chapter 14
principles of disease & epidemiology
# The Germ Theory of Disease

<table>
<thead>
<tr>
<th>Decade</th>
<th>Key Figures and Achievements</th>
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<tbody>
<tr>
<td>1830s</td>
<td>Agostino Bassi - fungal silkworm disease</td>
</tr>
<tr>
<td>1840s</td>
<td>Ignaz Semmelweis - handwashing during childbirth</td>
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<tr>
<td>1860s</td>
<td>Joseph Lister - phenol-sterilized surgical instruments</td>
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<tr>
<td></td>
<td>Louis Pasteur - protozoan silkworm disease</td>
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<tr>
<td>1876</td>
<td>Robert Koch - Koch’s Postulates</td>
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<tr>
<td></td>
<td><em>B. anthracis &amp; M. tuberculosis</em> work</td>
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</table>
## Symbiosis

<table>
<thead>
<tr>
<th>Type</th>
<th>Description</th>
<th>Example</th>
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<tbody>
<tr>
<td><strong>Commensalism</strong></td>
<td>One organism benefits, and the other is unaffected</td>
<td><em>(a) Staphylococcus epidermidis on the skin</em></td>
</tr>
<tr>
<td><strong>Mutualism</strong></td>
<td>Both organisms benefit</td>
<td><em>(b) E. coli bacteria (lavender) in the large intestine</em></td>
</tr>
<tr>
<td><strong>Parasitism</strong></td>
<td>One organism benefits at the expense of the other</td>
<td><em>(c) H1N1 virus particles (orange) on a host cell (green)</em></td>
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the etiology of disease: Koch’s Postulates

1. Microorganisms are isolated from a diseased or dead animal.

2a. The microorganisms are grown in pure culture.

2b. The microorganisms are identified.

3. The microorganisms are injected into a healthy laboratory animal.

4. The disease is reproduced in a laboratory animal; microorganisms are isolated from this animal.

5a. The microorganisms are grown in pure culture.

5b. Identical microorganisms are identified.
studying disease transmission

<table>
<thead>
<tr>
<th>Name</th>
<th>Timeframe</th>
<th>Contribution</th>
</tr>
</thead>
<tbody>
<tr>
<td>John Snow</td>
<td>1848–1849</td>
<td>mapped occurrence of cholera in London</td>
</tr>
<tr>
<td>Ignaz Semmelweis</td>
<td>1846–1848</td>
<td>handwashing decreased the incidence of puerperal fever</td>
</tr>
<tr>
<td>Florence Nightingale</td>
<td>1858</td>
<td>improved sanitation decreased the incidence of epidemic typhus</td>
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</tbody>
</table>

- **descriptive**: collection and analysis of data

- **experimental**: controlled experiments

- **analytical**: comparison of a diseased group and a healthy group
Cholera in Soho, 1854: 616 dead

Descriptive Study: data collection & analysis

Analysis of Study: did transmission stop?

Hypothesis Formation: stop disease transmission

Analytical/Experimental Study

* Figure: Number* of cases of norovirus infection associated with meals served by a national franchise restaurant, by setting and date of illness onset — Kent County, Michigan, May 2–10, 2005

* N = 170.
the language of epidemiology

epidemiology
pathogenicity

pathology
infectivity
communicable

etiology
contagious

infection
noncommunicable

disease
disease classification helps identification → stops transmission

- occurrence

- severity & duration

- extent of host involvement

- development & progression

- transmission
disease classification: occurrence

- **endemic disease**
  - low, constant
  - expected rate

- **epidemic disease**
  - exceeds expectations
  - local or widespread

- **pandemic disease**
  - epidemic on >1 continent
disease classification: severity

acute disease

chronic disease

subacute disease (definition varies)

latent disease

predisposing factors \( \uparrow \) severity
gender • age • immune/genetic status
disease classification: host involvement

localized vs. systemic infection
- bacteremia
- viremia
- toxemia
- septecemia

focal infection

mixed infection
- primary vs. secondary infection
  - primary (urinary tract) infection
  - secondary (vaginal) infection
- various microbes
disease classification: transmission

contact transmission

Direct contact
- Rabies, rat bite fever, typhus, gonorrhea, herpes, diphtheria, enterovirus infections, cutaneous anthrax, genital warts

Indirect contact by fomites
- Tetanus, common cold, enterovirus infections, ringworm

Droplets
- Common cold, influenza, measles, Q fever, pneumonia, whooping cough

vehicle transmission

Waterborne
- Cholera, shigellosis, leptospirosis, Campylobacter infections

Airborne, including dust particles
- Chickenpox, tuberculosis, coccidioidomycosis, histoplasmosis, influenza, measles

Foodborne
- Intoxication with aflatoxins and botulinum toxin, paralytic shellfish poisoning, staphylococcal food poisoning, typhoid fever, salmonellosis, typhus, toxoplasmosis, trichinosis, hepatitis A

vector transmission

Mechanical (on insect bodies)
- E. coli diarrhea, salmonellosis, trachoma

Biological
- Plague, malaria, yellow fever, typhus fever, Rocky Mountain spotted fever, Chagas' disease, Lyme disease
nosocomial infections
1.7 mill infections, 99,000 deaths; $4.5-11 billion

<table>
<thead>
<tr>
<th>Microorganisms in hospital environment</th>
<th>Compromised host</th>
<th>Chain of transmission</th>
</tr>
</thead>
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<table>
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<tr>
<th>Total Infections</th>
<th>Antibiotic Resistance</th>
</tr>
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<tbody>
<tr>
<td>S. aureus</td>
<td>25%</td>
</tr>
<tr>
<td>other Staphylococcus</td>
<td>16%</td>
</tr>
<tr>
<td>Enterococcus</td>
<td>10%</td>
</tr>
<tr>
<td>Gram-negative rods</td>
<td>23%</td>
</tr>
<tr>
<td>C. difficile</td>
<td>13%</td>
</tr>
</tbody>
</table>

Source: Data from CDC, National Nosocomial Infection Surveillance.
avoiding nosocomial infections

this includes hand-hygiene procedures

Follow effective hand-hygiene procedures

Follow hand-hygiene procedures before catheter insertion or manipulation

Implement written catheter-care protocols, including guidelines on catheter insertion

* These guidelines have been adapted from recent guidelines published by professional societies and organizations committed to improving patient safety and quality of care.⁸ We report only those strategies with grade I quality of evidence (i.e., from one or more properly randomized, controlled trials) or grade II quality of evidence (i.e., from one or more well-designed, nonrandomized clinical trials). ICU denotes intensive care unit, and VAP ventilator-associated pneumonia.

† This strategy is considered grade I in the American Thoracic Society guidelines¹⁵ but grade III in the guidelines published more recently by the collaborative group of societies and organizations.⁹

‡ Central venous or arterial catheters should not be routinely replaced.
chapter 14 learning objectives

1. Define the following terms: epidemiology, pathology, etiology, pathogenesis, infection, host, disease, communicable, contagious, and non-communicable.

2. Compare the following classes of disease severity: acute, chronic, subacute, and latent disease. How do predisposing factors affect the severity of disease?

3. Describe the work done by Robert Koch to formulate his Postulates. List and explain these postulates and discuss relevant exceptions.

4. How are descriptive and analytical/experimental epidemiological studies related to one another? What kinds of data are collected in each?

5. What is the ultimate goal of epidemiology?

6. Contrast endemic, epidemic, and pandemic disease occurrence. How does herd immunity affect disease occurrence?

7. Describe the three different ways that infectious agents are transmitted from one host to another, including their subcategories.

8. Describe the progression of disease in a given host, as related to time and number of infectious organisms.

9. Define and contrast the following: local infection, systemic infection, focal infection, mixed infection, primary infection, and secondary infection.

10. How are bacteremia, septicemia, toxemia and viremia related to systemic disease?

11. Why do nosocomial infections occur?

12. Why are urinary tract infections, pneumonia, and sepsis such common nosocomial infections?

13. How does herd immunity relate to the containment of infectious disease?

14. How do host involvement, signs, and symptoms relate to the idea of a disease syndrome?
chapter 16:
nonspecific defenses of the host
• susceptibility: lack of resistance to a disease
• resistance: ability to ward off disease
• non-specific (innate) resistance: any/all pathogens
• specific (adaptive) resistance: specific pathogen “immunity”
1st defense: physical barriers & normal flora

**INNATE IMMUNE SYSTEM**
- Lysozyme in tears kills Gram-positive bacteria
- Removal of particles by turbinates and humidification
- Mucus and cilia capture organisms and remove them
- Skin: physical barrier
- Stomach acid kills ingested pathogens
- Fatty acids inhibit growth of many bacteria
- Competition and toxic products from intestinal flora
- Flushing action of urinary flow removes organisms
- Low vaginal pH from lactobacilli prevents colonization by pathogens

**NORMAL FLORA**
- **NASOPHARYNX**
  - Streptococci
  - Haemophilus
  - Neisseria
  - Mixed anaerobes
  - Candida
  - Actinomyces
- **SKIN**
  - Staphylococci
  - Streptococci
  - Corynebacteria
  - Propionibacteria
  - Yeasts
- **UPPER BOWEL**
  - Enterobacteriaceae
  - Enterococci
  - Candida
- **LOWER BOWEL**
  - Bacteroides
  - Bifidobacteria
  - Clostridium
  - Peptostreptococci
- **VAGINA**
  - Lactobacilli
  - Streptococci
  - Corynebacteria
  - Candida
  - Actinomyces
  - Mycoplasma hominis

**Whole body:**
- Molecular and cellular defence
- Pattern recognition molecule e.g. TLRs
- Neutrophils
- Macrophages
innate defense: inflammation
dolor, calor, tumor, rubor

- Injured agents
  - Cells damaged
  - Release kinins, histamine, and other chemicals
    - Blood vessels dilate
    - Capillaries become “leaky”
      - Increased blood flow into area
        - Redness
        - Heat
      - Edema (fluid in tissue spaces)
        - Pain
        - Swelling
          - Brings more nutrients and oxygen to area
            - Increases metabolic rate of tissue cells
              - Possible temporary limitation of joint movement
                - Fibrin barrier
                - Healing
          - Clotting proteins enter area
            - Neutrophils and then monocytes (and other WBCs) enter area
              - Removal of damaged/dead tissue cells and pathogens from area
white blood cells
innate defense: **phagocytosis**

details

**CELLULAR RECEPTORS**

**Pattern Recognition Receptor (PRR)**

**Toll Like Receptor (TLR)**

**FOREIGN MOLECULES**

**Pathogen-Associated Molecular Patterns (PAMPs)**

**ACTIVATE PHAGOCYTES**

cytokine release ↑ innate response
monocytes are phagocytic

“scouts” resident in tissue
PRR activation
  phagocytize pathogens
  recruit innate defenses
  present antigen
macrophages
  usually stay in tissue
  → present pathogen to B cells
dendritic cells
  migrate to lymph nodes
  → present pathogen to T cells

avoidance by microbes animation
avoidance by microbes (video)
innate defense: fever

fever ≠ hyperthermia

advantages

INCREASES
- transferrins (↓ free Fe)
- IL-1 activity
- Interferon
- tissue repair

DECREASES
- release of Fe & Zn

disadvantages

tachycardia
- tachypnea
- acidosis
- dehydration
- 44–46°C fatal (111°F)
innate defense: complement

Activation
- alternative pathway
- direct activation
- lectin pathway
- innate activation
- classical pathway
- adaptive activation

Results
innate defense: interferons

1. Viral RNA from an infecting virus enters the cell.
2. The infecting virus replicates into new viruses.
3. The infecting virus also induces the host cell to produce interferon mRNA (IFN-mRNA), which is translated into alpha and beta interferons.
4. Interferons released by the virus-infected host cell bind to plasma membrane or nuclear membrane receptors on uninfected neighboring host cells, inducing them to synthesize antiviral proteins (AVPs). These include oligoadenylate synthetase and protein kinase.
5. New viruses released by the virus-infected host cell infect neighboring host cells.
6. AVPs degrade viral mRNA and inhibit protein synthesis—and thus interfere with viral replication.
the non-specific defenses: a summary
chapter 16 learning objectives

1. Define the following terms: resistance, susceptibility, nonspecific resistance, specific resistance (immunity).
2. Describe the physical and chemical factors involved in the first innate resistance to disease.
3. Describe the process of inflammation - be familiar with the terms dolor, calor, tumor, and rubor. What about the release of cytokines causes each of these signs? Why are these effects useful?
4. Describe the three pathways through which complement can be activated.
5. Describe the stepwise production of fever. Why is fever useful? When isn’t it, and why?
6. Describe the production of interferon and antiviral proteins. Why is this still considered an innate (and not specific) defense?
7. What three ways does complement work to rid the body of pathogens?
8. Define and describe the stepwise mechanism of phagocytosis, describe the process. Include in your discussion the role of PRRs, TLRs, and PAMPs. Discuss the similarities and differences between dendritic cells and macrophages.