chapter 14
principles of disease & epidemiology
the history of the study of infectious disease

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

**SYMBIOSIS**

**Commensalism:** One organism benefits, and the other is unaffected

(a) *Staphylococcus epidermidis* on the skin

**Mutualism:** Both organisms benefit

(b) *E. coli* bacteria (lavender) in the large intestine

**Parasitism:** One organism benefits at the expense of the other

(c) H1N1 virus particles (orange) on a host cell (green)

© 2013 Pearson Education, Inc.
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>Year</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>
</tr>
</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

Hypothesis Formation: stop disease transmission

Analysis of Study: did transmission stop?

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.
<table>
<thead>
<tr>
<th>the language of epidemiology</th>
</tr>
</thead>
<tbody>
<tr>
<td>epidemiology</td>
</tr>
<tr>
<td>pathogenicity</td>
</tr>
<tr>
<td>pathology</td>
</tr>
<tr>
<td>infectivity</td>
</tr>
<tr>
<td>etiology</td>
</tr>
<tr>
<td>communicable</td>
</tr>
<tr>
<td>infection</td>
</tr>
<tr>
<td>contagious</td>
</tr>
<tr>
<td>disease</td>
</tr>
<tr>
<td>non-communicable</td>
</tr>
</tbody>
</table>
understanding infectious diseases

helps identification → stops transmission

CLASSIFICATION, PATTERNS & SPREAD OF DISEASE

occurrence

severity & duration

extent of host involvement

development & progression

transmission
disease classification: occurrence
How widespread is the disease?

- **endemic disease**: low, constant expected rate
- **epidemic disease**: exceeds expectations, local or widespread
- **pandemic disease**: epidemic on >1 continent
disease classification: severity
how does a particular disease run its course?

Acute:

Chronic:

Subacute:

Latent:

Persistent:

predisposing factors ↑ severity
gender • age • immune/genetic status
disease classification: host involvement
How much of the body is affected?

localized vs. systemic infection

bacteremia
viremia
toxemia
septecemia

focal infection

subclinical infection

primary vs. secondary infection

primary (urinary tract) infection

secondary (vaginal) infection

various microbes (no S&S)
disease classification: progression
What does the disease look like in the host?
disease classification: transmission

How is the disease spread?

contact transmission

- direct contact
- indirect fomite contact
- indirect droplet contact

vehicle transmission

- waterborne
- airborne
- foodborne

vector transmission

- mechanical vector
- biological vector
Healthcare-Associated Infections (HAIs)

- 2,000,000 infections / >70,000 deaths per year
- 36% increase since 2000
- $4.5-11 billion per year
avoiding nosocomial infections

this includes hand-hygiene procedures

**Table 3. Evidence-Based Guidelines for the Prevention of Hospital-Acquired Infections.**

<table>
<thead>
<tr>
<th>Ventilator-Associated Pneumonia</th>
<th>Central Venous Catheter–Associated Bloodstream Infection</th>
<th>Catheter-Associated Urinary Tract Infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Follow effective hand-hygiene procedures</td>
<td>Implement written catheter-care protocols, including guidelines on catheter insertion</td>
<td></td>
</tr>
<tr>
<td>Conduct active surveillance for VAP and institute preventive measures</td>
<td></td>
<td></td>
</tr>
<tr>
<td>In hospitals with suboptimal infection control using basic practices, use an endotracheal tube with in-line and subglottic suctioning for all eligible patients</td>
<td>Follow hand-hygiene procedures before catheter insertion or manipulation</td>
<td>Avoidance of the femoral vein in adults</td>
</tr>
<tr>
<td>Use noninvasive ventilation in appropriately selected patients with respiratory failure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ensure that patient is in a semirecumbent position, unless contraindicated</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Use an all-inclusive catheter kit and maximal sterile-barrier precautions during catheter insertion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Use a chlorhexidine-based antiseptic for skin preparation in patients &gt;2 mo of age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>After insertion, disinfect catheter hubs, needleless connectors, and injection ports before accessing the catheter; remove nonessential catheters</td>
<td></td>
<td></td>
</tr>
<tr>
<td>For nontunneled catheters in adults, change transparent dressings and perform site care with a chlorhexidine antiseptic every 5 to 7 days (every 2 days for gauze dressings), or more frequently if dressing is soiled, loose, or damp;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Replace administration sets not used for blood products or lipids at intervals not longer than 96 hr</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Use antimicrobial ointments for hemodialysis-catheter insertion sites</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Perform surveillance for bloodstream infection</td>
<td></td>
<td></td>
</tr>
<tr>
<td>In hospitals with suboptimal infection control using basic practices, bathe ICU patients &gt;2 mo of age with a chlorhexidine preparation daily, use antiseptic-impregnated or antimicrobial-impregnated catheters for adult patients, use chlorhexidine-containing sponge dressings in patients &gt;2 mo of age, and use antimicrobial locks for central venous catheters</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* These guidelines have been adapted from recent guidelines published by professional societies and organizations committed to improving patient safety and quality of care. 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 guidelines but grade III in the guidelines published more recently by the collaborative group of societies and organizations.

‡ 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, persistent, 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 sporadic, 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
### Host Defenses

<table>
<thead>
<tr>
<th>Innate Immunity</th>
<th>Adaptive Immunity (Chapter 17)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>First line of defense</strong></td>
<td><strong>Second line of defense</strong></td>
</tr>
<tr>
<td>• Intact skin</td>
<td>• Phagocytes, such as neutrophils, eosinophils, dendritic cells, and macrophages</td>
</tr>
<tr>
<td>• Mucous membranes and their secretions</td>
<td>• Inflammation</td>
</tr>
<tr>
<td>• Normal microbiota</td>
<td>• Fever</td>
</tr>
<tr>
<td>• Antimicrobial substances</td>
<td></td>
</tr>
</tbody>
</table>

- **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

**VAGINA**
- Lactobacilli
- Streptococci
- Corynebacteria
- Candida
- Actinomycetes
- Mycoplasma hominis

**NORMAL FLORA**

**NASOPHARYNX**
- Streptococci
- Haemophilus
- Neisseria
- Mixed anaerobes
- Candida
- Actinomycetes

**SKIN**
- Staphylococci
- Streptococci
- Corynebacteria
- Propionibacteria
- Yeasts

**UPPER BOWEL**
- Enterobacteriaceae
- Enterococci
- Candida

**LOWER BOWEL**
- Bacteroides
- Bifidobacteria
- Clostridium
- Peptostreptococci
innate defense: **inflammation**

*dolor, calor, tumor, rubor*
white blood cells
innate defense: **phagocytosis**

**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
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.