Immune Responses to Infectious Disease

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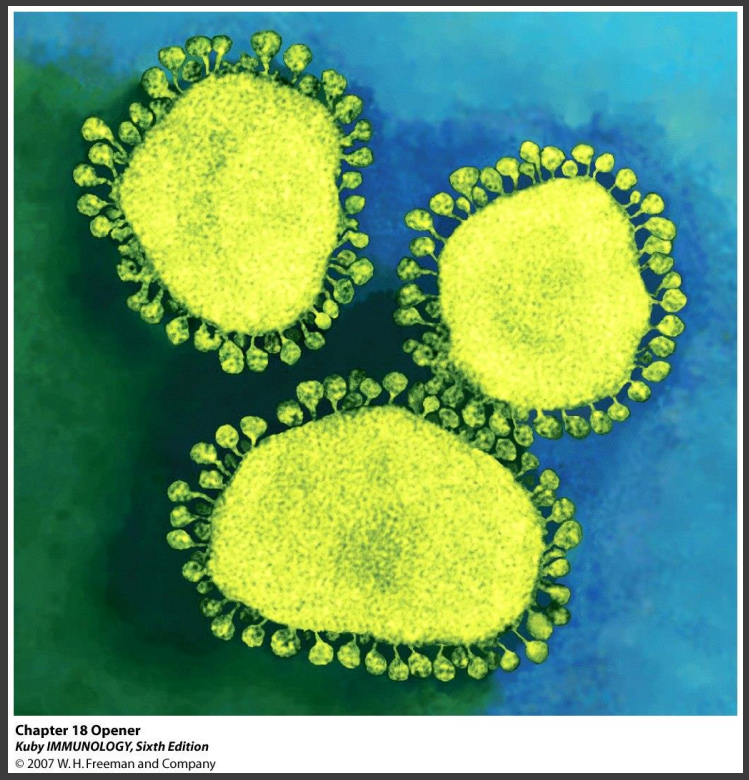
IMMUNOLOGY

Kindt • Goldsby • Osborne

Kuby IMMUNOLOGY

Sixth Edition

Immune Response to Infectious Diseases



Chapter 18 Opener
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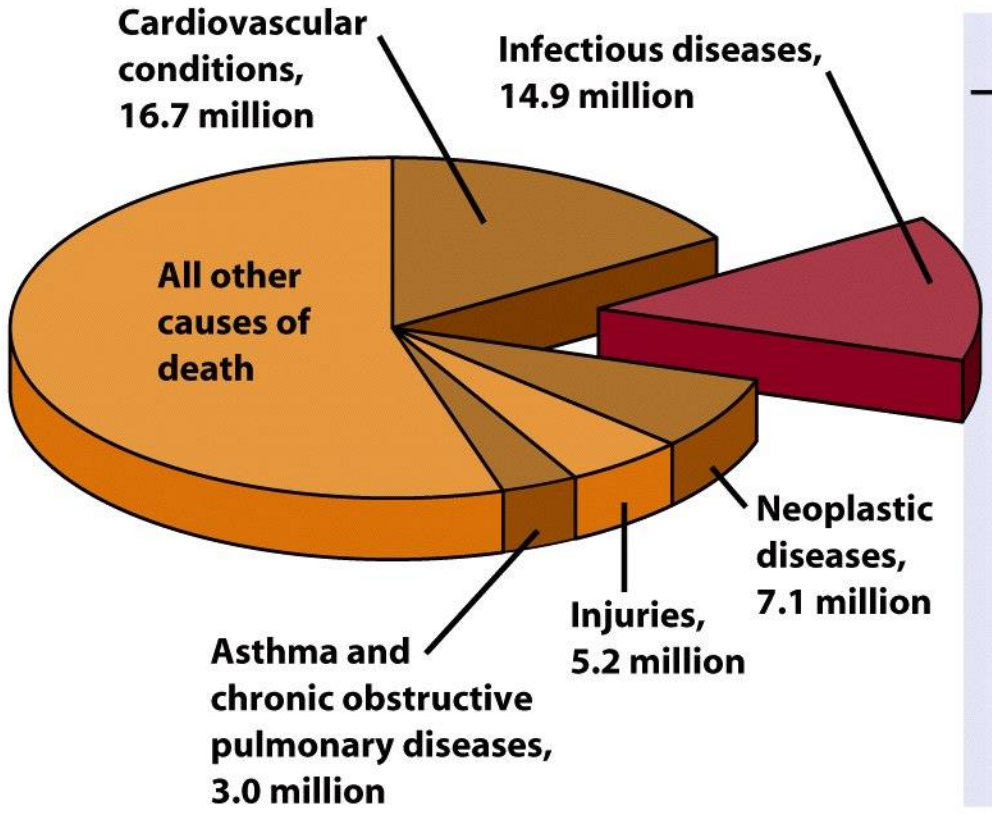
- Pathogens use variety of strategies to escape immune system



Infectious diseases	Annual deaths
Respiratory infections	3.96
HIV/AIDS	2.77
Diarrheal diseases	1.80
Tuberculosis	1.56
Vaccine-preventable childhood diseases	1.12
Malaria	1.27
STDs (other than HIV)	0.18
Meningitis	0.17
Hepatitis B and C	0.16
Tropical parasitic diseases	0.13
Dengue	0.02
Other infectious diseases	1.76

Figure 18-1
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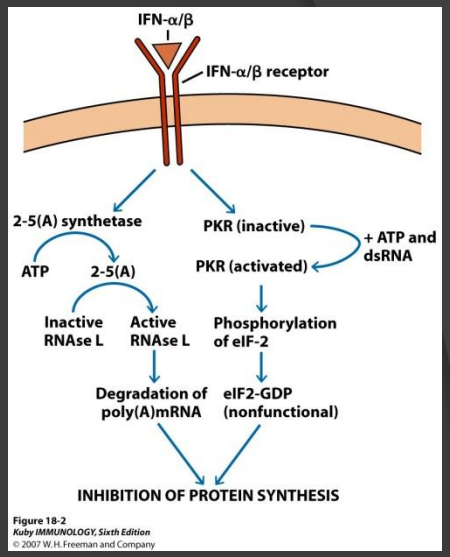
Viral Infections

- Long latency period before severe illness
  - HIV
- Efficient transmission during short illness
  - Influenza
- Life cycle in other host, vectors
  - West nile

Viral Infections



- Activation of NK cells
- Induction of interferons
  - Bind to IFN receptor
  - Activate JAK-STAT pathway
  - Induces transcription of genes of host cell
    - Enzyme that degrades viral RNA
- Can be neutralized by antibodies
- If viral DNA is integrated into host, cell must be killed

TABLE 18-1 Mechanisms of humoral and cell-mediated immune responses to viruses

Response type	Effector molecule or cell	Activity
Humoral	Antibody (especially secretory IgA)	Blocks binding of virus to host cells, thus preventing infection or reinfection
	IgG, IgM, and IgA antibody	Blocks fusion of viral envelope with host cell's plasma membrane
	IgG and IgM antibody	Enhances phagocytosis of viral particles (opsonization)
	IgM antibody	Agglutinates viral particles
	Complement activated by IgG or IgM antibody	Mediates opsonization by C3b and lysis of enveloped viral particles by membrane-attack complex
Cell mediated	IFN-γ secreted by T_H or T_C cells	Has direct antiviral activity
	Cytotoxic T lymphocytes (CTLs)	Kill virus-infected self cells
	NK cells and macrophages	Kill virus-infected cells by antibody-dependent cell-mediated cytotoxicity (ADCC)

Table 18-1
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Viral Infections

- Evading host defenses
  - Block or inhibit production of interferons
  - Inhibition of antigen presentation
  - Evade complement
  - Cause general immunosuppression

Influenza – "Flu"

- Respiratory illness
- Responsible for some of the worse pandemics in history
- Spherical virion surrounded by lipid bilayer acquired from host
  - 2 glycoproteins – hemagglutin (HA) and neuraminidase (NA)
  - Antigenic variation in these (mutations leading to new strains) cause problems in developing sustained immunity in the population

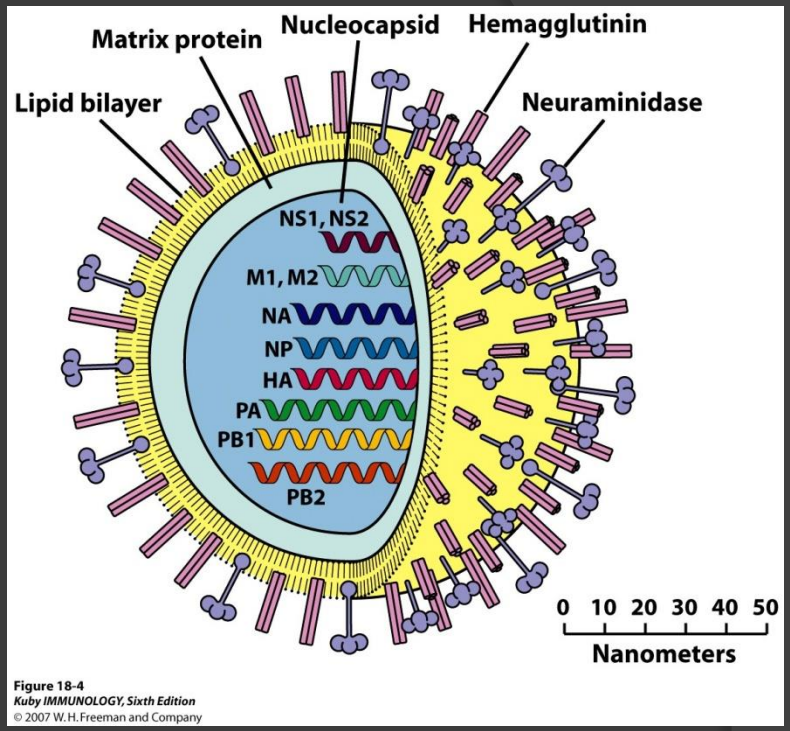

Figure 18-4
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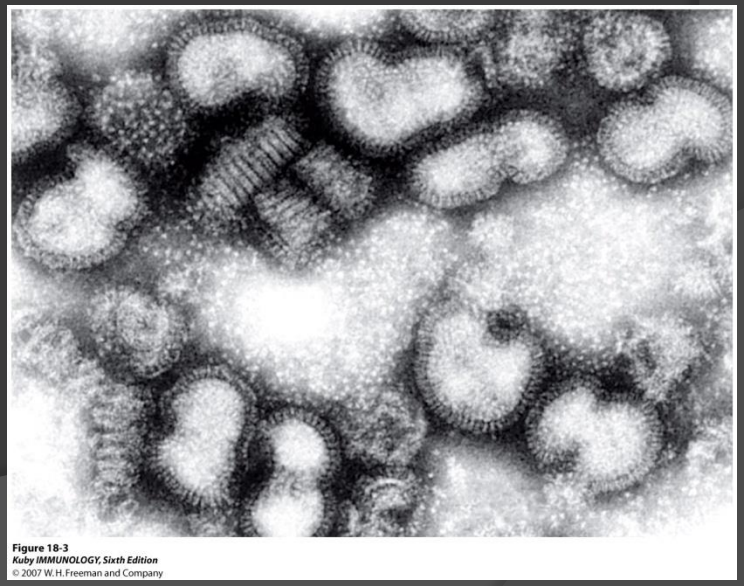
Figure 18-3
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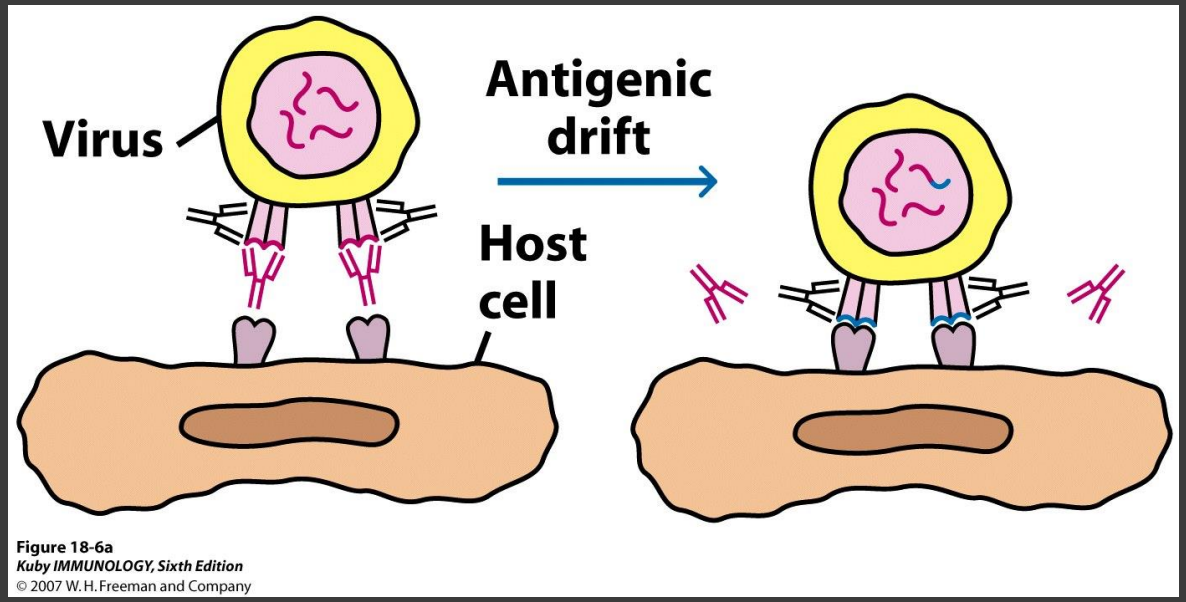

Figure 18-6a
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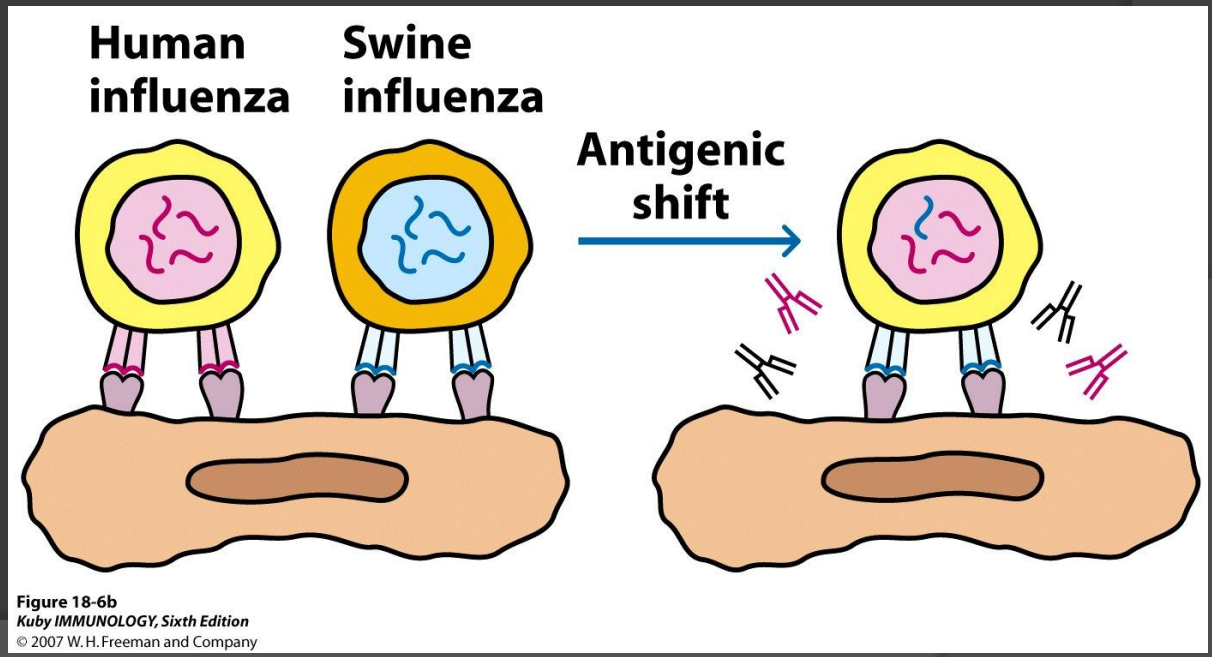

Figure 18-6b
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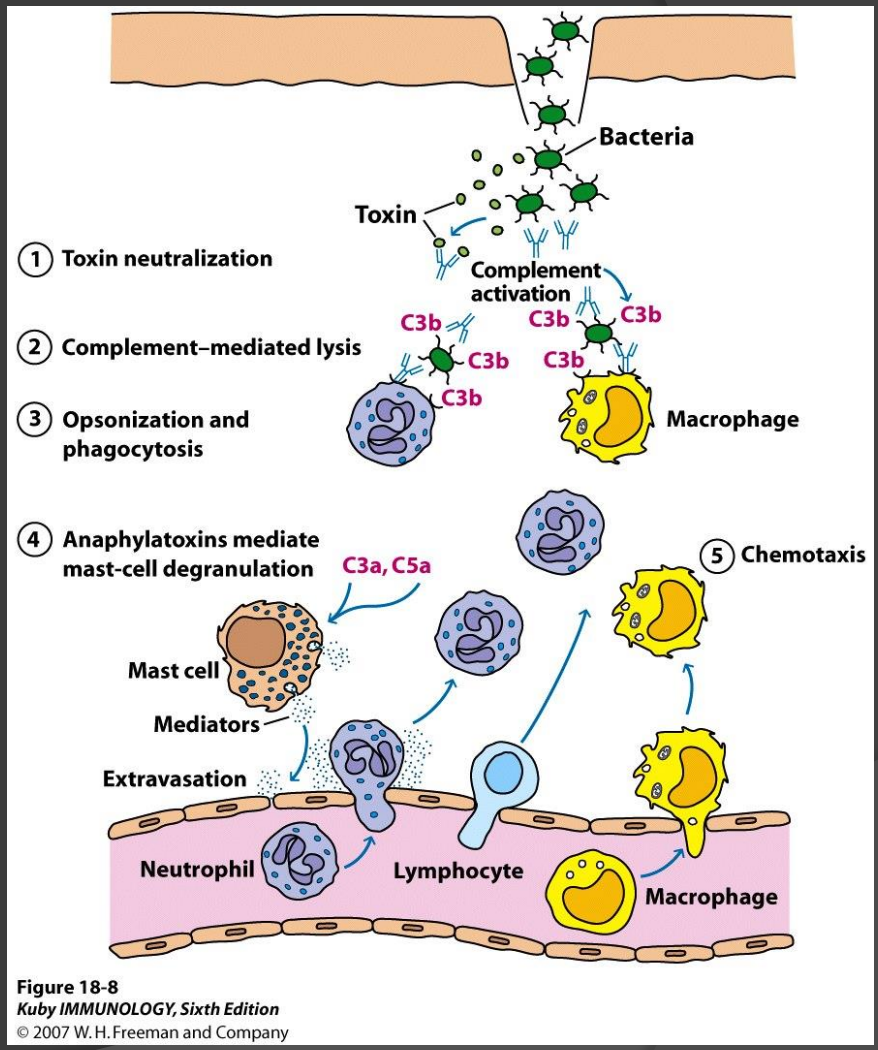
Bacterial Infections

- Immunity mainly achieved by antibodies
  - Unless bacteria is capable of intracellular growth
- Depending on # of organisms entering and virulence, different levels of host defense enlisted
  - If inoculum size and virulence is low, phagocytes may be able to eliminate the bacteria



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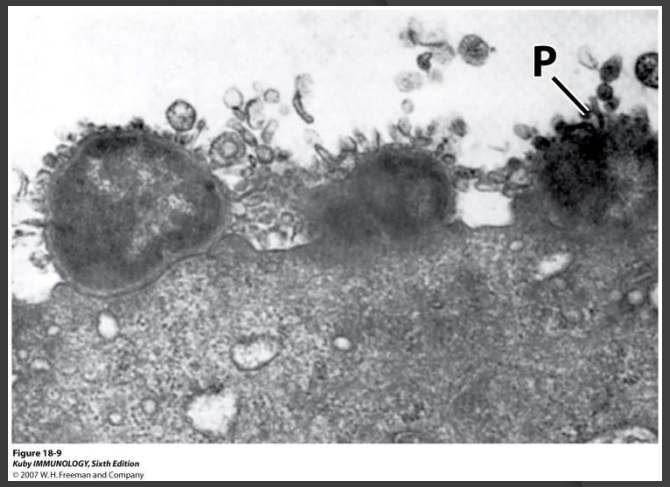
Bacterial Infections



- 4 steps:
  - Attachment to host cells
  - Proliferation
  - Invasion of host tissue
  - Toxin-induced damage to host cells
- Host defenses act at each of these sites, some bacteria have developed ways to avoid

TABLE 18-3 Host immune responses to bacterial infection and bacterial evasion mechanisms

Infection process	Host defense	Bacterial evasion mechanisms
Attachment to host cells	Blockage of attachment by secretory IgA antibodies	Secretion of proteases that cleave secretory IgA dimers (*Neisseria meningitidis, N. gonorrhoeae, Haemophilus influenzae*) Antigenic variation in attachment structures (pili of *N. gonorrhoeae*)
Proliferation	Phagocytosis (Ab- and C3b-mediated opsonization)	Production of surface structures (polysaccharide capsule, M protein, fibrin coat) that inhibit phagocytic cells Mechanisms for surviving within phagocytic cells Induction of apoptosis in macrophages (*Shigella flexneri*)
	Complement-mediated lysis and localized inflammatory response	Generalized resistance of gram-positive bacteria to complement-mediated lysis Insertion of membrane-attack complex prevented by long side chain in cell-wall LPS (some gram-negative bacteria)
Invasion of host tissues	Ab-mediated agglutination	Secretion of elastase that inactivates C3a and C5a (*Pseudomonas*)
Toxin-induced damage to host cells	Neutralization of toxin by antibody	Secretion of hyaluronidase, which enhances bacterial invasiveness

Table 18-3
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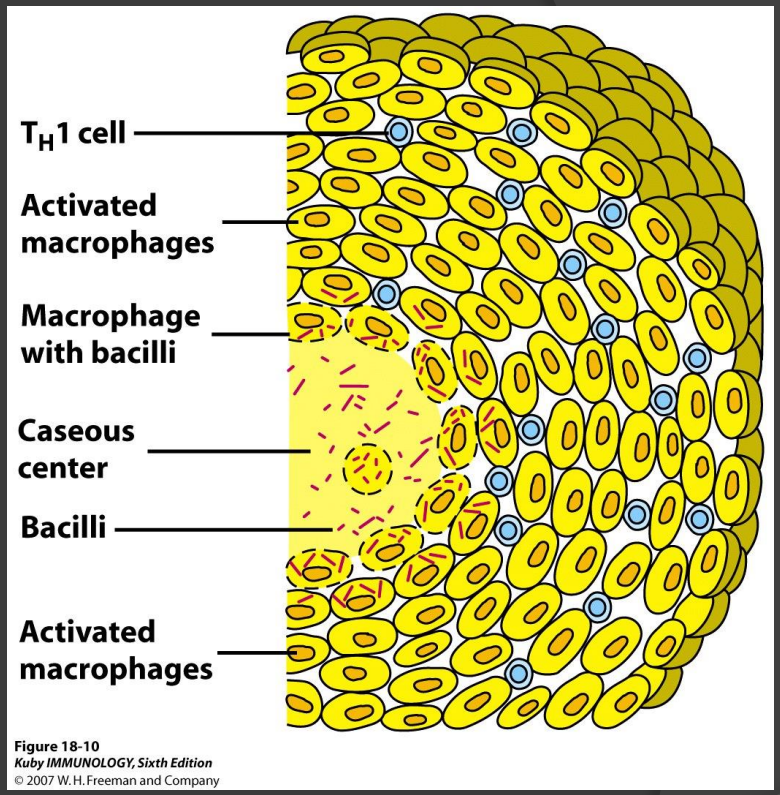
Immune responses can contribute to bacterial pathogenesis

- Overproduction of cytokines
  - Septic shock, food poisoning, toxic shock
- Intracellular bacteria
  - Chronic antigenic activation of CD4+ T cells
  - Leads to tissue destruction
  - Characteristics of delayed-type hypersensitivity
  - Leads to development of granuloma and necrosis

Tuberculosis

- Intracellular bacillus
- CD4+ T cell response
  - Responsible for most of the tissue damage
  - This necrosis can be seen when tested for TB



- Tubercle formed in pulmonary tuberculosis

Parasitic Disease

- Protozoan and helminthic organsims
- Malaria – *Plasmodium*, protozoan
  - Complex life cycle

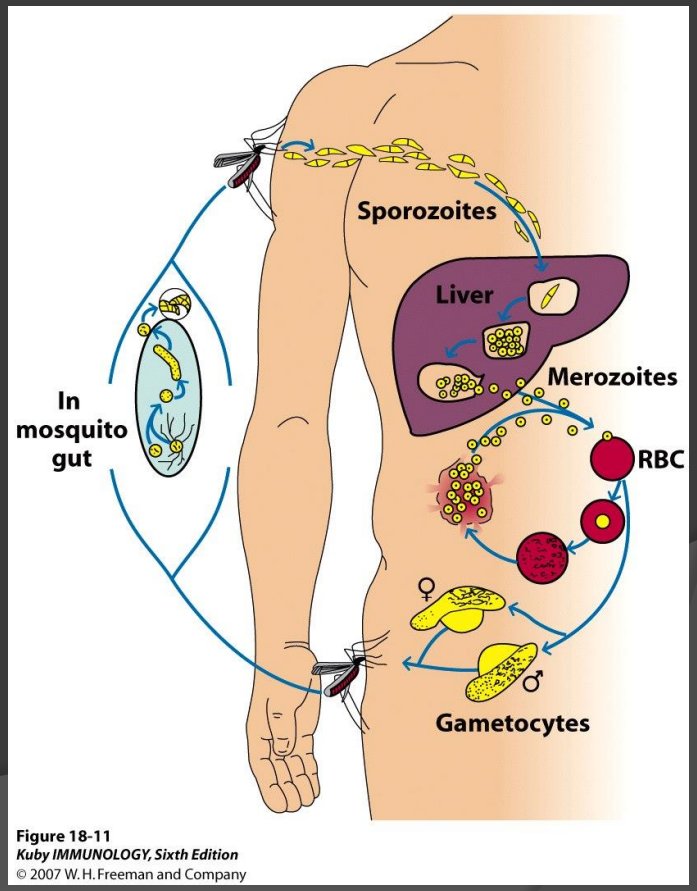


Figure 18-11
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Parasitic Infections

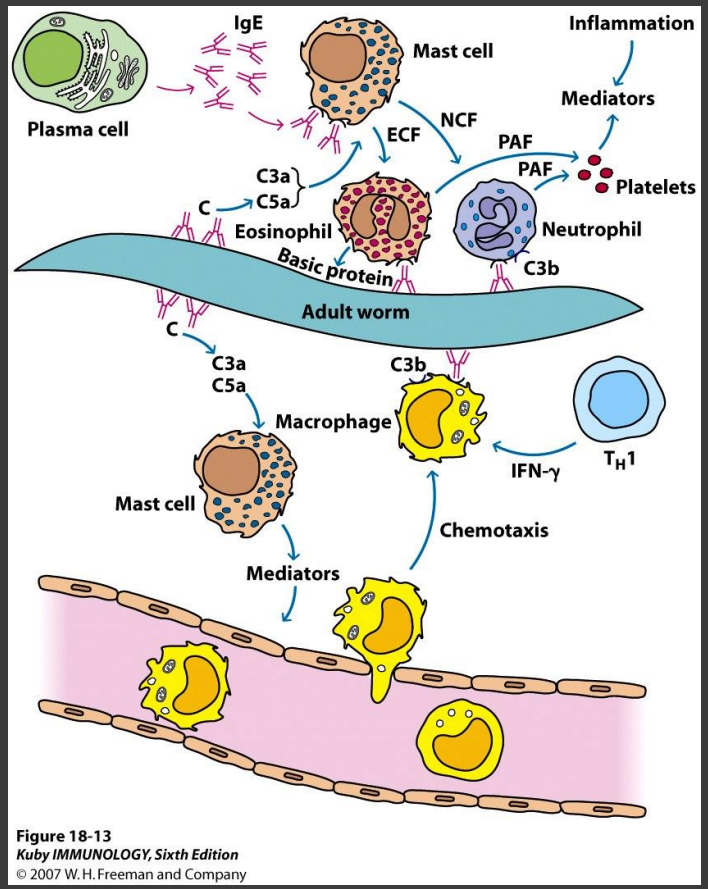

Figure 18-13
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- Helminthes
  - IgE plays big role

Fungal Infections

- Most fungal infections of healthy individuals resolve rapidly
- Barriers of innate immunity control most fungi
- Mannose-binding protein recognizes some major fungal pathogens

TABLE 18-4 Classification of fungal diseases

Site of infection	Superficial	Epidermis, no inflammation
	Cutaneous	Skin, hair, nails
	Subcutaneous	Wounds, usually inflammatory
	Deep or systemic	Lungs, abdominal viscera, bones, CNS
Route of acquistion neous	Exogenous	Environmental, airborne, cutaneous or percuta-
	Endogenous	Latent reactivation, commensal organism
Virulence	Primary	Inherently virulent, infects healthy host
	Opportunistic	Low virulence, infects immunocompromised host

Table 18-4
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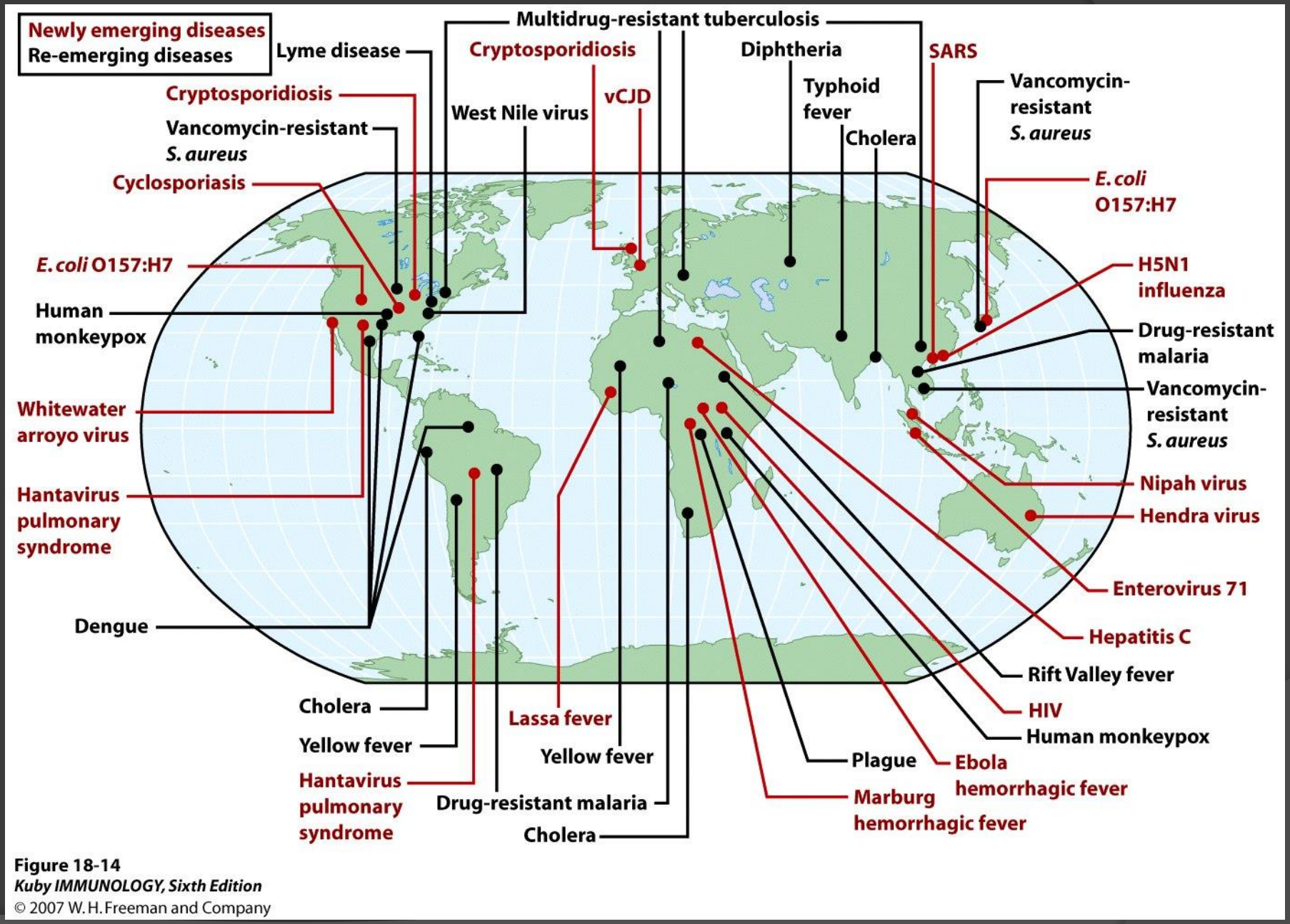

Figure 18-14
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Bioterrorism

- Something to be concerned with….

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