Immunity to Infectious Diseases

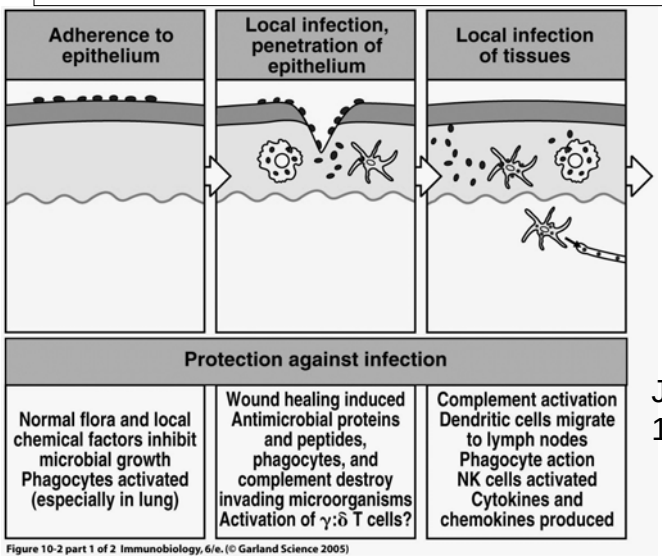
BIOS 486A/586A

K.J.Goodrum 2005

Topic Outline

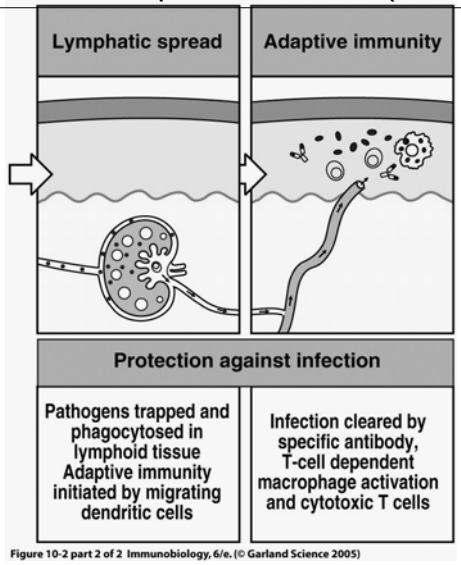
- Routes and sites of infection
- Mechanisms of tissue injury in infection
- Timing of immune responses to infection
- Regulation of cell-mediated (T_H1) vs. humoral immunity (T_H2) in infections
- Effector mechanisms for immunity to different pathogens
- Microbial evasion of immune responses
- Immunizations/vaccines

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



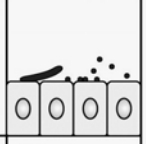
Janeway, Fig. 10.2

Primary Route of Infection: Microbial Adherence and Invasion of epithelial tissues (continued).



Janeway, Fig. 10.2

Janeway. Fig. 10.4. Infection compartments

	Extracellular		Intracellular	
	Interstitial spaces, blood, lymph	Epithelial surfaces	Cytoplasmic	Vesicular
Site of infection				
Organisms	Viruses Bacteria Protozoa Fungi Worms	*Neisseria gonorrhoeae* *Mycoplasma* spp. *Streptococcus pneumoniae* *Vibrio cholerae* *Escherichia coli* *Helicobacter pylori* *Candida albicans* Worms	Viruses *Chlamydia* spp. *Rickettsia* spp. *Listeria monocytogenes* Protozoa	*Mycobacterium* spp. *Salmonella typhimurium* *Yersinia pestis* *Listeria* spp. *Legionella pneumophila* *Cryptococcus neoformans* *Histoplasma* *Leishmania* spp. *Trypanosoma* spp.
Protective immunity	Antibodies Complement Phagocytosis Neutralization	Antibodies, especially IgA Antimicrobial peptides	Cytotoxic T cells NK cells	T-cell and NK-cell dependent macrophage activation

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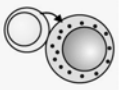
Janeway. Fig. 10.5. Mechanisms of Pathogen-induced tissue Damage

	Direct mechanisms of tissue damage by pathogens		
	Exotoxin production	Endotoxin	Direct cytopathic effect
Pathogenic mechanism			
Infectious agent	*Streptococcus pyogenes* *Staphylococcus aureus* *Corynebacterium diphtheriae* *Clostridiumtetani* *Vibrio cholerae*	*Escherichiacoli* *Haemophilus influenzae* *Salmonella typhi* *Shigella* *Pseudomonas aeruginosa* *Yersinia pestis*	Variola Varicella-zoster Hepatitis B virus Polio virus Measles virus Influenza virus Herpes simplex virus Human herpes virus 8 (HHV8)
Disease	Tonsilitis, scarlet fever Boils, toxic shock syndrome, food poisoning Diphtheria Tetanus Cholera	Gram-negative sepsis Meningitis, pneumonia Typhoid Bacillary dysentery Wound infection Plague	Smallpox Chickenpox, shingles Hepatitis Poliomyelitis Measles, subacute sclerosing panencephalitis Influenza Cold sores Kaposi's sarcoma

Figure 10-5 part 1 of 2 Immunobiology, 6/e. (© Garland Science 2005)

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

	Indirect mechanisms of tissue damage by pathogens		
	Immune complexes	Anti-host antibody	Cell-mediated immunity
Pathogenic mechanism			
Infectious agent	Hepatitis B virus Malaria *Streptococcus pyogenes* *Treponema pallidum* Most acute infections	*Streptococcus pyogenes* *Mycoplasma pneumoniae*	*Mycobacterium tuberculosis* *Mycobacterium leprae* Lymphocytic choriomeningitis virus *Borrelia burgdorferi* *Schistosoma mansoni* Herpes simplex virus
Disease	Kidney disease Vascular deposits Glomerulonephritis Kidney damage in secondary syphilis Transient renal deposits	Rheumatic fever Hemolytic anemia	Tuberculosis Tuberculoid leprosy Aseptic meningitis Lyme arthritis Schistosomiasis Herpes stromal keratitis

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

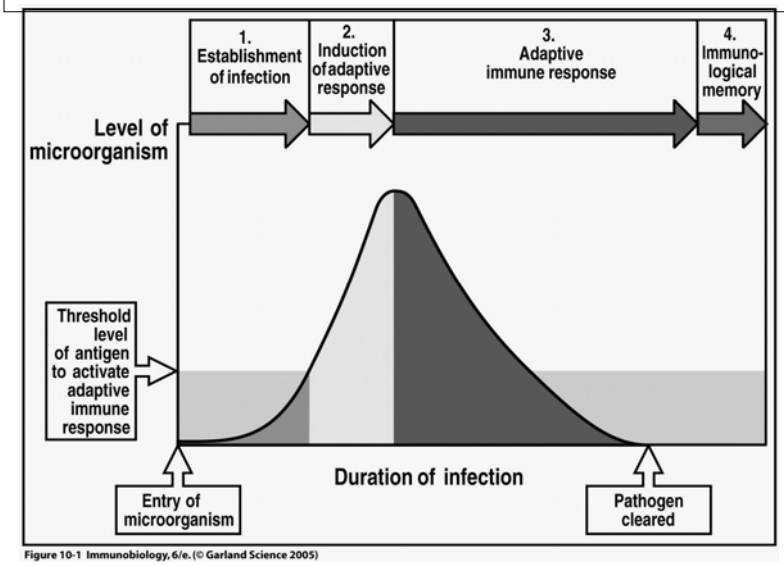
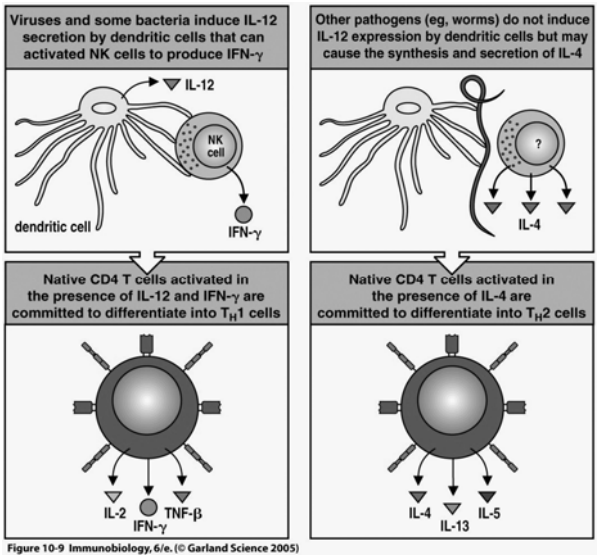


Figure 10-1 Immunobiology, 6/e. (© Garland Science 2005)

Janeway. Fig.10.9. Infection induced Th1 vs. Th2 responses.



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Janeway. Fig. 10.17. Protective Effector Mechanisms against various infectious microbes

	Infectious agent	Disease	Humoral immunity				Cell-mediated immunity	
			IgM	IgG	IgE	IgA	CD4 T cells (macrophages)	CD8 killer T cells
Viruses	Variola	Smallpox						
	Varicella zoster	Chickenpox						
	Epstein–Barr virus	Mononucleosis						
	Influenza virus	Influenza						
	Mumps virus	Mumps						
	Measles virus	Measles						
	Polio virus	Poliomyelitis						
	Human immunodeficiency virus	AIDS						

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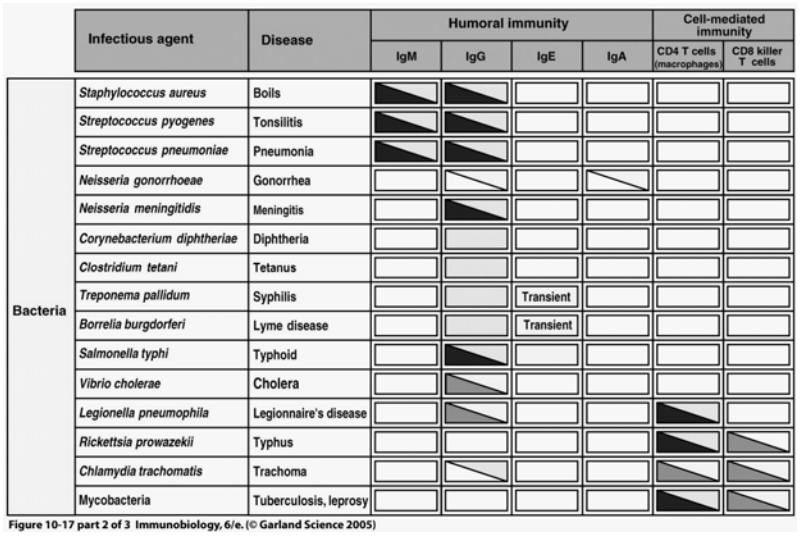
Janeway. Fig. 10.17. Protective Effector Mechanisms against various infectious microbes (continued)



	Infectious agent	Disease	Humoral immunity				Cell-mediated immunity	
			IgM	IgG	IgE	IgA	CD4 T cells (macrophages)	CD8 killer T cells
Bacteria	*Staphylococcus aureus*	Boils						
	Streptococcus pyogenes	Tonsilitis						
	Streptococcus pneumoniae	Pneumonia						
	Neisseria gonorrhoeae	Gonorrhea						
	Neisseria meningitidis	Meningitis						
	Corynebacterium diphtheriae	Diphtheria						
	Clostridium tetani	Tetanus						
	Treponema pallidum	Syphilis			Transient			
	Borrelia burgdorferi	Lyme disease			Transient			
	Salmonella typhi	Typhoid						
	Vibrio cholerae	Cholera						
	Legionella pneumophila	Legionnaire's disease						
	Rickettsia prowazekii	Typhus						
	Chlamydia trachomatis	Trachoma						
	Mycobacteria	Tuberculosis, leprosy						

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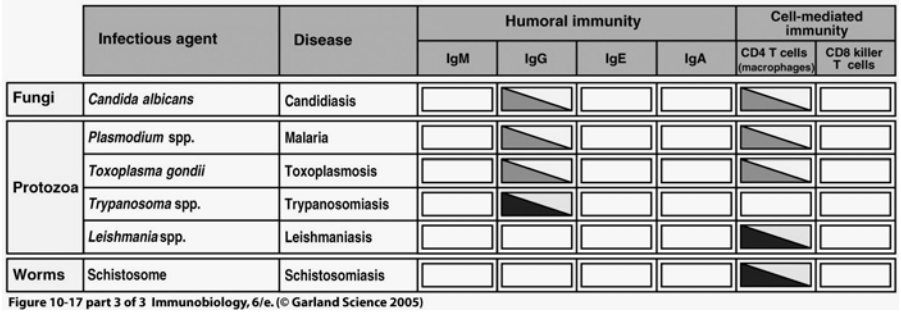
Janeway. Fig. 10.17. Protective Effector Mechanisms against various infectious microbes (continued)



	Infectious agent	Disease	Humoral immunity				Cell-mediated immunity	
			IgM	IgG	IgE	IgA	CD4 T cells (macrophages)	CD8 killer T cells
Fungi	*Candida albicans*	Candidiasis						
Protozoa	*Plasmodium* spp.	Malaria						
	Toxoplasma gondii	Toxoplasmosis						
	Trypanosoma spp.	Trypanosomiasis						
	Leishmania spp.	Leishmaniasis						
Worms	Schistosome	Schistosomiasis						

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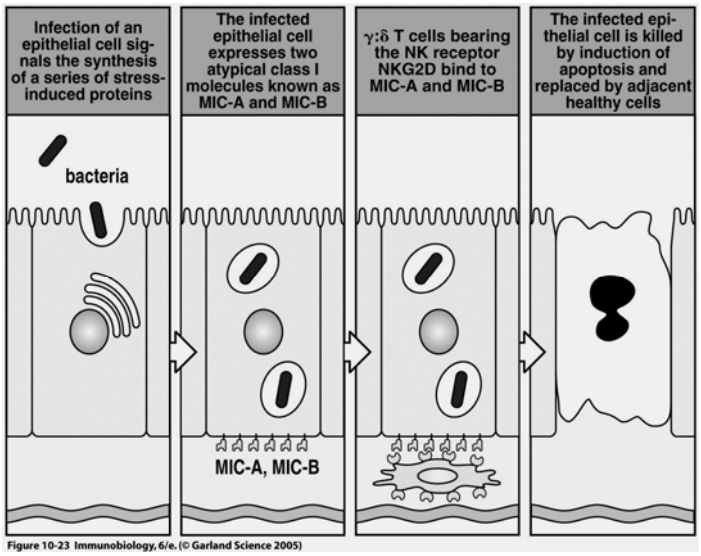
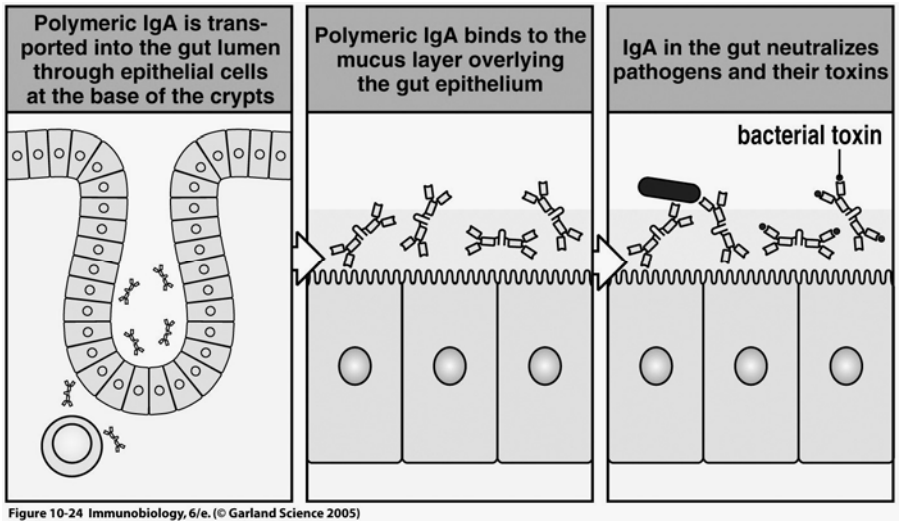
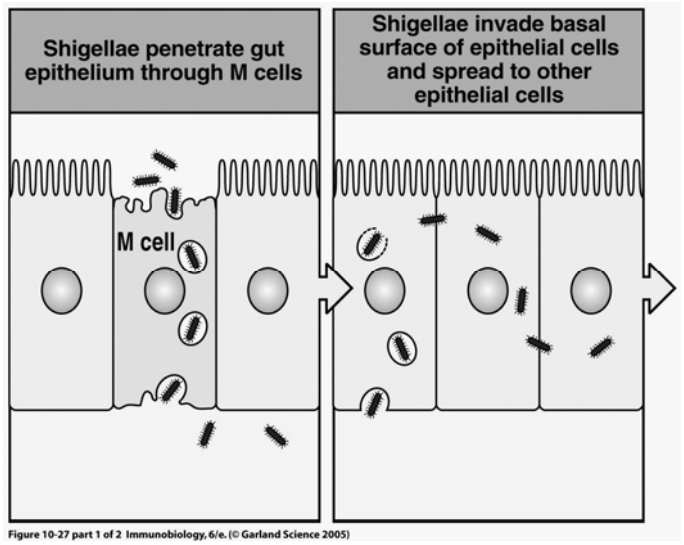
Janeway. Fig. 10.23. Mucosal γδT cell function.



Janeway. Fig. 10.24. Mucosal Secretory IgA function



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



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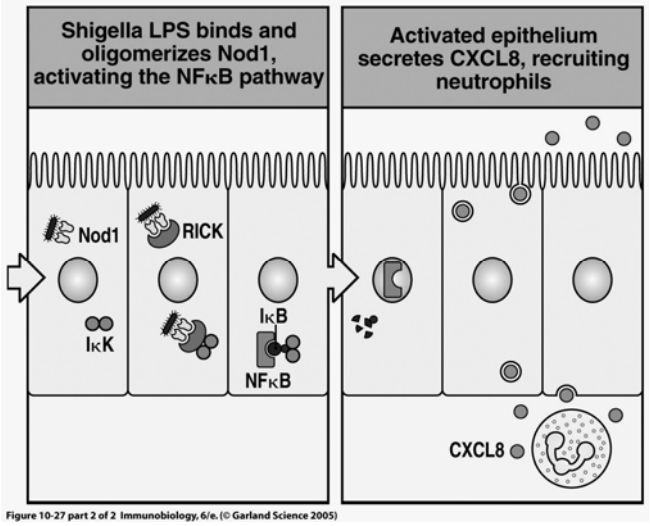
Janeway. Fig. 10.27. Recognition of intracellular infection by Nod1.(continued)



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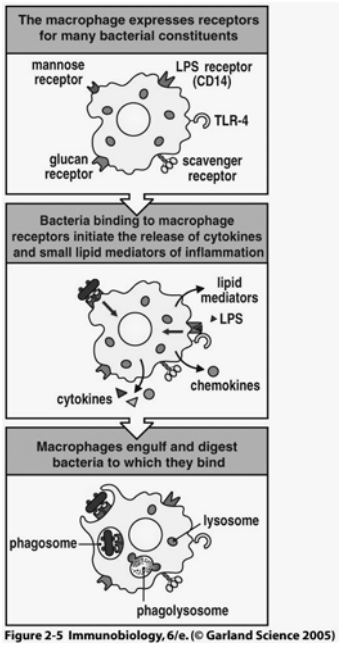

Figure 2-5 Immunobiology, 6/e. (© Garland Science 2005)

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

Janeway. Fig. 2.18. Microbial activation of complement pathways for inflammation.

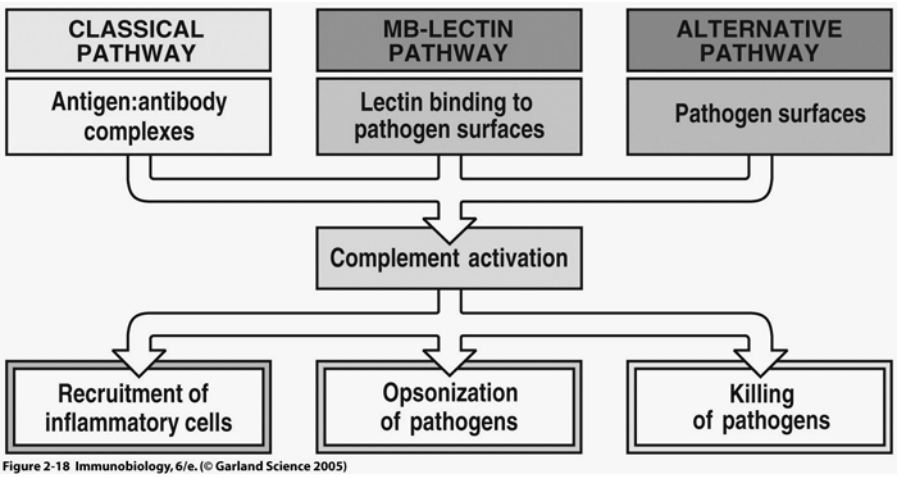

Figure 2-18 Immunobiology, 6/e. (© Garland Science 2005)

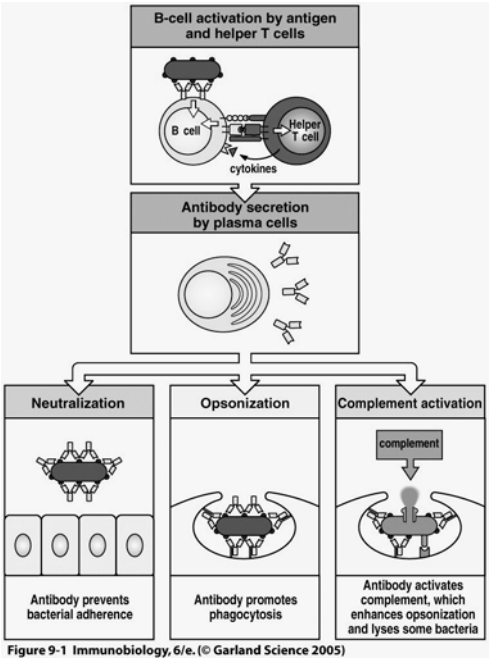

Figure 9-1 Immunobiology, 6/e. (© Garland Science 2005)

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

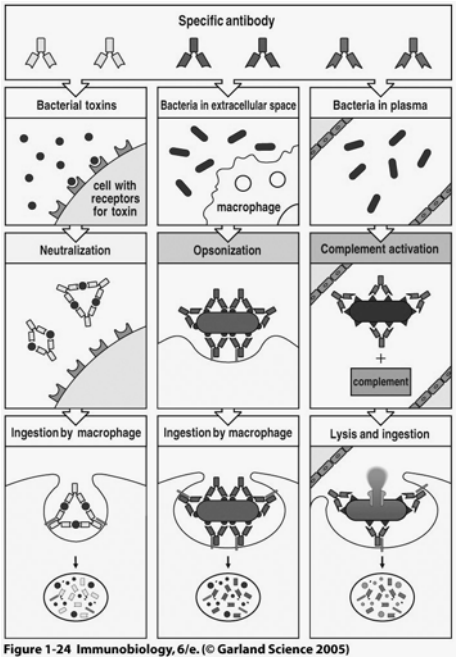

Figure 1-24 Immunobiology, 6/e. (© Garland Science 2005)

Janeway. Fig. 1.24 Protective effector mechanisms of antibody.

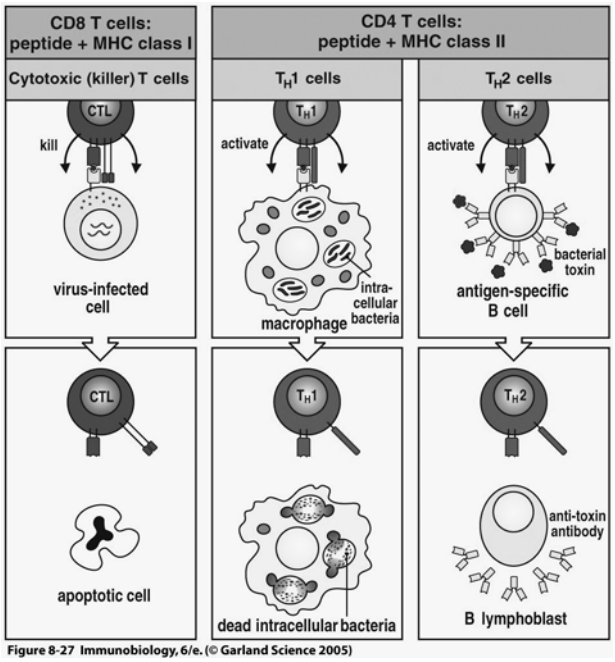

Figure 8-27 Immunobiology, 6/e. (© Garland Science 2005)

Janeway. Fig. 8.27. Effector T cell populations and effector mechanisms.

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

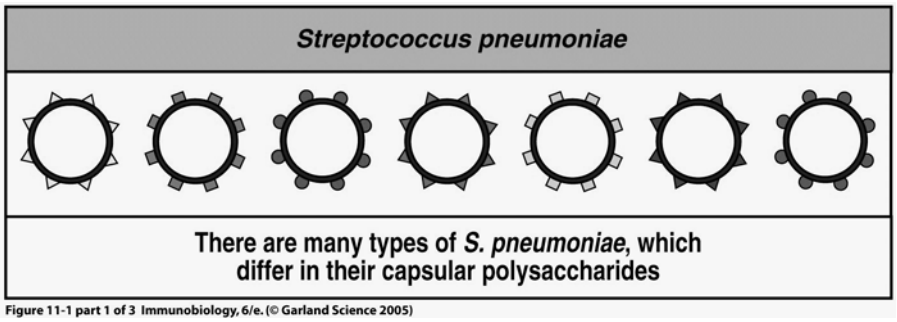

Figure 11-1 part 1 of 3 Immunobiology, 6/e. (© Garland Science 2005)

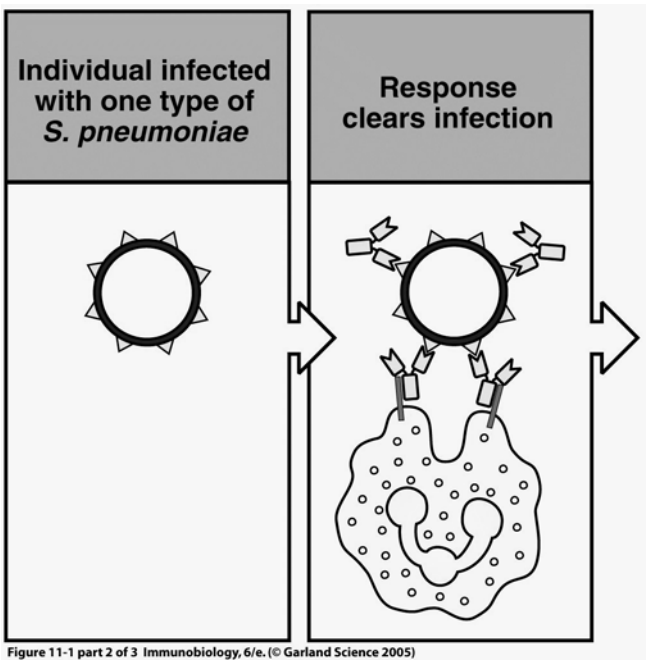

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Fig.11.1 continued

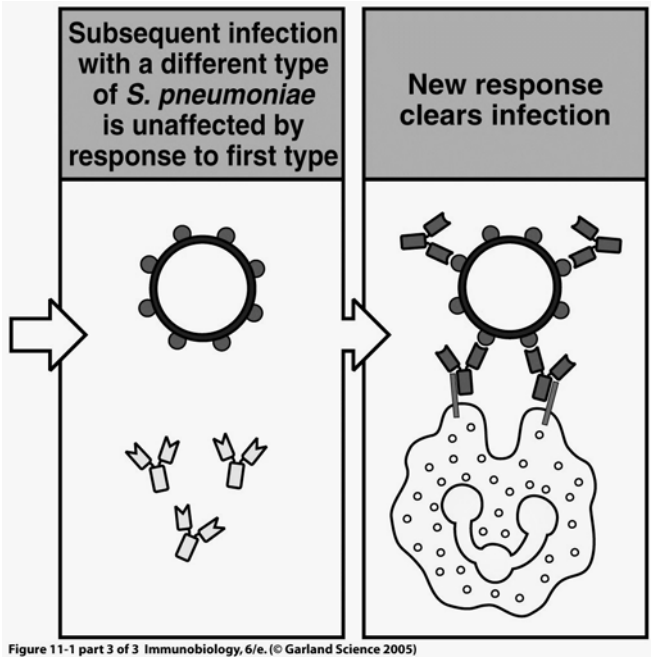

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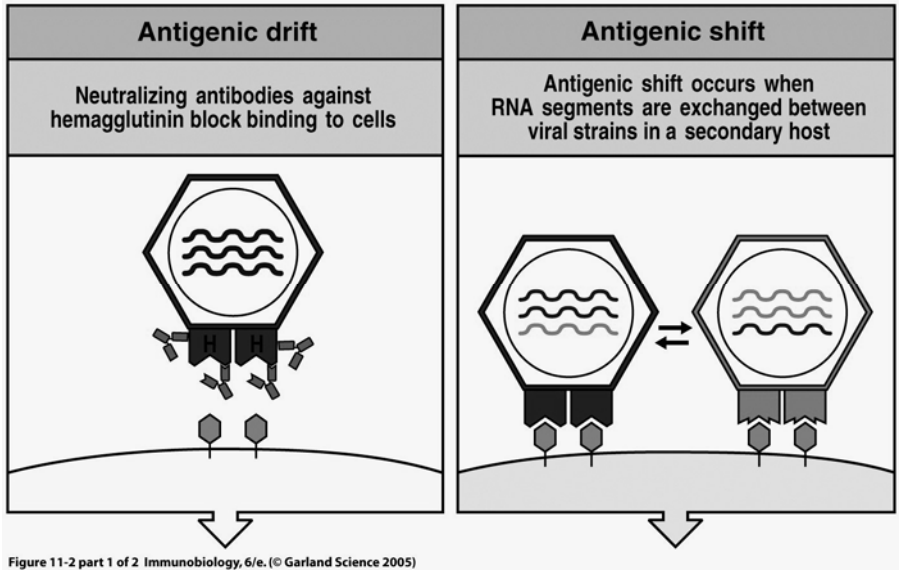
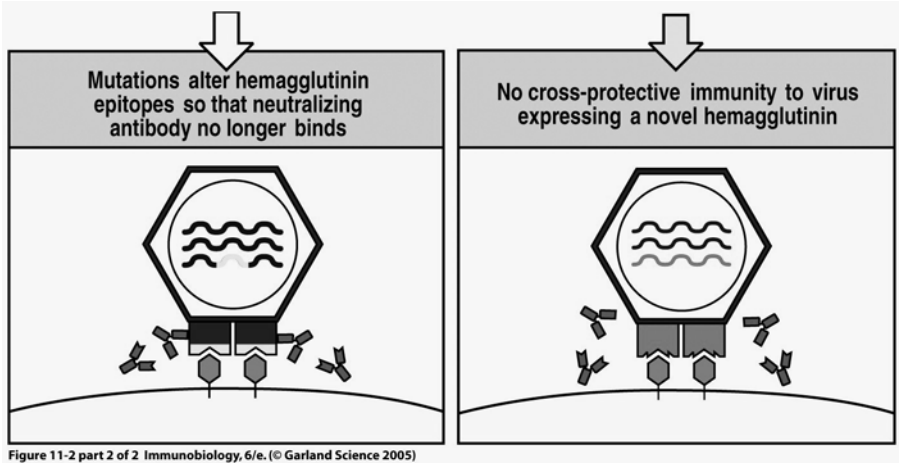
Fig. 11.1 continued

Janeway. Fig. 11.2. Immune Evasion via antigen drift/shift.



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



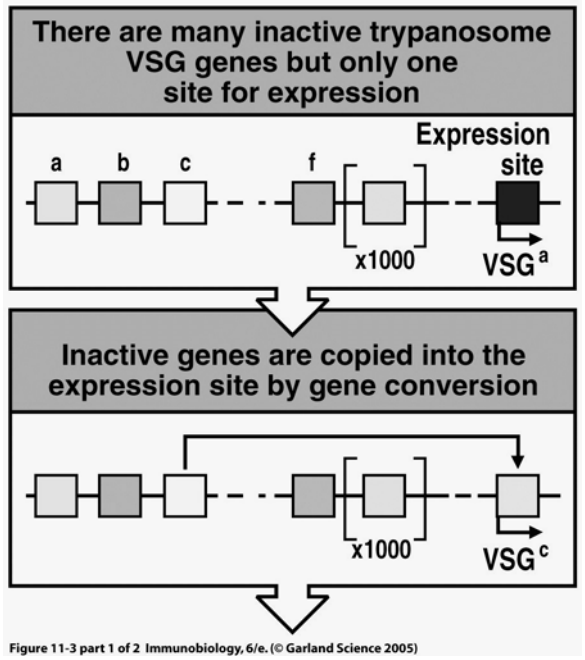
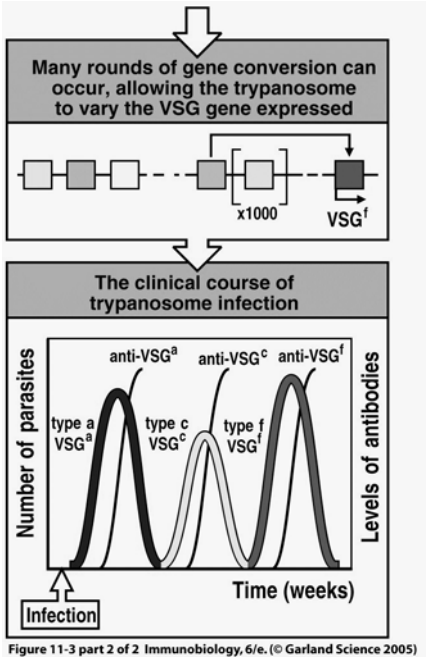


Figure 11-3 part 1 of 2 Immunobiology, 6/e. (© Garland Science 2005)

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



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

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

Viral strategy	Specific mechanism	Result	Virus examples
Inhibition of humoral immunity	Virally encoded Fc receptor	Blocks effector functions of antibodies bound to infected cells	Herpes simplex Cytomegalovirus
	Virally encoded complement receptor	Blocks complement-mediated effector pathways	Herpes simplex
	Virally encoded complement control protein	Inhibits complement activation by infected cell	Vaccinia

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Janeway. Fig. 11.5. Immune evasion mechanisms of herpes viruses. (continued)

Viral strategy	Specific mechanism	Result	Virus examples
Inhibition of inflammatory response	Virally encoded chemokine receptor homolog, eg, β-chemokine receptor	Sensitizes infected cells to effects of β-chemokine; advantage to virus unknown	Cytomegalovirus
	Virally encoded soluble cytokine receptor, eg, IL-1 receptor homolog, TNF receptor homolog, interferon-γ receptor homolog	Blocks effects of cytokines by inhibiting their interaction with host receptors	Vaccinia Rabbit myxoma virus
	Viral inhibition of adhesion molecule expression, eg, LFA-3 ICAM-1	Blocks adhesion of lymphocytes to infected cells	Epstein–Barr virus
	Protection from NFκB activation by short sequences that mimic TLRs	Blocks inflammatory responses elicited by IL-1 or bacterial pathogens	Vaccinia

Figure 11-5 part 2 of 3 Immunobiology, 6/e. (© Garland Science 2005)

Janeway. Fig. 11.5. Immune evasion mechanisms of herpes viruses. (continued)

Viral strategy	Specific mechanism	Result	Virus examples
Blocking of antigen processing and presentation	Inhibition of MHC class I expression	Impairs recognition of infected cells by cytotoxic T cells	Herpes simplex Cytomegalovirus
	Inhibition of peptide transport by TAP	Blocks peptide association with MHC class I	Herpes simplex
Immunosuppression of host	Virally encoded cytokine homolog of IL-10	Inhibits T_H1 lymphocytes Reduces interferon-γ production	Epstein–Barr virus

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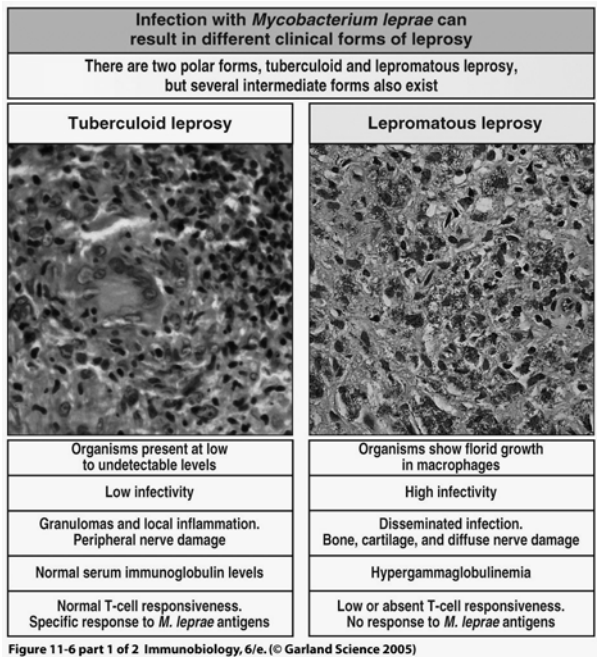
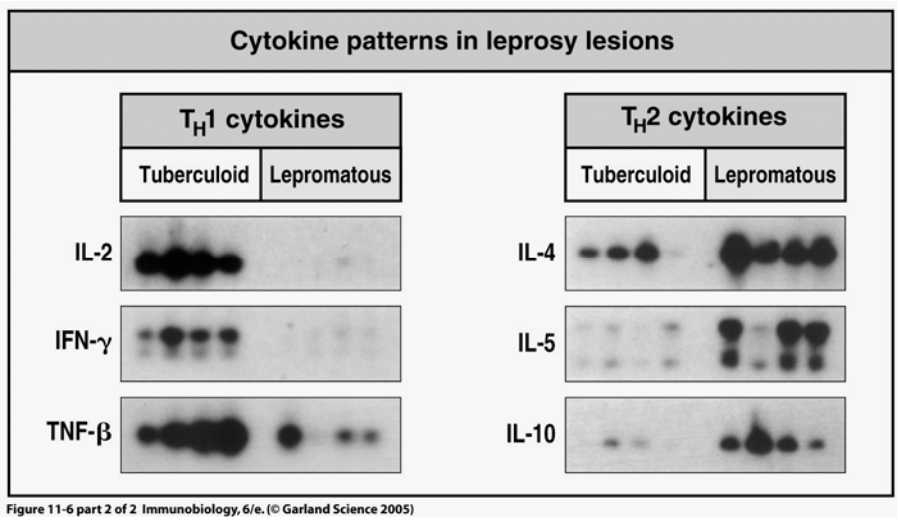


Figure 11-6 part 1 of 2 Immunobiology, 6/e. (© Garland Science 2005)

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

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



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Janeway. Fig. 14.21. Childhood vaccination schedule in USA.

Current immunization schedule for children (USA)

Vaccine given	1 month	2 months	4 months	6 months	12 months	15 months	18 months	4–6 years	11–12 years	14–16 years
Diphtheria–tetanus–pertussis (DTP/DTaP)									*	
Inactivated polio vaccine										
Measles/mumps/rubella (MMR)										
Pneumococcal conjugate										
Haemophilus B conjugate (HiBC)										
Hepatitis B										
Varicella										

Figure 14-21 Immunobiology, 6/e. (© Garland Science 2005)

Janeway. Fig. 14.23.

Features of effective vaccines	
Safe	Vaccine must not itself cause illness or death
Protective	Vaccine must protect against illness resulting from exposure to live pathogen
Gives sustained protection	Protection against illness must last for several years

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Features of effective vaccines	
Induces neutralizing antibody	Some pathogens (such as poliovirus) infect cells that cannot be replaced (eg, neurons). Neutralizing antibody is essential to prevent infection of such cells
Induces protective T cells	Some pathogens, particularly intracellular, are more effectively dealt with by cell-mediated responses
Practical considerations	Low cost per dose Biological stability Ease of administration Few side-effects

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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).