Immunity to Infectious Diseases
BIOS 486A/586A
K.J. Goodrum 2006

Routes and sites of infection

Topic Outline

- Routes and sites of infection
- Mechanisms of tissue injury in infection
- Timing of immune responses to infection
- Regulation of cell-mediated (T_H1) vs. humoral immunity (T_H2) in infections
- Effector mechanisms for immunity to different pathogens
- Microbial evasion of immune responses
- Immunizations/vaccines

Primary Route of Infection: Microbial Adherence and Invasion of epithelial tissues (lung, gut, other)

Janeway, Fig. 10.2
Primary Route of Infection: Microbial Adherence and Invasion of epithelial tissues (continued).

Janeway, Fig. 10.2

Janeway, Fig. 10.4. Infection compartments

Janeway, Fig. 10.5. Mechanisms of Pathogen-induced tissue Damage

Mechanisms of tissue injury in infection
Janeway. Fig. 10.1. Time course of immune response to acute infection.

Janeway. Fig. 10.5. Mechanisms of Pathogen-induced tissue damage (continued)

Timing of immune responses to infection

Regulation of cell-mediated (T_{H1}) vs. humoral immunity (T_{H2}) in infections
Janeway. Fig. 10.9. Infection induced Th1 vs. Th2 responses.

Janeway. Fig. 11.6. The effect of T helper subpopulations on leprosy outcome. (continued)

Cytokine patterns in leprosy lesions

<table>
<thead>
<tr>
<th>T$_h$1 cytokines</th>
<th>T$_h$2 cytokines</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Tuberculoid</strong></td>
<td><strong>Lepromatous</strong></td>
</tr>
<tr>
<td>IL-2</td>
<td>IL-4</td>
</tr>
<tr>
<td>IFN-γ</td>
<td>IL-5</td>
</tr>
<tr>
<td>TNF-β</td>
<td>IL-10</td>
</tr>
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</table>

Effector mechanisms for immunity to different pathogens
Janeway. Fig. 10.24. Mucosal Secretory IgA function

Polymeric IgA is transported into the gut lumen through epithelial cells at the base of the crypt.

Polymeric IgA binds to the mucus layer overlying the gut epithelium.

IgA in the gut neutralizes pathogens and their toxins.

bacterial toxin

Janeway. Fig. 10.27. Recognition of intracellular infection by Nod1.

Shigella penetrate gut epithelium through M cells and spread to other epithelial cells.

Shigella invade basal surface of epithelial cells and spread to other epithelial cells.

Janeway. Fig. 2.5. Innate recognition of microbes and phagocytosis by macrophages

Shigella LPS binds and oligomerizes Nod1, activating the NFκB pathway.

Activated epithelium secretes CXCL8, recruiting neutrophils.

The macrophage expresses receptors for many bacterial components.

Shigella invasion involves interactions with these receptors and signals that mediate infection.

Macrophage engulf and digest pathogens, which they digest.

Janeway. Fig. 10.27. Recognition of intracellular infection by Nod1. (continued)
Janeway. Fig. 2.18. Microbial activation of complement pathways for inflammation.

Janeway. Fig. 9.1. Protective effector mechanisms of antibody.

Janeway. Fig. 1.24 Protective effector mechanisms of antibody.

Janeway. Fig. 8.27 Effector T cell populations and effector mechanisms.
Microbial evasion of immune responses

Janeway. Fig. 11.1. Immune evasion via multiple antigenic variants of microbes (serotypes).

<table>
<thead>
<tr>
<th>Streptococcus pneumoniae</th>
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<tbody>
<tr>
<td><img src="image1" alt="Diagram of Streptococcus pneumoniae variants" /></td>
</tr>
</tbody>
</table>

There are many types of S. pneumoniae, which differ in their capsular polysaccharides.

Fig. 11.1 continued

Individual infected with one type of S. pneumoniae → Response clears infection → Subsequent infection with a different type of S. pneumoniae is unaffected by response to first type → New response clears infection

Fig. 11.1 continued
Fig. 11.2. Immune Evasion via antigen drift/shift.

Antigenic drift
- Neutralizing antibodies against hemagglutinin block binding to cells

Antigenic shift
- Antigenic shift occurs when RNA segments are exchanged between viral strains in a secondary host

Janeway. Fig. 11.3. Immune evasion via sequential DNA rearrangements of microbial antigens.

There are many inactive trypanosome VSG genes but only one site for expression

Expression site
- a, b, c, f
- x1000
- VSG

Inactive genes are copied into the expression site by gene conversion

Janeway. Fig. 11.3. Immune evasion via sequential DNA rearrangements of microbial antigens. (continued)
Janeway. Fig. 11.5. Immune evasion mechanisms of herpes viruses. (continued)

**Table: Inhibition of Inflammatory Responses**

<table>
<thead>
<tr>
<th>Viral strategy</th>
<th>Specific mechanism</th>
<th>Result</th>
<th>Virus examples</th>
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<tbody>
<tr>
<td>Inhibition of humoral immunity</td>
<td>Viremically encoded Fc receptor</td>
<td>Blocks effector function of antibodies bound to infected cells</td>
<td>Herpes simplex, Cytomegalovirus</td>
</tr>
<tr>
<td></td>
<td>Viremically encoded complement receptor</td>
<td>Blocks complement-mediated effector pathways</td>
<td>Herpes simplex</td>
</tr>
<tr>
<td></td>
<td>Viremically encoded complement control protein</td>
<td>Inhibits complement activation by infected cells</td>
<td>Vaccinia</td>
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**Table: Blocking of Antigen Processing and Presentation**

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<tr>
<td>Blocking of antigen presentation</td>
<td>Inhibition of MHC class I expression</td>
<td>Impairs recognition of infected cells by cytotoxic T cells</td>
<td>Herpes simplex, Cytomegalovirus</td>
</tr>
<tr>
<td>Immunosuppression of host</td>
<td>Viremically encoded cytokine homolog of IL-10</td>
<td>Inhibits T-cell lymphocyte production, reduces interferon-γ production</td>
<td>Epstein-Barr virus</td>
</tr>
</tbody>
</table>

**Immunizations/vaccines**
Summary

- Immunity to infection depends on a combination of innate mechanisms (phagocytosis, complement, etc.) and antigen specific adaptive responses (antibody, effector T lymphocytes).
- The immune system regulates which specific responses predominate (humoral vs. cell-mediated) based on the body compartment infected (intracellular vs. extracellular) and on cytokine signals present at initial antigen contact (Th1 vs. Th2 responses).
Summary-continued

- Disease-causing microbes have virulence mechanisms that resist or evade innate and/or specific immune effector functions.
- Recovery from natural infection or artificial immunization promote specific longterm immunity to re-infection (immunological memory).