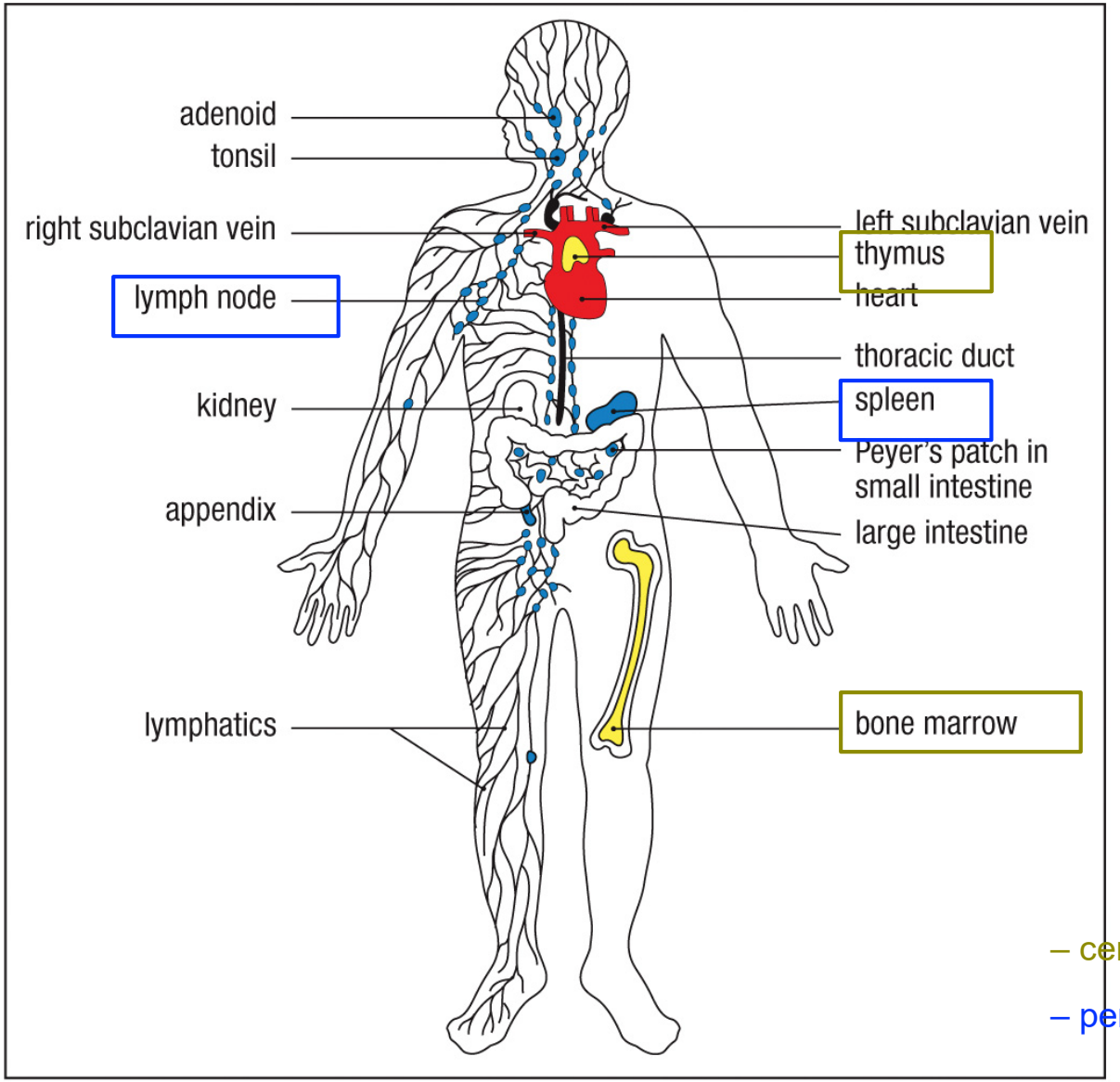
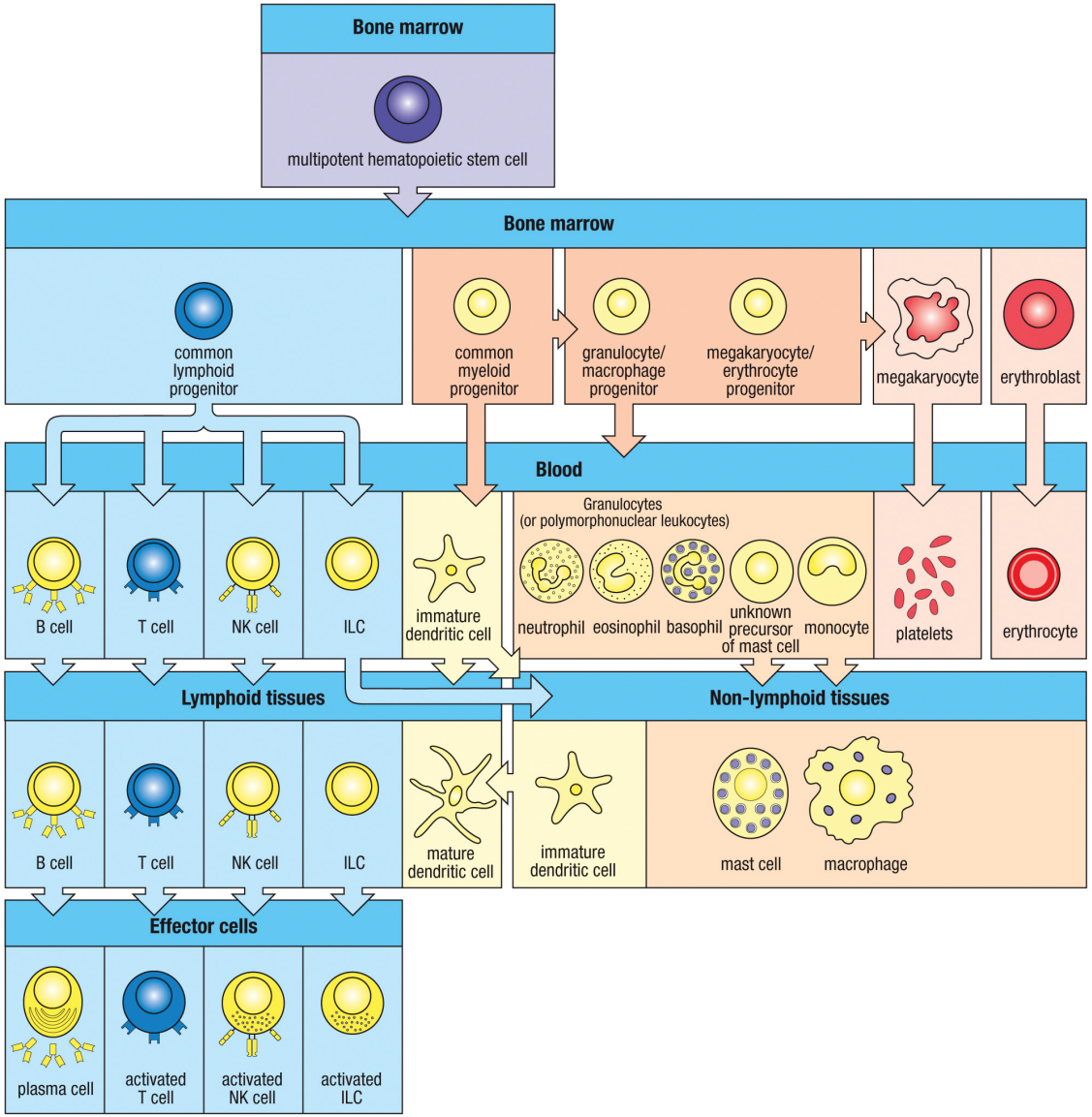
Lymphoid Tissue



– central lymphoid organ

– peripheral lymphoid organ

Hematopoiesis



Outline

Course of the immune response

- Pathogen entry point
- First encounter w/ immune system: local infection & inflammation
- Full activation of immune response: peripheral lymphoid organs
- Immunological memmory

Timing of Adult Immune Response

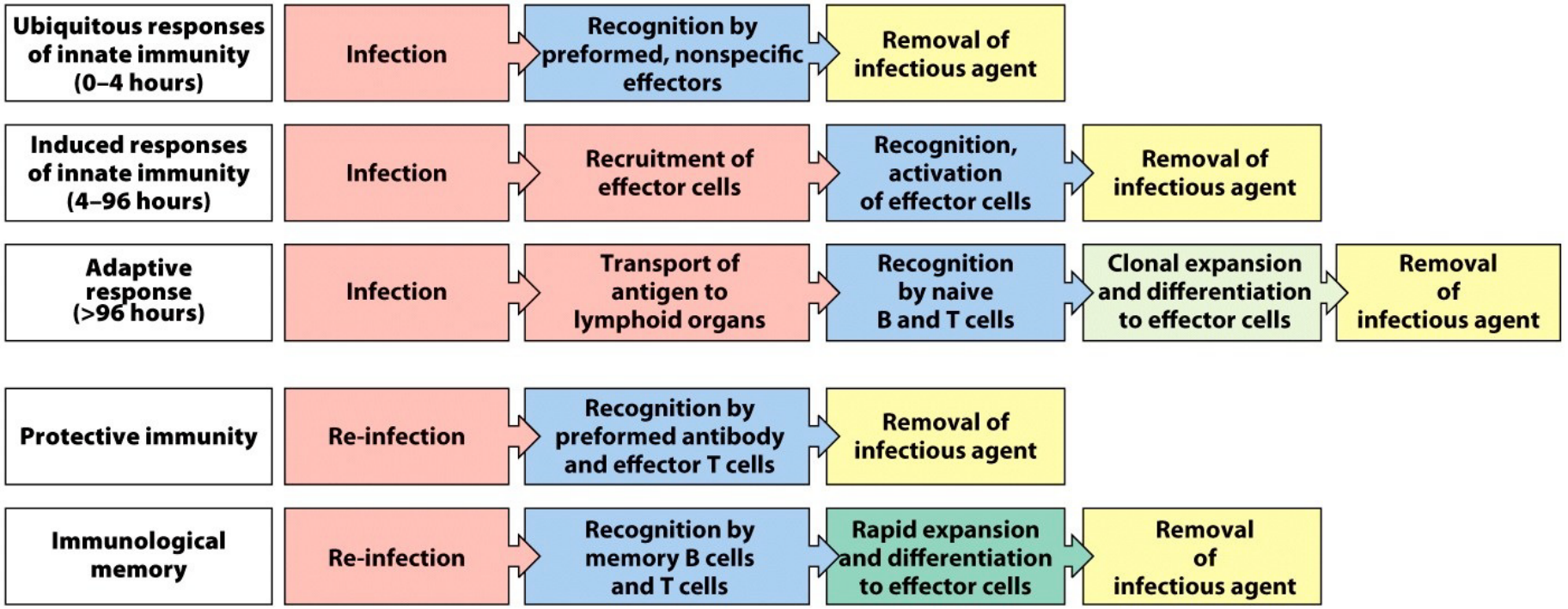
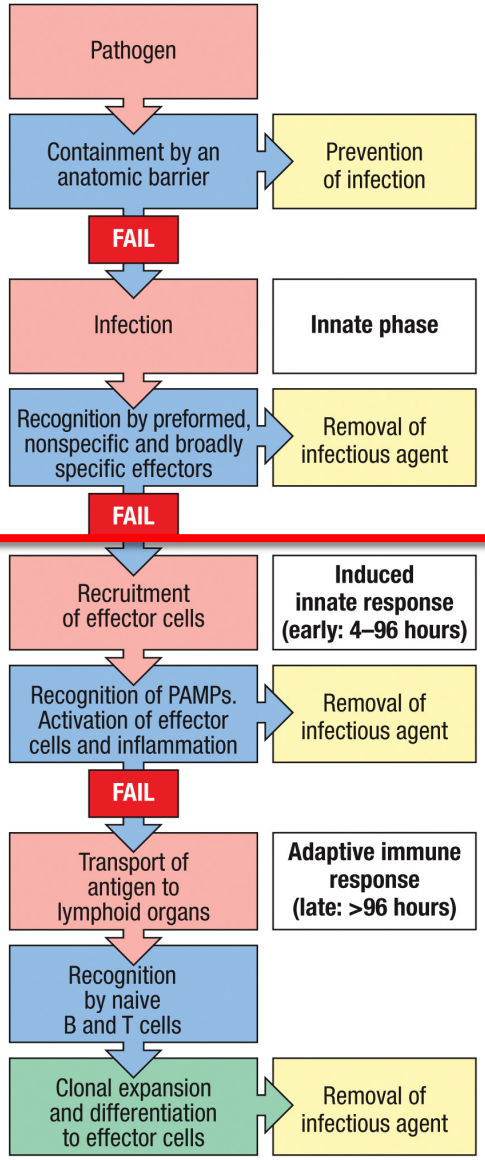


Figure 10.41 The Immune System, 3ed. (© Garland Science 2009)

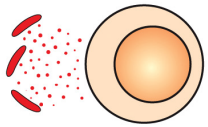
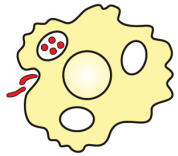
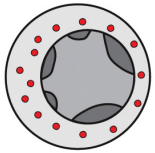
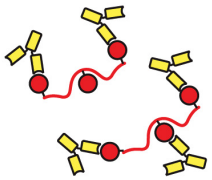
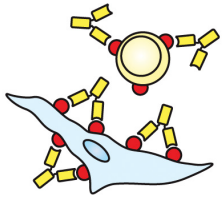
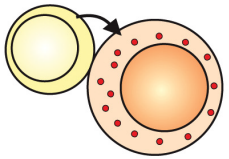
Activation of the Immune Response



Not apparent

symptoms

Pathogens Damage Tissues

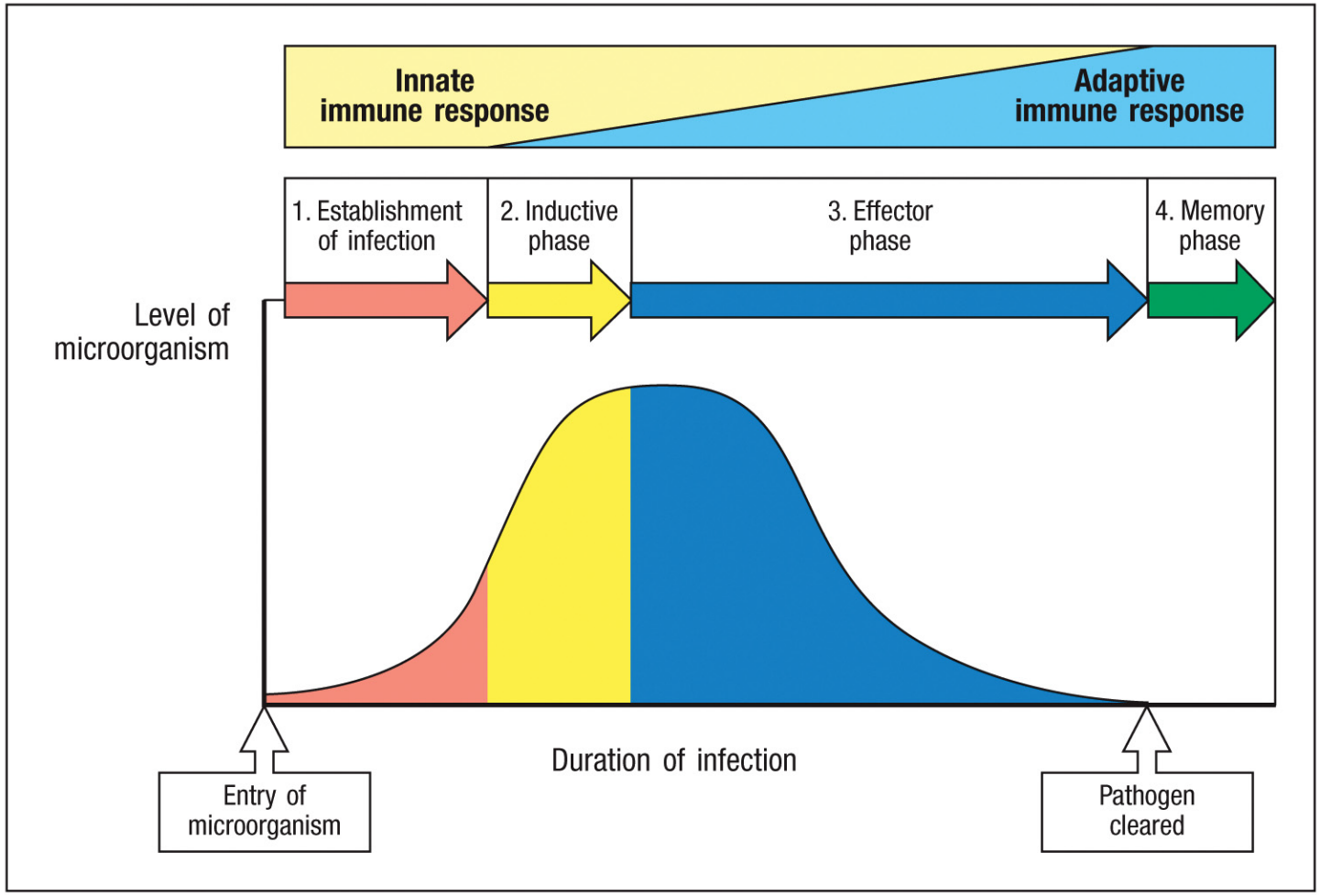
	Direct mechanisms of tissue damage by pathogens			Indirect mechanisms of tissue damage by pathogens		
	Exotoxin production	**Endotoxin**	**Direct cytopathic effect**	**Immune complexes**	**Anti-host antibody**	**Cell-mediated immunity**
Pathogenic mechanism						
Infectious agent	*Streptococcus pyogenes* *Staphylococcus aureus* *Corynebacterium diphtheriae* *Clostridium tetani* *Vibrio cholerae*	*Escherichia coli* *Haemophilus influenzae* *Salmonella enterica* ssp. *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)	Hepatitis B virus *Plasmodium* *Streptococcus pyogenes* *Treponema pallidum* Most acute infections	*Streptococcus pyogenes* *Mycoplasma pneumoniae*	Lymphocytic choriomeningitis virus Herpes simplex virus *Mycobacterium tuberculosis* *Mycobacterium leprae* *Borrelia burgdorferi* *Schistosoma mansoni*
Disease	Tonsilitis, scarlet fever Boils, toxic shock syndrome, food poisoning Diphtheria Tetanus Cholera	Gram-negative sepsis Meningitis, pneumonia Typhoid fever Bacillary dysentery Wound infection Plague	Smallpox Chickenpox, shingles Hepatitis Poliomyelitis Measles, subacute sclerosing panencephalitis Influenza Cold sores Kaposi's sarcoma	Kidney disease Vascular deposits Glomerulonephritis Kidney damage in secondary syphilis Transient renal deposits	Rheumatic fever Hemolytic anemia	Aseptic meningitis Herpes stromal keratitis Tuberculosis Tuberculoid leprosy Lyme arthritis Schistosomiasis

Inflammation

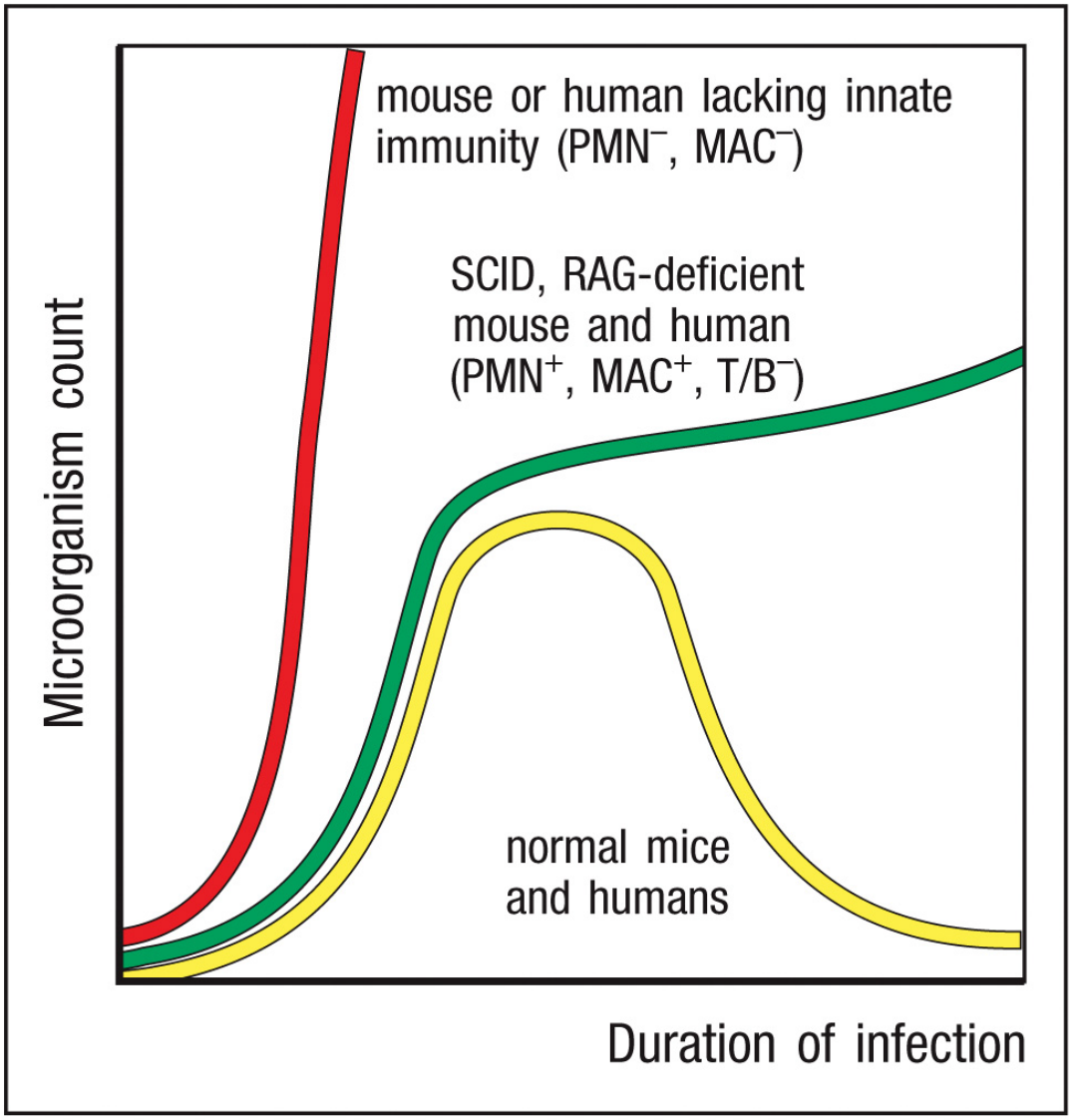
- **Commensal organisms cause little host damage while pathogens damage host tissues by a variety of mechanisms**
-

A.True/B.False: Our immune system efficiently kills all categories of microbes that attempt to colonize our bodies.

Course of Acute Infection



Consequences of Immunodeficiency



Outline

Course of the immune response

- Pathogen entry point
- First encounter w/ immune system: local infection & inflammation
- Full activation of immune response: peripheral lymphoid organs
- Immunological memory

Pathogen Entry Points

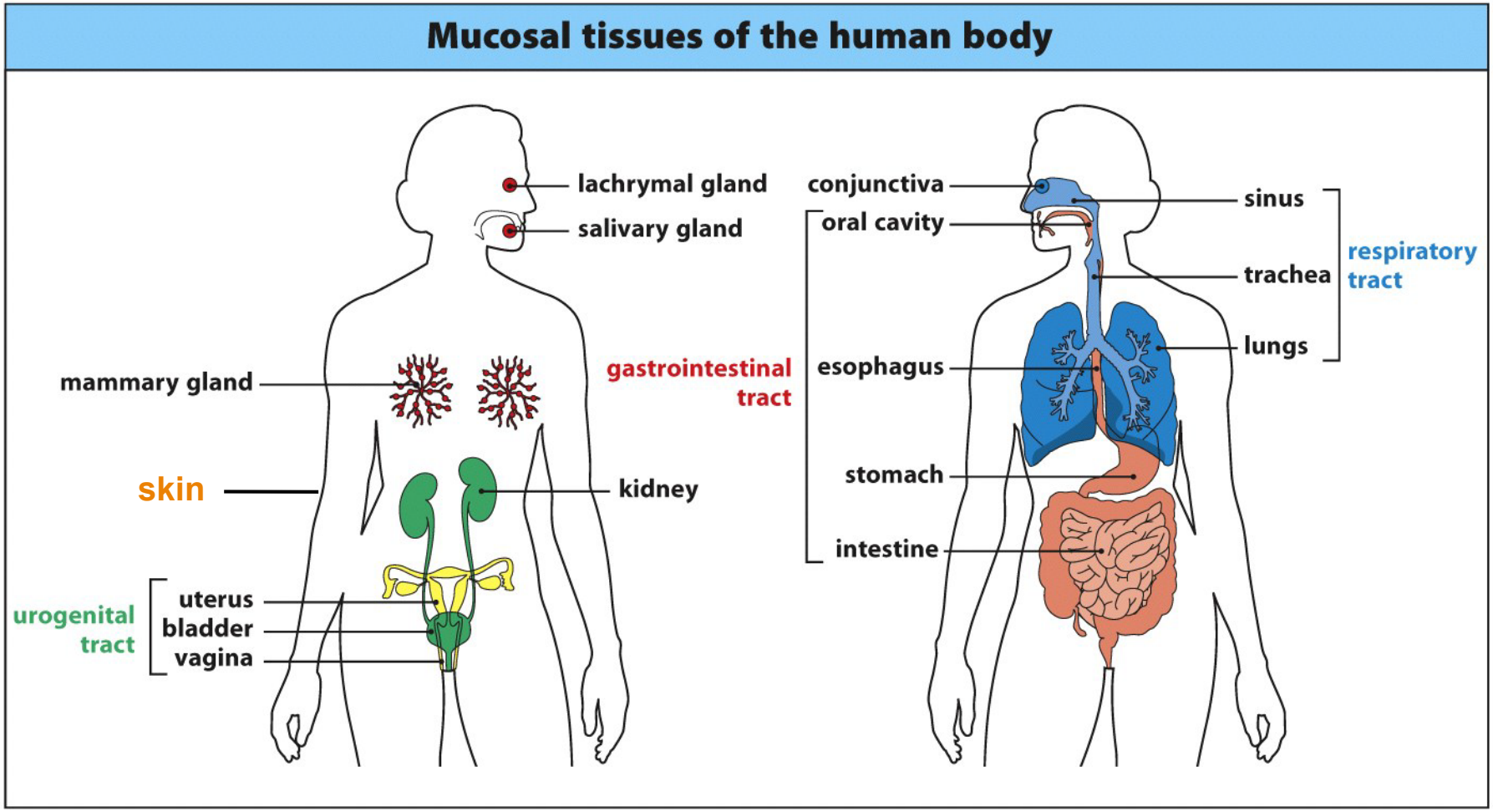
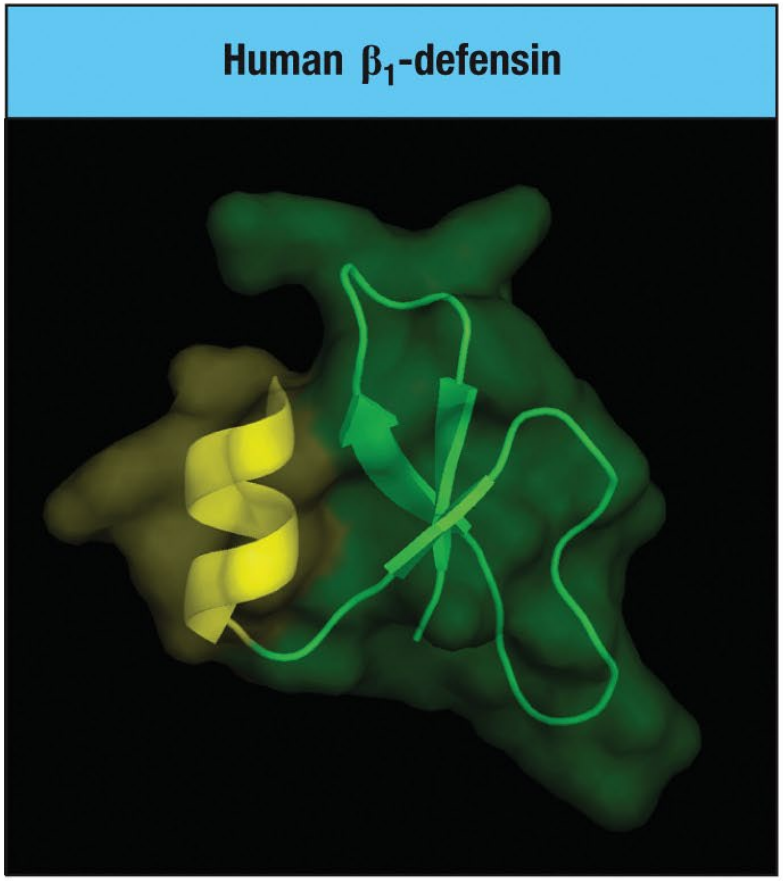


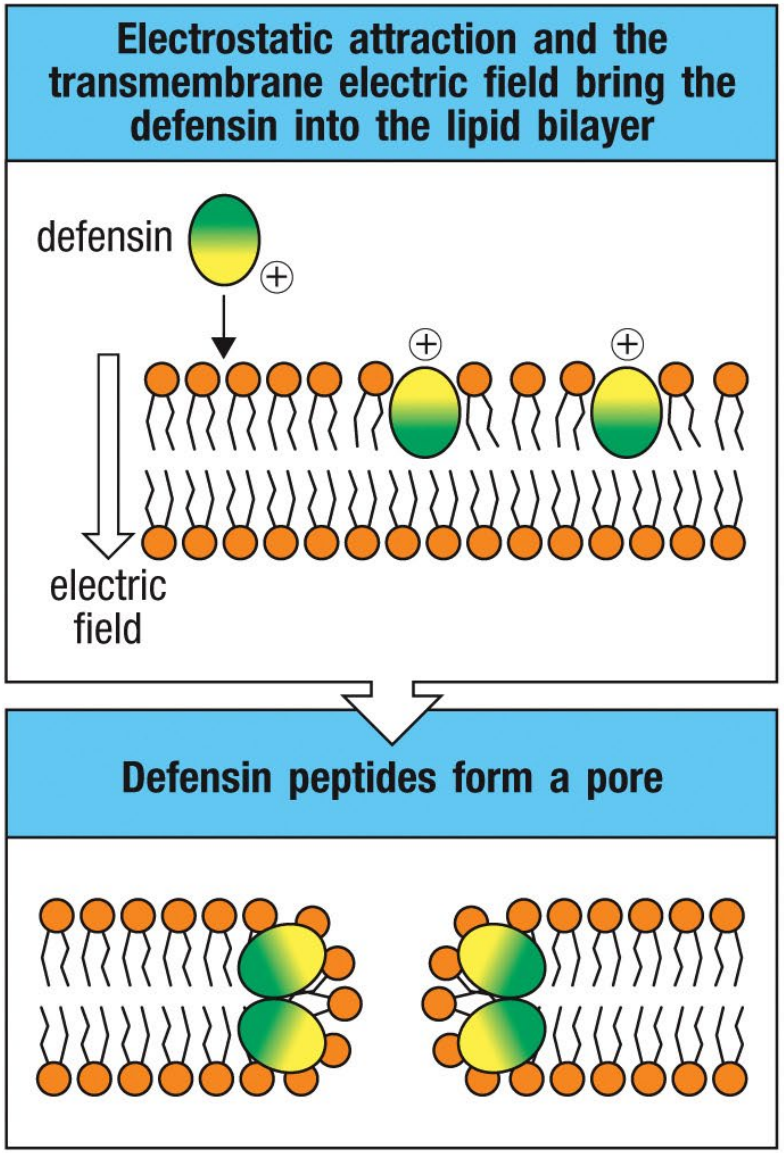
Figure 12.1 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

Barriers: The First Line of Defense

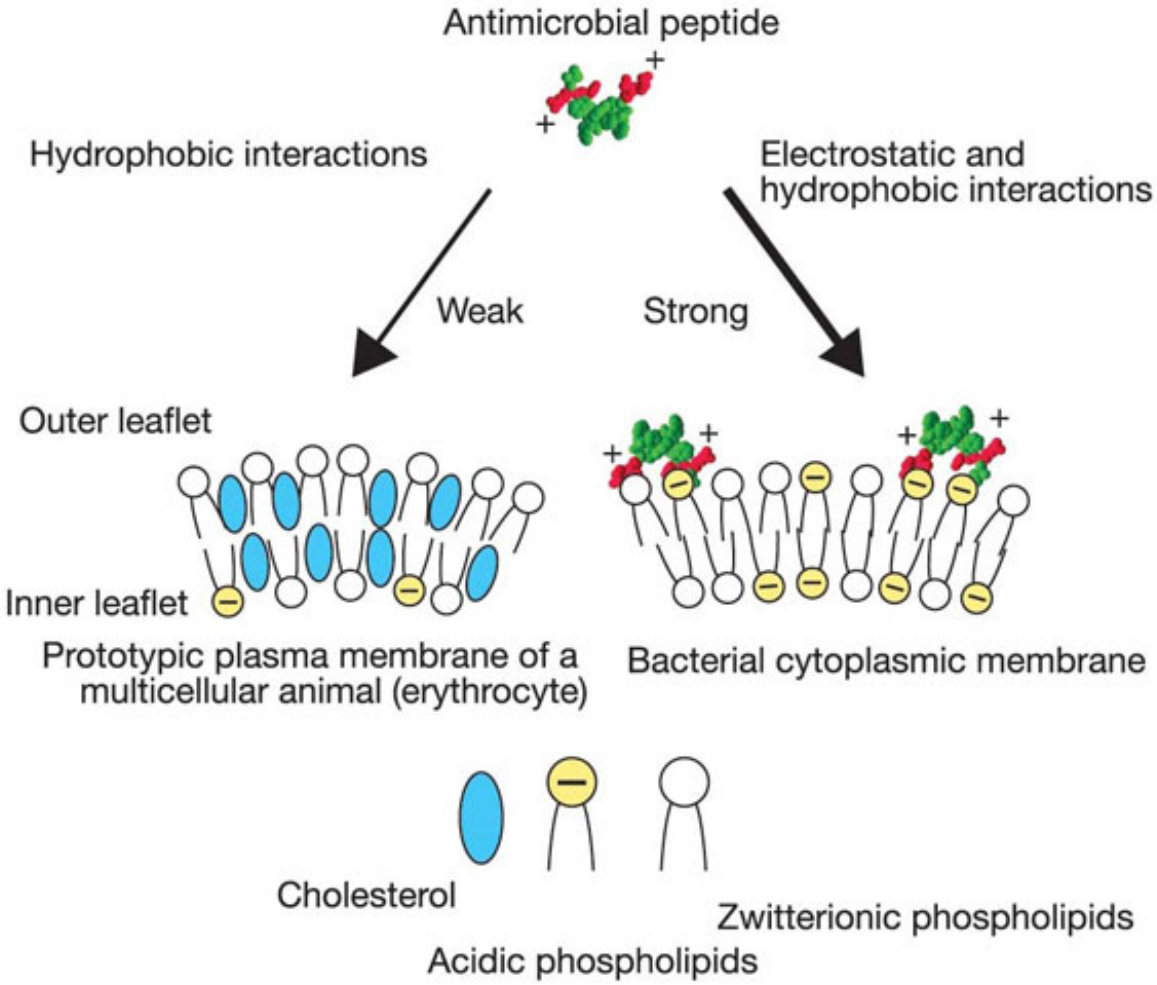
	Skin	Gut	Lungs	Eyes/nose/oral cavity
	Stratified epithelium	Single cell layer of columnar epithelium	Upper airway: pseudostratified columnar epithelium Lower airway: single cell layer of columnar epithelium	Pseudostratified columnar epithelium
Mechanical	Epithelial cells joined by tight junctions			
	Longitudinal flow of air or fluid	Longitudinal flow of air or fluid	Movement of mucus by cilia	Tears Nasal cilia
Chemical	Fatty acids	Low pH	Pulmonary surfactant	Enzymes in tears and saliva (lysozyme)
		Enzymes (pepsin)		
	β-defensins Lamellar bodies Cathelicidin	α-defensins (cryptdins) RegIII (lecticidins) Cathelicidin	α-defensins Cathelicidin	Histatins β-defensins
Microbiological	Normal microbiota			

Defensin- Amphipathic Peptides



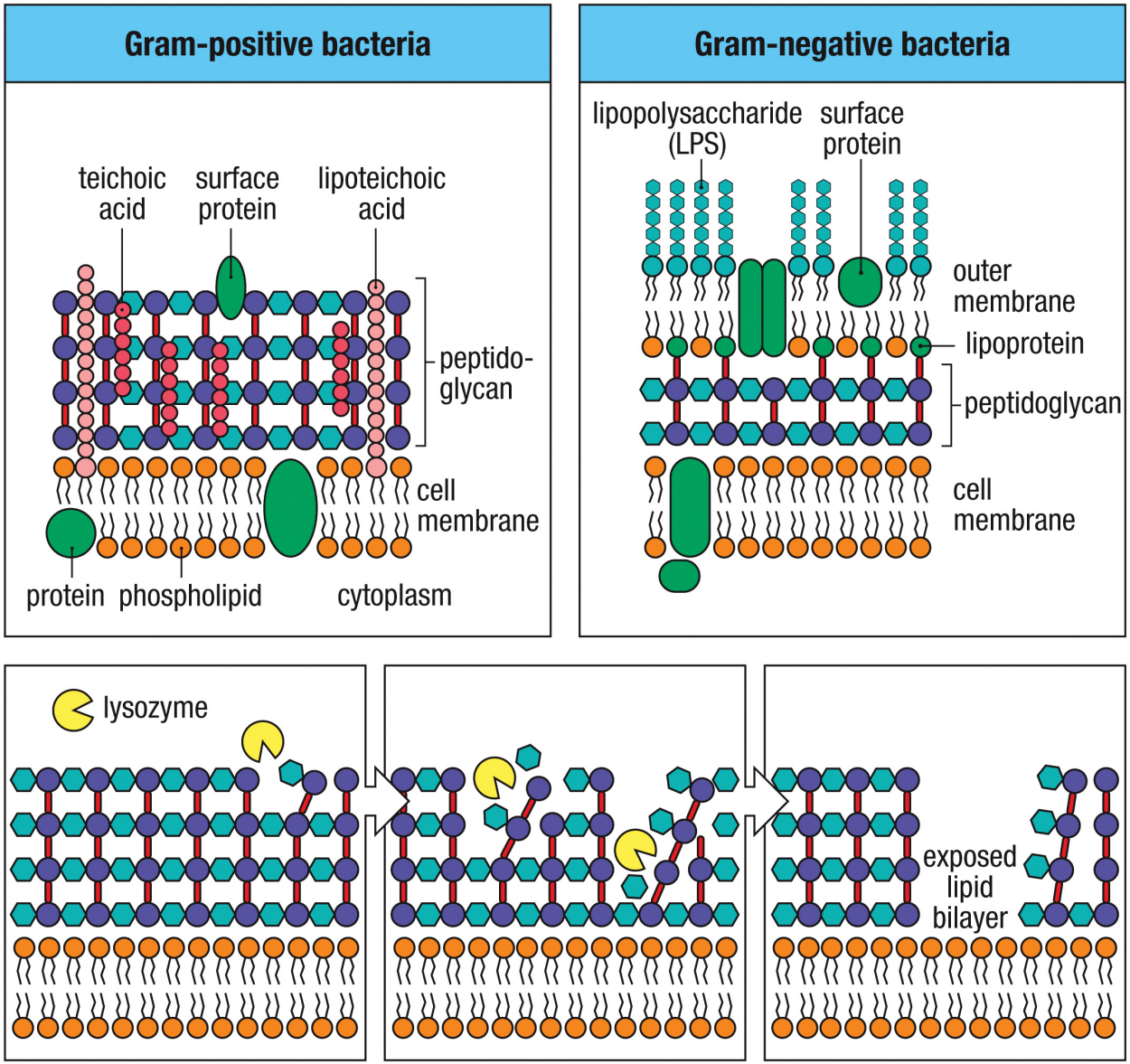


Specificity of Defensins



Nature **415**, 389-395 (24 January 2002) | doi:10.1038/415389a

Lysozyme


Gram-positive bacteria
teichoic acid
surface protein
lipoteichoic acid
peptido-glycan
cell membrane
protein
phospholipid
cytoplasm
Gram-negative bacteria
lipopolysaccharide (LPS)
surface protein
outer membrane
lipoprotein
peptidoglycan
cell membrane
lysozyme
exposed lipid bilayer

Microbiota


CS253604
DEADLY DIARRHEA:
C. DIFFICILE CAUSES IMMENSE SUFFERING, DEATH
IMPACT
500,000
Caused close to half a million illnesses in one year.
Comes back at least once in about 1 in 5 patients who get C. difficile.
Caused 15,000 deaths in one year
1 in 11 people 65 and older died within a month of C. difficile infection diagnosis.
RISK
People on antibiotics are 7-10 times more likely to get C. difficile while on the drugs and during the month after.
Being in healthcare settings, especially hospitals or nursing homes.
More than 80% of C. difficile deaths occurred in people 65 and older.
SPREAD
Touching unclean surfaces, especially those in healthcare settings, contaminated with feces from an infected person.
Dirty hands.
Failing to notify other healthcare facilities when patients with C. difficile transfer from one facility to another.
PREVENT
Improve prescribing of antibiotics.
Use best tests for accurate results to prevent spread.
Rapidly identify and isolate patients with C. difficile.
Wear gloves and gowns when treating patient with C. difficile. Remember that hand sanitizer doesn't kill C. difficile.
Clean room surfaces with EPA-approved, spore-killing disinfectant (such as bleach), where C. difficile patients are treated.
http://www.cdc.gov/HAI/organisms/cdiff/Cdiff_infect.html
www.cdc.gov/media
CDC
U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

Question

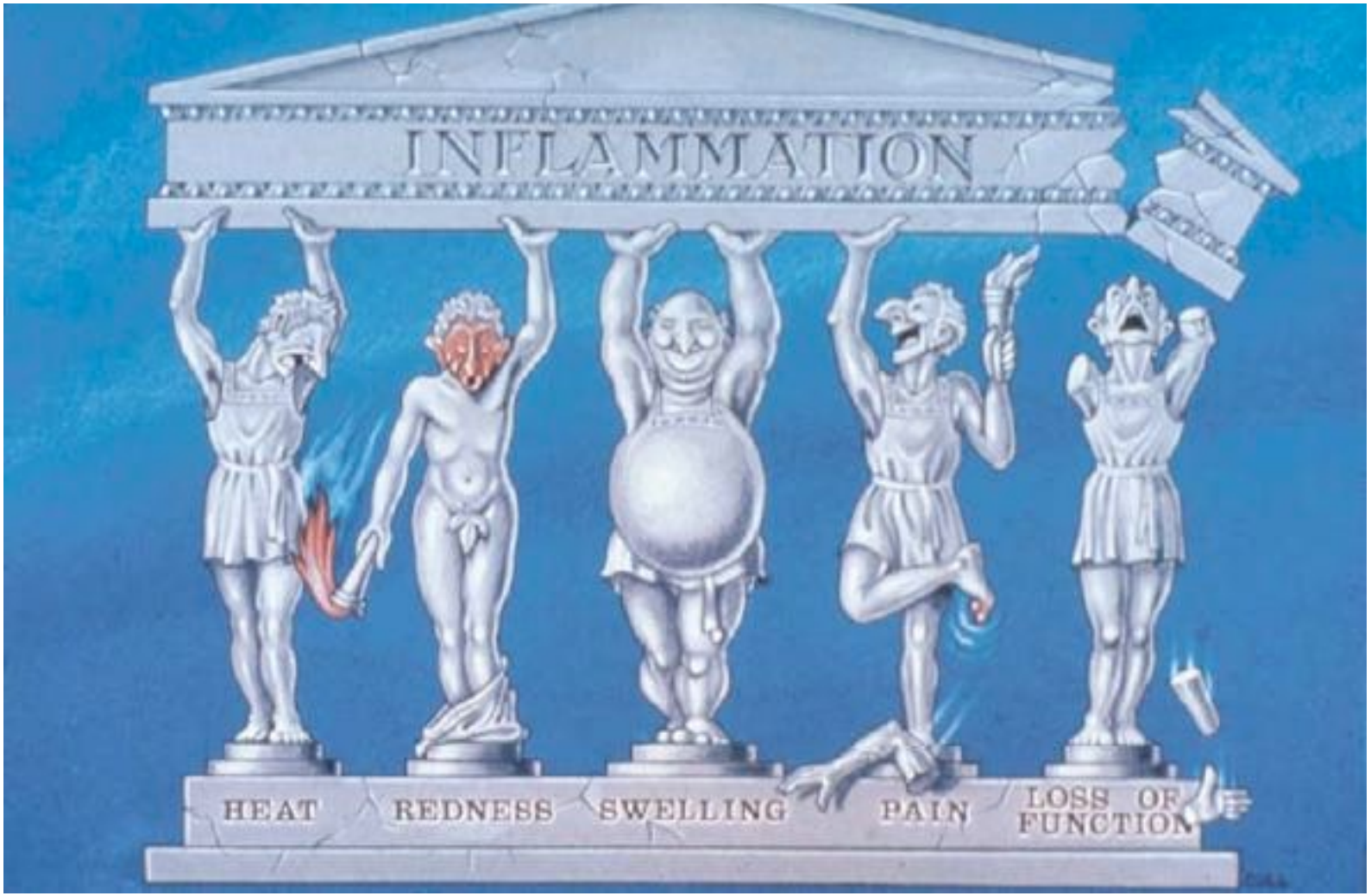
- What are the three barriers that a pathogen has to across to establish an infection?

Outline

Course of the immune response

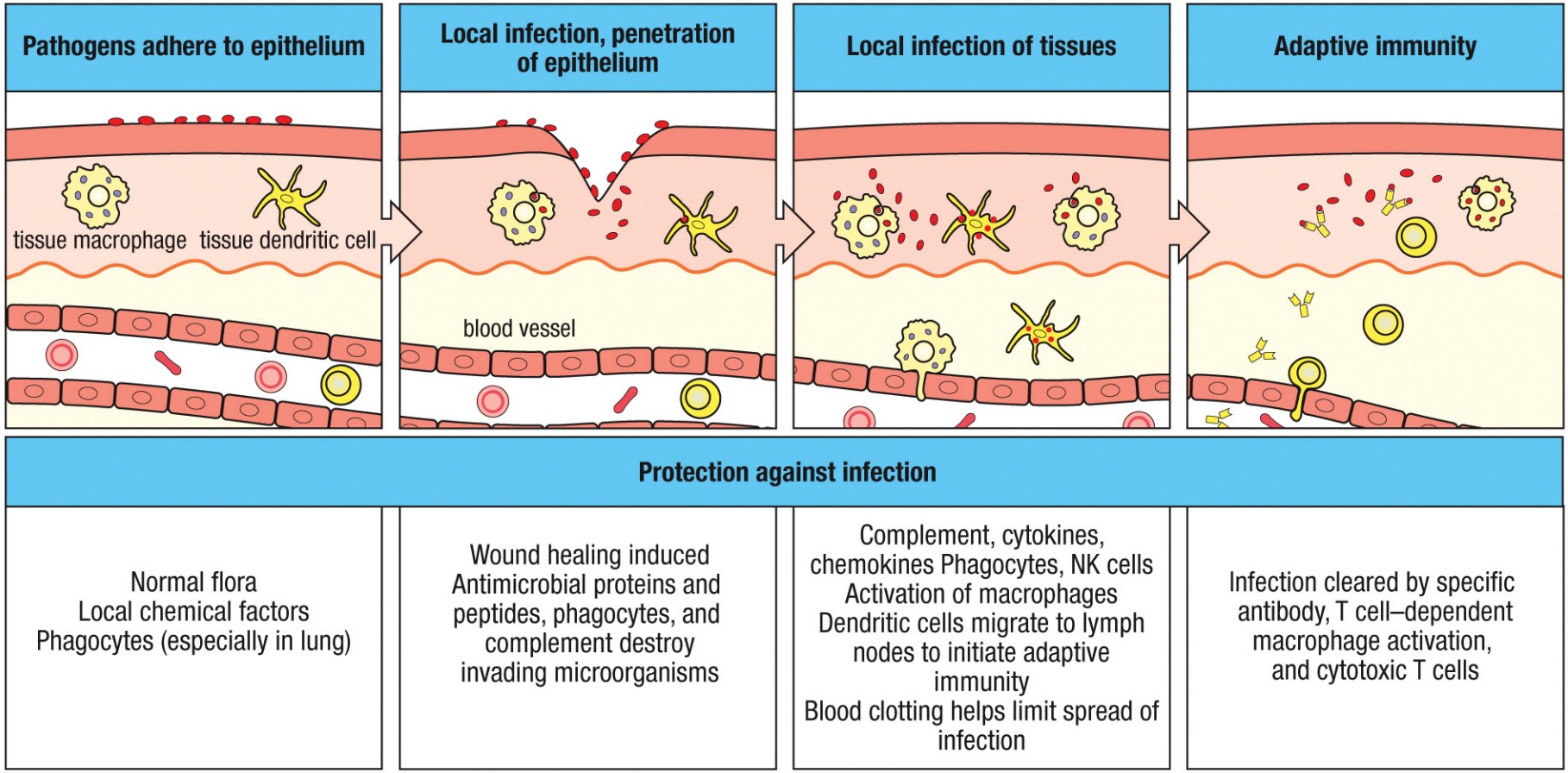
- Pathogen entry point
- First encounter w/ immune system: local infection & inflammation
- Full activation of immune response: peripheral lymphoid organs
- Immunological memory

Inflammation Greek Style

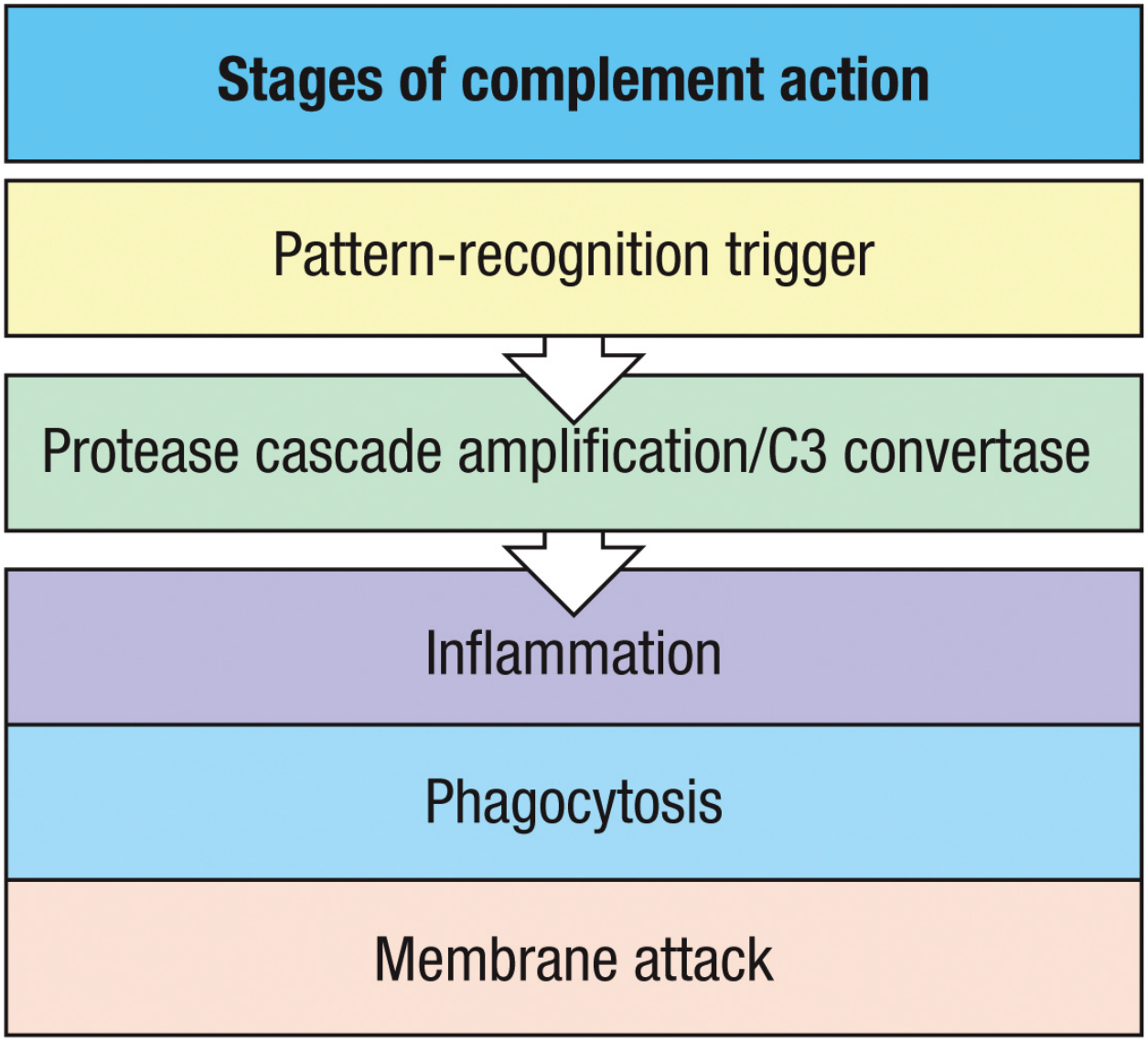


http://www6.ufrgs.br/favet/imunovet/molecular_immunology/inflammation_cartoon.jpg

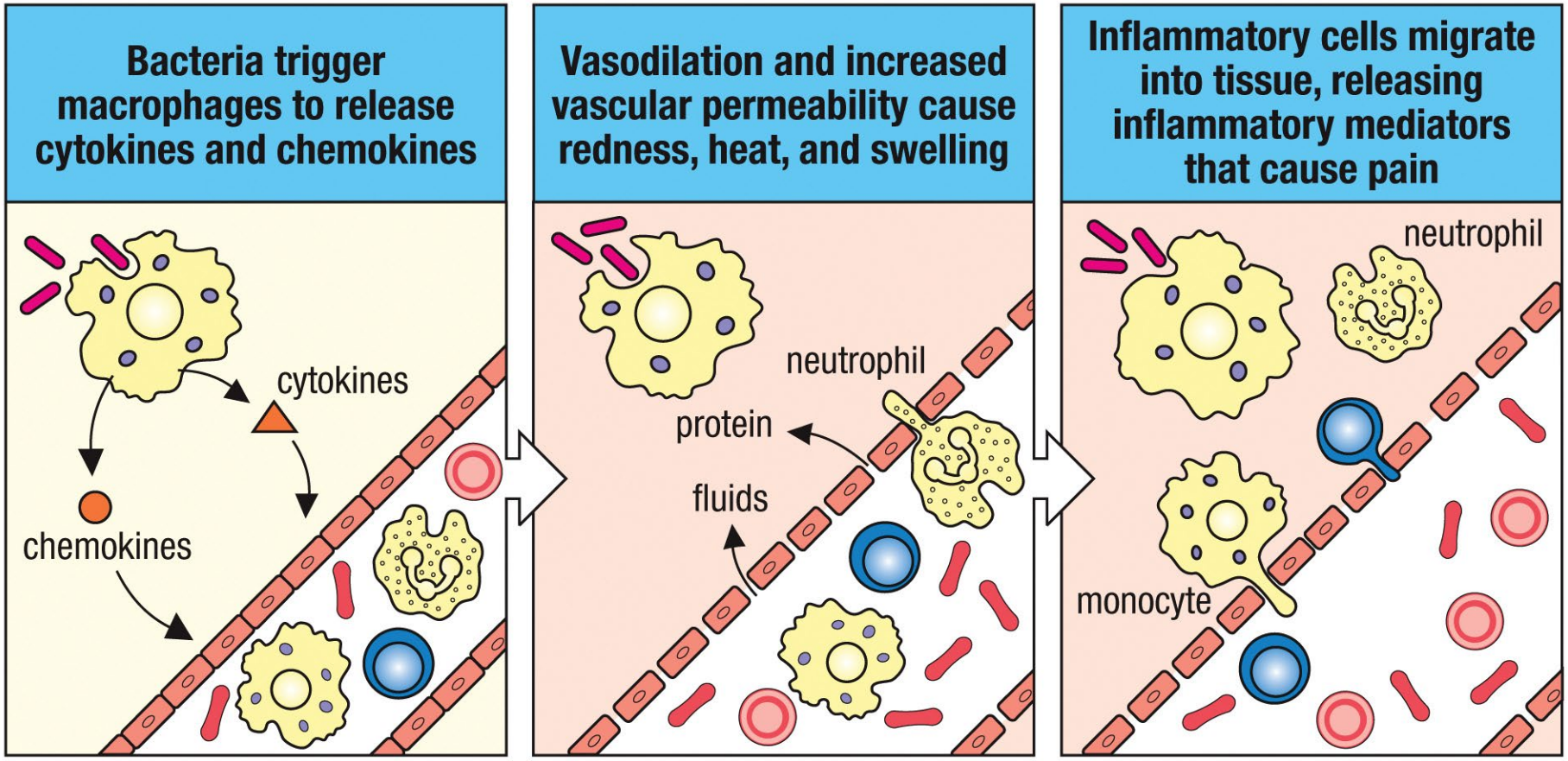
Series of Immune Activation



Humoral Innate Immunity: Complement System



Cytokines and Innate Immune Cells

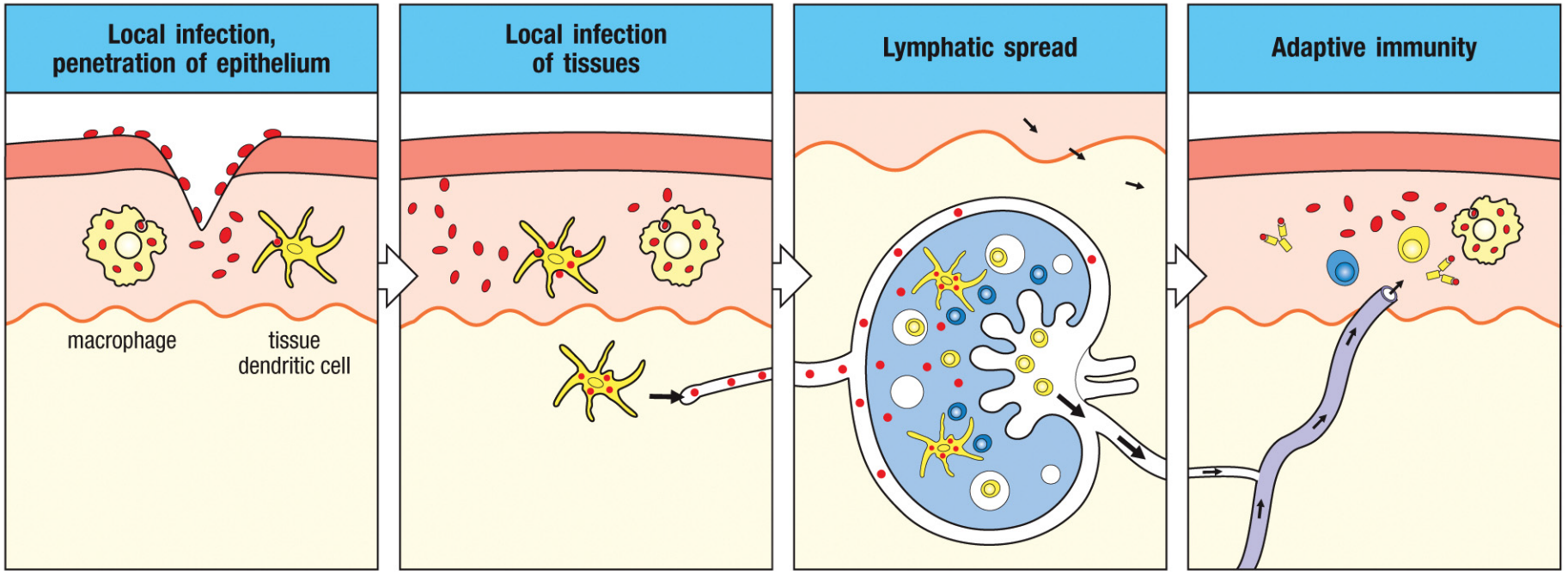


Outline

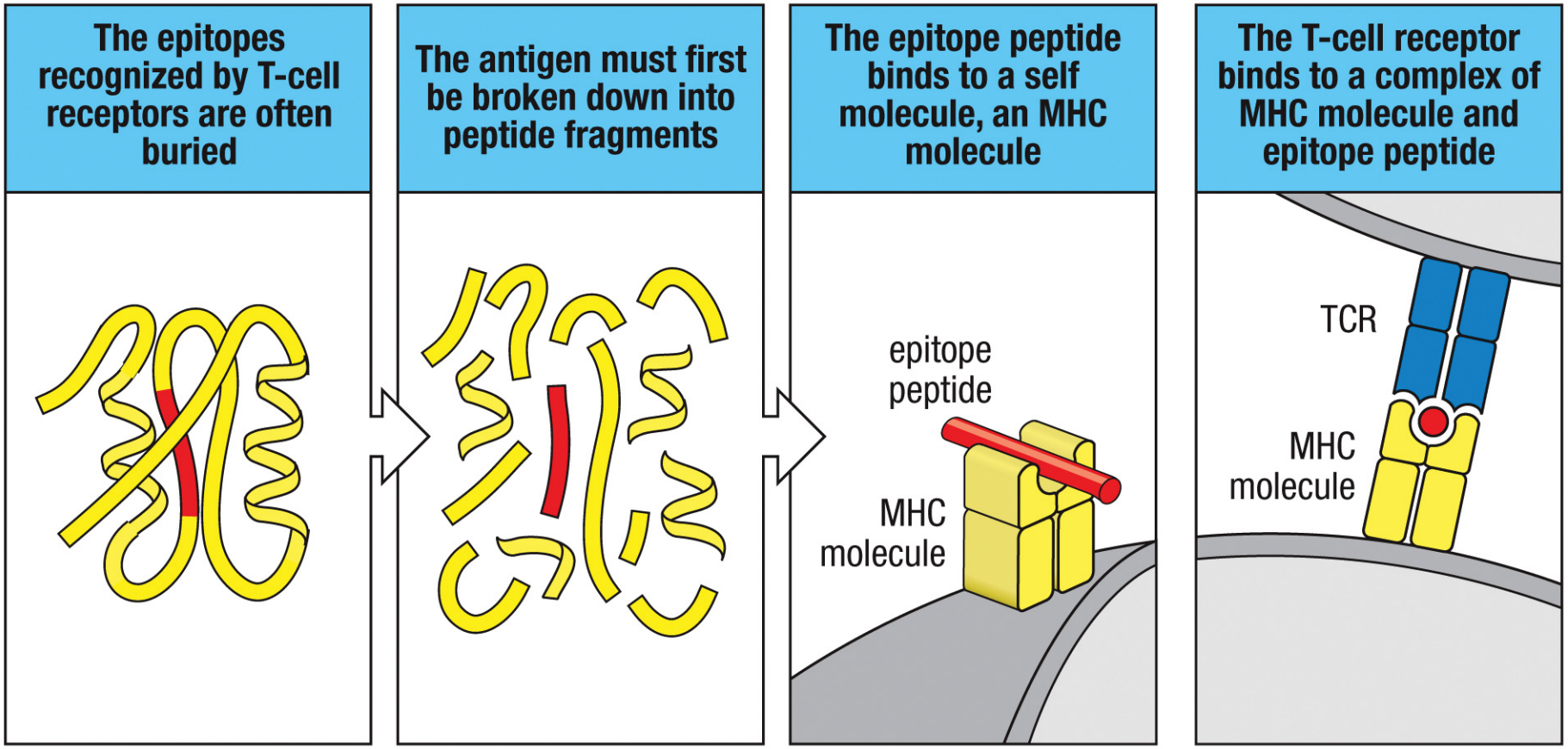
Course of the immune response

- Pathogen entry point
- First encounter w/ immune system: local infection & inflammation
- Full activation of immune response: peripheral lymphoid organs
- Immunological memory

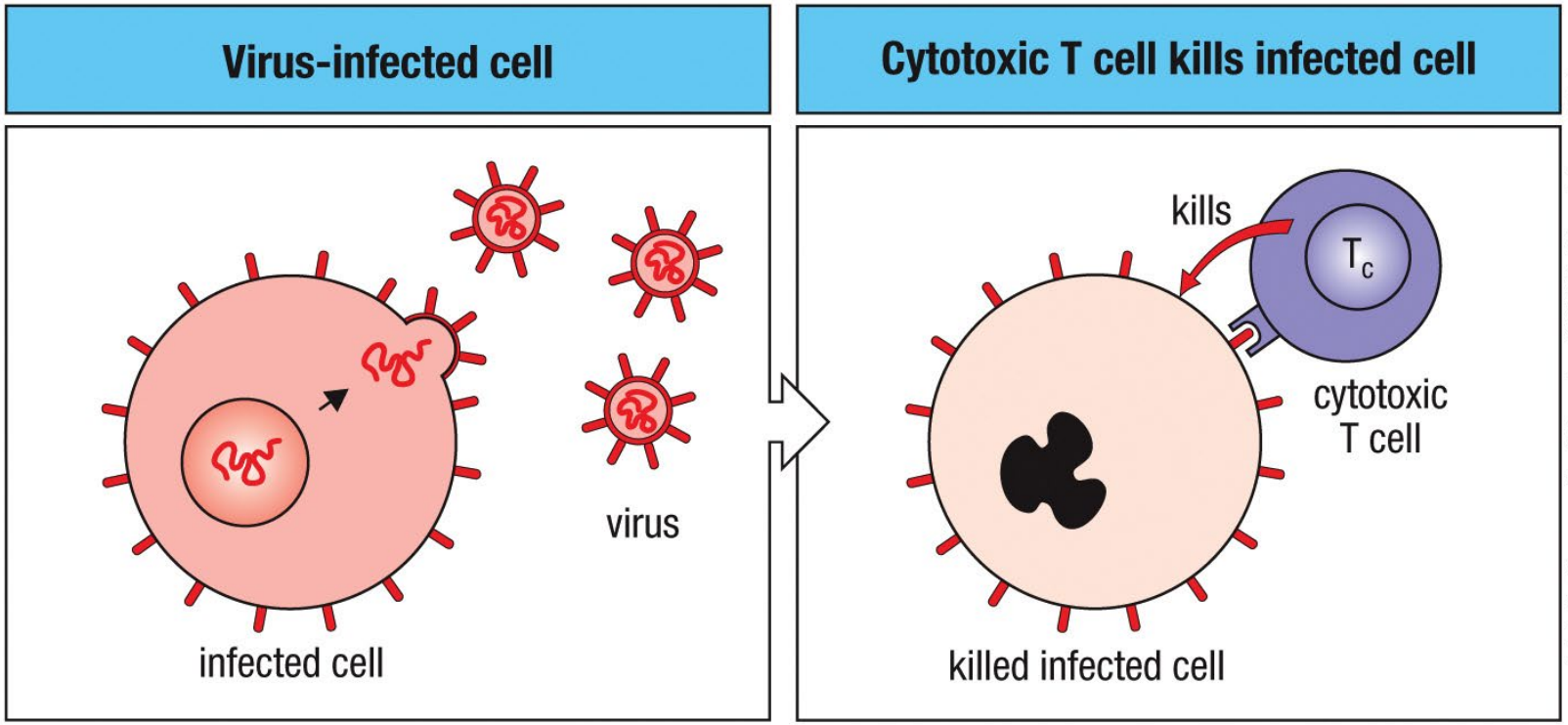
Activation of the Immune Response

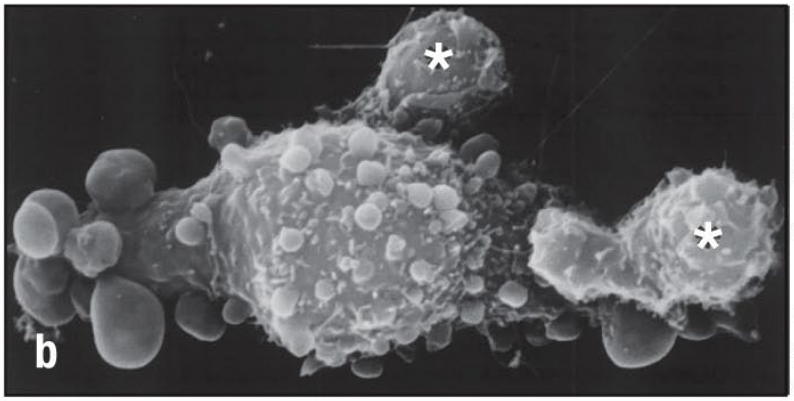


Antigen Recognition by TCR

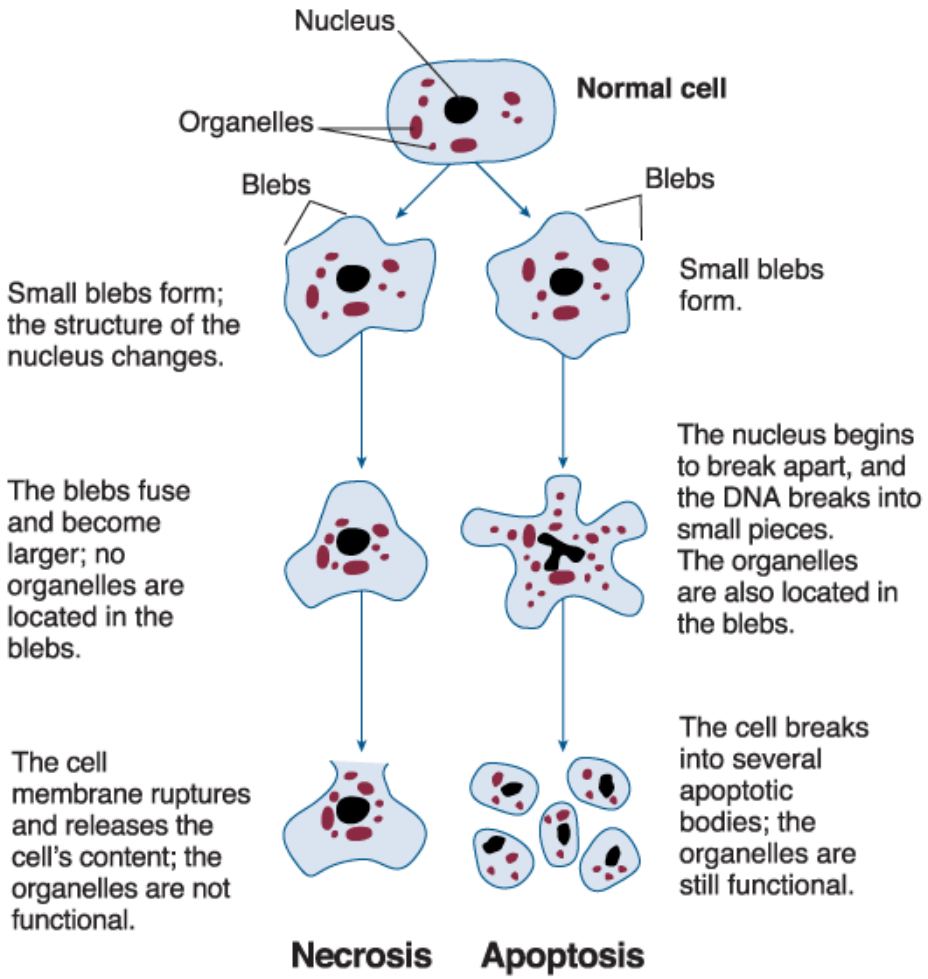


Cytotoxic T Cells Interact With MHC Class I





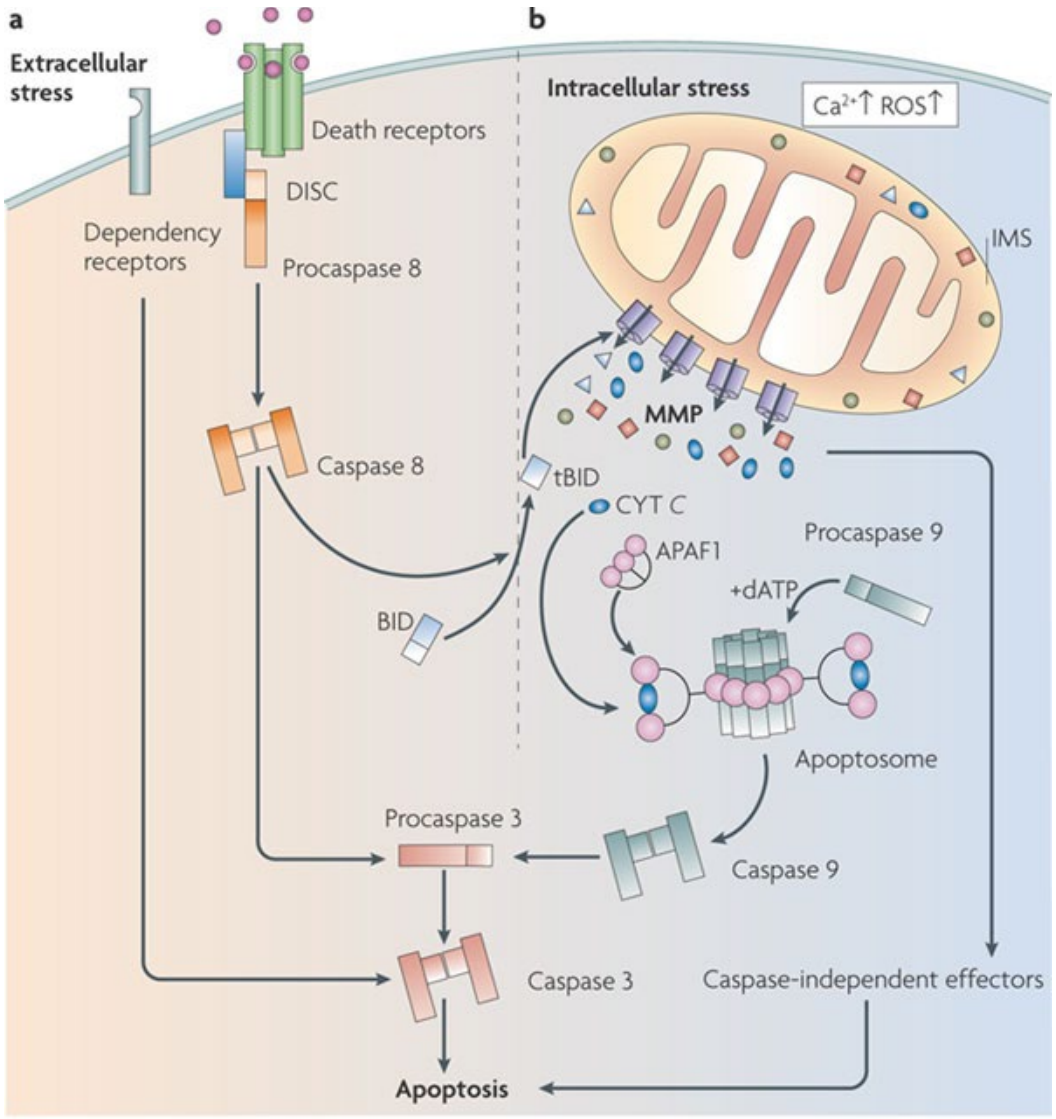
Cell Death Pathways



Alcohol Research & Health 25(3):175–184 (2001)

Apoptosis Pathways

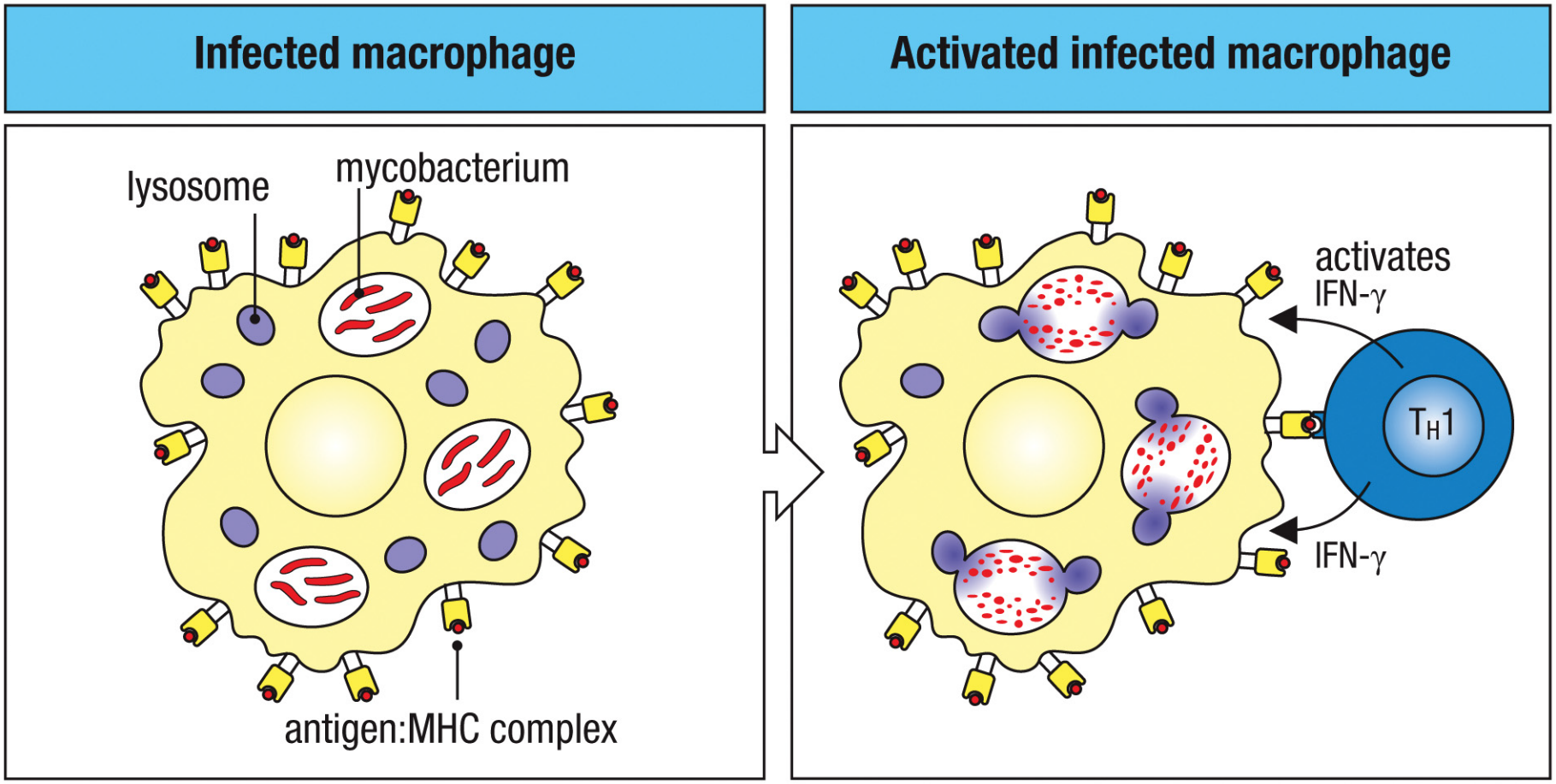
Death Receptor Pathway



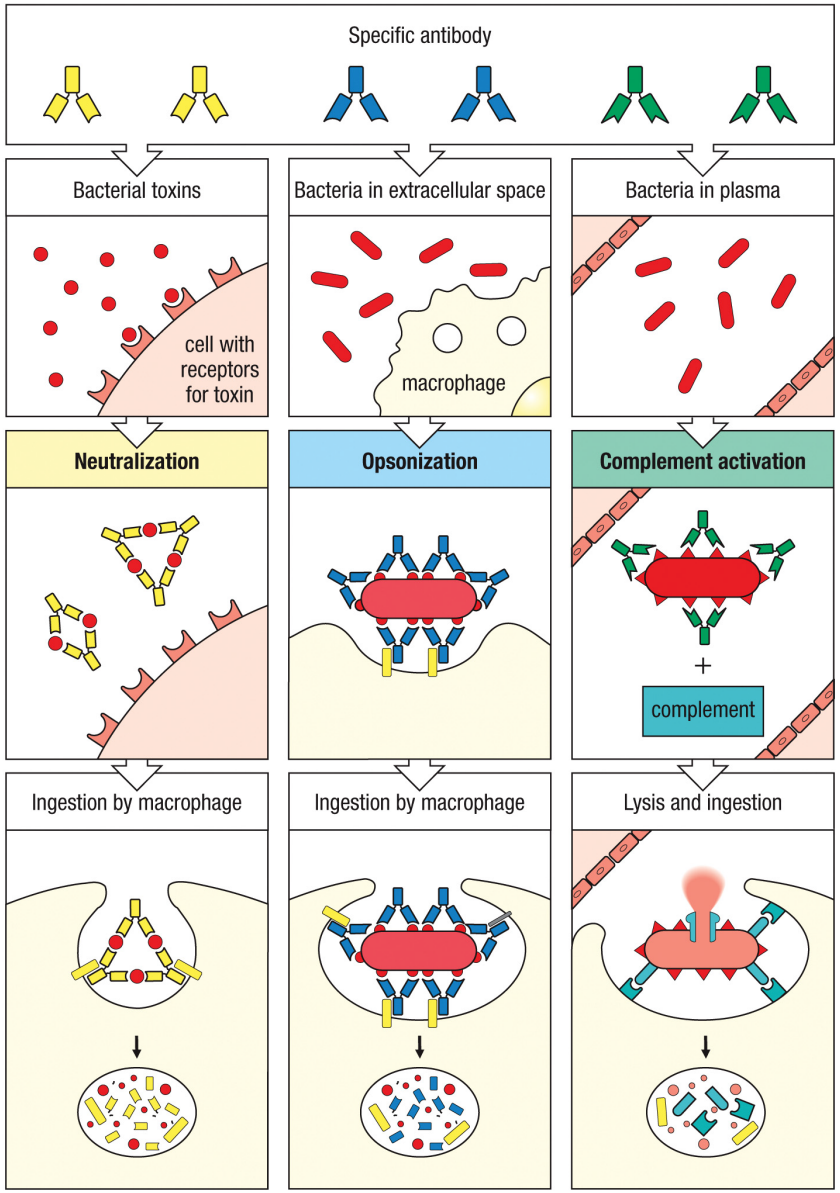
Mitochondrial Pathway

Nature Reviews Neuroscience **10**, 481-494 (July 2009) | doi:10.1038/nrn2665

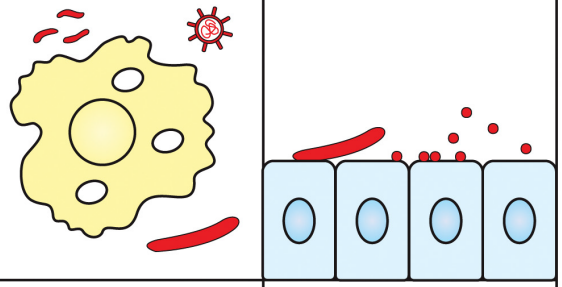
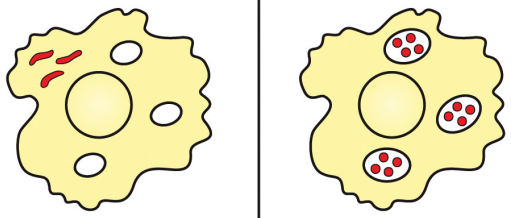
Helper T Cells Interact With MHC Class II



Humoral Mechanism of Clearing Infection



Specific Defenses Against Specific Pathogens

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

Specific Defenses Against Specific Pathogens

	Phases of the immune response		
	Innate phase (Immediate: 0–4 hours)	**Induced innate phase (Early: 4–96 hours)**	**Adaptive immune phase (Late: >96 hours)**
	Nonspecific Innate No memory No specific T cells	Nonspecific + specific Inducible No memory No specific T cells	Specific Inducible Memory Specific T cells
Barrier functions	Skin, epithelia, mucins, acid	Local inflammation (C5a) Local TNF-α	IgA antibody in luminal spaces IgE antibody on mast cells Local inflammation
Response to extracellular pathogens	Phagocytes Alternative and MBL complement pathway Lysozyme Lactoferrin Peroxidase Defensins	Mannose-binding lectin C-reactive protein T-independent B-cell antibody Complement	IgG antibody and Fc receptor–bearing cells IgG, IgM antibody + classical complement pathway
Response to intracellular bacteria	Macrophages	Activated NK-dependent macrophage activation IL-1, IL-6, TNF-α, IL-12	T-cell activation of macrophages by IFN-γ
Response to virus-infected cells	Natural killer (NK) cells	IFN-α and IFN-β IL-12–activated NK cells	Cytotoxic T cells IFN-γ

Question

Who fights who?

A. Cytotoxic T cells

B. Antibodies

C. T helper cells

D. Complement

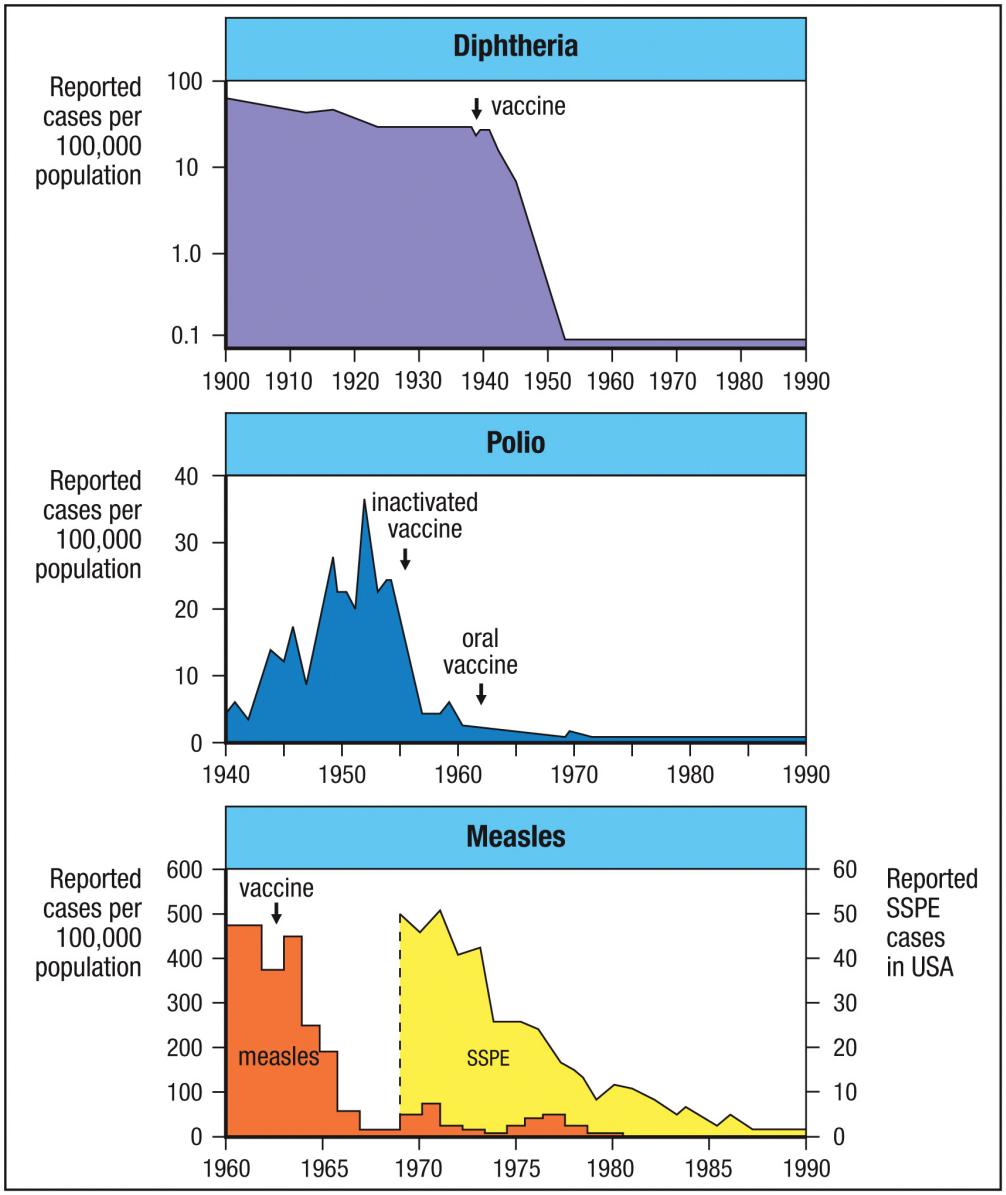
1. Virus
2. Intracellular bacteria in cytosol
3. Intracellular bacteria in phagosome
4. parasites

Outline

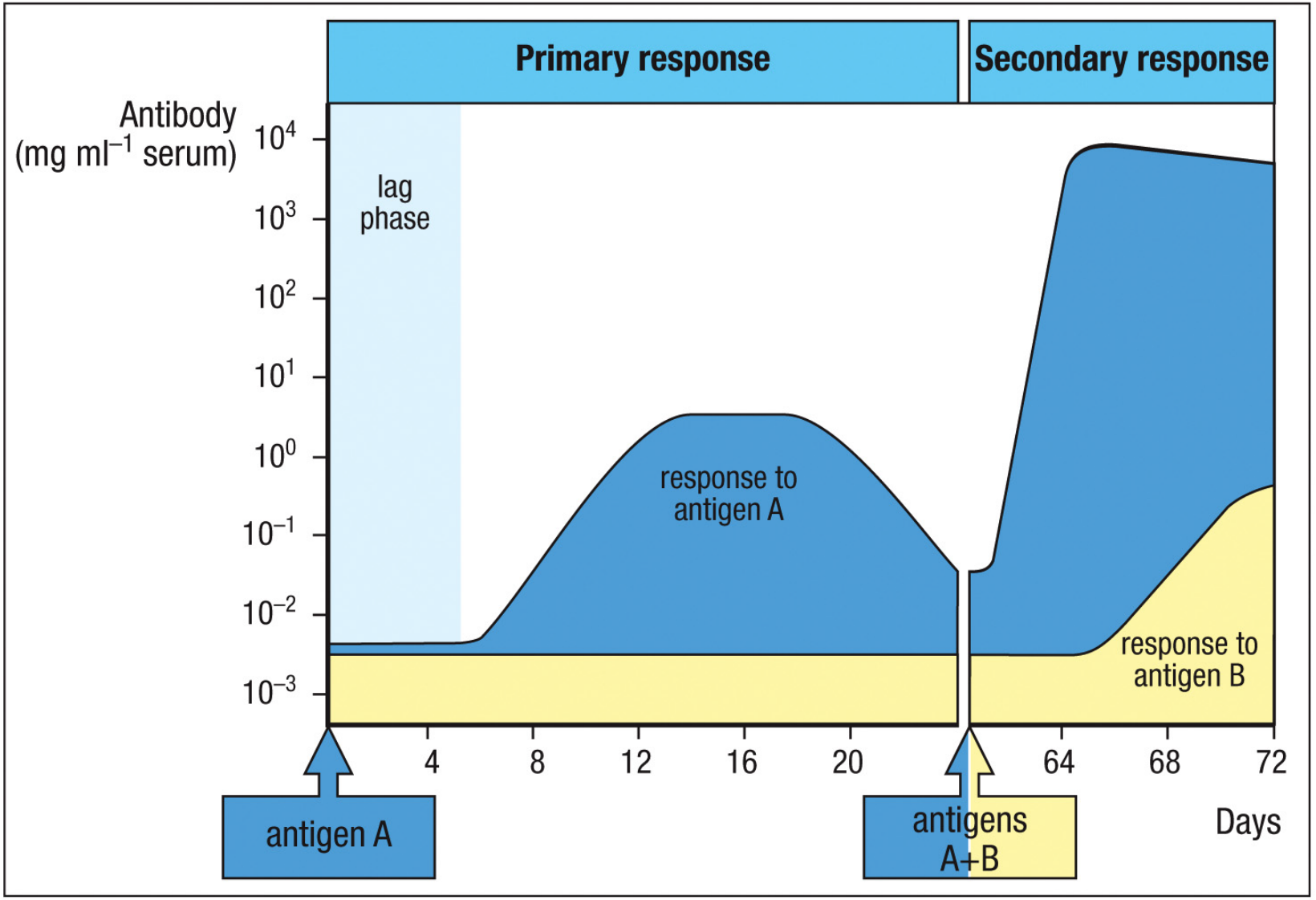
Course of the immune response

- Pathogen entry point
- First encounter w/ immune system:
  local infection & inflammation
- Full activation of immune response:
  peripheral lymphoid organs
- Immunological memory

Vaccination is the most effective means of controlling infectious diseases



Course of Immunization



Course of Smallpox Vaccination