Immunity to Infectious Diseases
BIOS 486A/586A
K.J. Goodrum 2005

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

Janeway. Fig. 10.1. Time course of immune response to acute infection.

Janeway. Fig. 10.9. Infection induced Th1 vs. Th2 responses.
Janeway, Fig. 10.17. Protective Effector Mechanisms against various infectious microbes (continued)

<table>
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<tr>
<th>Infectious agent</th>
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Janeway. Fig. 10.23. Mucosal γδT cell function.

Janeway. Fig. 10.24. Mucosal Secretory IgA function

Janeway. Fig. 10.27. Recognition of intracellular infection by Nod1.
Janeway. Fig. 10.27. Recognition of intracellular infection by Nod1. (continued)

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

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

**Streptococcus pneumoniae**

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

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**Fig. 11.1 continued**

Individual infected with one type of *S. pneumoniae*

Response clears infection

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**Fig. 11.1 continued**

Subsequent infection with a different type of *S. pneumoniae* is unaffected by response to first type

New response clears infection

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Janeway. 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. 11.2. Immune Evasion via antigen drift/shift. (continued)

Mutations alter hemagglutinin epitopes so that neutralizing antibody no longer binds

No cross-protective immunity to virus expressing a novel hemagglutinin

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

Expression

Inactive genes are copied into the expression site by gene conversion

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

Janeway. Fig. 11.5. Immune evasion mechanisms of herpes viruses.

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<tr>
<td>Inhibition of humoral immunity</td>
<td>Virolyzed Fc receptor</td>
<td>Blocks effector function of antibodies bound to infected cells</td>
<td>Herpes simplex, Cytomegalovirus</td>
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<td>Virolyzed complement receptor</td>
<td>Blocks complement-mediated effector pathways.</td>
<td>Herpes simplex.</td>
</tr>
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<td>Virolyzed complement control protein</td>
<td>Inhibits complement activation by infected cells</td>
<td>Vaccinia.</td>
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Janeway. Fig. 11.5. Immune evasion mechanisms of herpes viruses. (continued)

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<td>Inhibition of inflammatory response</td>
<td>Virolyzed chaperone receptor forming, e.g., 2-mercaptoethanol</td>
<td>Sensitizes infected cells to effects of chaperone/antigenglue to virus interior</td>
<td>Cytomegalovirus</td>
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<td>Virolyzed encoded sytolic receptor, e.g., 30-430 receptor forming TM receptor forming receptor forming</td>
<td>Blocks effects of viral asymmetry inhibition through receptor interaction</td>
<td>Vaccinia, Rabies, human herpes virus.</td>
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<td>Virolyzed inhibition of adhesive nuclear expression, e.g., LFA-1</td>
<td>Blocks adhesion of effector to infected cells</td>
<td>Epstein-Barr virus.</td>
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<td>Anti-inflammatory response protection from IFN-gamma activation by INF-γ receptor-blocked</td>
<td>Blocks inflammatory responses elicited by activation of inflammatory pathways</td>
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<td>Blocking of antigen</td>
<td>Inhibitory MHC class I expression</td>
<td>Inhibits recognition of herpes by cytotoxic T cell</td>
<td>Herpes simplex, Cytomegalovirus</td>
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<td>processing and presentation</td>
<td>Inhibition of peptide transport by TAP</td>
<td>Blocks peptide association with MHC class I</td>
<td>Herpes simplex</td>
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<td>Immunosepression of host</td>
<td>Virally encoded cytokine synthesis of IL-10</td>
<td>Induces Th1/Th2 cytokine response interferon-γ production</td>
<td>Epstein-Barr virus</td>
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Janeway. Fig. 14.21. Childhood vaccination schedule in USA.

Janeway. Fig. 14.23. Continued.

Janeway. Fig. 14.23. Continued.
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).