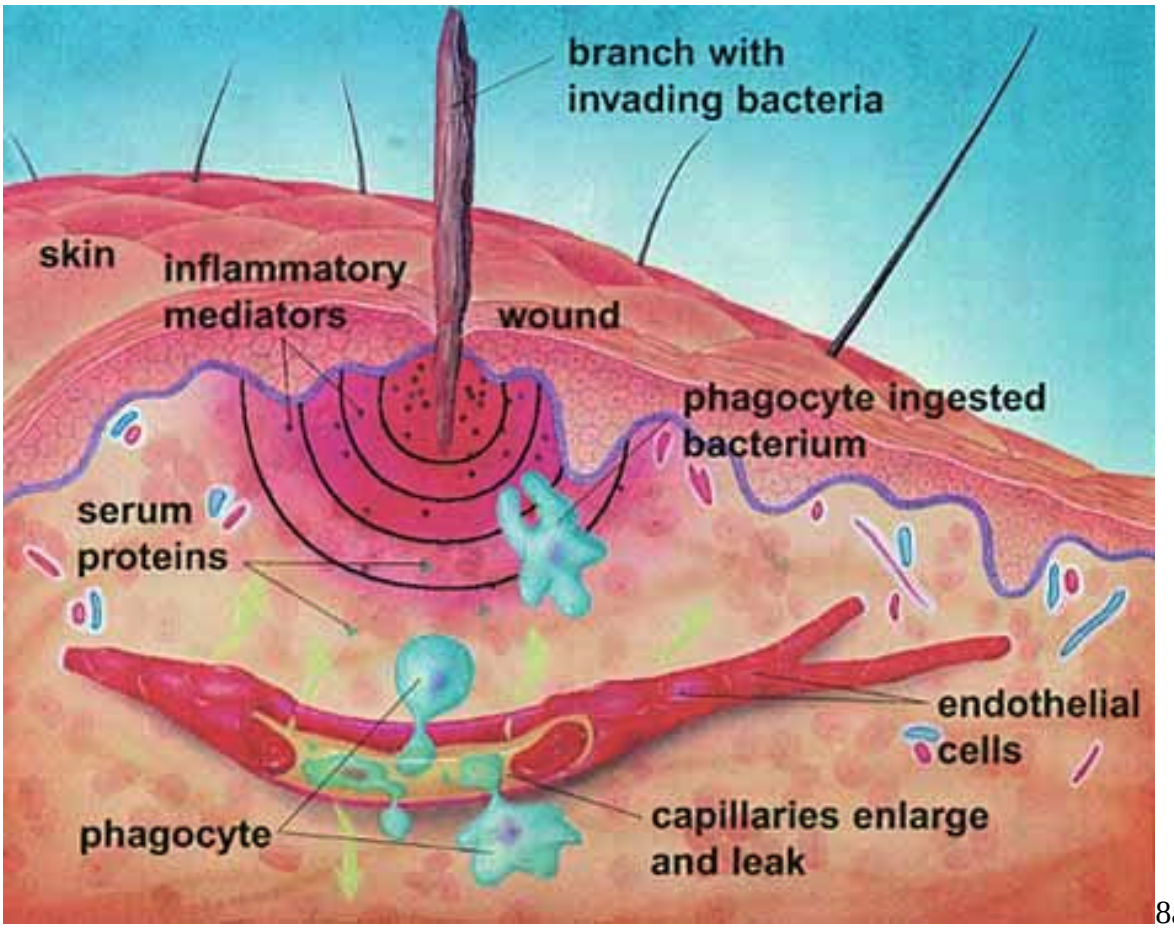
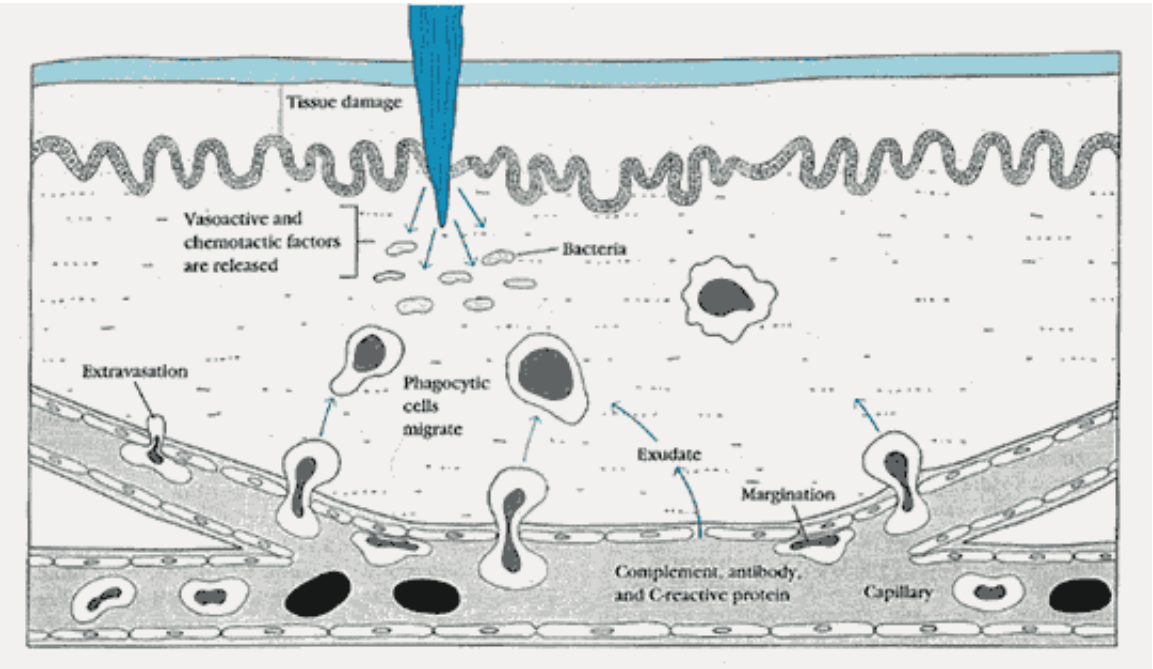

branch with
invading bacteria
skin
inflammatory
mediators
wound
phagocyte ingested
bacterium
serum
proteins
endothelial
cells
capillaries enlarge
and leak
phagocyte
8a



8b

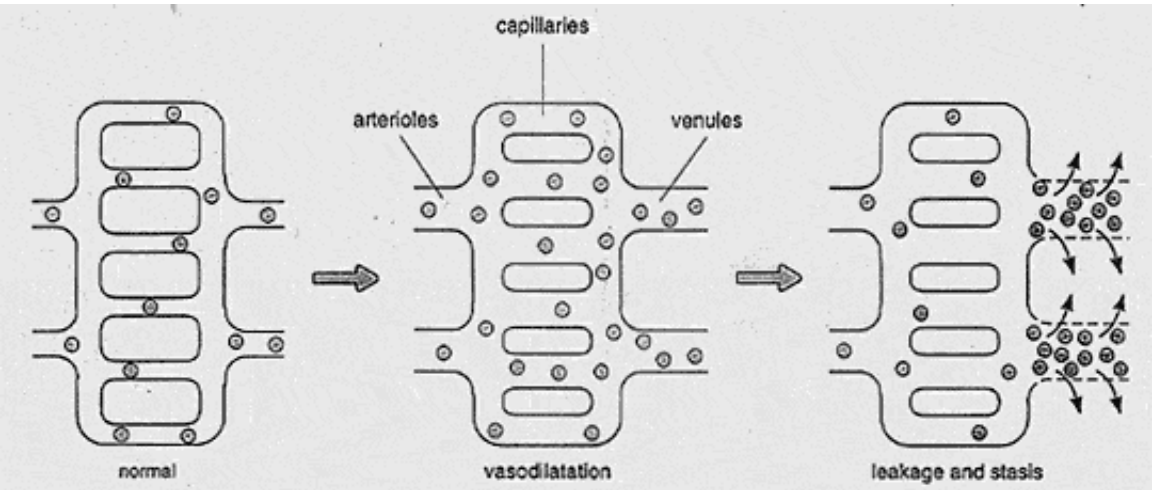


Figure 2–3. Vasodilatation and vascular leakage. Vasodilatation affects arterioles, capillaries, and venules. Leakage results from endothelial retraction that occurs only in postcapillary venules.

8c

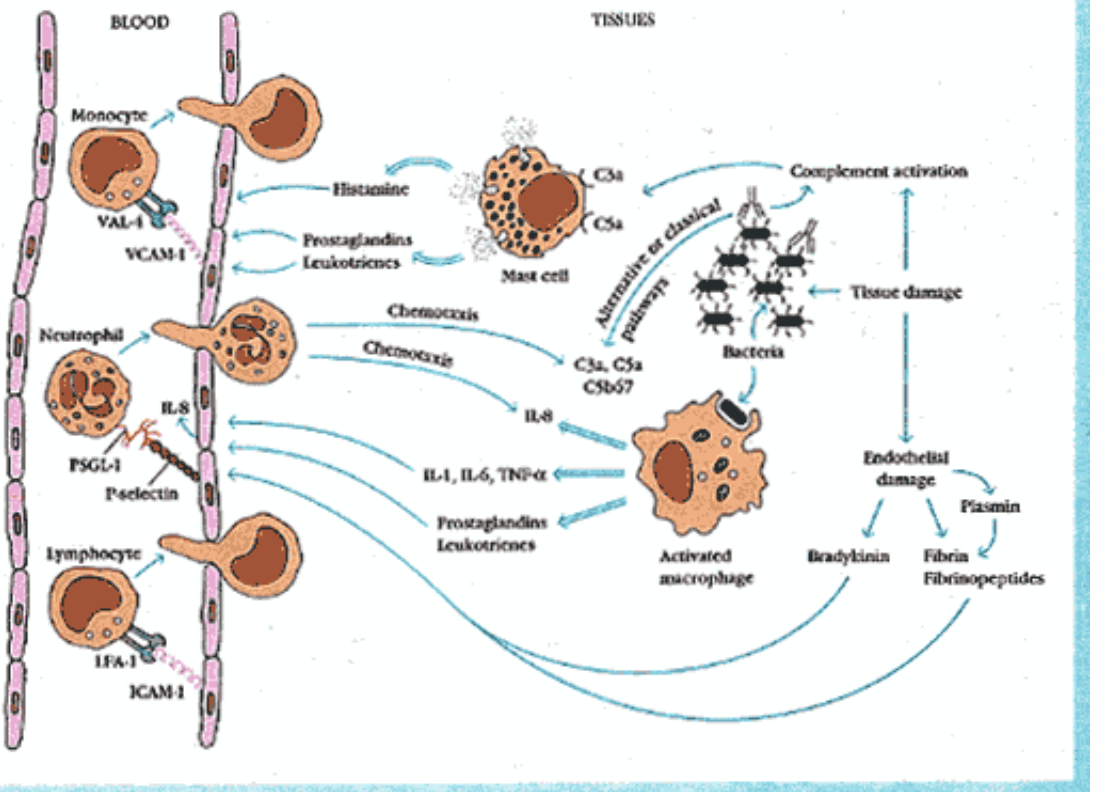
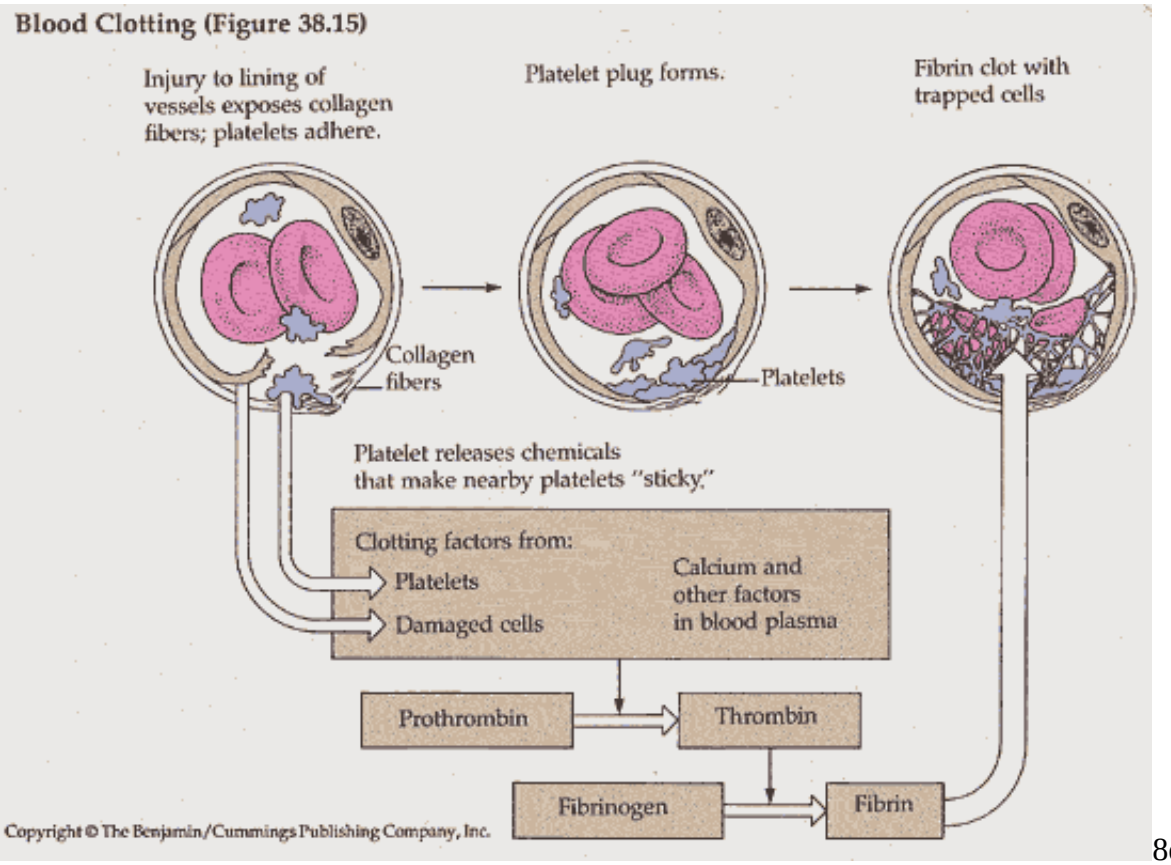


FIGURE 15-10

Overview of the cells and mediators involved in a local acute inflammatory response. Tissue damage leads to the formation of complement products that act as opsonins, anaphylatoxins, and chemotactic agents. Bradykinin and fibrinopeptides induced by endothelial damage mediate vascular changes. Neutrophils generally are the first leukocytes to migrate into the tissue, followed by monocytes and lymphocytes. Only some of the interactions involved in the extravasation of leukocytes are depicted.


Blood Clotting (Figure 38.15)
Injury to lining of vessels exposes collagen fibers; platelets adhere.
Platelet plug forms.
Fibrin clot with trapped cells
Collagen fibers
Platelets
Platelet releases chemicals that make nearby platelets "sticky."
Clotting factors from:
Platelets
Damaged cells
Calcium and other factors in blood plasma
Prothrombin
Thrombin
Fibrinogen
Fibrin
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8e

NON-SPECIFIC DEFENSES

A. **GENERAL BARRIERS**- nutrition, age, genetics, physiology, fever (discussed in text)

B. **CATEGORIES OF NON-SPECIFIC DEFENSES:**
(Layers of Protection)

1. **DEFENSES OF BODY SURFACES** - The physical and chemical barriers of the intact **skin and mucous membranes** (includes the normal flora)

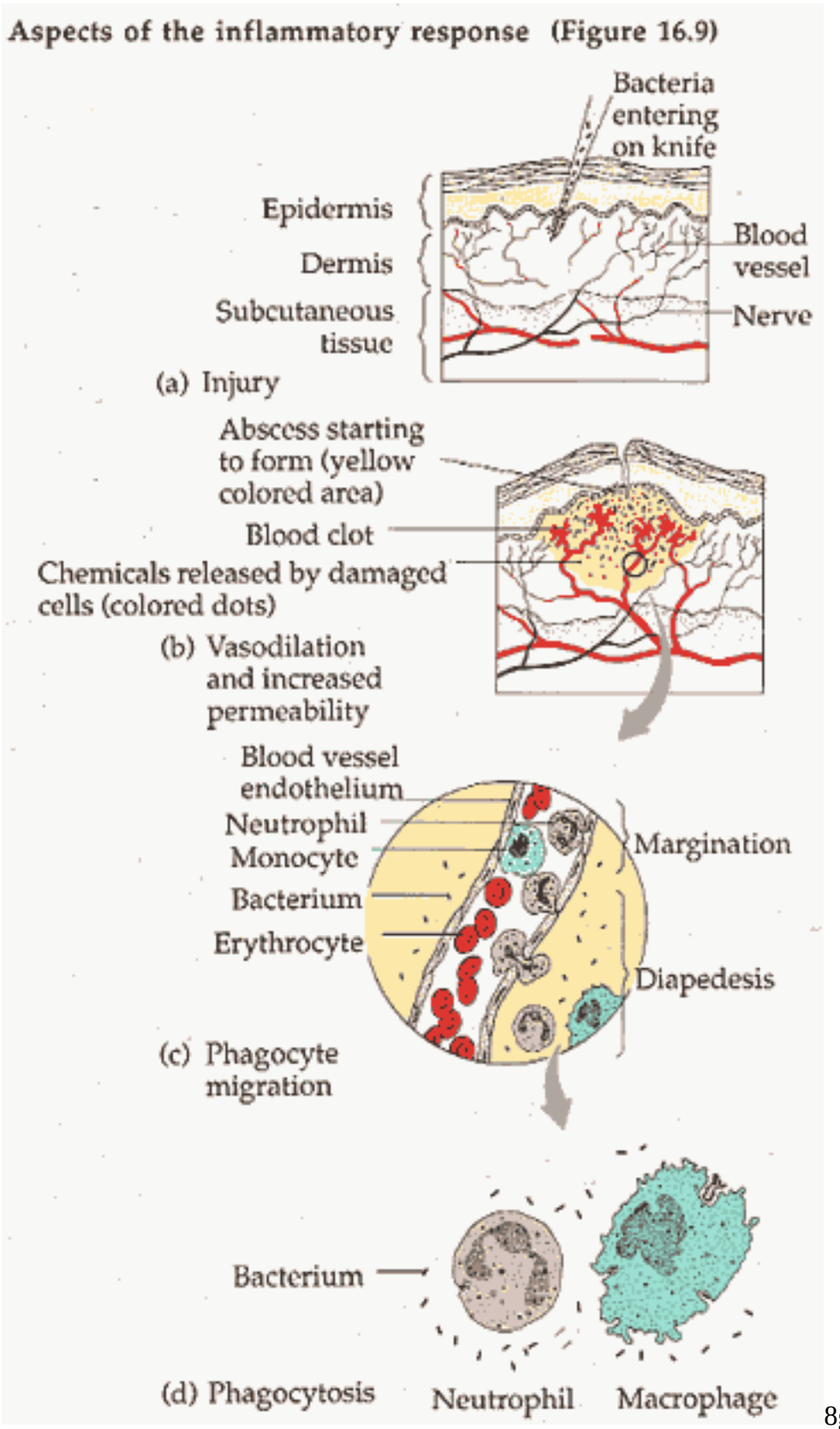
2. **DEFENSES OF TISSUE AND BLOOD**-

Inflammation- (L. inflammare-to set on fire) a localized protective response elicited by injury or destruction of tissues, which serves to destroy, dilute, or wall off both the injurious agent and the injured tissue. May be acute or chronic.

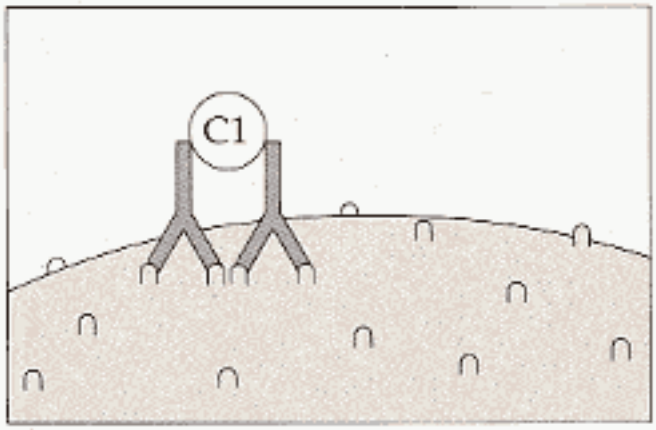
Includes:

a. **Phagocytosis** by neutrophils, macrophages,

b. **Soluble proteins** in tissue, blood, lymph, and other body fluids:
    1. transferrin and other iron-binding proteins
    2. complement activation

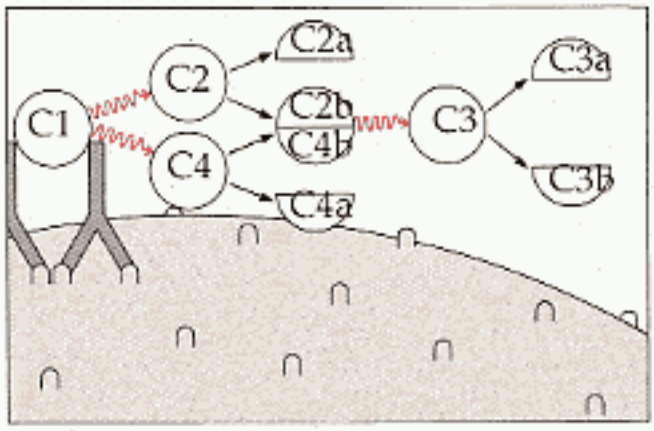

Aspects of the inflammatory response (Figure 16.9)
Bacteria entering on knife
Epidermis
Dermis
Subcutaneous tissue
Blood vessel
Nerve
(a) Injury
Abscess starting to form (yellow colored area)
Blood clot
Chemicals released by damaged cells (colored dots)
(b) Vasodilation and increased permeability
Blood vessel endothelium
Neutrophil
Monocyte
Bacterium
Erythrocyte
Margination
Diapedesis
(c) Phagocyte migration
Bacterium
(d) Phagocytosis
Neutrophil
Macrophage

8g



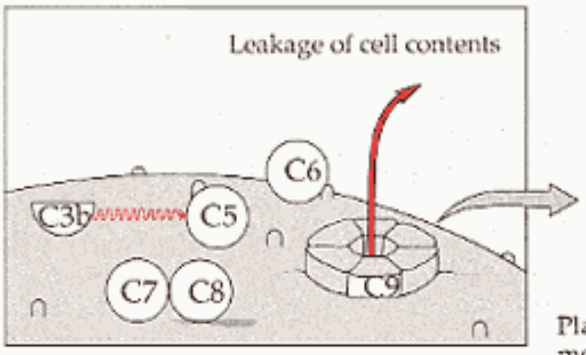
(a) Once antibodies recognize and attach to the antigen, complement protein C1 bonds to two adjacent antibodies.

8h-1

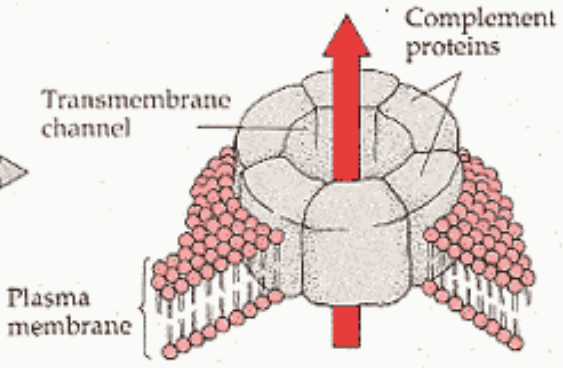


(b) C1 acts as an enzyme that splits the C2 and C4 proteins into fragments. Fragments C2b and C4b combine to form another enzyme, which splits C3 into two fragments. The active fragment is called C3b.

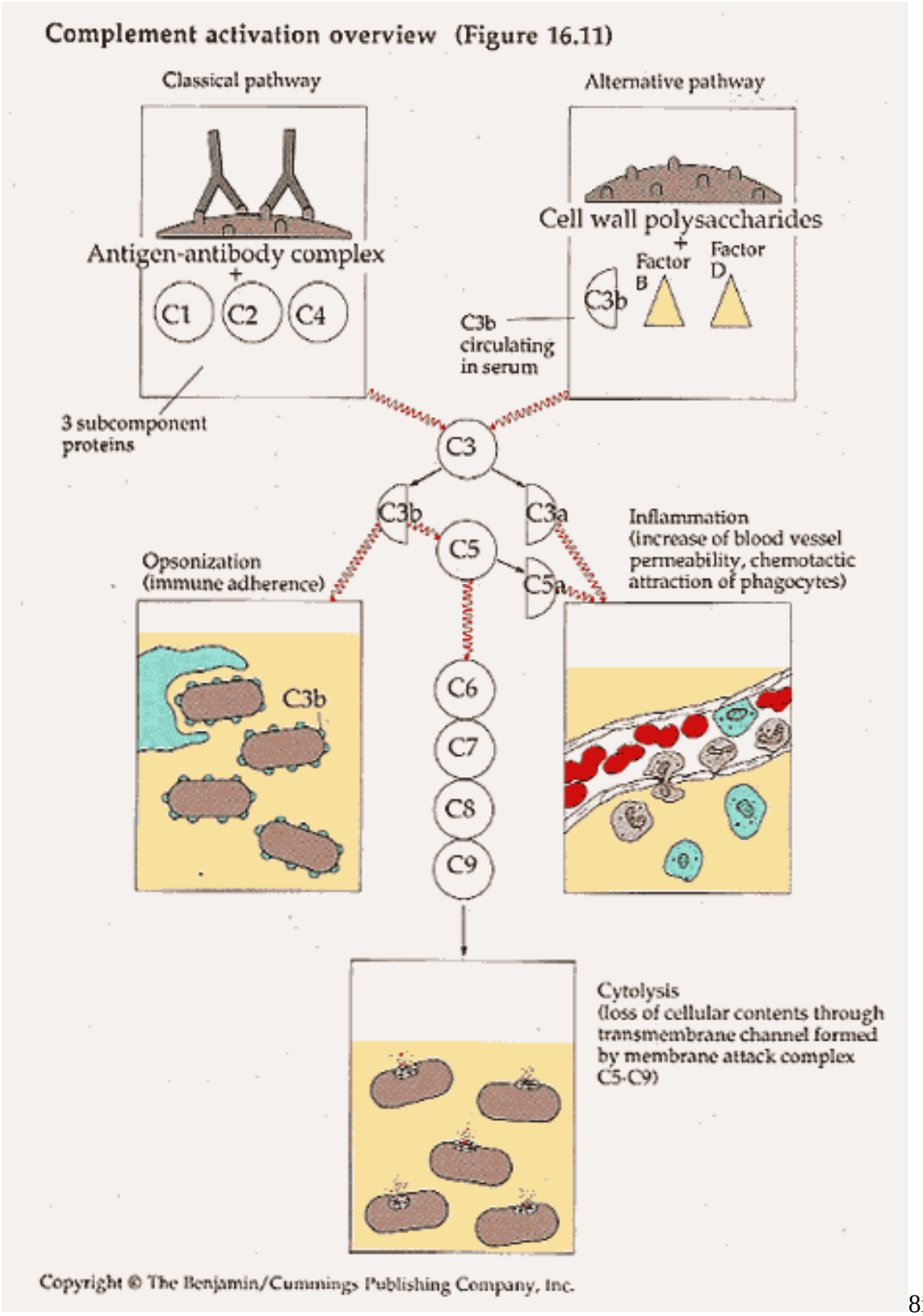
8h-2



(c) C3b initiates a series of reactions involving C5-C9, collectively called the membrane attack complex. This complex forms circular transmembrane channels (lesions) in the antigenic cell's membrane, with C9 proteins possibly playing a key role. The result is leakage of the cell's contents—cytolysis.



(d) Enlarged view of a transmembrane channel.


Complement activation overview (Figure 16.11)
Classical pathway
Alternative pathway
Antigen-antibody complex
+
C1
C2
C4
Cell wall polysaccharides
+
Factor B
Factor D
C3b
C3b circulating in serum
3 subcomponent proteins
C3
C3b
C3a
C5
C5a
Opsonization (immune adherence)
Inflammation (increase of blood vessel permeability, chemotactic attraction of phagocytes)
C3b
C6
C7
C8
C9
Cytolysis (loss of cellular contents through transmembrane channel formed by membrane attack complex C5-C9)
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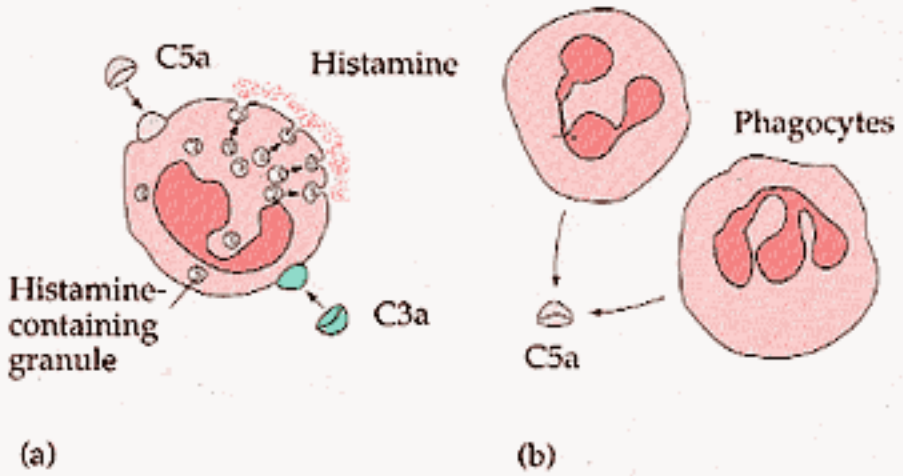
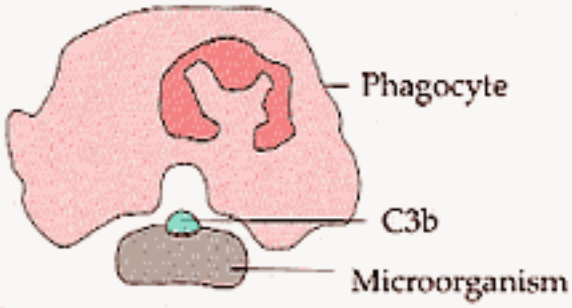
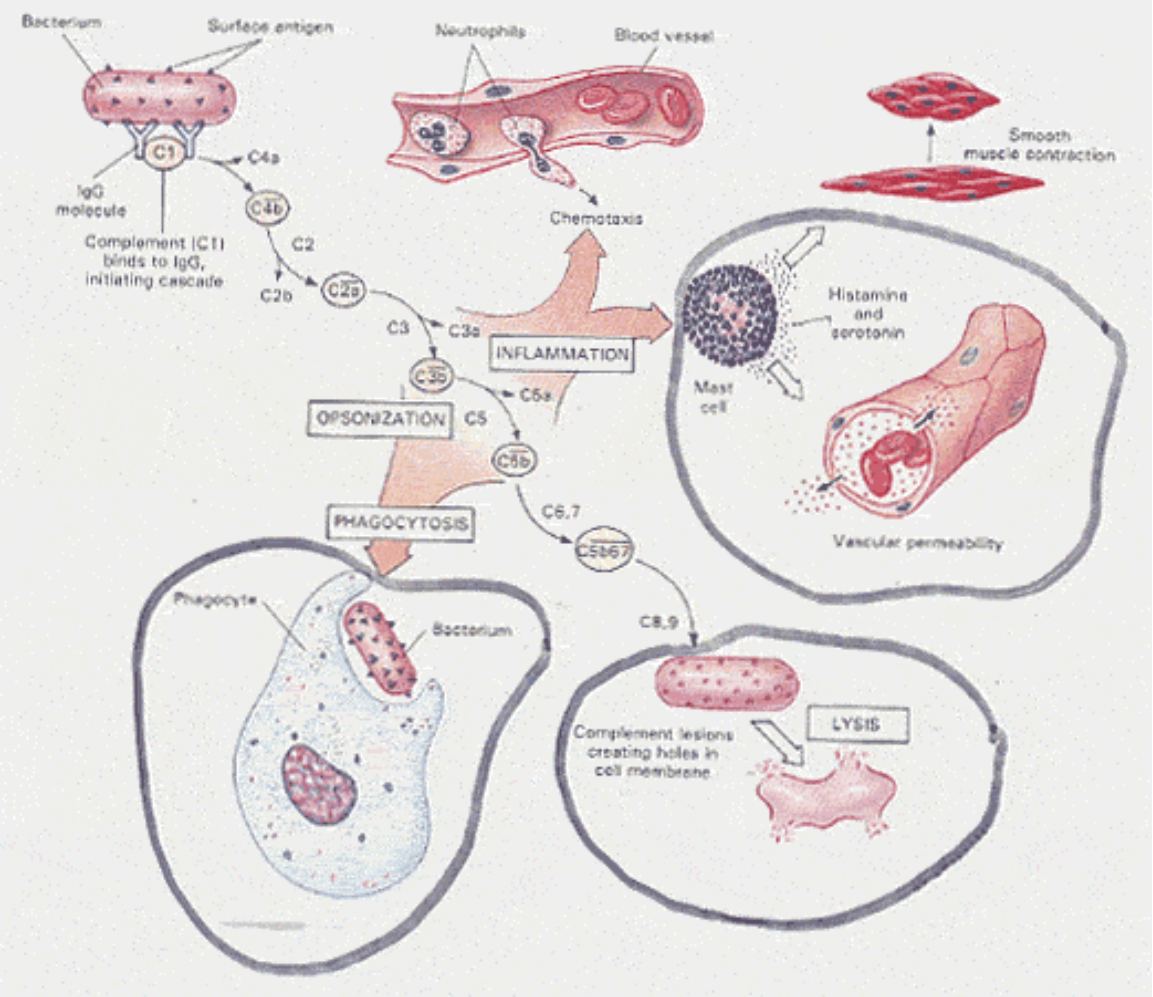
8i

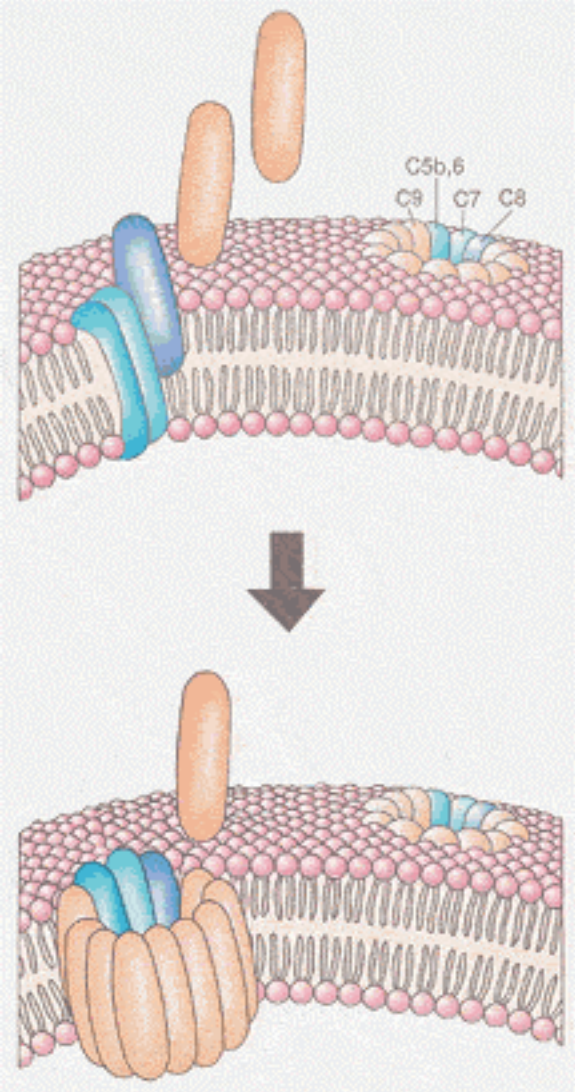
Stimulation of inflammatory response by complement (Figure 16.13)



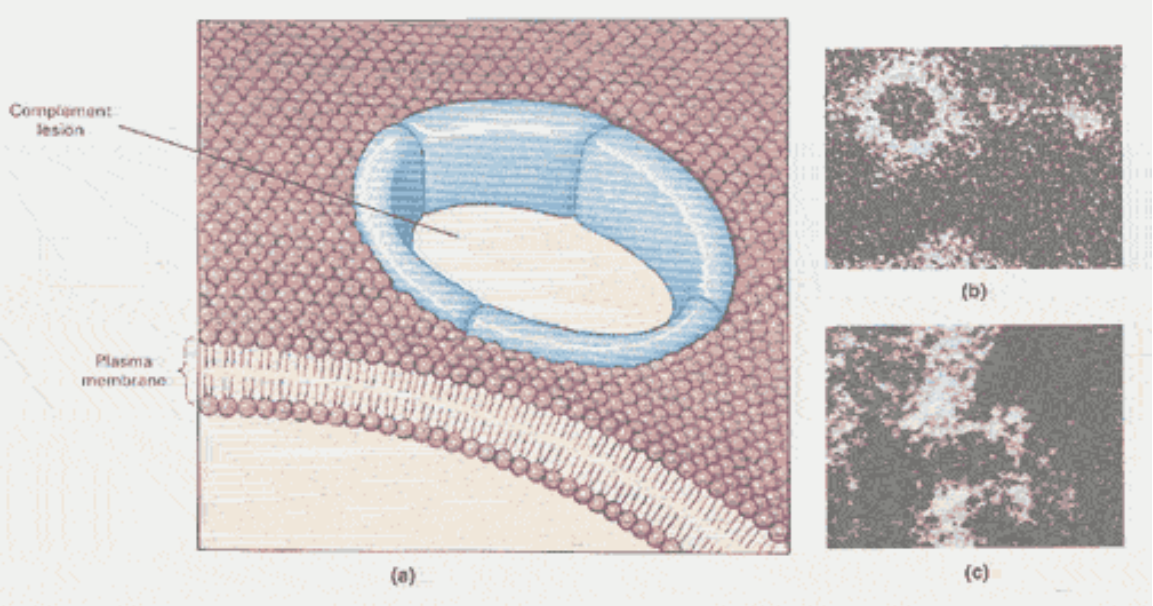
Opsonization by complement (Figure 16.14)



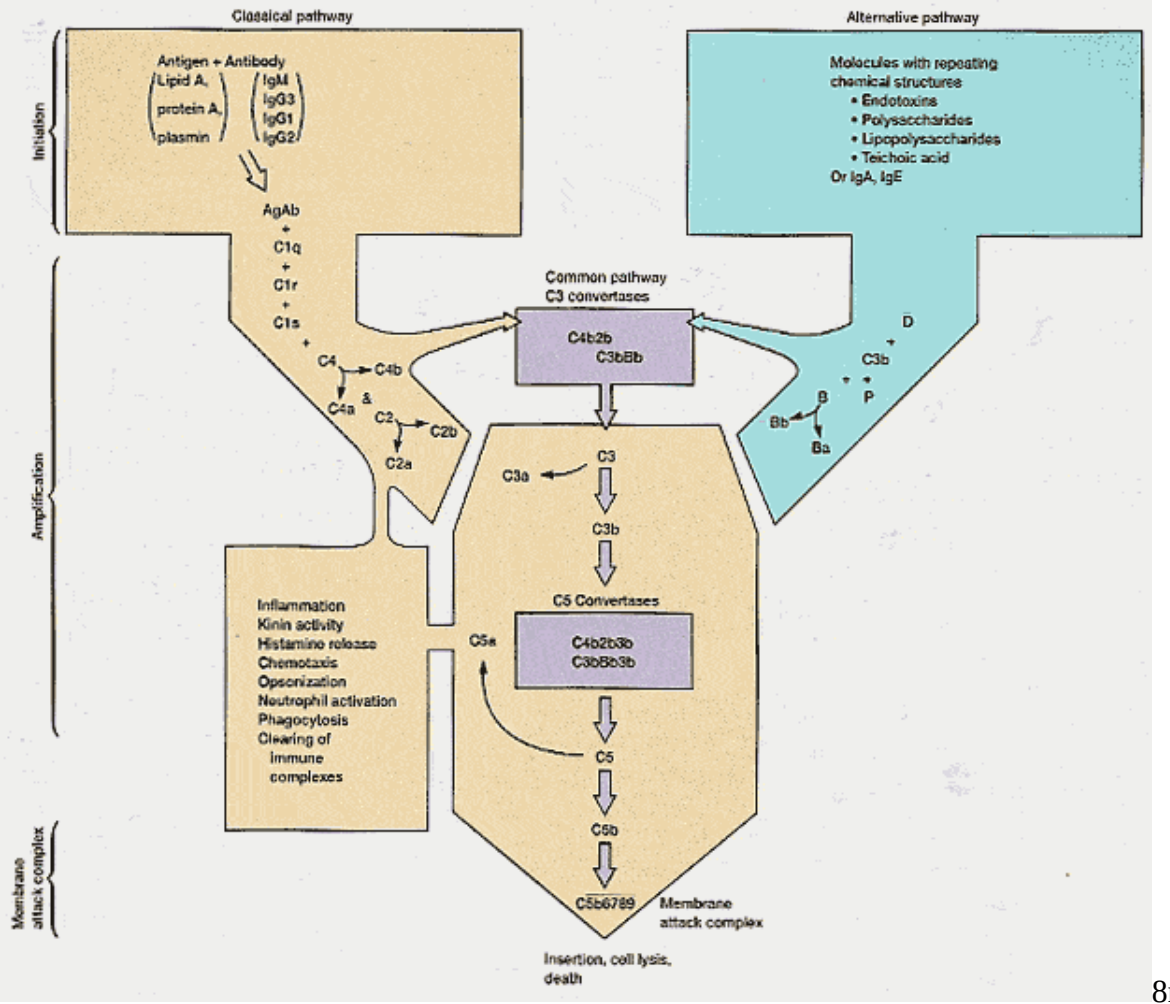

Bacterium
Surface antigen
Neutrophils
Blood vessel
Smooth muscle contraction
C1
C4a
IgG molecule
C4b
Complement (C1) binds to IgG, initiating cascade
C2
C2b
C2a
Chemotaxis
C3
C3a
INFLAMMATION
Histamine and serotonin
Mast cell
C3b
C5a
OPSONIZATION
C5
C5b
C6,7
PHAGOCYTOSIS
C5b67
Vascular permeability
Phagocyte
Bacterium
C8,9
Complement lesions creating holes in cell membrane
LYSIS
8k



8l


Complement lesion
Plasma membrane
(a)
(b)
(c)

8m


Classical pathway
Alternative pathway
Initiation
Amplification
Membrane attack complex
Antigen + Antibody
(Lipid A, protein A, plasmin)
(IgM IgG3 IgG1 IgG2)
AgAb
C1q
C1r
C1s
C4
C4b
C4a
&
C2
C2b
C2a
Molecules with repeating chemical structures
• Endotoxins
• Polysaccharides
• Lipopolysaccharides
• Teichoic acid
Or IgA, IgE
Common pathway
C3 convertases
C4b2b
C3bBb
D
C3b
B
P
Bb
Ba
C3
C3a
C3b
C5 Convertases
C4b2b3b
C3bBb3b
C5a
C5
C5b
C5b6789
Membrane attack complex
Inflammation
Kinin activity
Histamine release
Chemotaxis
Opsonization
Neutrophil activation
Phagocytosis
Clearing of immune complexes
Insertion, cell lysis, death

8n

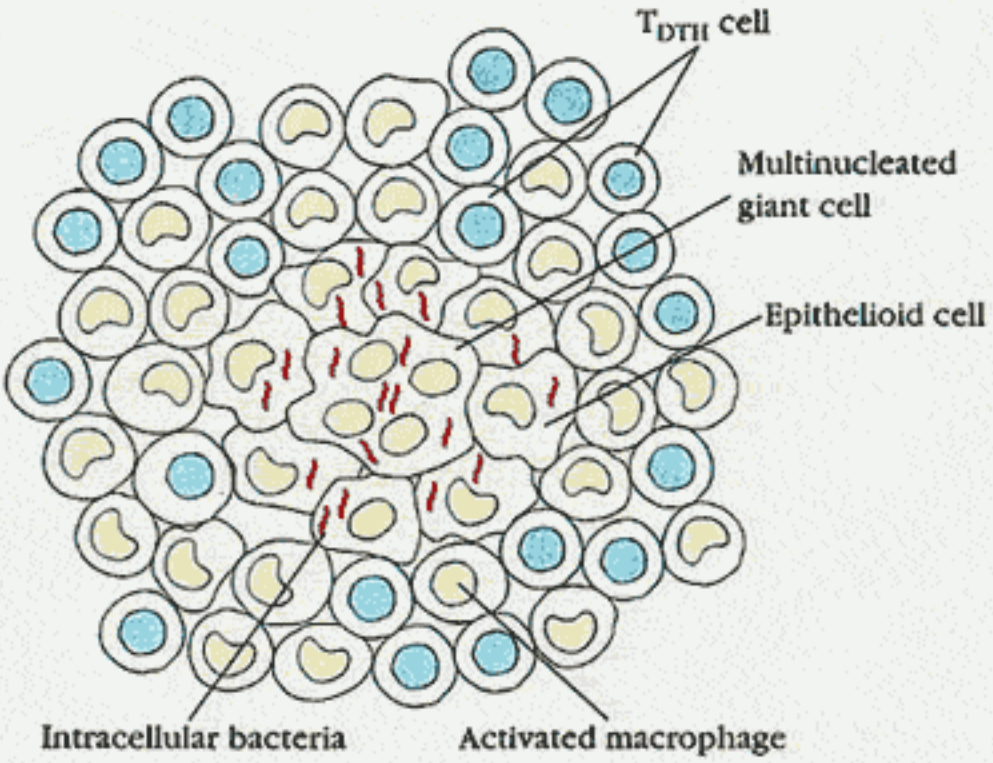


FIGURE 16-16

A prolonged DTH response can lead to formation of a granuloma, a nodule-like mass. Lytic enzymes released from activated macrophages in a granuloma can cause extensive tissue damage.

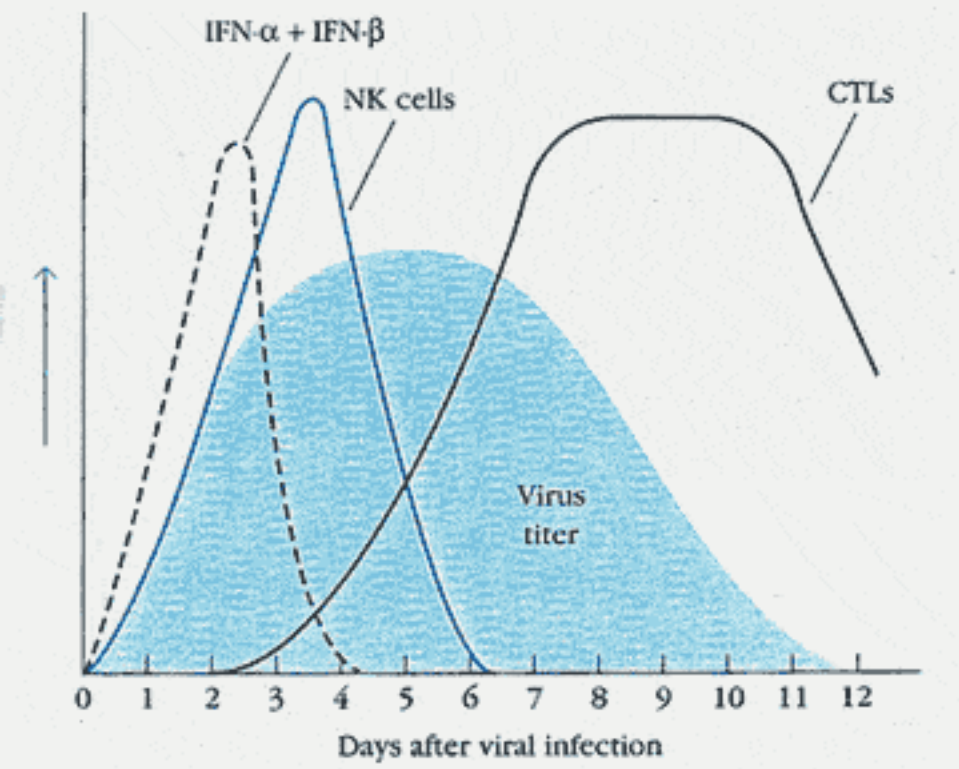
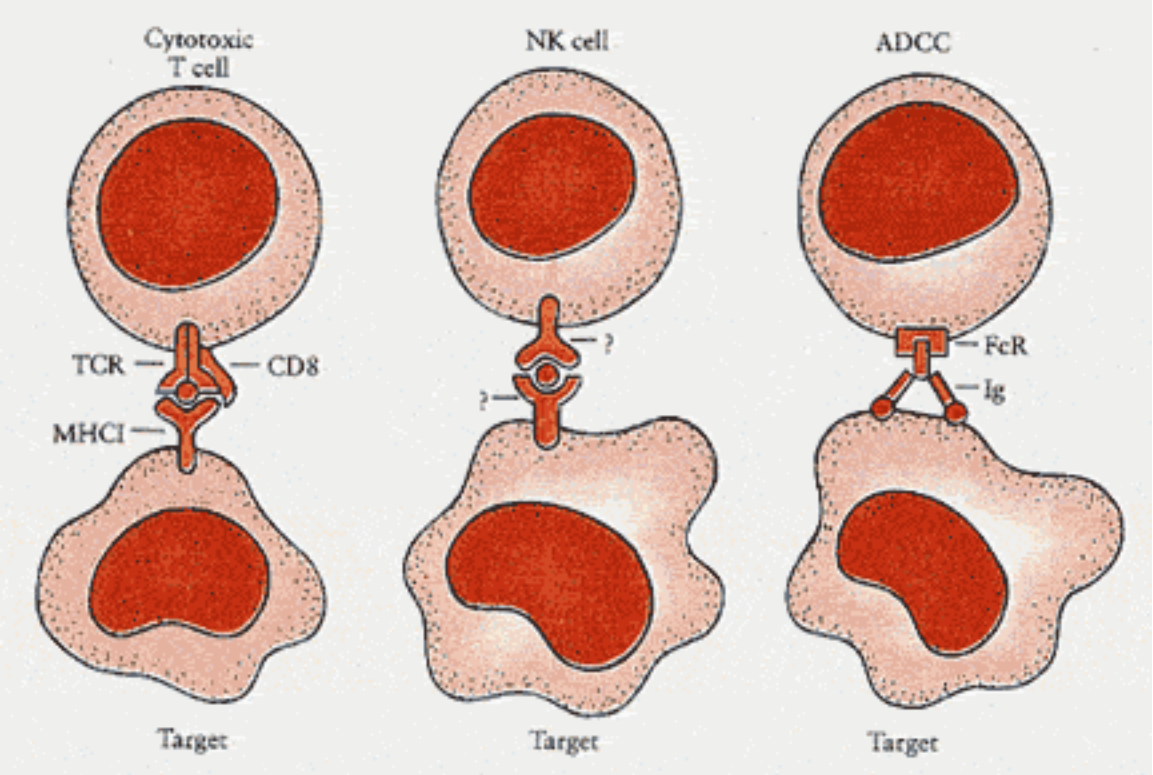


FIGURE 16-9

Time course of viral infection. IFN-α and IFN-β (dashed curve) are released from virus-infected cells soon after infection. These cytokines stimulate the NK cells, quickly leading to a rise in the NK-cell population (blue curve). NK cells help contain the infection during the period required for generation of CTLs (solid black curve). Once the CTL population reaches a peak, the virus titer (blue area) rapidly decreases.

8p


Cytotoxic
T cell
TCR
CD8
MHCI
Target
NK cell
?
?
Target
ADCC
FcR
Ig
Target
8q