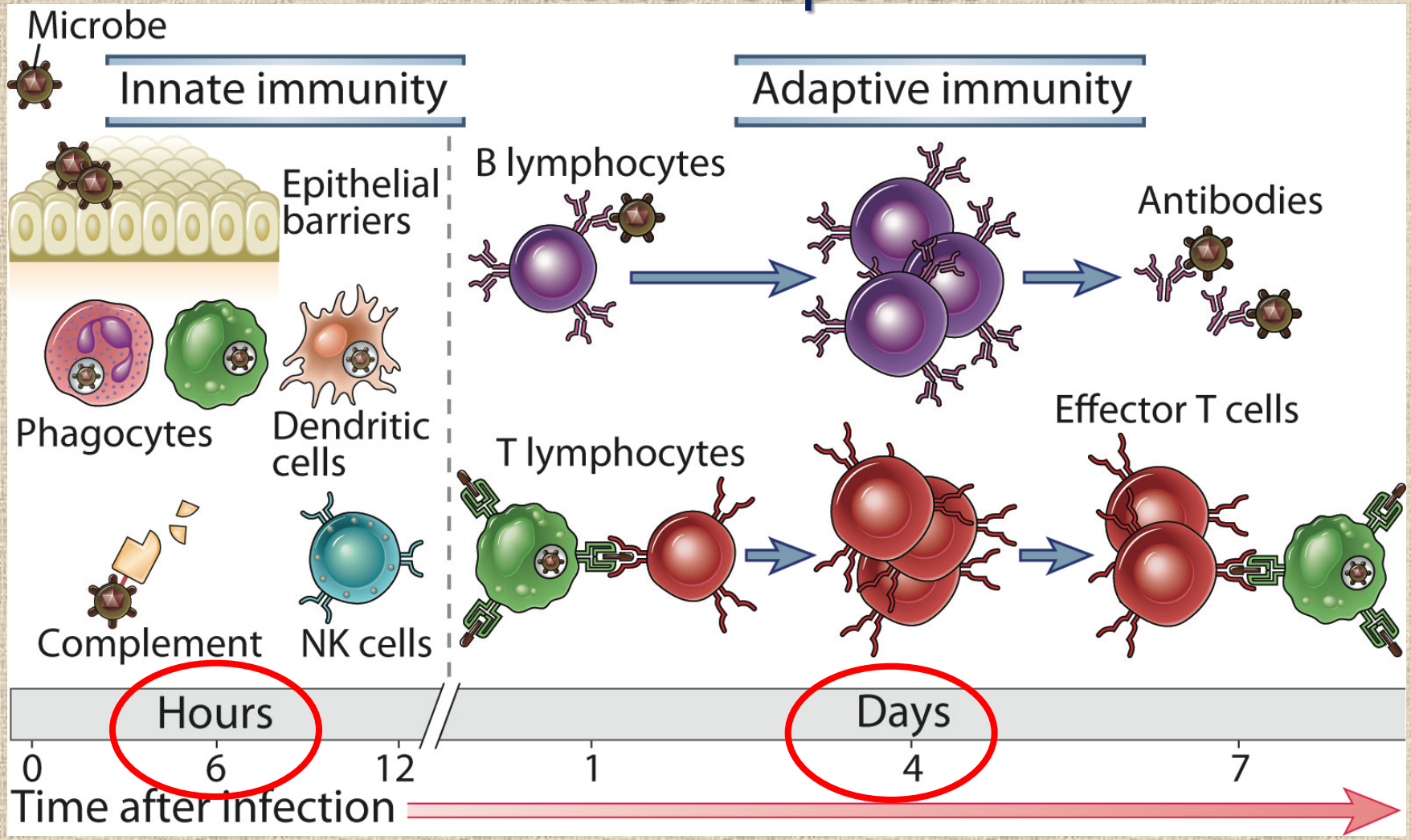
Basic immunology

Lecture 8.

Inflammatory reaction

Timea Berki

Time kinetic of the innate and adaprive immune response



Abbas, Lichtman, Pillai: Cellular and Molecular Immunology 7th Edition, 2012.

Routes of Antigen Entry

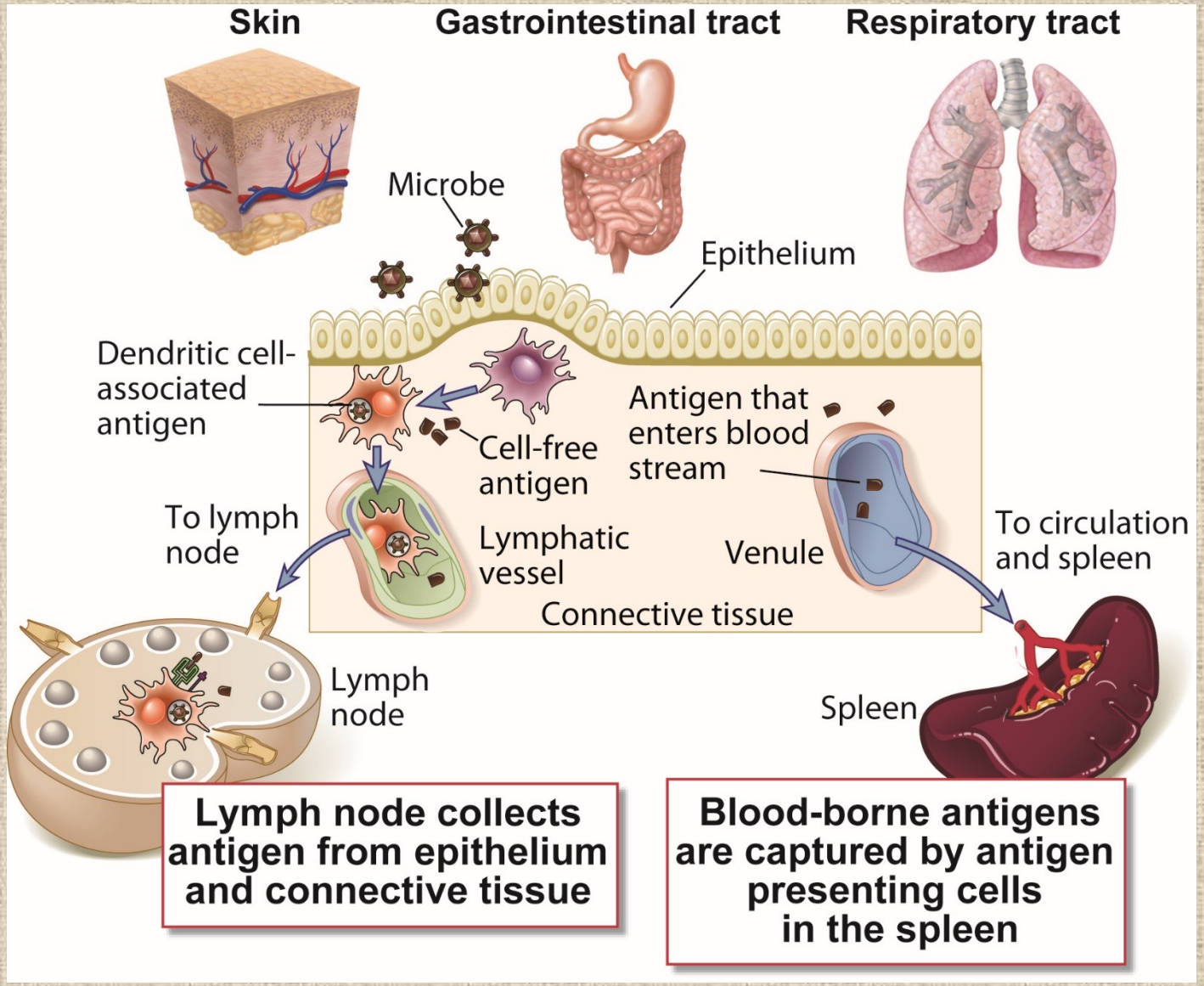
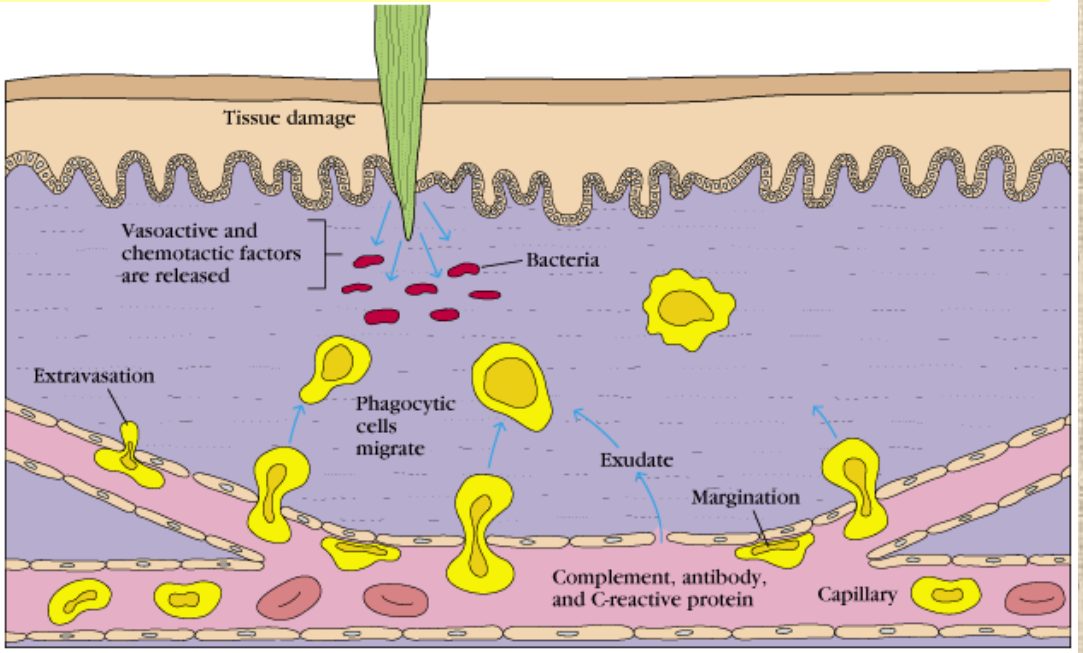


Fig. 6-3

Acute, local inflammation:

- Infection or tissue-injury initiate the cascade of non-specific reactions
- Immediate reaction
- Its role is to inhibit the spreading of infection and tissue injury

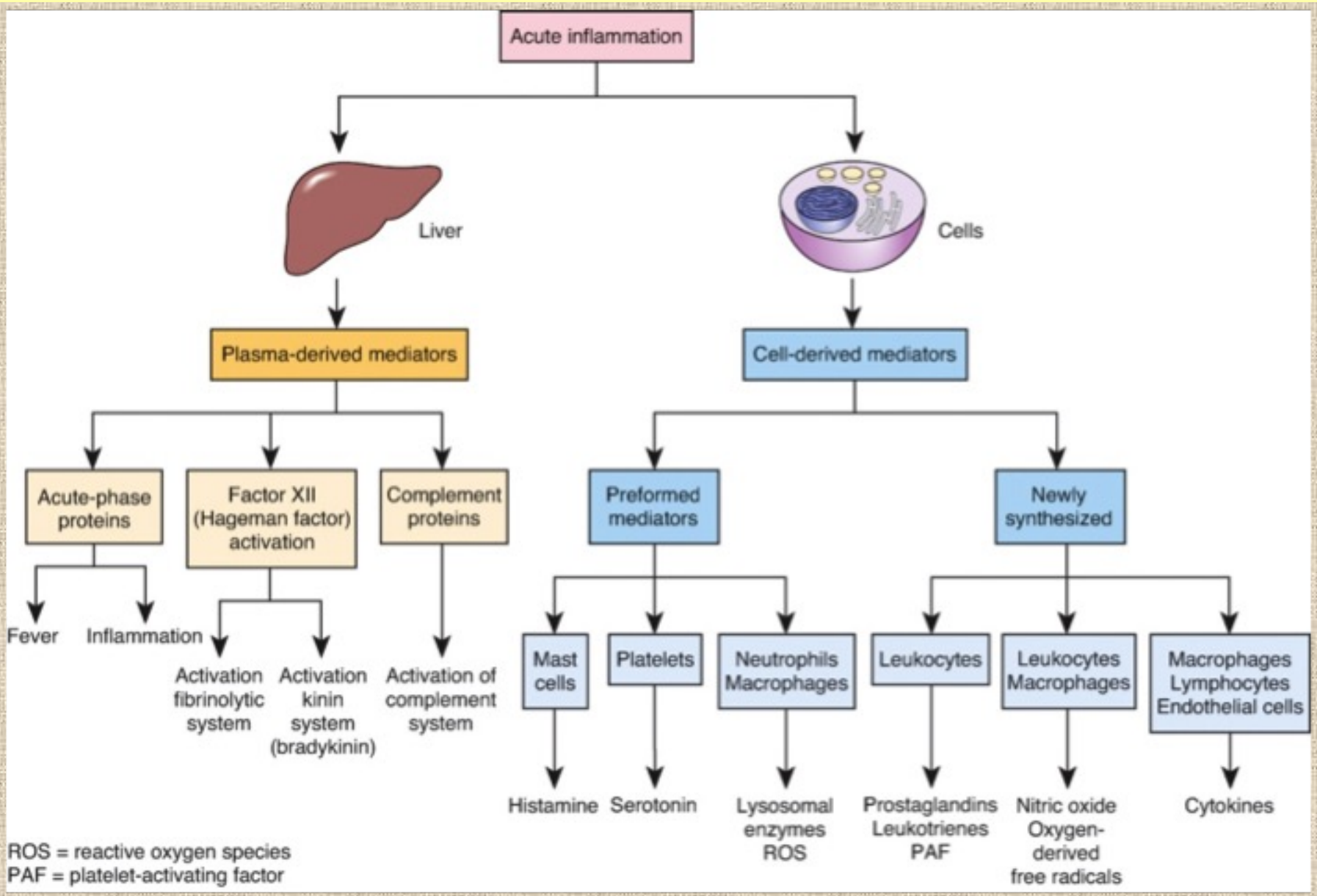


Celsus: 4 signs of inflammation: - rubor (red), calor (hot), dolor (painfull), tumor (swelling) + functio laesa (loss of function)

3 main events: - Vasodilation – minutes
- Increased capillary permeability, fluid efflux, oedema
- Phagocytes migration: - hours

Goldsby RA, Kindt TJ, Osborne BA: Kuby Immunology 4th Edition, 2000.

Mediators of inflammation



Molecular mediators of inflammation

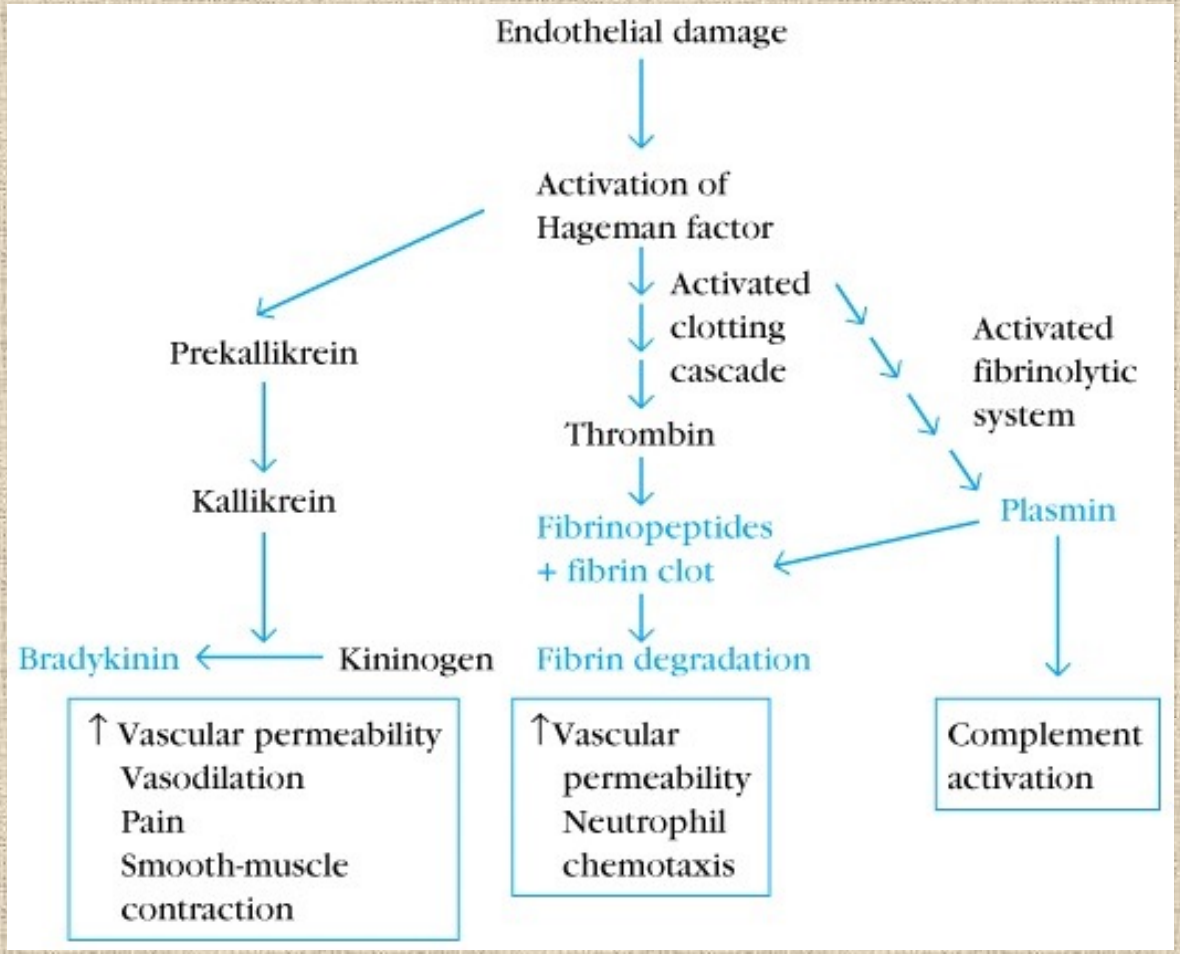
Plasma enzyme mediators:

- kinin kallikrein system
- Fibrinolytic system
- Complement cascade
- Clotting cascade

Lipid mediators:
leukotrienes,
prostaglandins (PGE)

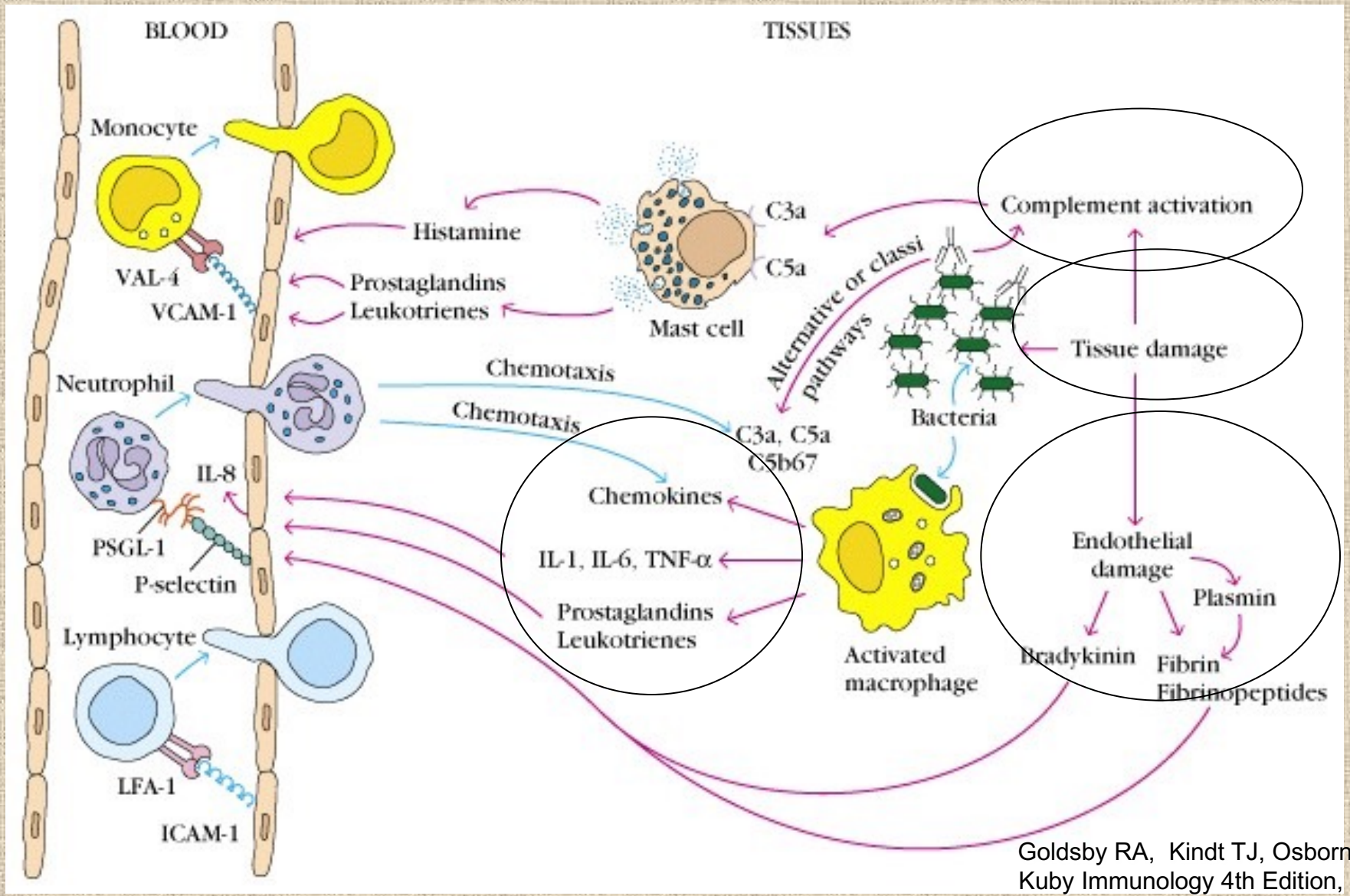
Chemoattractants:
-Chemokines: IL-8
-Complement components
- PAF (platelet activating factor)

Inflammatory cytokines:
IL-1, IL-6, TNFalpha



Goldsby RA, Kindt TJ, Osborne BA: Kuby Immunology 4th Edition, 2000.

Initation of acute inflammation



Goldsby RA, Kindt TJ, Osborne BA: Kuby Immunology 4th Edition, 2000.

Maturation of Macrophages and DCs

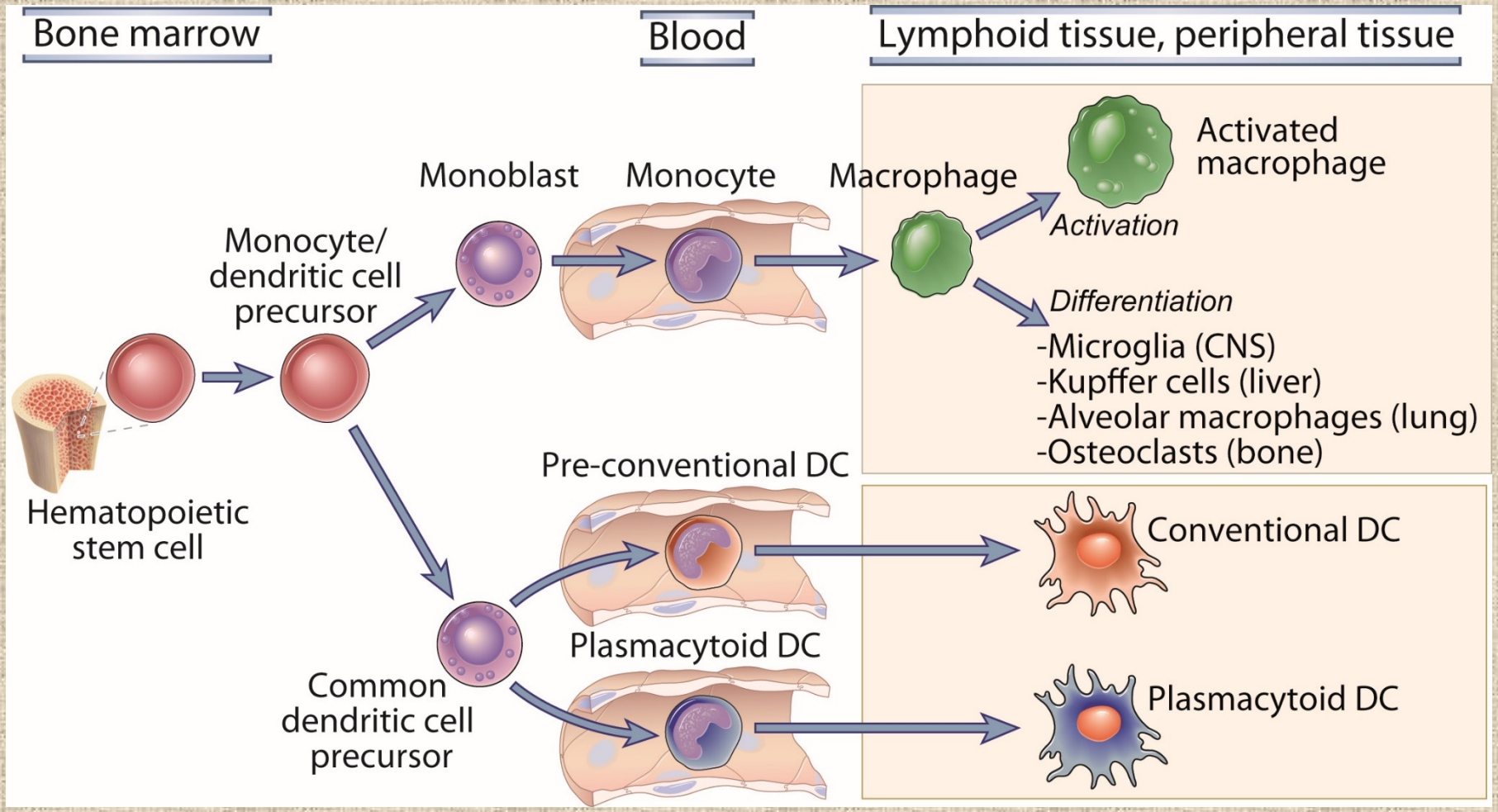
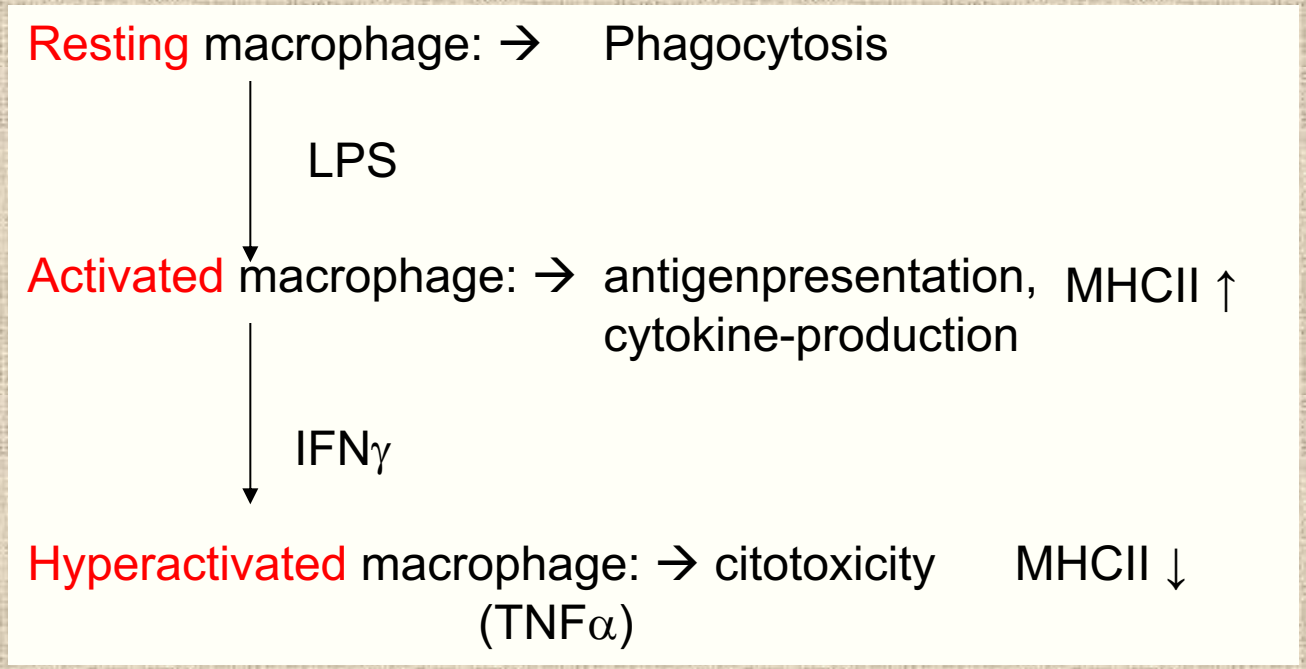


Fig. 2-2

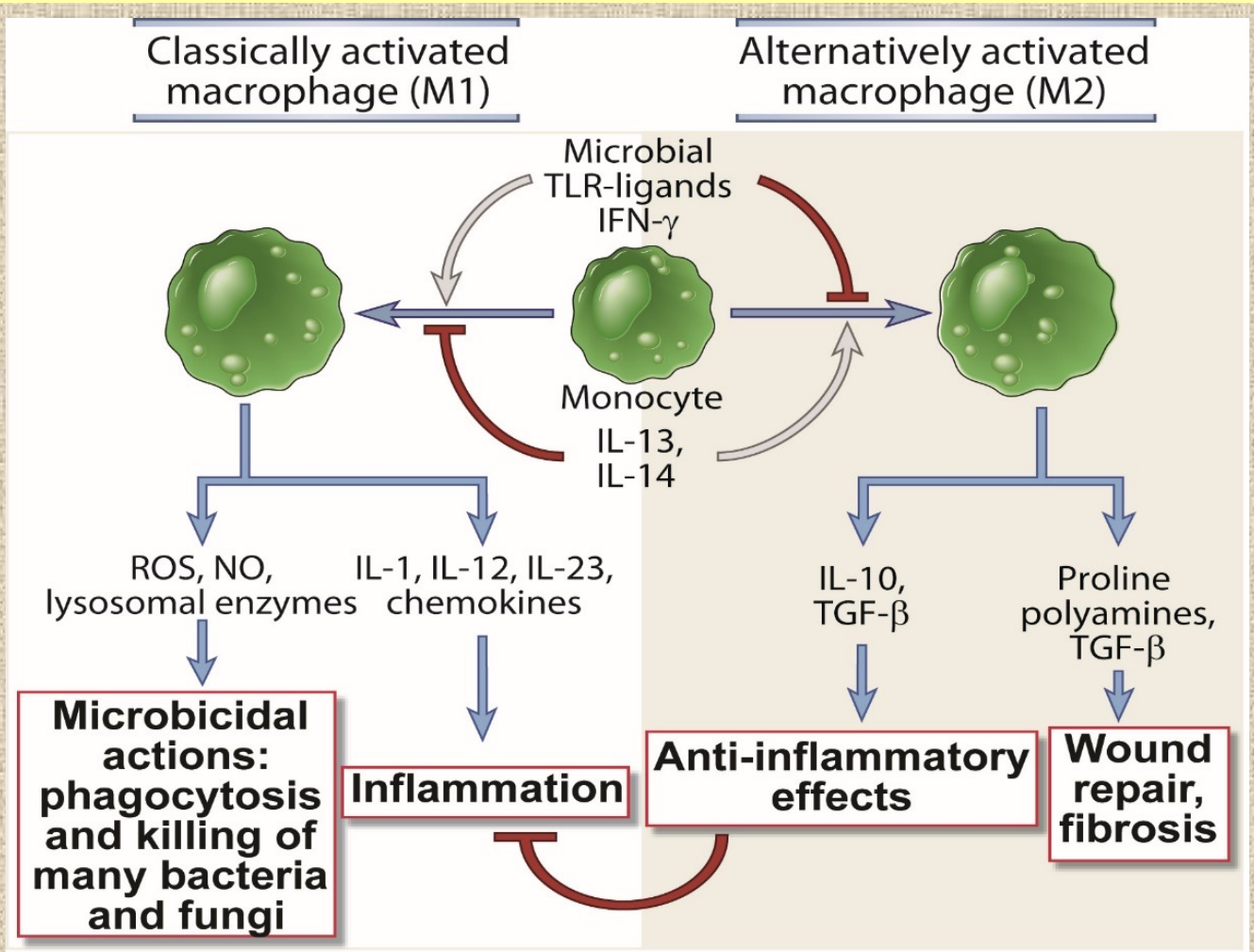
Role of macrophages in acute inflammation: classical activation



Abbas, Lichtman, Pillai: Cellular and Molecular Immunology 7th Edition, 2012.

Janeway CA Jr, Travers P, Walport M, Shlomchik MJ. Immunobiology, 2005.

Polarization of macrophages

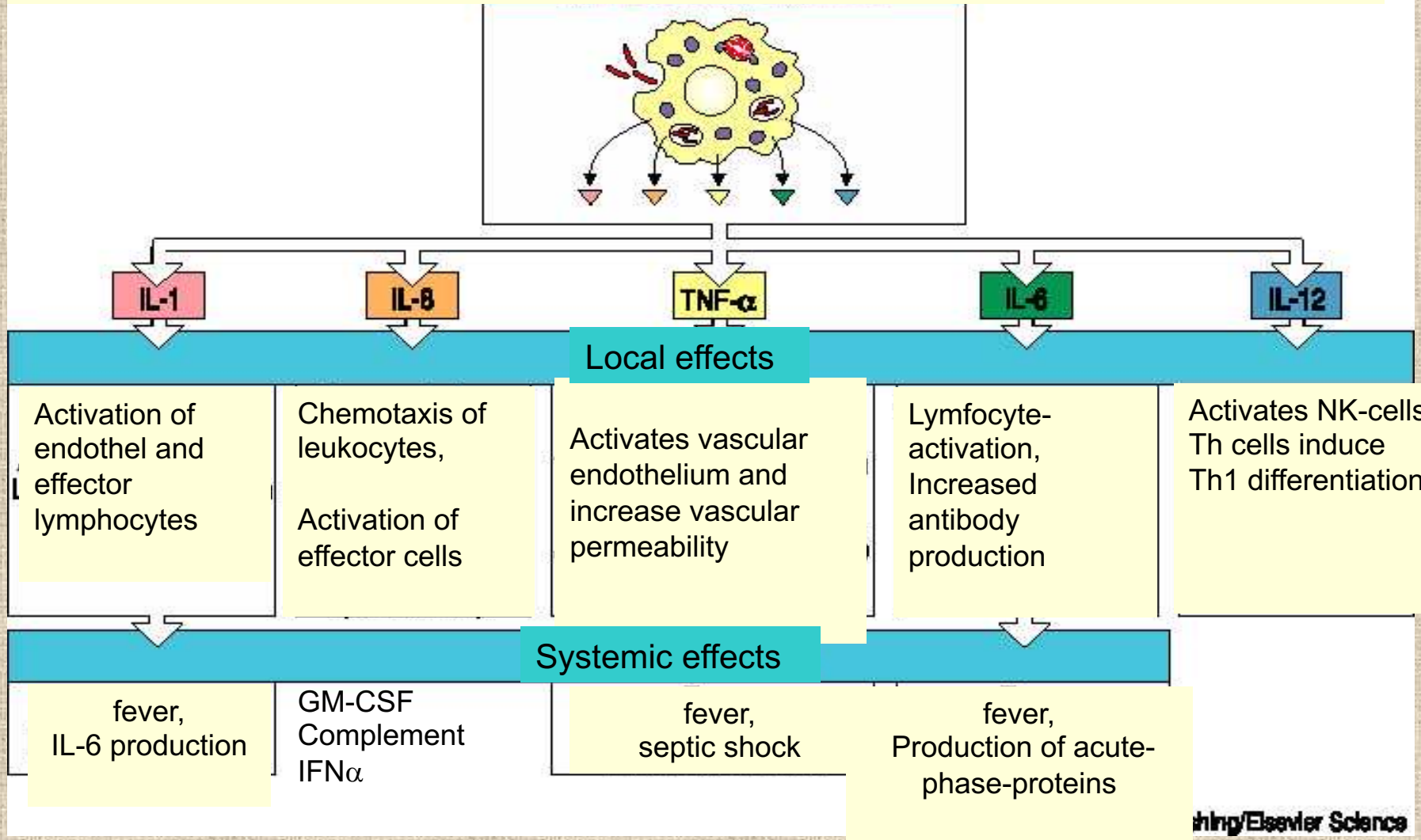


Abbas, Lichtman, Pillai: Cellular and Molecular Immunology 7th Edition, 2012.

Janeway CA Jr, Travers P, Walport M, Shlomchik MJ. Immunobiology, 2005.

Activated macrophages produce infalmmatory cytokines

LPS originated from Gram – bacterium LPS activates the macrophages, those produce various cytokines



Janeway CA Jr, Travers P, Walport M, Shlomchik MJ. Immunobiology, 2005.

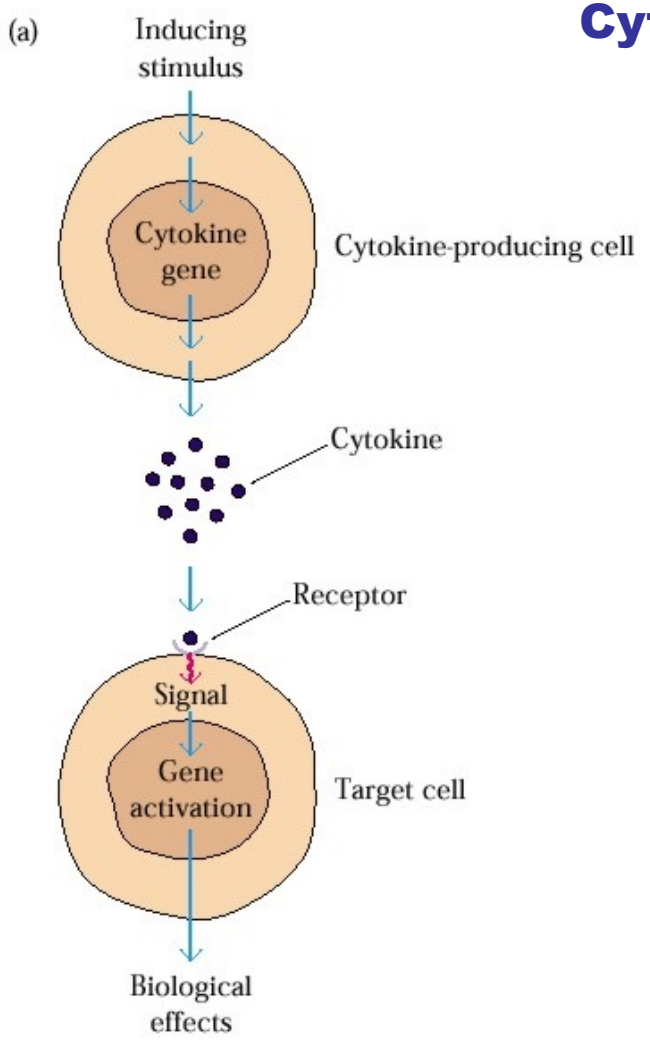
Basic characteristics of cytokies

- Low molecular weight (10-40 kDa) glycoproteins
- Isolated cells secrete them, due to gene activation
- They mediate cell-cell interaction:
- - sending information
- - regulation of immune response
- Mechanism of action:

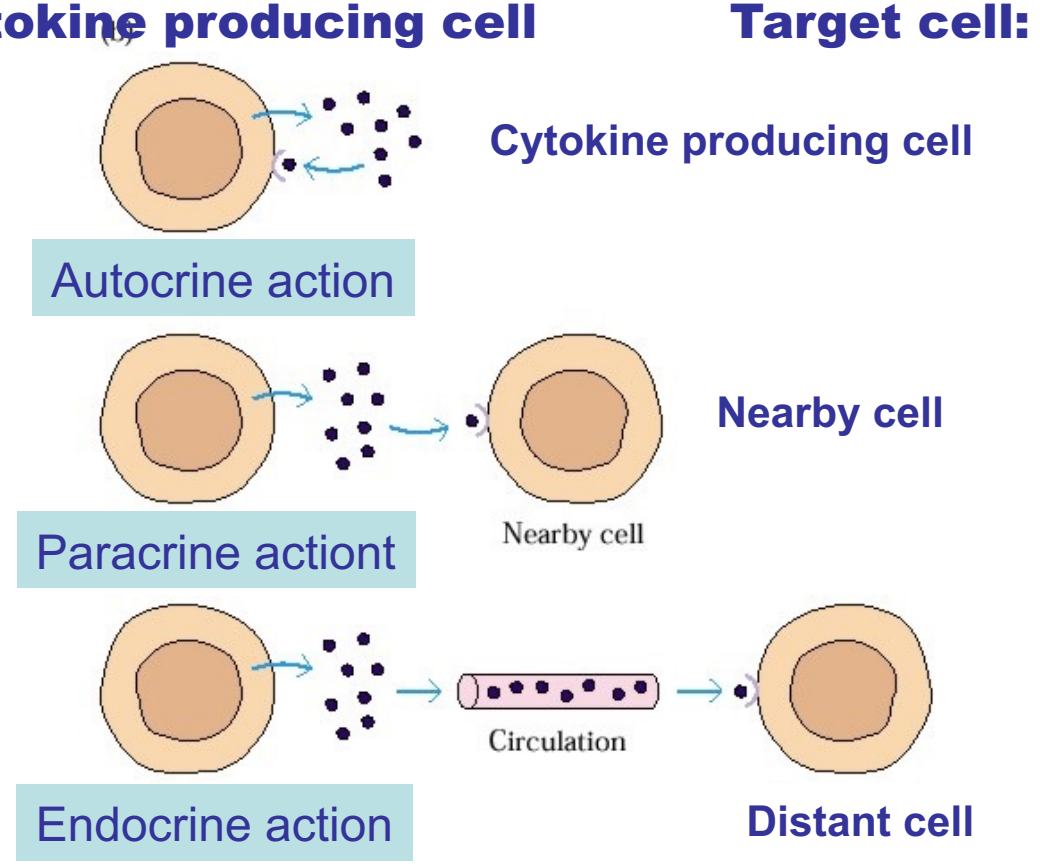
  - produced after transient gene activation
  - act through receptors triggering signal-transduction
  - high affinity
  - picomolar concentration

They act mostly locally.

Mechanism of cytokine action I.:



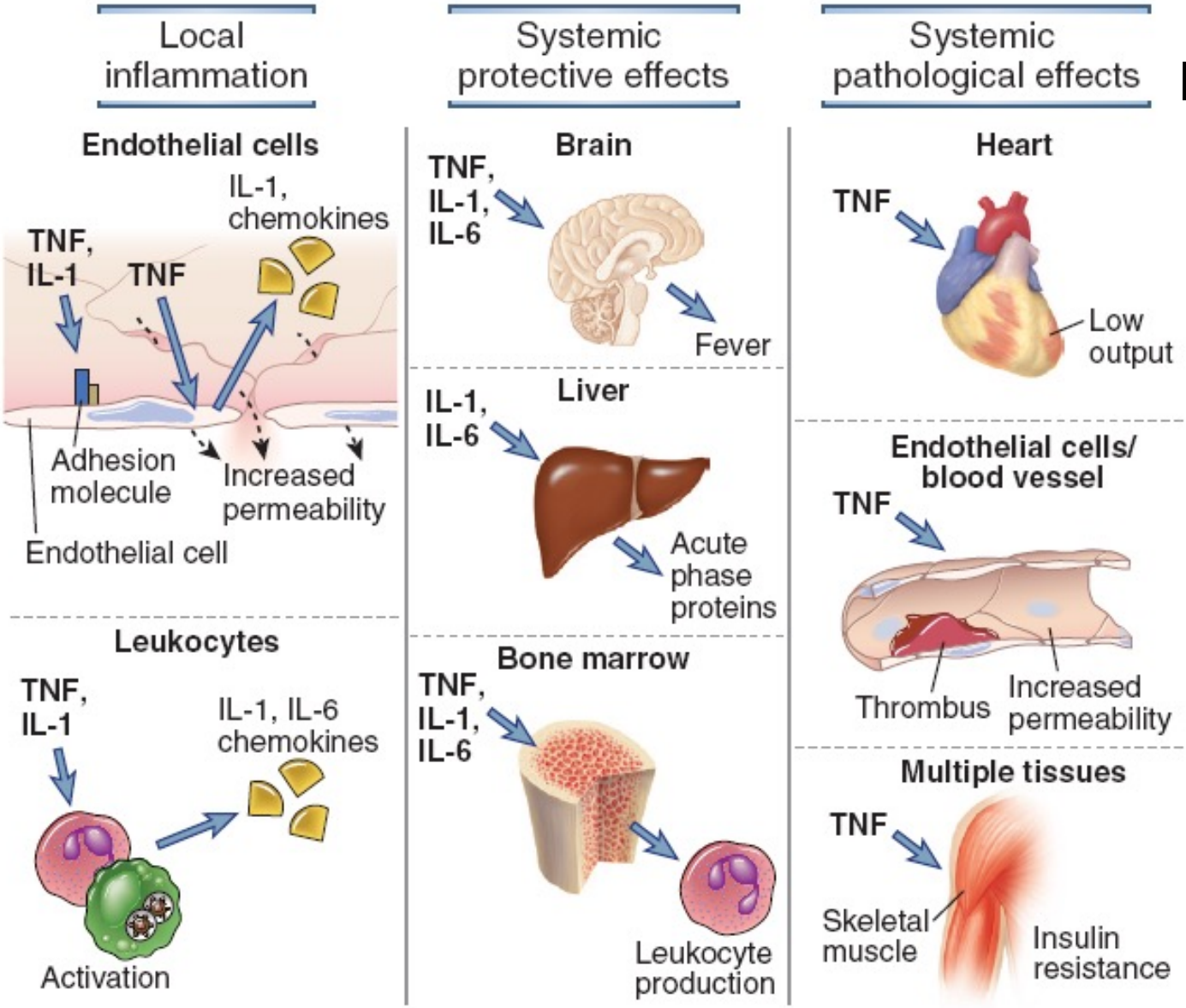
Cytokine producing cell **Target cell:**



Functional groups of cytokines

I. Regulators of natural immunity and inflammation	IFNα, IFNβ, IL-1α, IL-1β, IL-6, TNFα IL-12, Chemokines: CXCL8 (IL-8), CCL3,4 (MCP, MIP-1)
II. Regulators of lymphocyte activation and differentiation	TH1: IL-2, INFγ, TNFβ (LT) TH2: , IL-4, IL-5, IL-6, IL-13, IL-15 Treg: IL-10 and TGFβ
III. Regulators of haematopoiesis	IL-3, IL-7, GM-CSF, SCF

Local and systemic effects of TNF

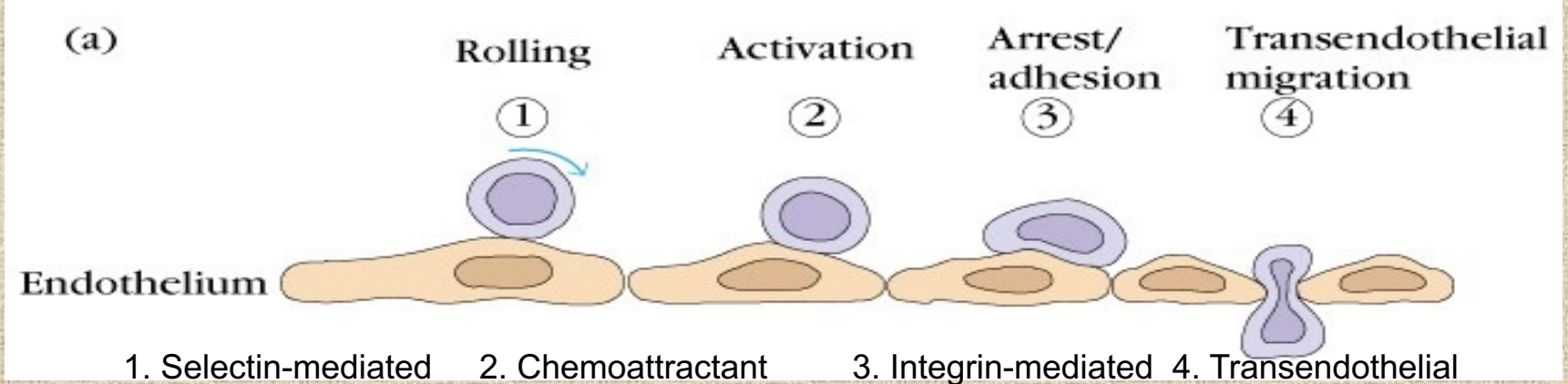


TNF inhibitors, Steroids

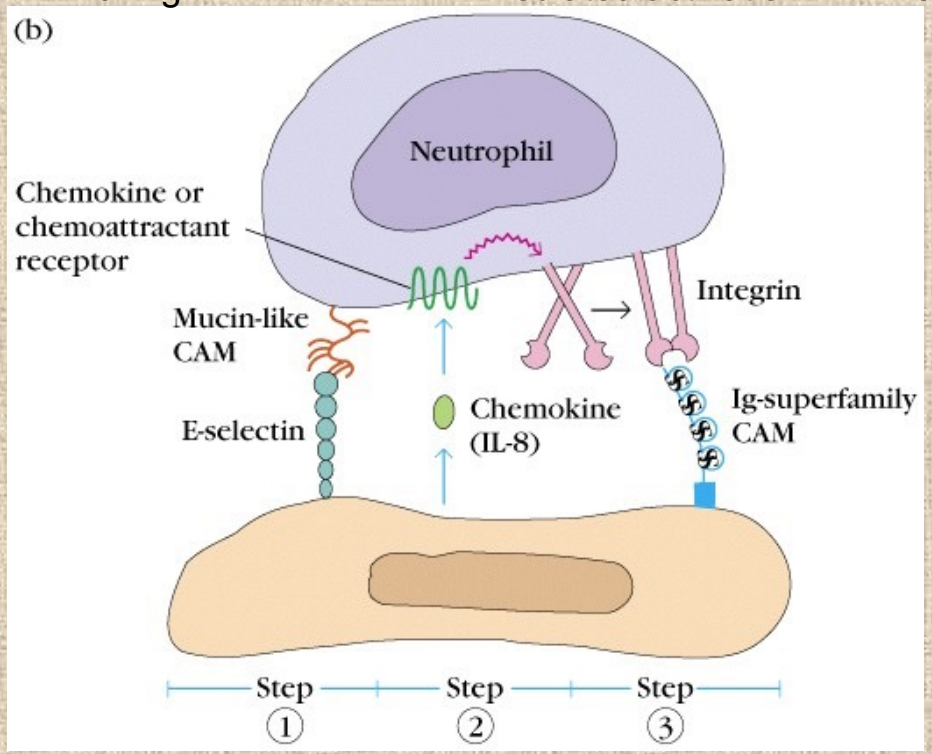
Abbas, Lichtman, Pillai: Cellular and Molecular Immunology 7th Edition, 2012.

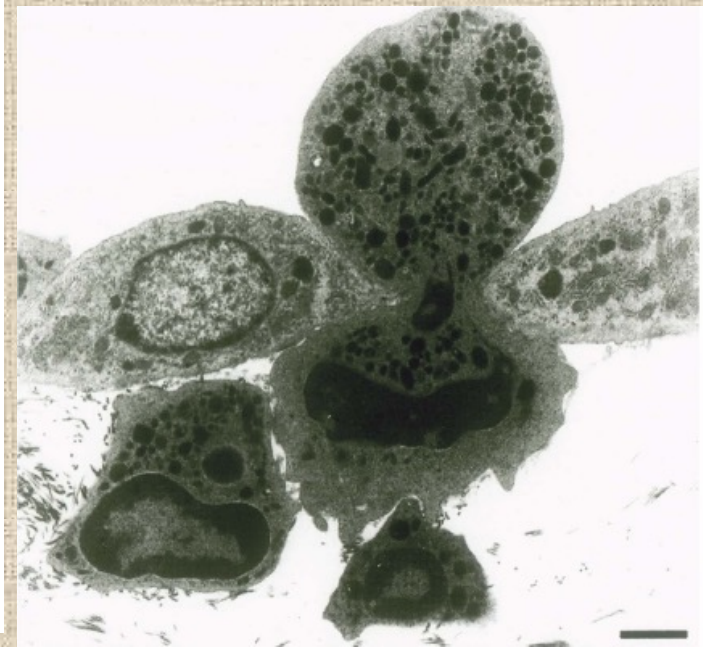
- **Extravasation, homing (leukocyte migration)**

Neutrophil extravasation through the inflamed endothelium



1. Selectin-mediated rolling
2. Chemoattractant mediated activation
3. Integrin-mediated adhesion
4. Transendothelial migration





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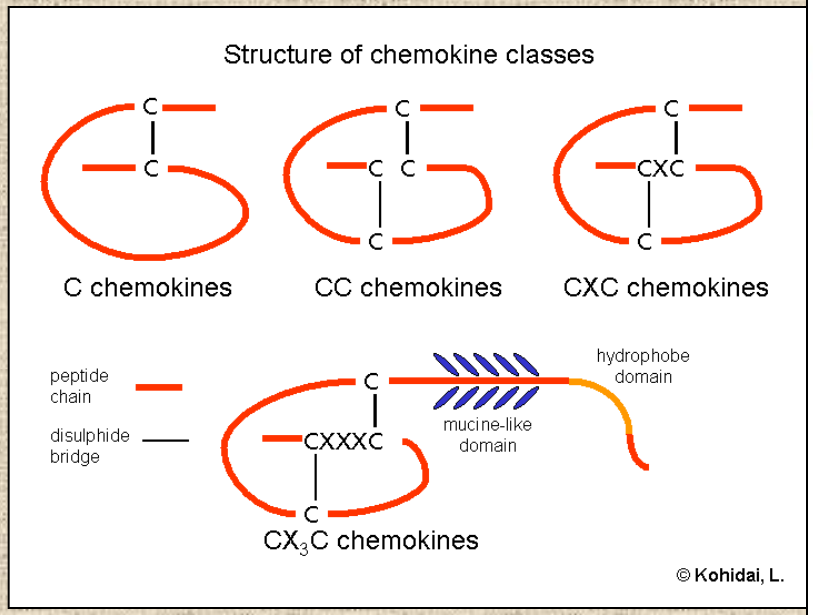
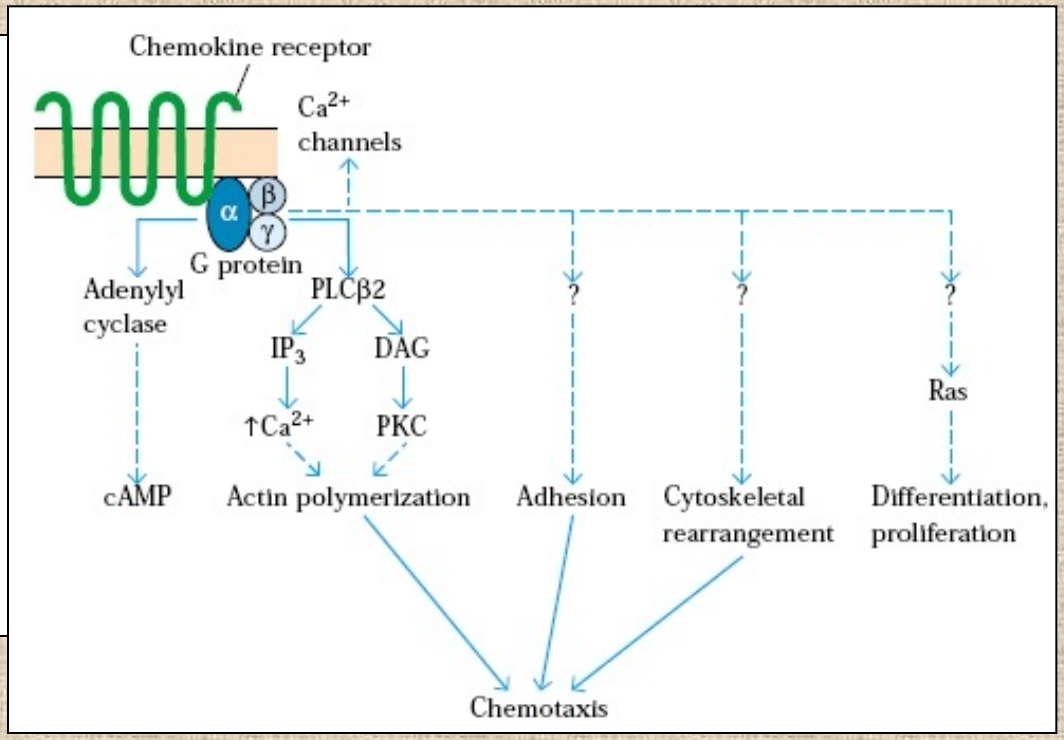
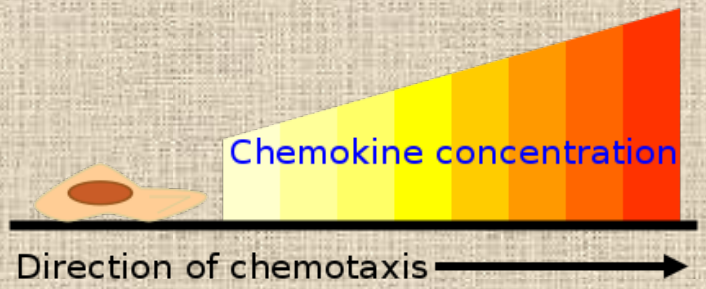
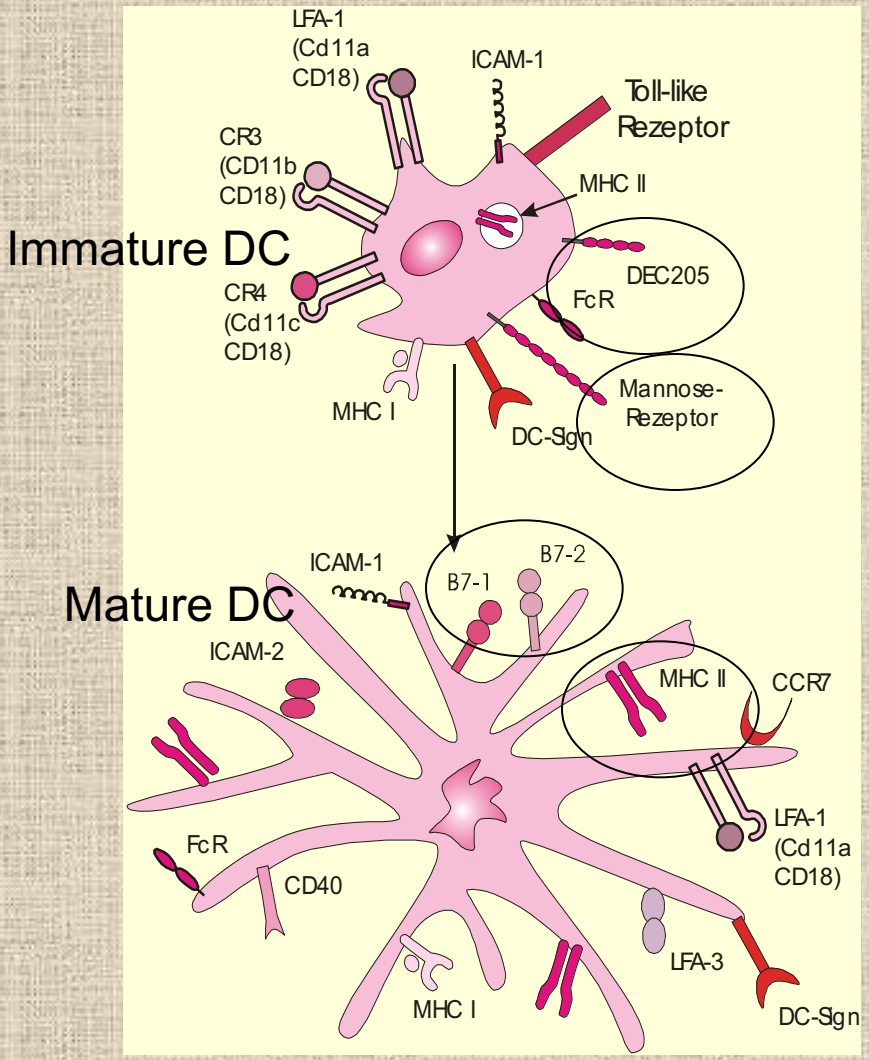
Chemokine action







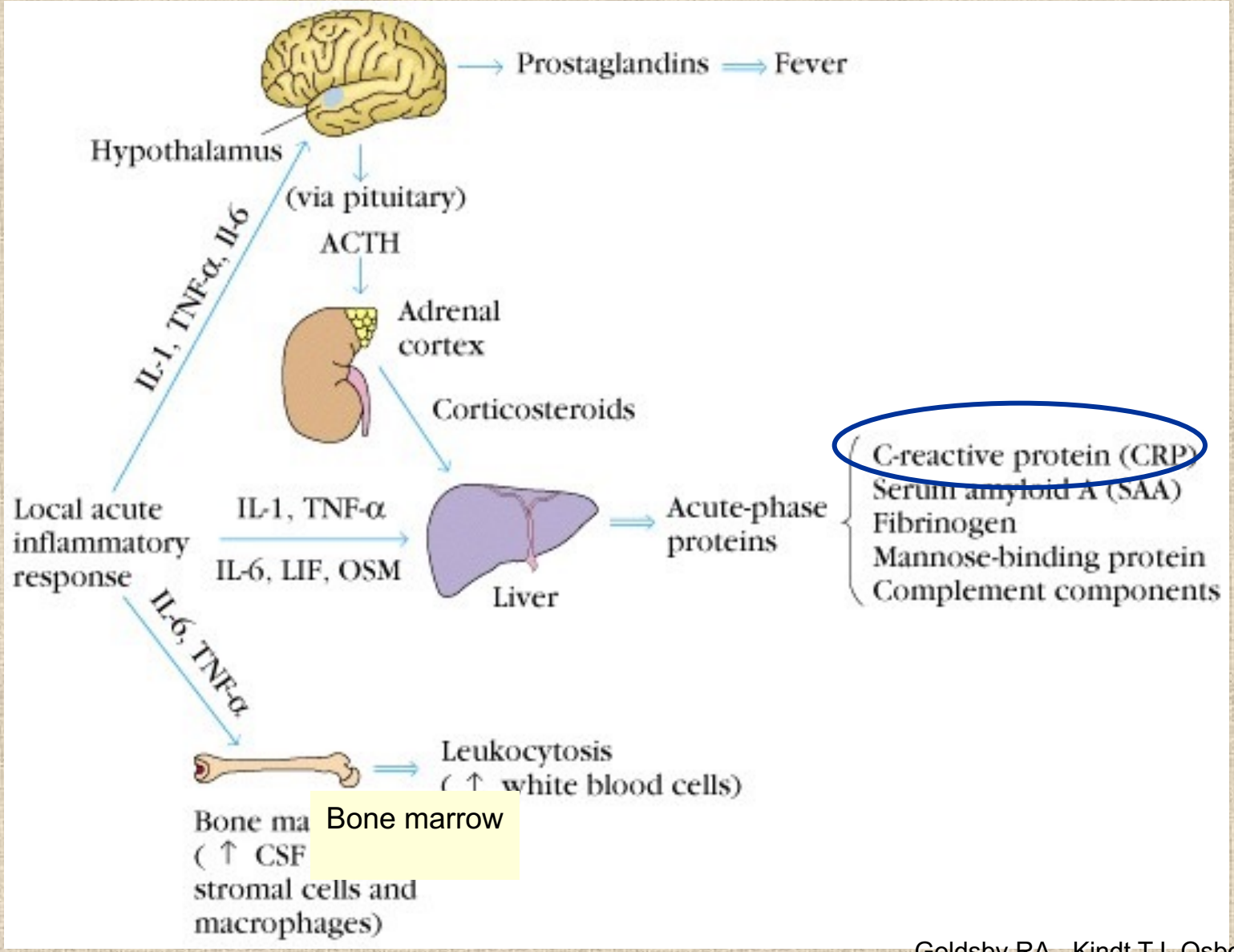
Dendritic cell activation



	Immature dendritic cell	Mature dendritic cell
Principal function	Antigen capture	Antigen presentation to T cells
Expression of Fc receptors, mannose receptors	++	–
Expression of molecules involved in T cell activation: B7, ICAM-1, IL-12	– or low	++
Class II MHC molecules Half-life	~10 hr	>100 hr
Number of surface molecules	~10^6	~7×10^6

- **Systemic inflammation**

Systemic acute inflammation = acute phase reaction



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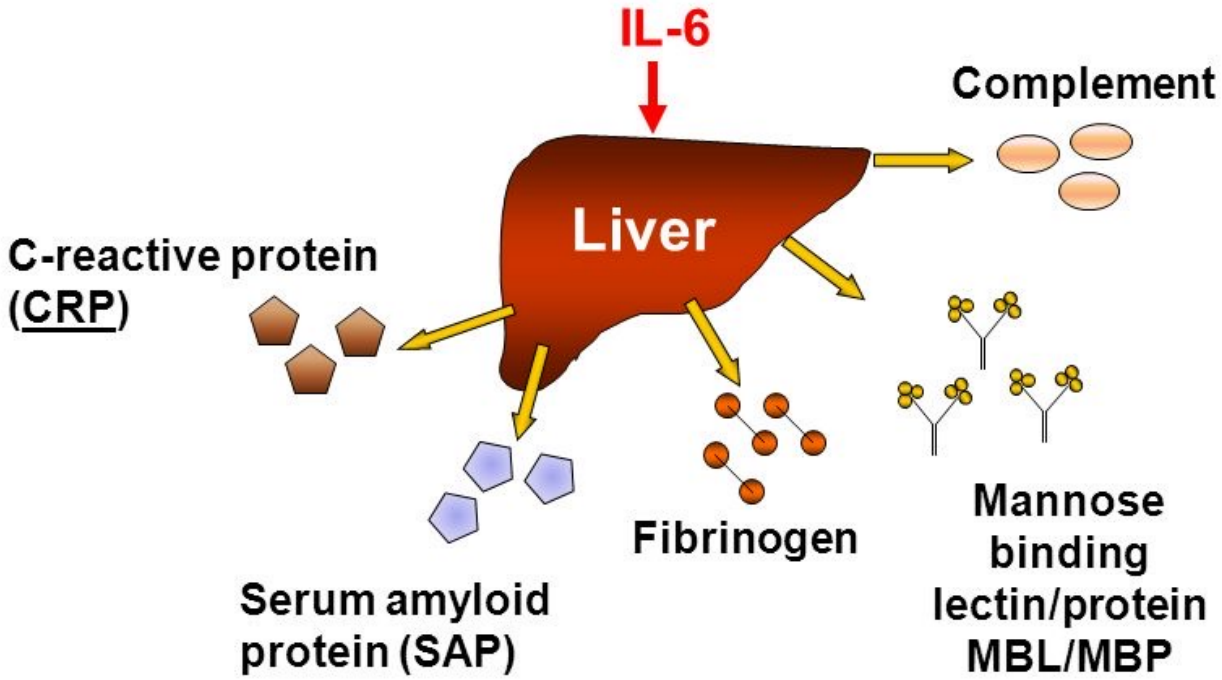
ACUTE PHASE REACTION

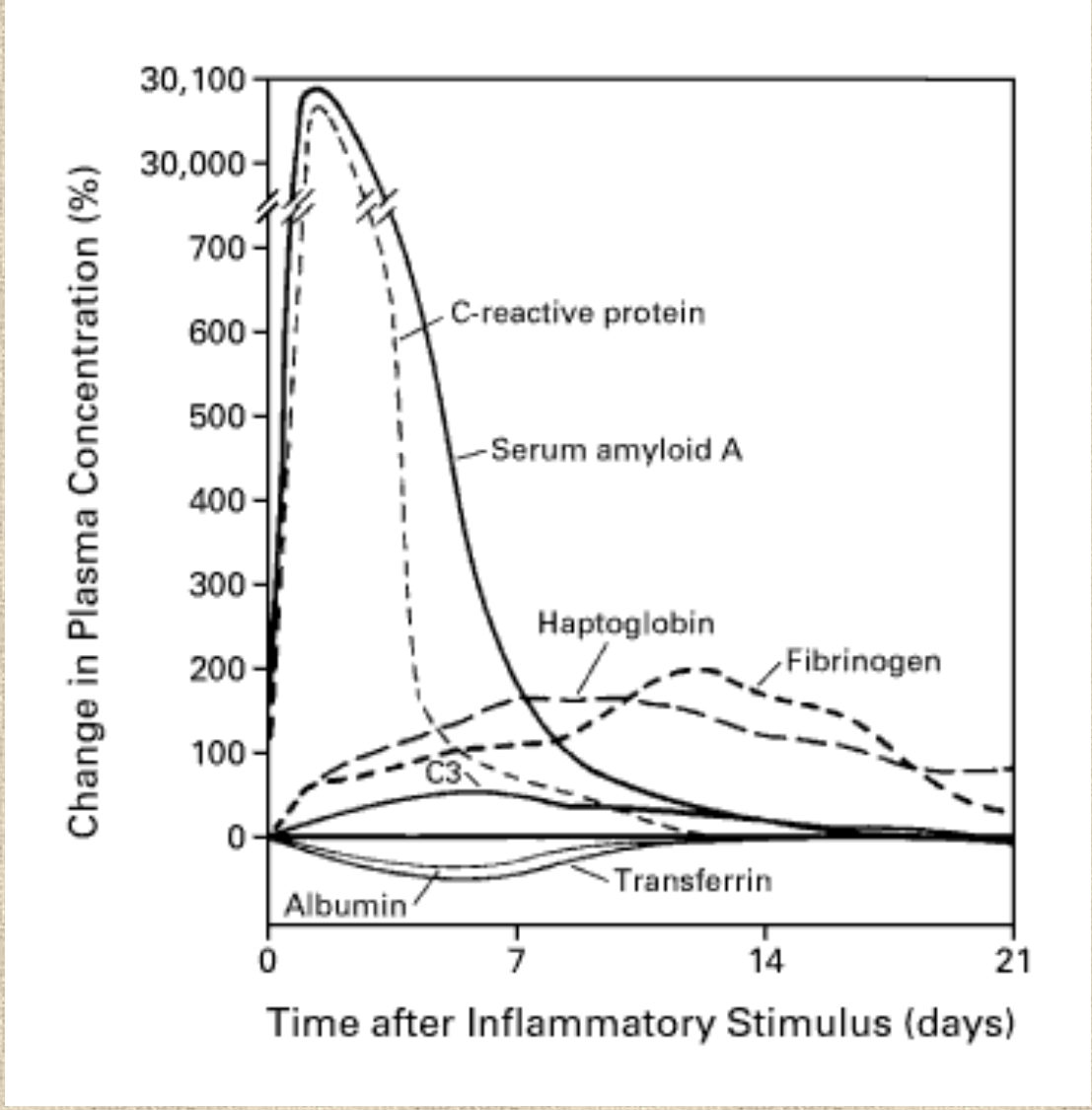


UNDER THE INFLUENCE OF IL-6 THE LIVER PRODUCES A BUNCH OF ACUTE-PHASE PROTEINS

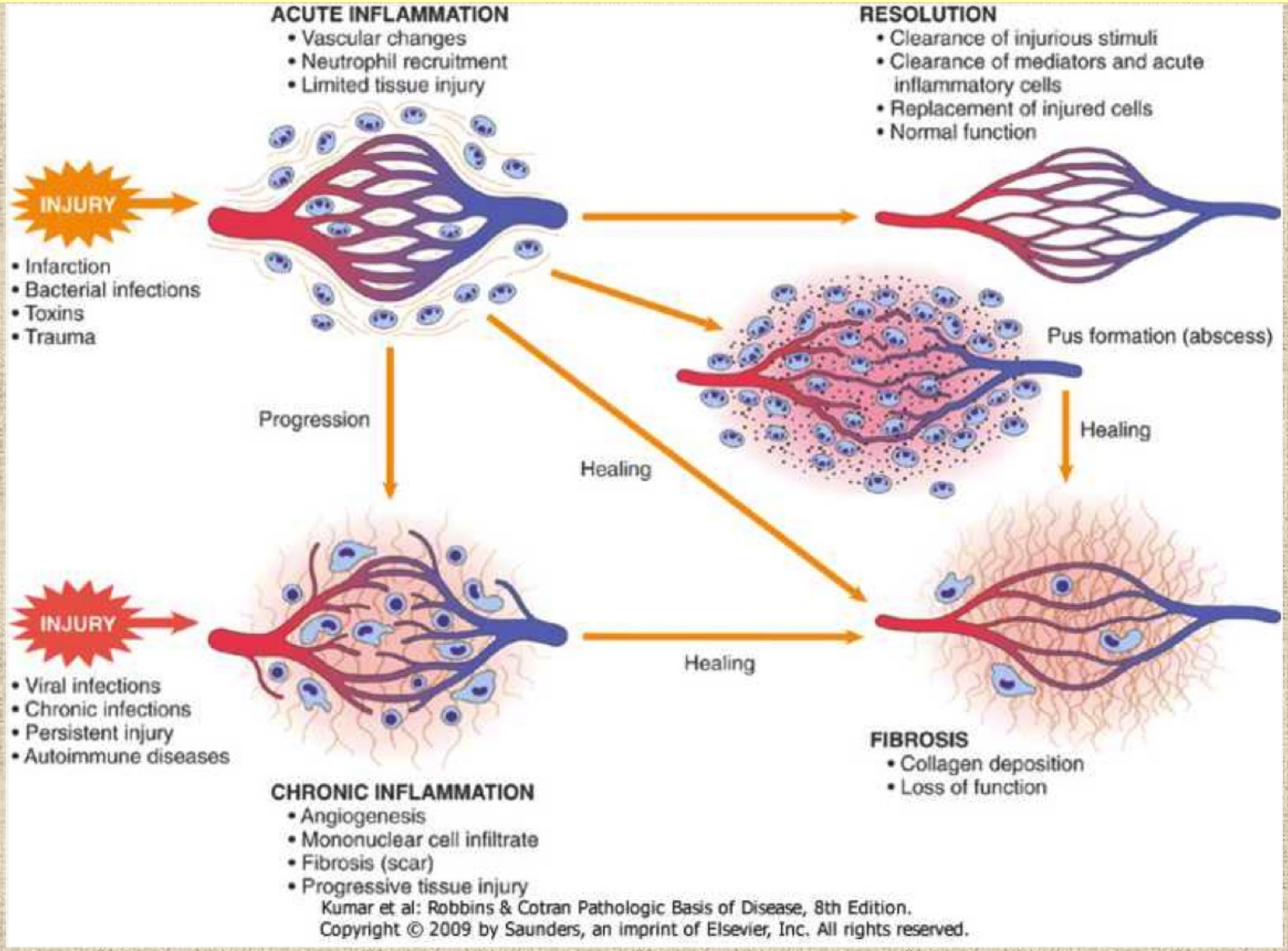
Systemic effects of acute inflammation *acute phase response*

- Fever (temperature > 37.8°C or >100 F)
  - Increased pulse, blood pressure
  - Chills
  - Anorexia
- Leukocytosis
  - neutrophilia and left shift of neutrophils points to bacterial infection
  - Lymphocytosis points to viral infection
  - Eosinophilia point to allergy or parasitic infection
- Acute phase protein production in liver
  - fibrinogen, CRP,SAA leads to increased ESR

Acute phase proteins in serum



Outcomes of acute inflammation



Causes of Chronic Inflammation

Unlike acute inflammation showing redness, swelling and pain, chronic inflammation can be invisible

Causes

- Autoimmune diseases e.g. such as rheumatoid arthritis, lupus
- Infectious agents e.g. H. pylori, viruses
- Atherosclerosis
- Environmental e.g. smoking
- Allergens
- Central adiposity: more macrophages localised in fat will thus produce more inflammatory mediators