specific portals on entry
  - Skin (Staph. sp., Haemophilus sp.)
  - Gastrointestinal tract (Salmonella, Shigella, Vibrio, polio, hepatitis A, Giardia lamblia)
  - Respiratory tract (Streps., Cryptococcus)
  - Urogenital (STDs, papillomavirus, Trichomonas, Neisseria)
  - Placenta (Syphilis, Herpes)

Some Portals
Mucous Membranes

- Line body cavities open to the environment
- Provide moist, warm environment hospitable to pathogens
- Respiratory tract is most common site of entry
  - Entry is through the nose, mouth, or eyes
- Gastrointestinal tract can be route of entry
  - Must survive acidic stomach pH

Transplacental fetus infection acquisition.

Inoculum size

- Infectious dose (ID)
  - minimum number of bacteria required to cause disease
  - Low ID = high virulence
Attachment

- Adhesion
  - Binding between specific molecules on both the host and pathogen
- Structures
  - Capsules
  - Pili or fimbriae
  - Hooks

Pathogen Adhesion

<table>
<thead>
<tr>
<th>Microbe</th>
<th>Disease</th>
<th>Adhesion Mechanism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neisseria</td>
<td>Gonorrhea</td>
<td>Fimbria attach to the epithelial surface</td>
</tr>
<tr>
<td>Staphylococci</td>
<td>Staphylococci</td>
<td>Surface attachment of fimbriae</td>
</tr>
<tr>
<td>Vibrio</td>
<td>Cholera</td>
<td>Fimbria attach to the epithelial surface</td>
</tr>
<tr>
<td>Brucella</td>
<td>Brucellosis</td>
<td>Fimbria attach to the epithelial surface</td>
</tr>
<tr>
<td>Salmonella</td>
<td>Typhoid Fever</td>
<td>Fimbria attach to the epithelial surface</td>
</tr>
<tr>
<td>Helicobacter</td>
<td>Helicobacter pylori</td>
<td>Fimbria attach to the epithelial surface</td>
</tr>
<tr>
<td>Enterococcus</td>
<td>Enterococcal endocarditis</td>
<td>Fimbria attach to the epithelial surface</td>
</tr>
<tr>
<td>Streptococcus</td>
<td>Streptococcal endocarditis</td>
<td>Fimbria attach to the epithelial surface</td>
</tr>
<tr>
<td>Influenza</td>
<td>Influenza virus</td>
<td>Fimbria attach to the epithelial surface</td>
</tr>
<tr>
<td>Poliovirus</td>
<td>Polio</td>
<td>Fimbria attach to the epithelial surface</td>
</tr>
<tr>
<td>HIV</td>
<td>AIDS</td>
<td>Fimbria attach to the epithelial surface</td>
</tr>
<tr>
<td>Clostridium</td>
<td>Gas gangrene</td>
<td>Fimbria attach to the epithelial surface</td>
</tr>
</tbody>
</table>
Adhesion & Infection

- Attachment proteins $\rightarrow$ adhesion
  - on viruses and many bacteria
  - Viral or bacterial ligands bind host cell receptors
    (Interaction can determine host cell specificity)
- Changing/blocking a ligand or its receptor can prevent infection
- Inability to make attachment proteins or adhesins renders microorganisms avirulent
- Some bacterial pathogens attach to each other to form a biofilm

Example Adhesion – Dental Plaque

Ways to survive the host defenses

- Antiphagocytic factors
  - Capsule
    - Prevent phagocytosis
  - Leukocidins
    - Toxic to phagocytes
    - Some microbes survive inside phagocytes
Causing disease

• Virulence factors
  – Exoenzymes
  – Toxins
  – Capsule

• Occurrence of infection

• Signs and symptoms

Exoenzymes

• Mucinase – digest protective coating on mucous membranes
• Keratinase – digest the principal component of skin and hair
• Collagenase – digest the principal fiber of connective tissue
• Hyaluronidase – digest the substance that cements cells together

Bacterial toxins

• Exotoxins
  – Gram positive and Gram negative cells
  – Released (excreted) by the bacterium; directly affect different host organs (ex. Hemolysins)
  – Highly toxic in small amounts

• Endotoxins
  – Gram negative cells
  – Released "after" the bacterium is lysed.
  – Membrane associated
    • Lipopolysaccharide (LPS)
  – Fever associated
Characteristics – bacterial exotoxins and endotoxins

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Exotoxin</th>
<th>Endotoxin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Toxicity</td>
<td>Toxic in minute amounts</td>
<td>Toxic in high doses</td>
</tr>
<tr>
<td>Effects on the Body</td>
<td>Systemic tissue destruction</td>
<td>Systemic tissue necrosis, inflammation</td>
</tr>
<tr>
<td>Chemical Composition</td>
<td>Small proteins</td>
<td>Lipopolysaccharide</td>
</tr>
<tr>
<td>Heat Inactivation at 4°C</td>
<td>Soluble</td>
<td>Stable</td>
</tr>
<tr>
<td>Toxin Formation</td>
<td>Can be converted to toxin*</td>
<td>Cannot be converted to toxin</td>
</tr>
<tr>
<td>Immune Response</td>
<td>Stimulates antibodies**</td>
<td>Does not stimulate antibodies</td>
</tr>
<tr>
<td>Fever Induction</td>
<td>Usually not</td>
<td>Yes</td>
</tr>
<tr>
<td>Manner of Release</td>
<td>Secreted from the cell</td>
<td>Released by cell damage</td>
</tr>
<tr>
<td>Typical Bacteria</td>
<td>A few gram-positive and gram-negative</td>
<td>All gram-negative bacteria</td>
</tr>
</tbody>
</table>

* A trend is an observation over a 95% confidence interval.
** An antibody is an antibody that reacts specifically with a toxin.

Establishment of infections vary depending on location, type of microbe, and length of time

Process of infections and disease

Establishment
- Localized
- Systemic
- Focal
- Mixed
- Primary and secondary
- Acute and chronic

Signs vs. Symptoms
- **Signs** – objective evidence of disease based on observation: (inflammation → edema, granulomas, abscesses)
- **Symptoms** – subjective evidence of disease based on the patient’s description: (inflammation → fever, pain, soreness, swelling)
- **Syndrome** – collected sign and symptoms
Common signs and symptoms with infectious diseases

| TABLE 13.8 Common Signs and Symptoms of Infectious Diseases |
|-----------------|-----------------|
| **Signs**       | **Symptoms**    |
| Fever           | Chills           |
| Septicemia      | Pain, ache, soreness, irritation |
| Microbes in tissue fluids | Malaise, fatigue |
| Chest sounds    | Skin eruptions   |
| Leukocytosis    | Leukopenia       |
| Swollen lymph nodes | Nausea         |
| Abscesses       | Tachycardia (increased heart rate) |
| Antibodies in serum | Sore throat |

Portals of exit

* (how to get out…)

• Enables pathogen to spread to other hosts
  – Respiratory
  – Salivary
  – Skin
  – Fecal
  – Urogenital
  – Blood
• Persistence

Exit Portals
Persistence

- Latency
  - Viral
    - Herpes virus
  - Bacterial
    - Tuberculosis
- Sequelae – long-term damage to tissues or organs

Virulence Factors

- Pathogenicity = Ability of microorganism to cause disease
- Virulence = Degree of pathogenicity
- Virulence factors:
  - Adhesion factors
  - Biofilms
  - Extracellular enzymes
  - Toxins
  - Antiphagocytic factors

Relative Virulence

More virulent:
- Francisella tularensis (rabbit fever)
- Vibrio parahaemolyticus
- Bacillus cereus
- Pseudomonas aeruginosa
- Clostridium difficile
- Candida albicans
- Lactobacillus, diptheriae

Less virulent:
Reservoirs

- Carriers (Asymptomatic, Incubation, Convalescent, Chronic, Passive)
- Vectors:
  - Biological
    - Participates in the pathogen’s life cycle
    - Infected with the pathogen
    - Transmitted by bites, defecation
  - Mechanical
    - Not part of pathogen’s life cycle
    - Not infected with the pathogen
- Nonliving (soil, water fomites)

Different types of carriers

Zoonotic infections - caused by vectors and animal reservoirs that spread infections to humans

<table>
<thead>
<tr>
<th>Disease</th>
<th>Primary Animal Reservoirs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rabies</td>
<td>All mammals</td>
</tr>
<tr>
<td>Yellow fever</td>
<td>Wild birds, mosquitos</td>
</tr>
<tr>
<td>Malaria</td>
<td>Mice</td>
</tr>
<tr>
<td>Haemorrhagic Fever</td>
<td>Rodents, flies</td>
</tr>
<tr>
<td>Lassa fever</td>
<td>Rodents, flies</td>
</tr>
<tr>
<td>West Nile fever</td>
<td>Wild birds, mosquitos</td>
</tr>
</tbody>
</table>

- Rocky Mountain spotted fever
- Tickborne encephalitis: domestic animals
- Tickborne typhus: domestic animals
- Tickborne relapsing fever: cattle, sheep, pigs
- Flea-borne: rodents, rats
- Suckhothai fever: variety of mammals, birds, and rodents
- Tularemia: rodents, birds, arthropods

- Malaria: Domestic mammals
- Typhus: Domestic mammals
- Sib-sib: Domestic and wild mammals
- Scrub typhus: Cattle, ovine, fish
- Relapsing fever: Domestic mammals
Acquisition and transmission

- Communicable:
  - Infected host transmits an infectious agent to another host
  - Receiving host must become infected
- Non-communicable:
  - Host acquires infectious agent (self, reservoir)
- Patterns of transmission:
  - horizontal, vertical, direct, indirect

3 Types of Transmission

- Contact (direct, indirect, droplet)
- Vehicular (air, water, food)
- Vector (biological, mechanical)

Patterns of Transmission

- **Horizontal**: Disease is spread through a population from one infected person to another (kissing, sneezing)
- **Vertical**: Disease is transmitted from parent to offspring (ovum, sperm, placenta, milk)
- **Direct**: sex, kissing, droplets, vector fomites
- **Indirect**: contaminated materials, fomites, air (droplets, aerosols)
THE sneeze (droplet)

humongous amounts of moist, aerosolized droplets, plus dry droplets that form droplet nuclei

Some Other Mechanisms

• Refrigeration/Storage

Germ Farm

Poor hygiene

Dirty Utensils

Improper cooking

Disease Classification

• body system they affect
• Taxonomic categories
• longevity and severity
• How they are spread to their host
• The effects they have on populations (rather than on individuals)
Nosocomial infections
(aka: hospital acquired infections)

- Infectious diseases that are acquired or developed from a hospital stay
  - Urinary tract infections
  - Respiratory infections
  - Surgical incisions

Most common nosocomial infections

- Acinetobacter baumannii
- Clostridium difficile
- Gastroenteritis
- Hospital-acquired pneumonia (HAP)
- Legionella
- Methicillin Resistant Staphylococcus aureus (MRSA)
- Pseudomonas aeruginosa
- Staphylococcus aureus
- Stenotrophomonas maltophilia
- Tuberculosis
- Urinary tract infection
- Vancomycin-Resistant Enterococcus
- Ventilator associated pneumonia

Hospital isolation procedures to reduce nosocomial infections

<table>
<thead>
<tr>
<th>Type of Isolation</th>
<th>Levels of Isolation Used in Clinical Settings</th>
<th>To Prevent Spread of</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enteric Precautions</td>
<td>Gowns and gloves must be worn by all persons having direct contact with patient, family members, and visitors, not working in special precautions taken for disposing of these</td>
<td>Nosocomial diseases: hepatitis, tuberculosis, meningitis, invasive pulmonary aspergillosis</td>
</tr>
<tr>
<td>Respiratory Precautions</td>
<td>Private room with closed door is necessary; gowns and gloves are required; respiratory equipment should be used with caution and should be disinfected</td>
<td>Tuberculosis, measles, mumps, meningitis, pertussis, rubella, chickenpox</td>
</tr>
<tr>
<td>Draining and Secretion Precautions</td>
<td>Gowns and gloves are required for all persons; masks are mandatory; non-airborne and airborne procedures must be followed for disinfected</td>
<td>Nosocomial and community infections: gas gangrene, herpes zoster, head trauma</td>
</tr>
<tr>
<td>Isolation</td>
<td>Private room with closed door is required; gowns, gowns, and gowns are required; patients are not allowed to leave the room, backrooms, downstreem, or those with contagious diseases</td>
<td>Mostly highly contagious or contagious, includes: rhinovirus, influenza, streptococcus pneumonia, respiratory syncytial virus, chickenpox, measles, rubella, varicella, hantavirus, pertussis, typhoid, tuberculosis</td>
</tr>
<tr>
<td>Reverse Isolation</td>
<td>Same guidelines as for and isolation room may be required by both healthcare workers and healthcare workers; the room is usually closed and there is limited access to the room; the room may be used to care for patients who are not expected to survive or patients diagnosed with healthcare-associated infection (HAI) who are resistant to the antibiotics</td>
<td></td>
</tr>
</tbody>
</table>

Isolation precautions are based on the presence of a pathogen in the patient. Always check the hospital's specific guidelines before entering the room. All visitors and patients must wash their hands upon entering and leaving the room.
Infectious Disease Terms

Acute
Subacute
Chronic
Subclinical
Latent
Communicable
Contagious

Koch’s postulates (revisited)

- Method used to determine the etiologic agent
- Ex. Toxic shock syndrome, AIDS, Lyme disease, Legionnaires

- Koch’s Postulates:
  a) same pathogen in every case of disease
  b) isolated in pure culture
  c) isolated organism must cause same disease
  d) must be re-isolated from infected animal

  Exceptions exist….  

Epidemiology

- The study of disease in populations
  - Frequency data
  - Distribution data
    - Statistics
    - Strategies
    - Reservoir
    - Carriers
    - Vectors
    - Acquisition and transmission
    - Nosocomial
    - Koch’s postulates
- Center for Disease Control and Prevention (CDC)
Statistical data represented graphically can be used to predict trends.

The frequency of a disease in a population can be used to define endemic, epidemic, sporadic, and pandemic diseases.

Commonly reported diseases that are tracked in the United States.
Common STDs include viruses, protozoan, fungi, and bacteria.

**TABLE 13.5  Incidence of Common Sexually Transmitted Diseases**

<table>
<thead>
<tr>
<th>STD</th>
<th>Estimated Number of New Cases per Year in U.S.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Human papillomavirus</td>
<td>5,500,000</td>
</tr>
<tr>
<td>Trichomoniasis</td>
<td>5,000,000</td>
</tr>
<tr>
<td>Herpes simplex</td>
<td>1,000,000</td>
</tr>
<tr>
<td>Chlamydiosis</td>
<td>783,000</td>
</tr>
<tr>
<td>Gonorrhea</td>
<td>361,000</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>77,000</td>
</tr>
<tr>
<td>AIDS</td>
<td>41,002</td>
</tr>
<tr>
<td>Syphilis</td>
<td>32,200</td>
</tr>
</tbody>
</table>

**MMWR Reporting Example**