

Kenneth Murphy and Casey Weaver

# Janeway's Immunobiology

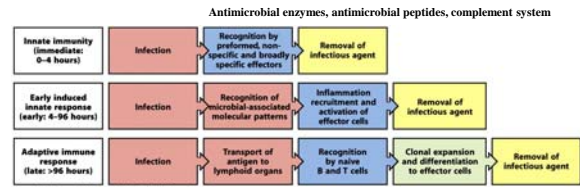
NINTH EDITION

## CHAPTER 2

### Innate Immunity: The First Lines of Defense

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## The response to an initial infection



Innate immune system: Germline-encoded receptors  
 Adaptive immune system: variable antigen specific receptors from gene segments rearrangements and clonal selection

## Tissue damage by pathogens

Pathogenic mechanism	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
Infectious agent	<i>Streptococcus pyogenes</i> <i>Staphylococcus aureus</i> <i>Corynebacterium diphtheriae</i> <i>Clostridium botulinum</i> <i>Vibrio cholerae</i>	<i>Escherichia coli</i> <i>Haemophilus influenzae</i> <i>Salmonella typhi</i> <i>Shigella</i> <i>Pseudomonas aeruginosa</i> <i>Yersinia pestis</i>	<i>Varicella-zoster virus</i> <i>Hepatitis B virus</i> <i>Poliomyelitis virus</i> <i>Measles virus</i> <i>Influenza virus</i> <i>Herpes simplex virus</i> <i>Human herpes virus 8 (HHV8)</i>	<i>Hepatitis B virus</i> <i>Malaria</i> <i>Streptococcus pyogenes</i> <i>Tricomonas pallidum</i> <i>Most acute infections</i>	<i>Streptococcus pyogenes</i> <i>Mycoplasma pneumoniae</i>	<i>Lymphocytic choriomeningitis virus</i> <i>Herpes simplex virus</i> <i>Mycobacterium tuberculosis</i> <i>Mycobacterium leprae</i> <i>Borrelia burgdorferi</i> <i>Schistosoma mansoni</i>
Disease	Tonsillitis, 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 Polymyositis Measles, sclerosing pancreatitis 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 Tuberculous lymphoma Lyme arthritis Schistosomiasis

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## The epithelial surfaces of the body make up the first line of defense

**Physical barrier:** Epithelial cells are held together by tight junctions form a seal against the external environment – skin, linings of the body's tubular structures including gastrointestinal, respiratory, urogenital tracts.

Internal epithelia are known as mucosal epithelia because they secrete a viscous fluid called mucus, which contains many glycoproteins called mucins.

**Chemical barrier:** The acid pH of the stomach, digestive enzymes, bile salts, fatty acids, lysolipids etc.

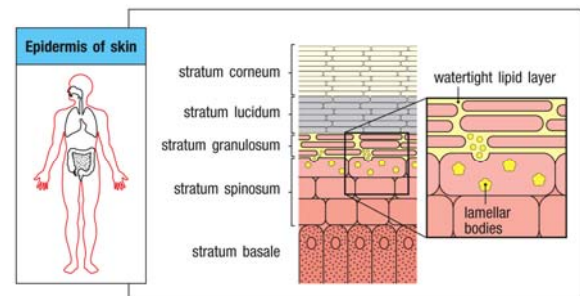
Antibacterial and antifungal peptides; cryptidins or α-defensins, β-defensins

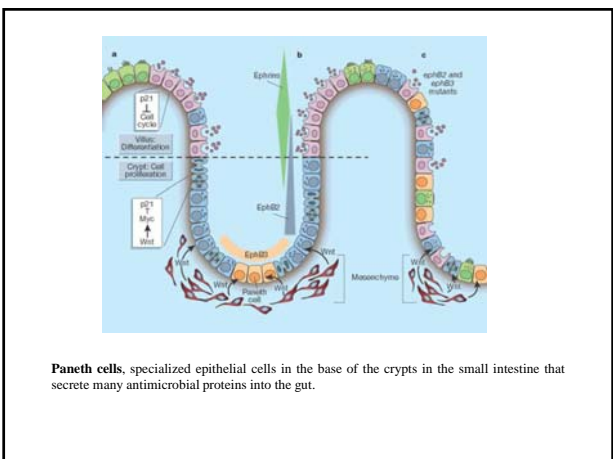
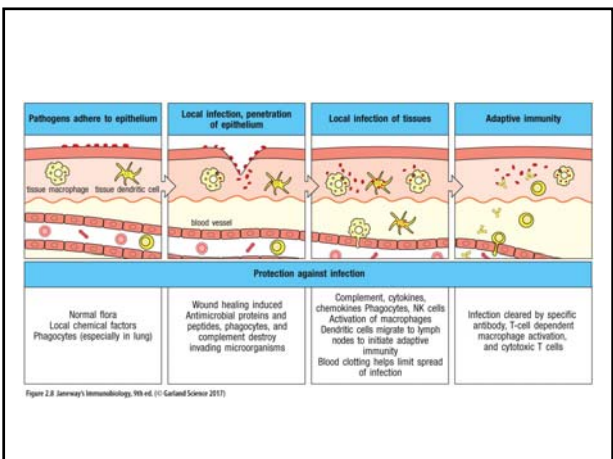
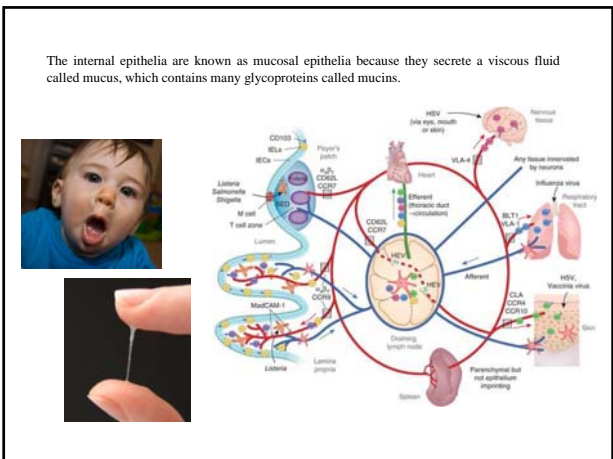
**Microbiological barrier:** Commensal bacteria which is normal flora of nonpathogenic bacteria that compete with pathogenic microorganisms for nutrients and for attachment sites on epithelial cells.

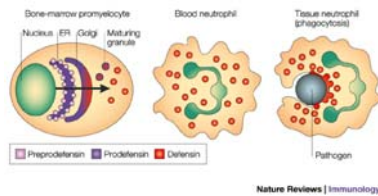
## Many barriers for the first defense line

	Skin	Gut	Lungs	Eyes/nose/oral cavity
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)
	β-defensins Lamellar bodies Cathelicidin	α-defensins (cryptidins) RegIII (lecticidins) Cathelicidin	α-defensins Cathelicidin	Histatins β-defensins
Microbiological	Normal microbiota			

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Antimicrobial peptides are secreted by epithelial cells and also some innate immune cells. **Defensins, cathelicidins, and histatins.**

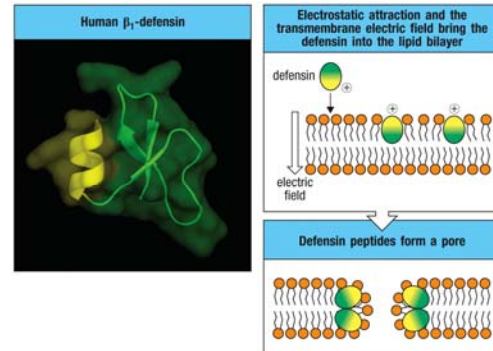


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**Defensins** are amphipathic peptides that disrupt the cell membranes of microbes. Evolutionarily conserved class. Short cationic peptides of around 30-40 amino acids.

### Complement system and innate immunity

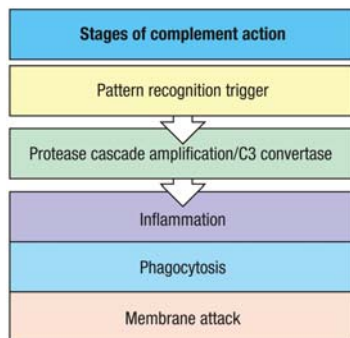


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### Complement system and innate immunity

Complement system: the first-line of defense

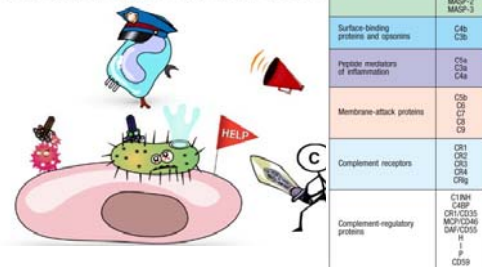


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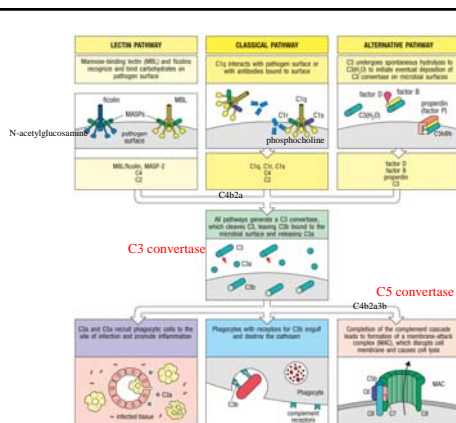


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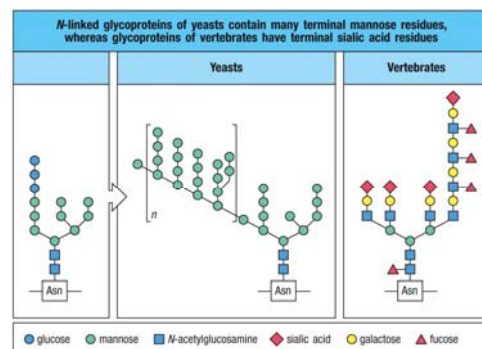
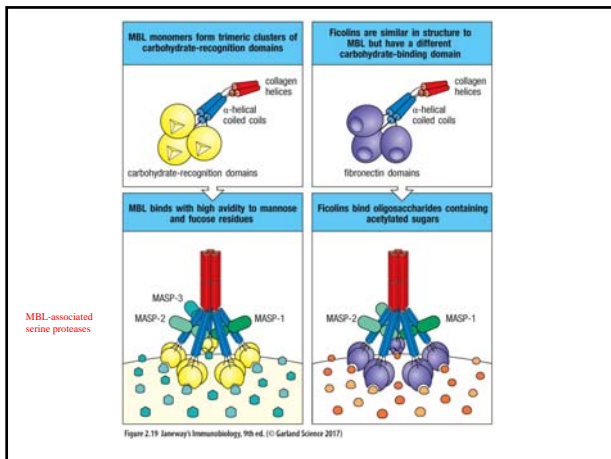
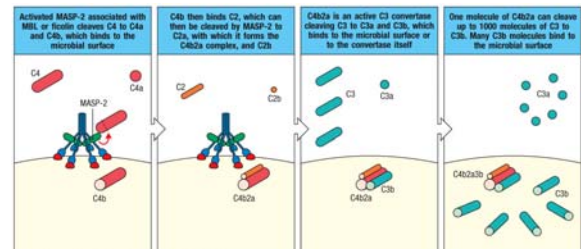


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**Mannose binding lectin (MBL)** which is synthesized in the liver and have a binding avidity for repetitive carbohydrate structures on a wide variety of microbial surfaces.

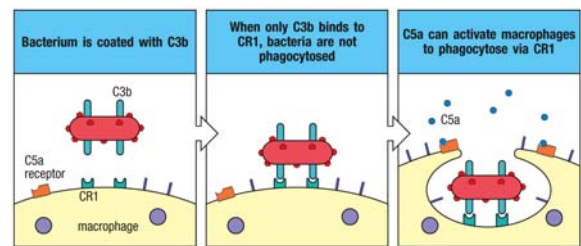
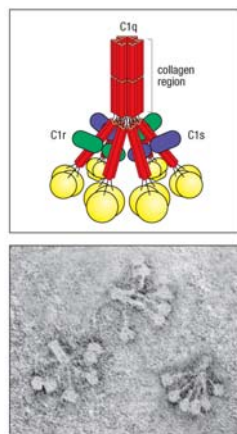


### The actions of the C3 convertase result in the binding of large numbers of C3b molecules to the pathogen surface

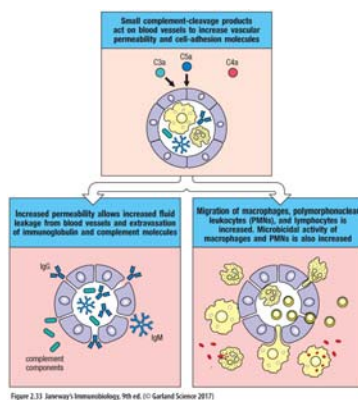


The lectin pathway is activated by soluble recognition receptor for microbial surfaces and C3 convertase generates C3b to be attached on them.

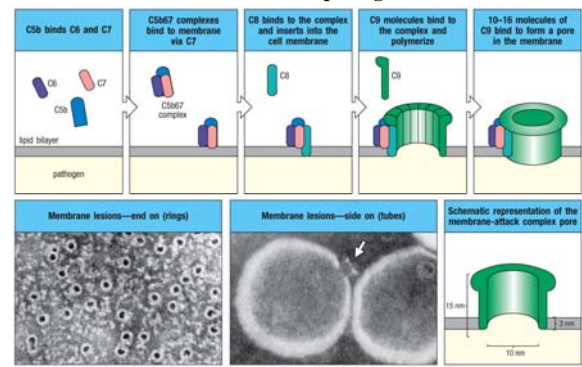
The classical pathway is initiated by activation of the C1 complex and is homologous to the lectin pathway.



C3b can be bound by the complement receptor CR1 on the surface of phagocytes, but this on its own is insufficient to induce phagocytosis. Anaphylatoxin C5a will activate the cell to phagocytose microorganisms.



### The terminal complement proteins polymerize to form pores in membranes that can kill certain pathogens



### Summary

- The complement system is one of the major mechanisms by plasma proteins that can be activated directly by pathogens or indirectly by pathogen bound antibody.
- Lectin pathway, Classical pathway, Alternative pathway
- C3 convertase generates C3b molecules to attach on the pathogen to be phagocytosed. The small fragments of C3, C4, and C5 recruit phagocytes to sites of infection and activate them by binding to specific receptors. C5 convertase lead to assemble a membrane attack complex to result in the lysis of pathogens.
- The activity of complement system is modulated by regulatory proteins that prevent tissue damage.