Basic immunology

Lecture 4.

Innate immunity, inflammatory reaction

Timea Berki

Innate and Adaptive Immunity

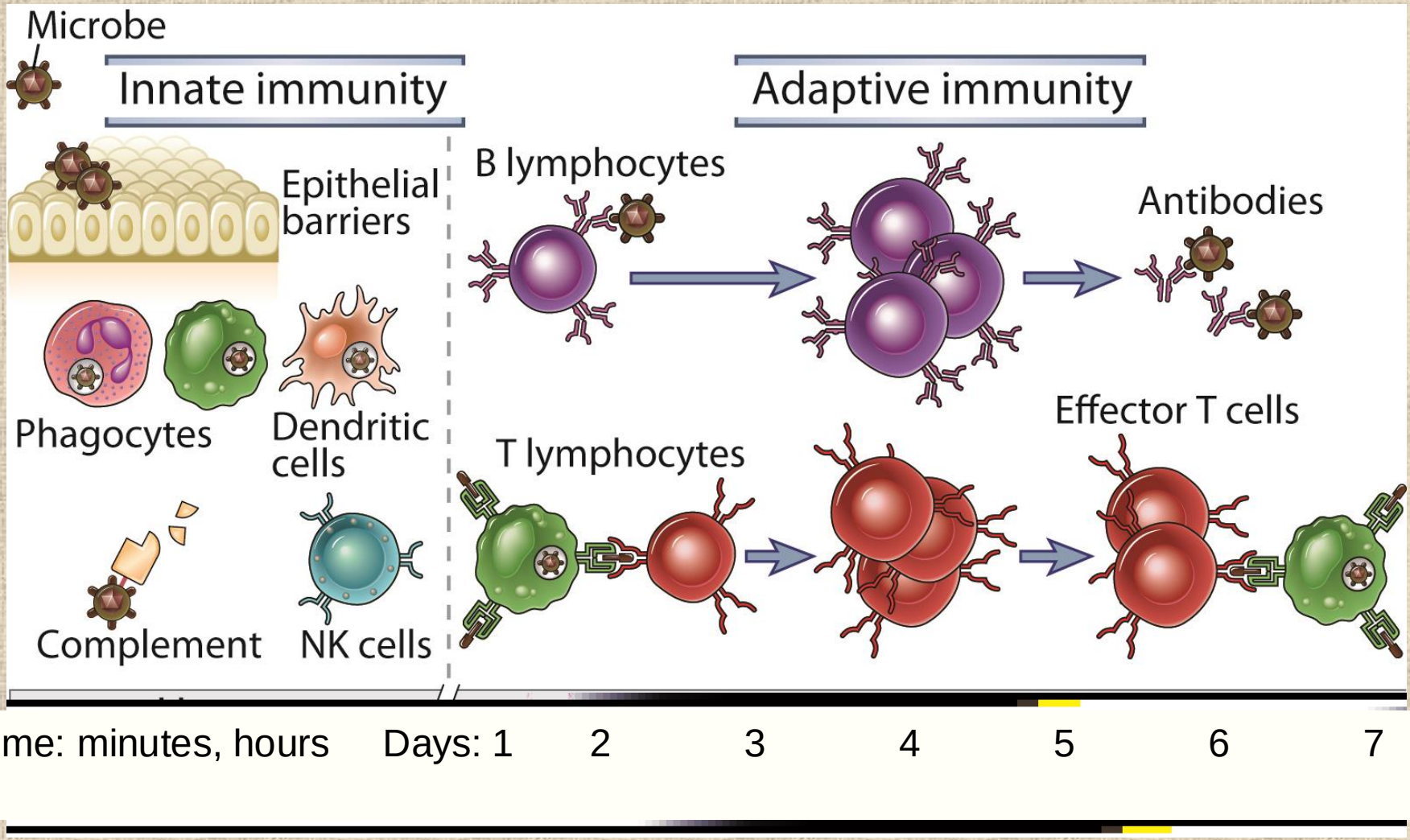


Fig. 1-1

Routes of Antigen Entry

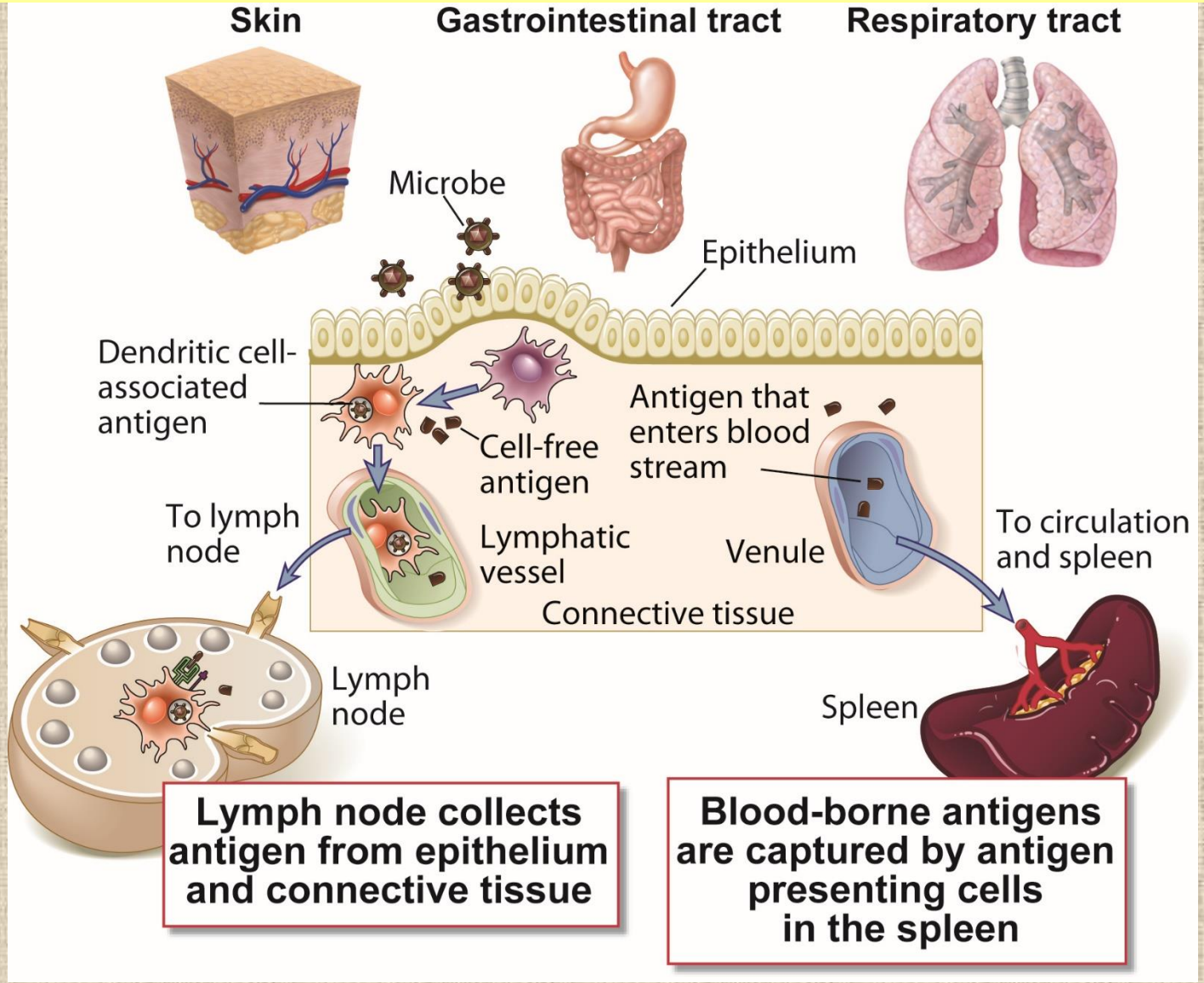


Fig. 6-3

Activation of the immune system

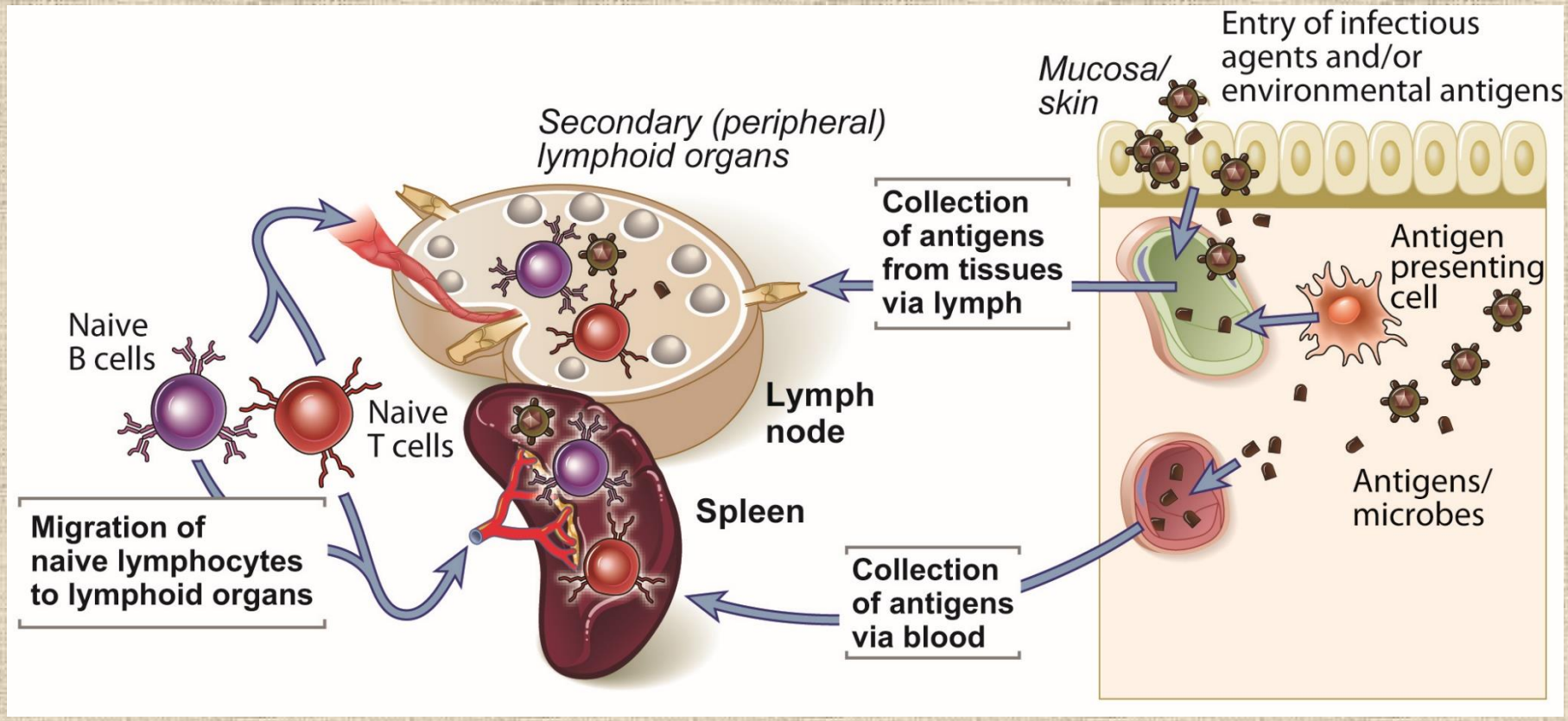


Fig. 2-6

Effector phase: cells and antibodies reach the site of infection

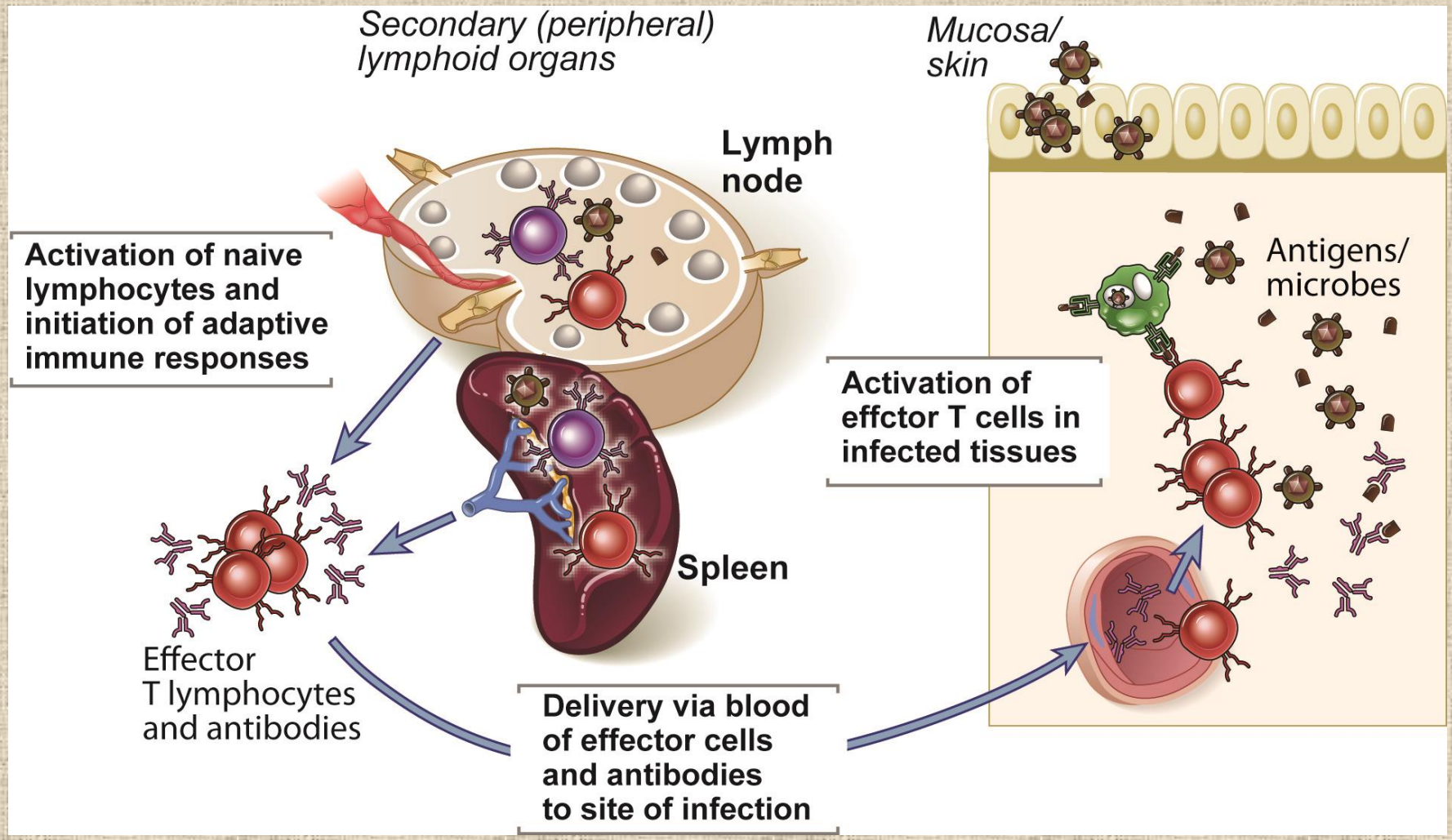
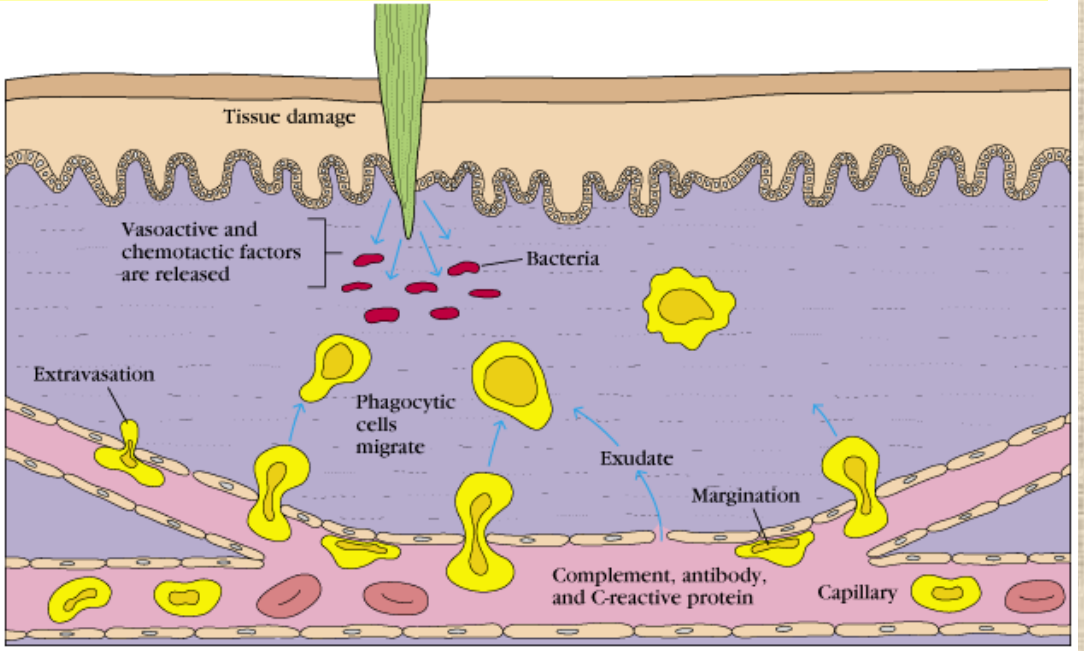


Fig. 2-6

- **Local acute inflammation**

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.

Molecular mediators of inflammation

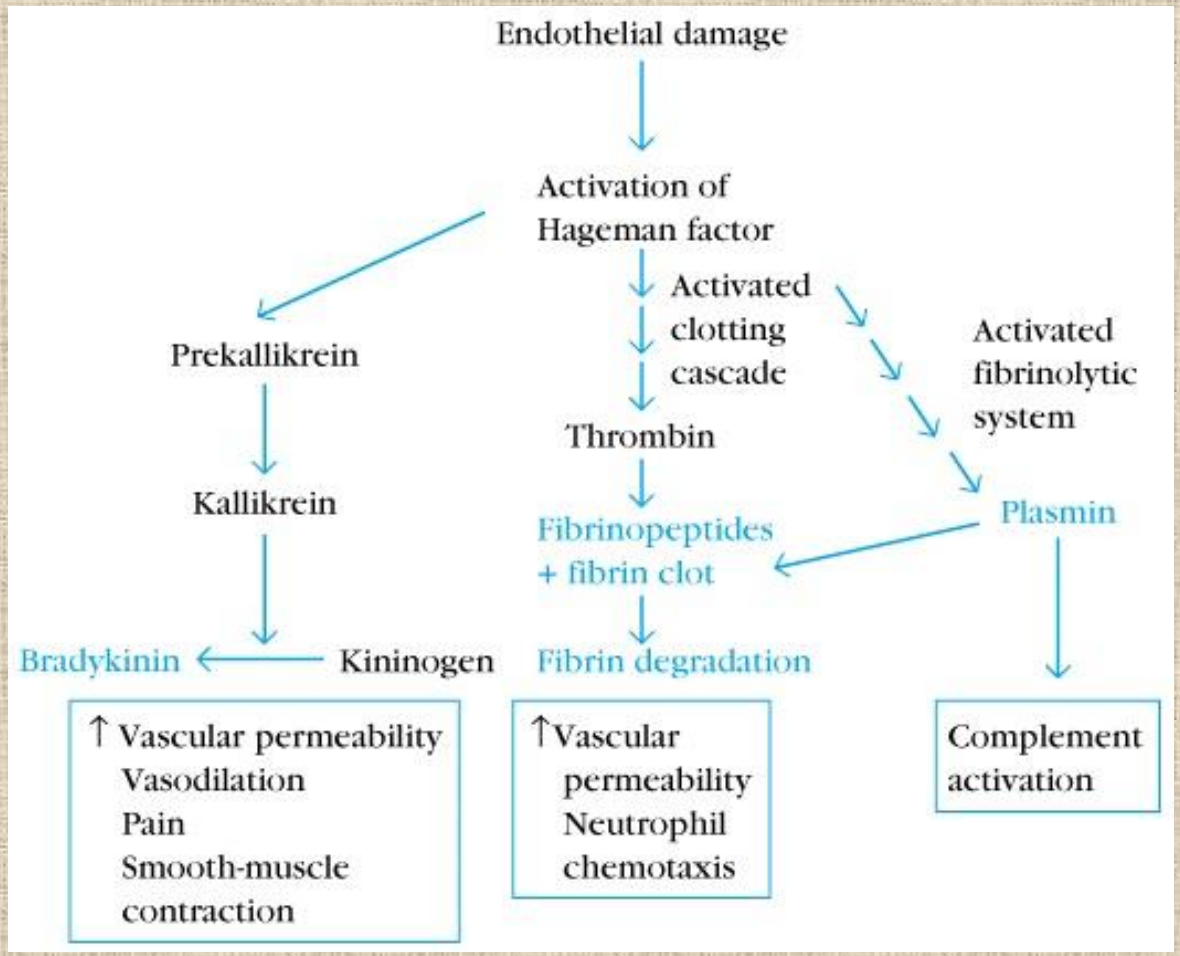
Plasma enzyme mediators:

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

Lipid mediators:
leukotrienes,
prostaglandins (PGE)

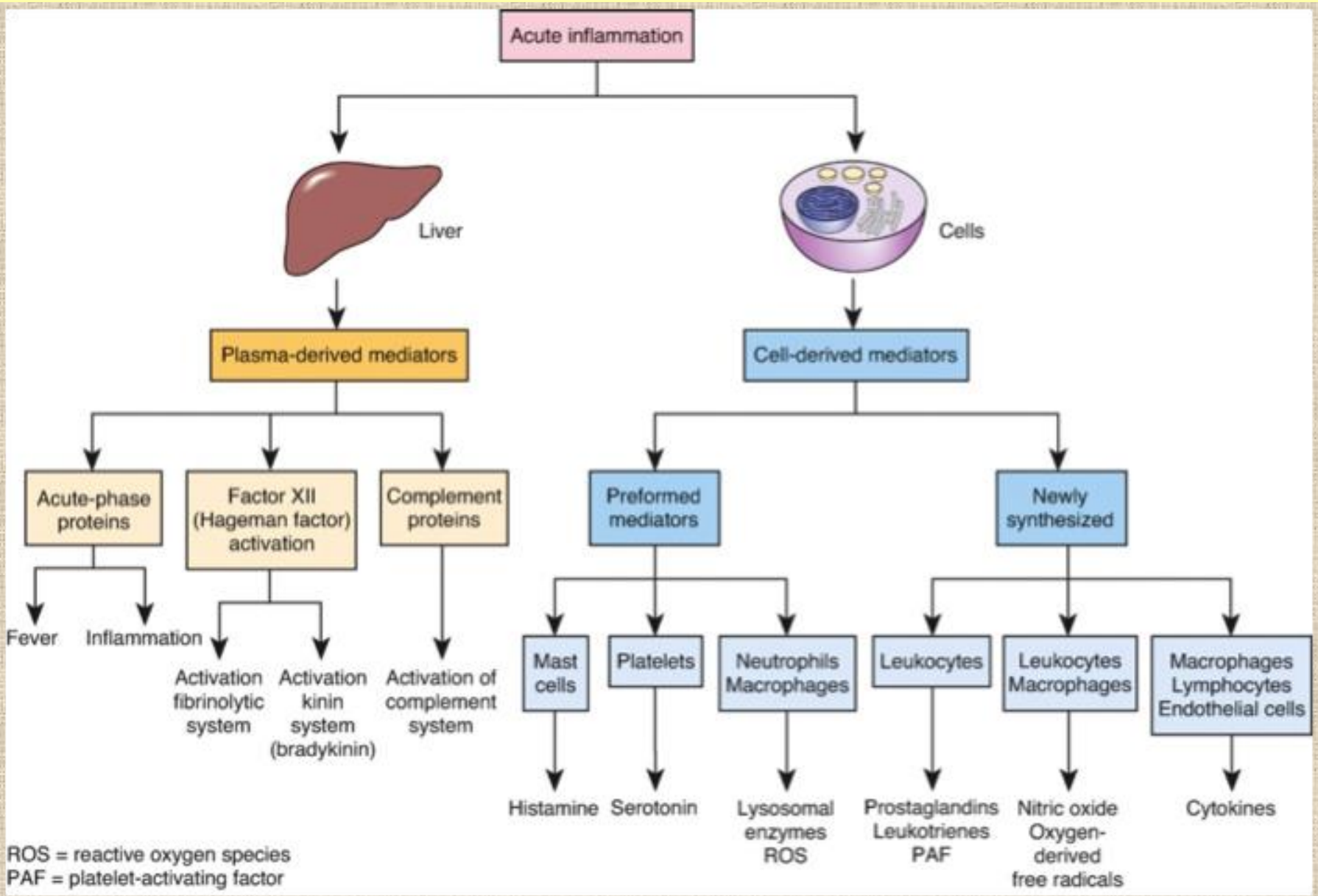
Chemoattractants:
-Chemokines: IL-8
-Complement components
- PAF (platelet activating factor)

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

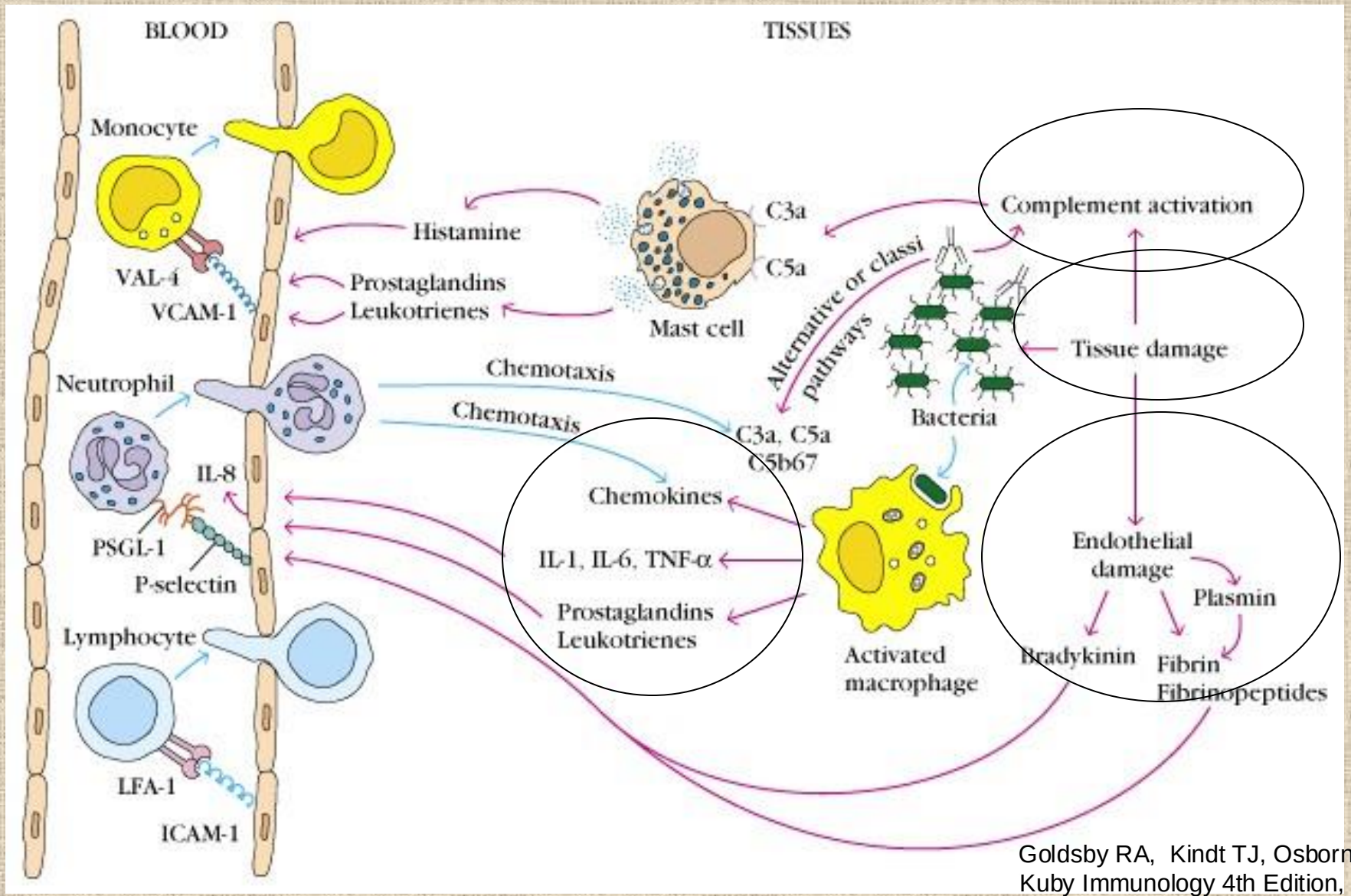


Goldsby RA, Kindt TJ, Osborne BA: Kuby Immunology 4th Edition, 2000.

Mediators of inflammation



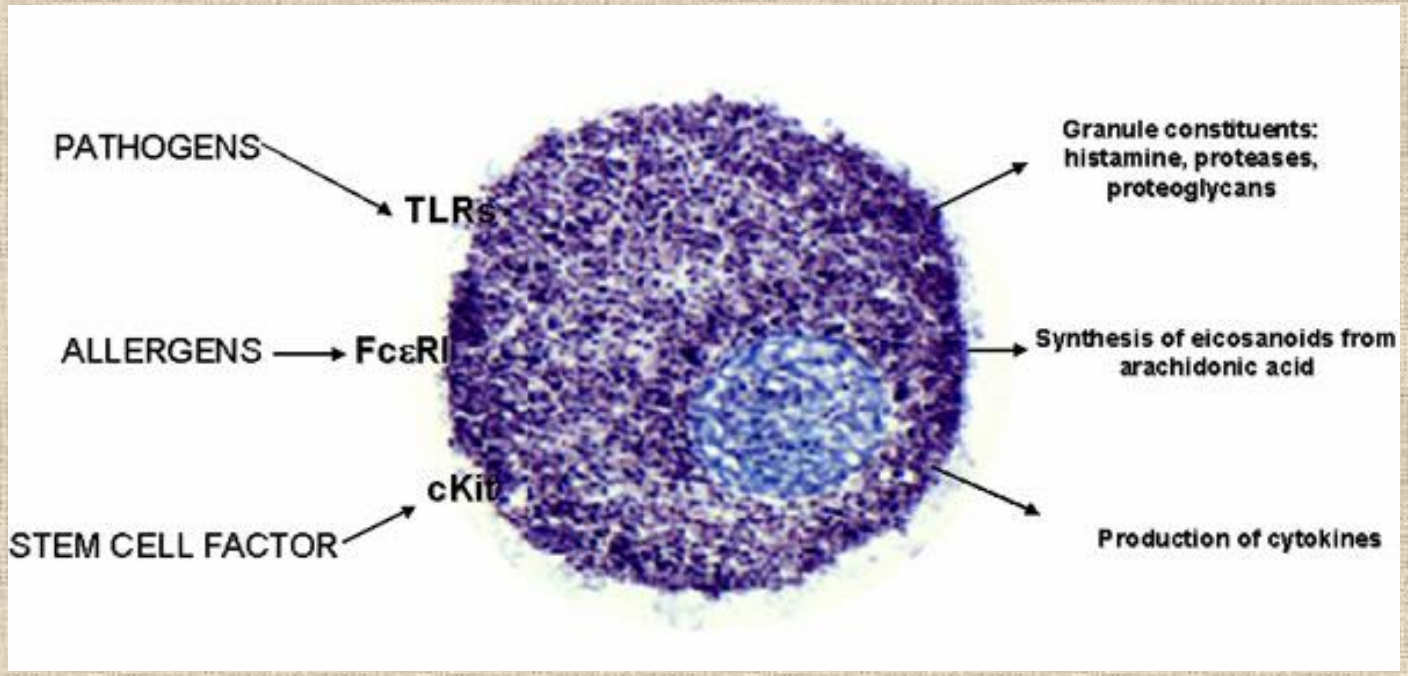
Initation of acute inflammation



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

Mast cells and their activation

TLR4 – LPS →IL-1β, TNF-α, IL-6 and IL-13, without mast cell degranulation
TLR2 – peptidoglycan → mast cell degranulation and production of IL-4 and IL-5, IL-6, IL-13
TLR3,7,9 – Poly (I:C), CpG oligonucleotid → release of pro-infalmmatory cyítokines and chemokines



they express several hundred thousand high affinity receptors for IgE (FcεR1) and thus respond to IgE-directed antigens

express the pathogen-recognizing Toll-like receptors (TLRs) which probably account for the ability of mast cells to mount an effective innate immune response

Maturation of Macrophages and DCs

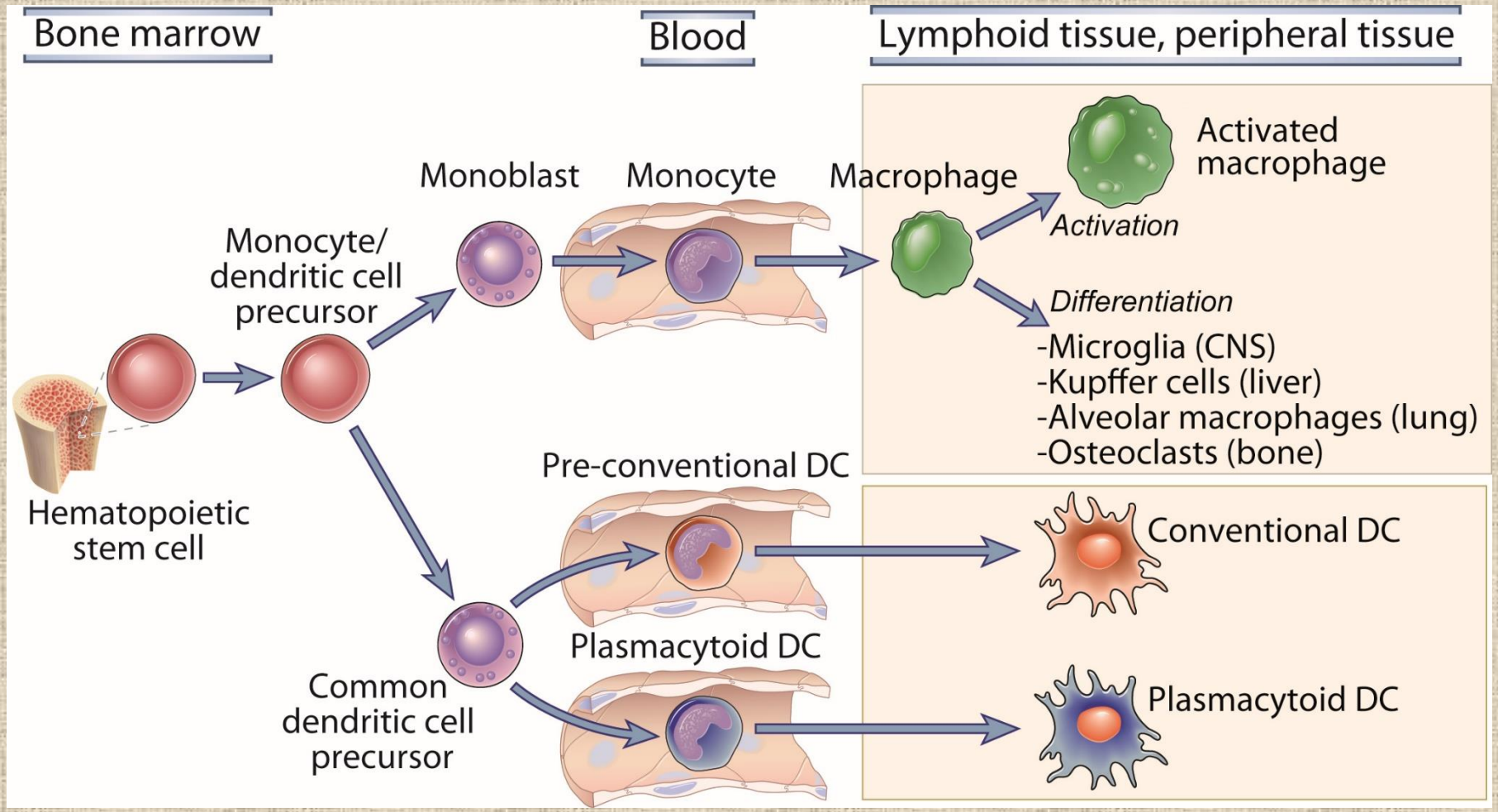
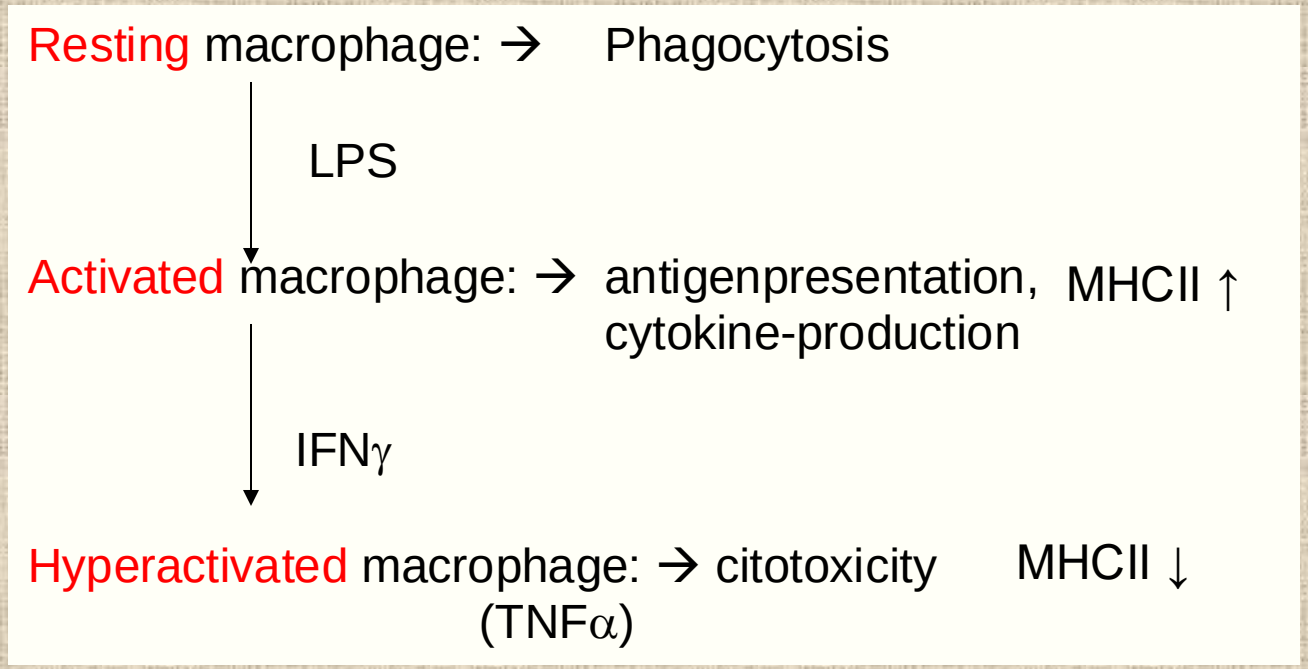


Fig. 2-2

Role of macrophages in acute inflammation: classical activation

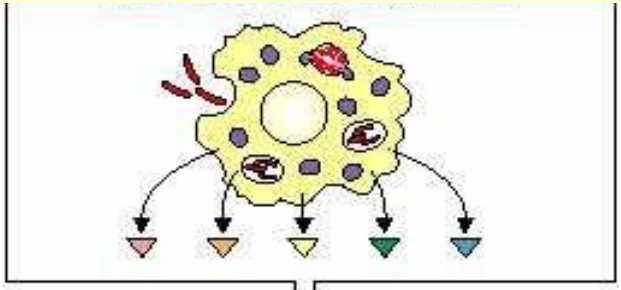


Abbas, Lichtman, Pillai: Cellular and Molecular Immunology 7th Edition, 2012.

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

Activated macrophages produce infalmmatory cytokines

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



IL-1 | IL-8 | TNF-α | IL-6 | IL-12

Local effects

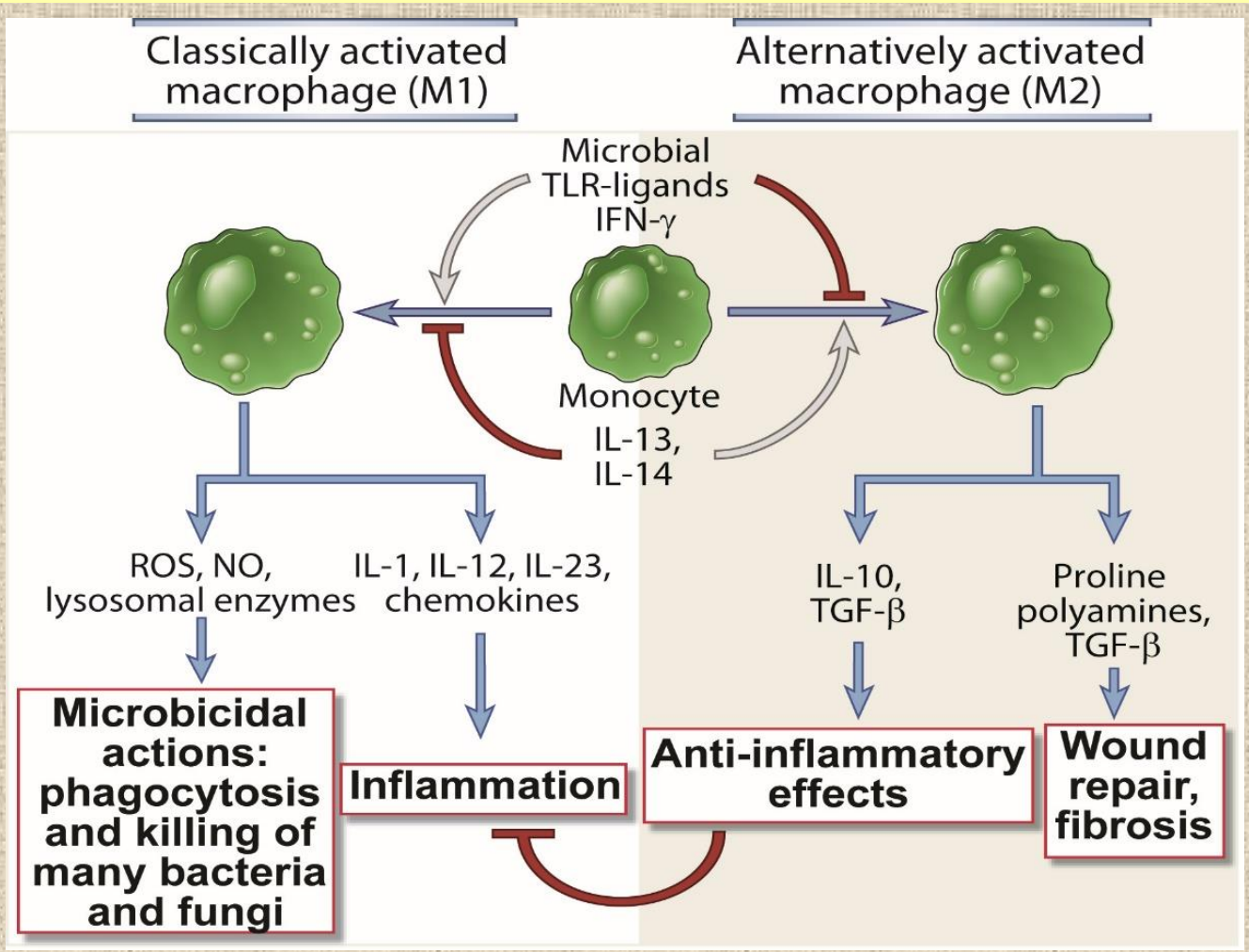
IL-1	IL-8	TNF-α	IL-6	IL-12
Activation of endothel and effector lymphocytes	Chemotaxis of leukocytes, Activation of effector cells	Activates vascular endothelium and increase vascular permeability	Lymfocyte-activation, Increased antibody production	Activates NK-cells, Th cells induce Th1 differentiation

Systemic effects

IL-1	IL-8	TNF-α	IL-6
fever, IL-6 production	GM-CSF Complement IFNα	fever, septic shock	fever, Production of acute-phase-proteins

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

Polarization of macrophages



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

Leukocyte Recruitment Into Tissues

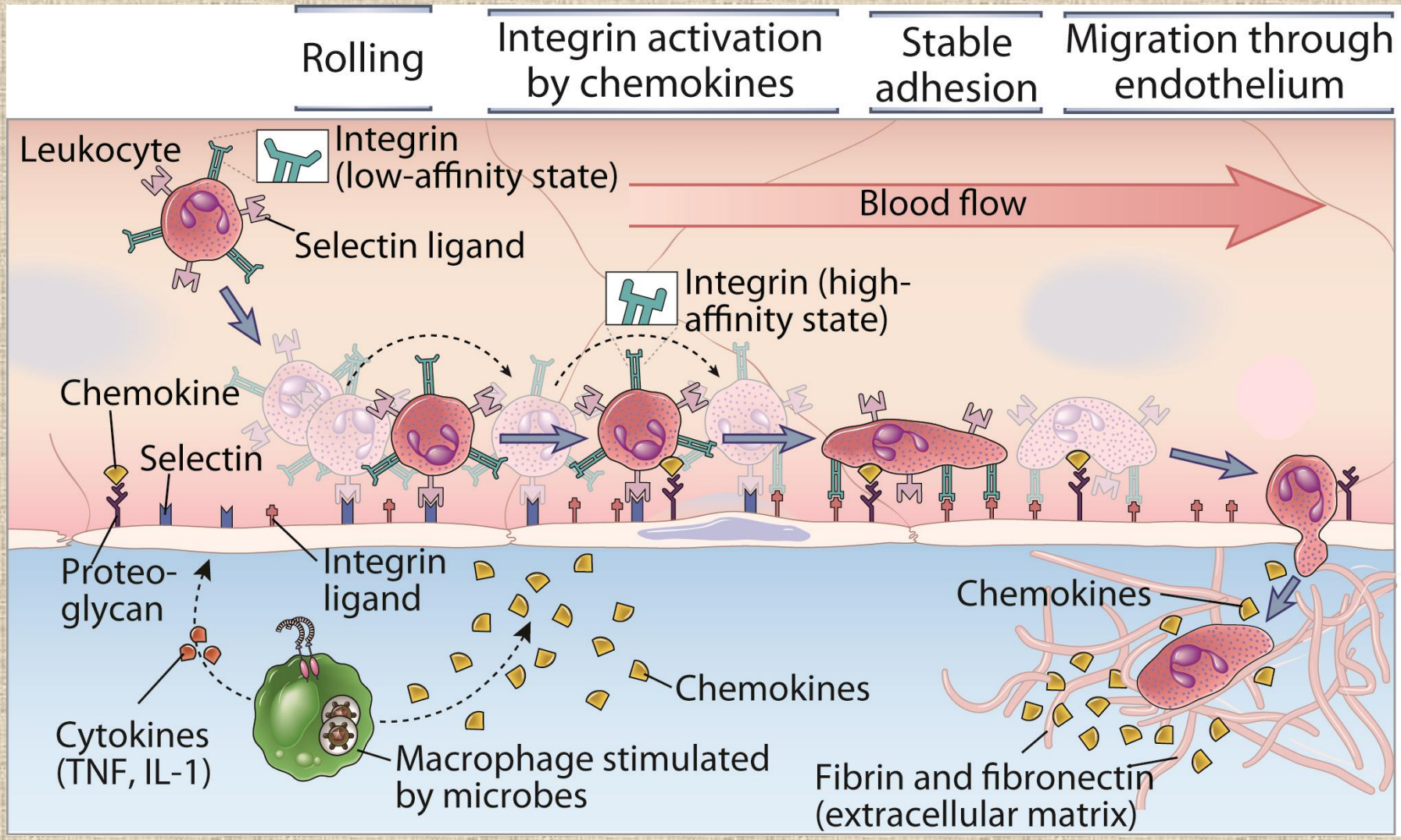
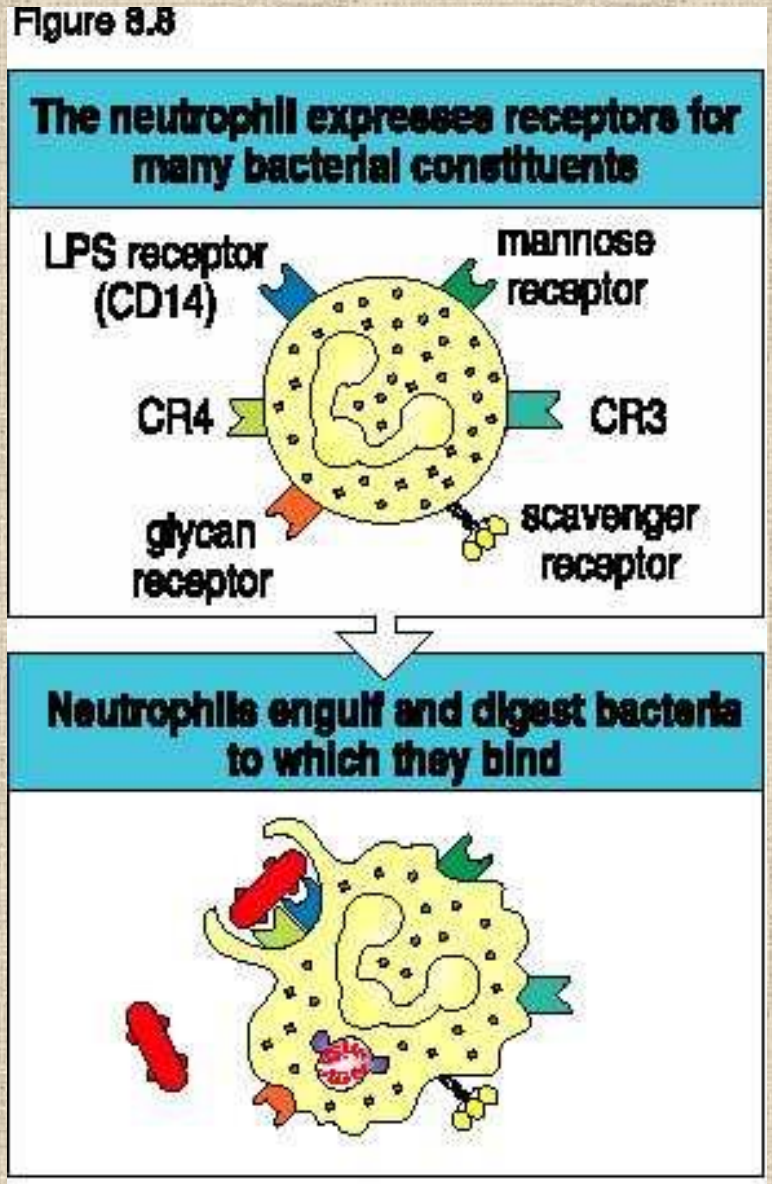


Fig. 3-3

Role of Neutrophils



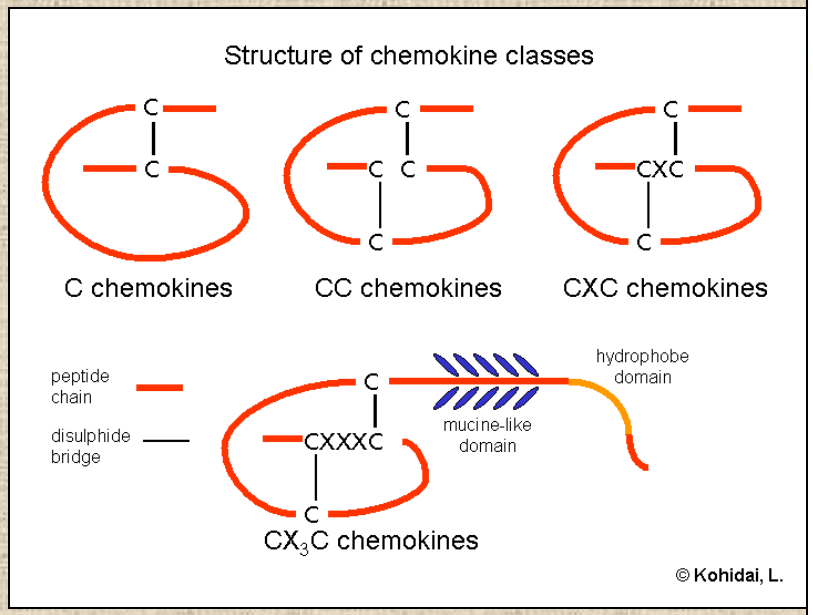
1. Phagocytosis / Receptor mediated endocytosis

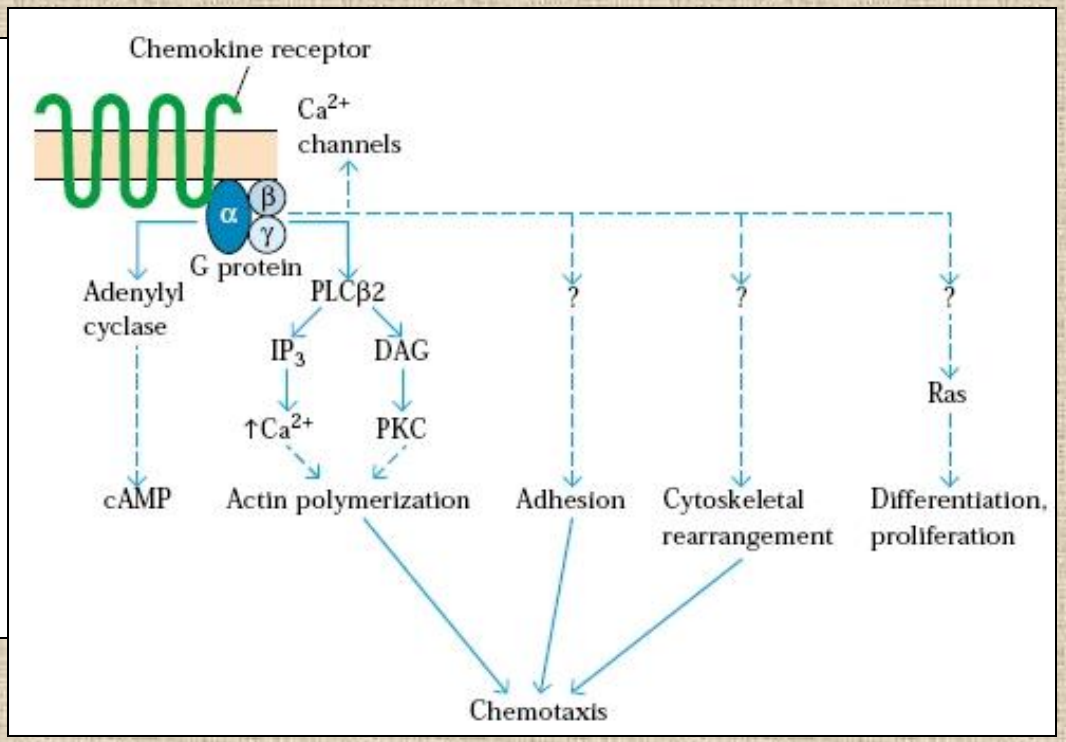
2. Degranulation

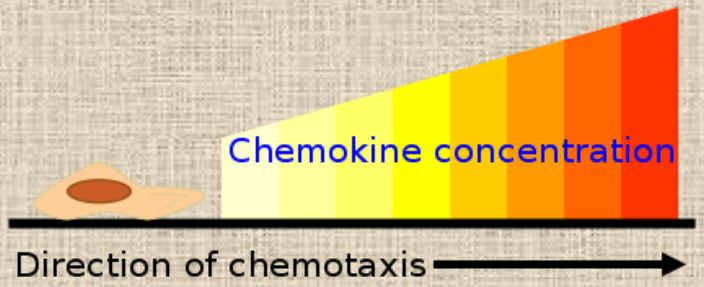
3. NET formation

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

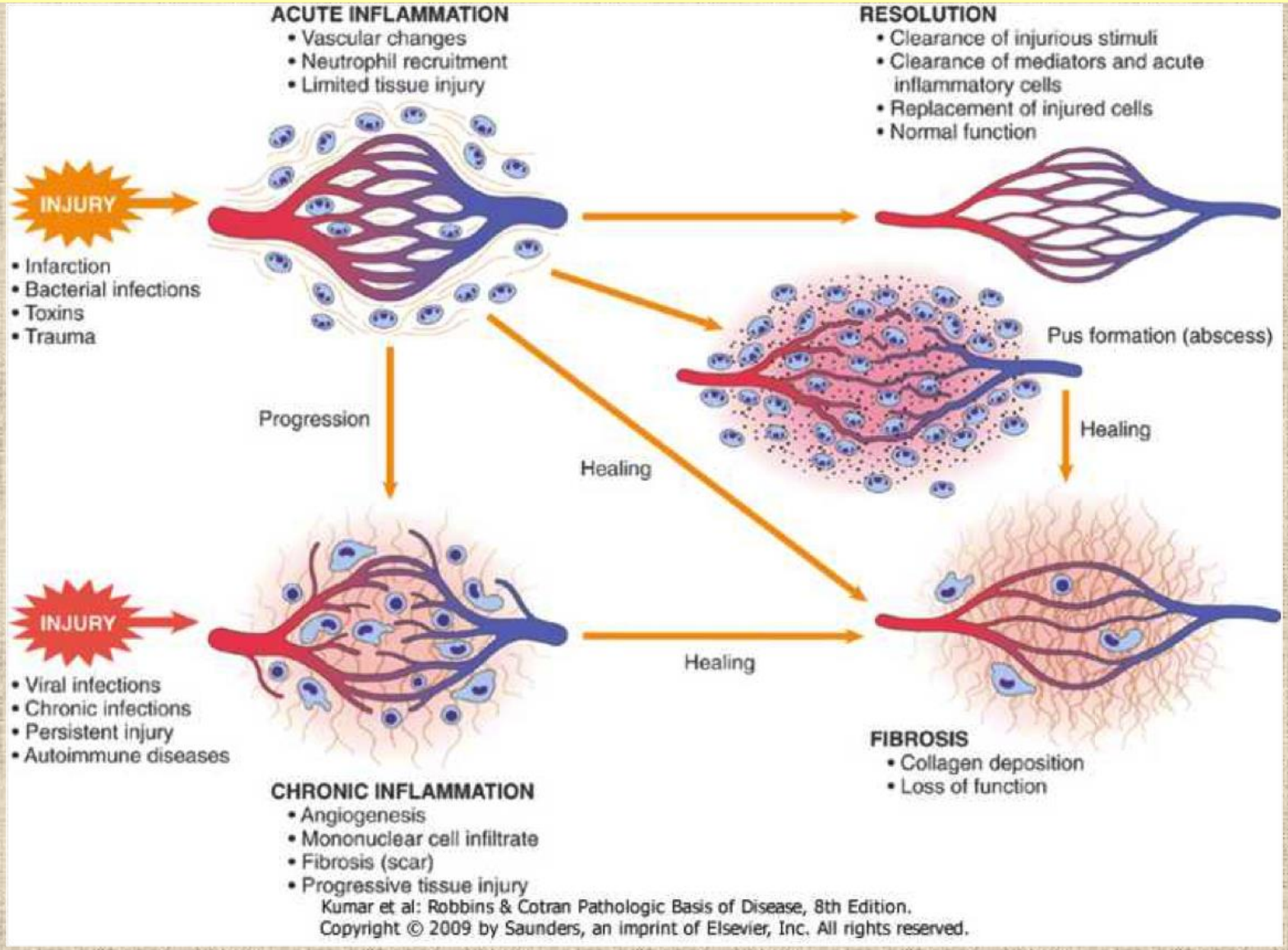
Chemokine action





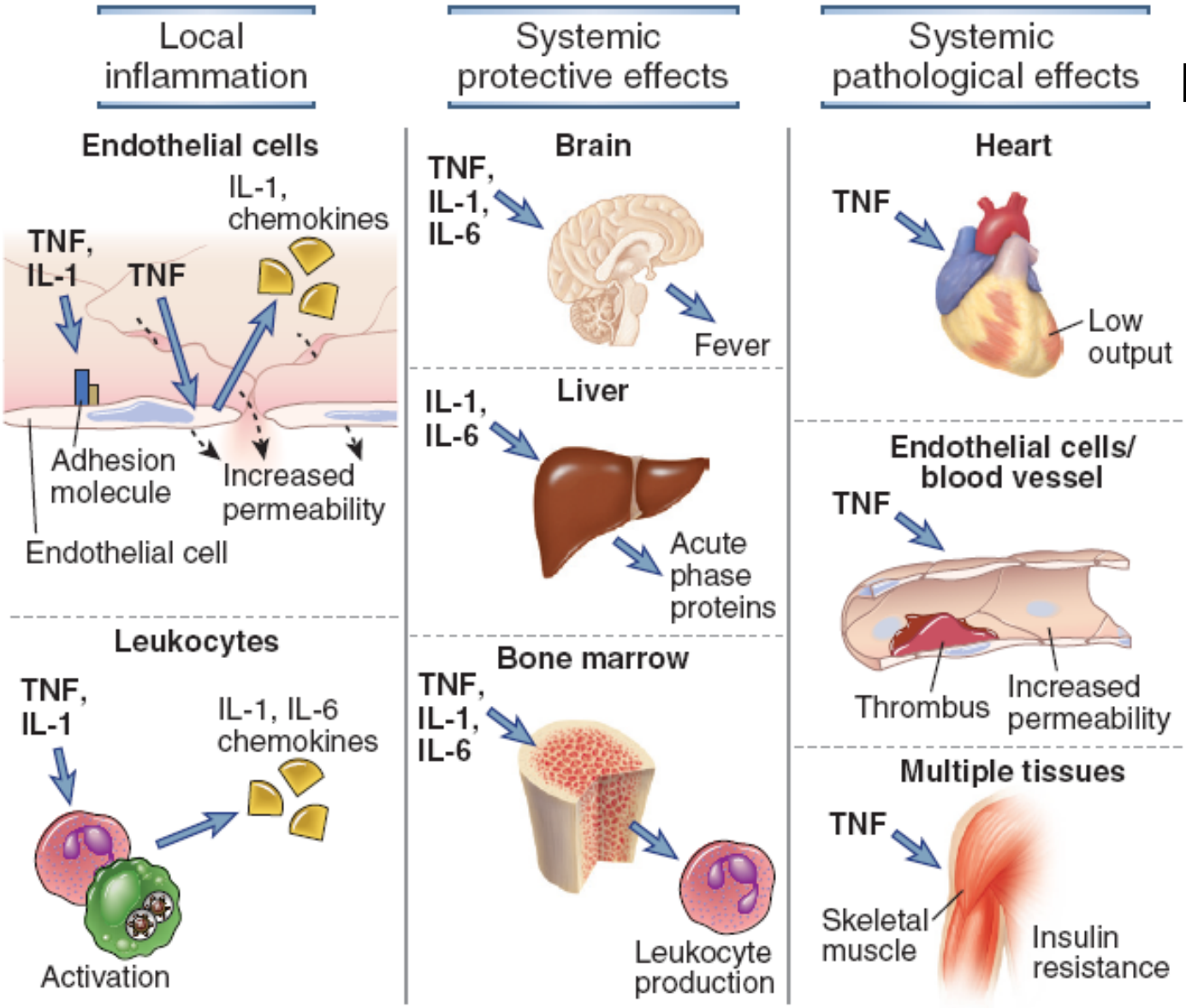


Outcomes of acute inflammation



- **Systemic inflammation**

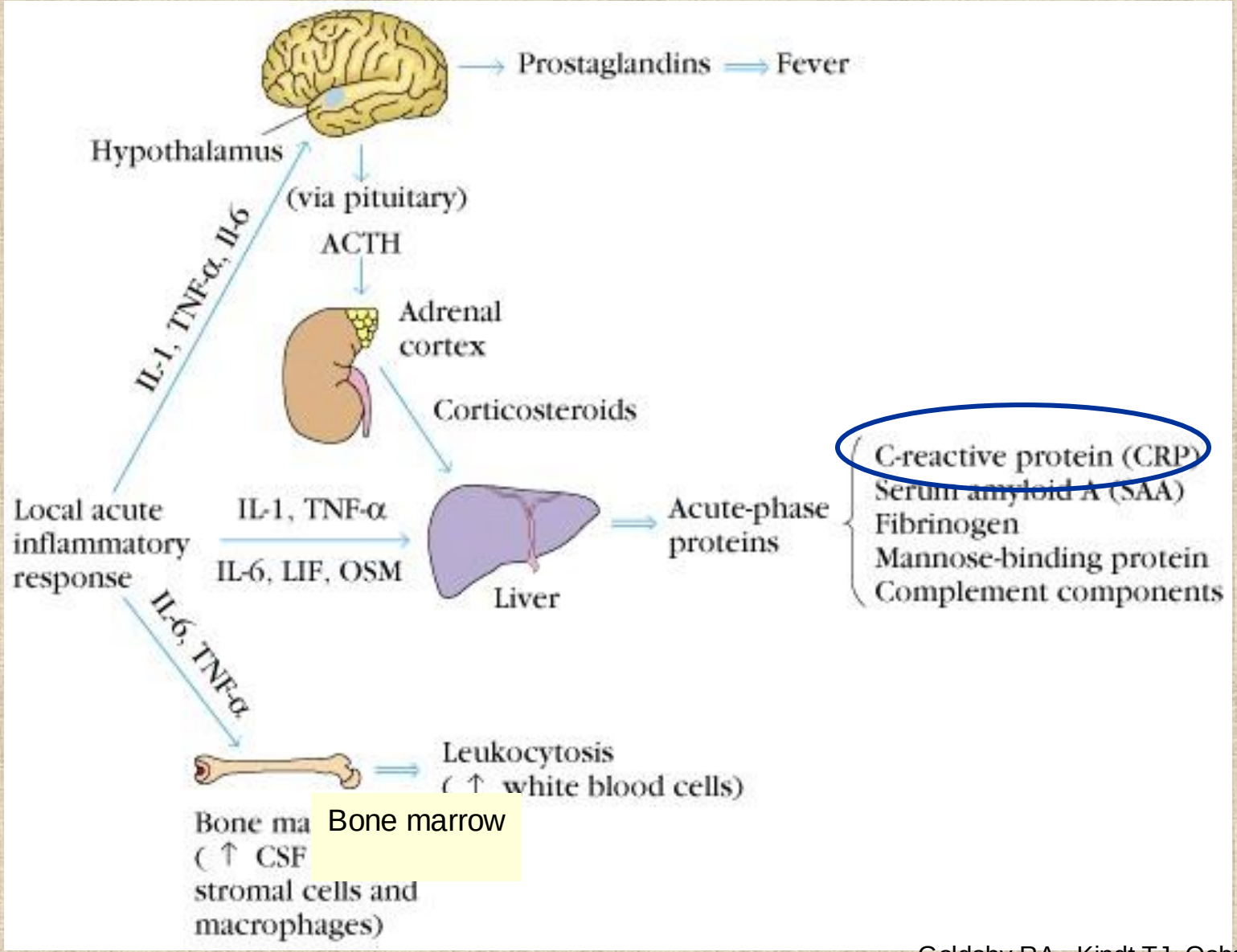
Local and systemic effects of TNF



TNF inhibitors, Steroids

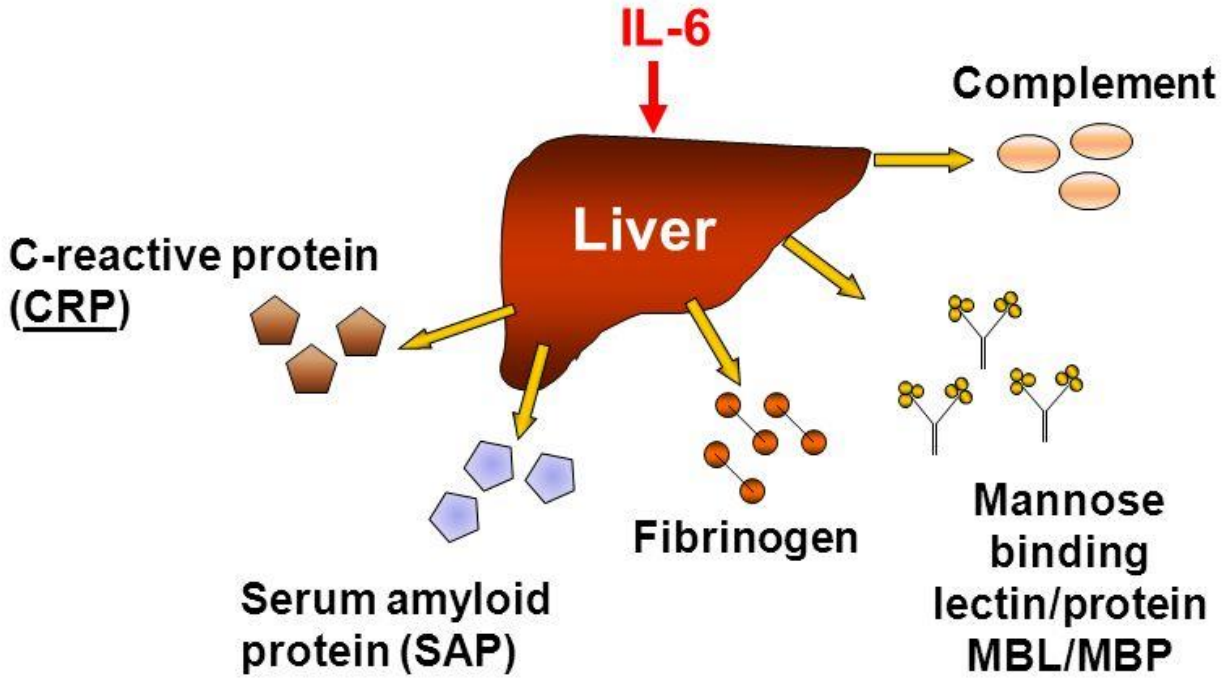
Abbas, Lichtman, Pillai: Cellular and Molecular Immunology 7th Edition, 2012.

Systemic acute inflammation = acute phase reaction



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

ACUTE PHASE REACTION

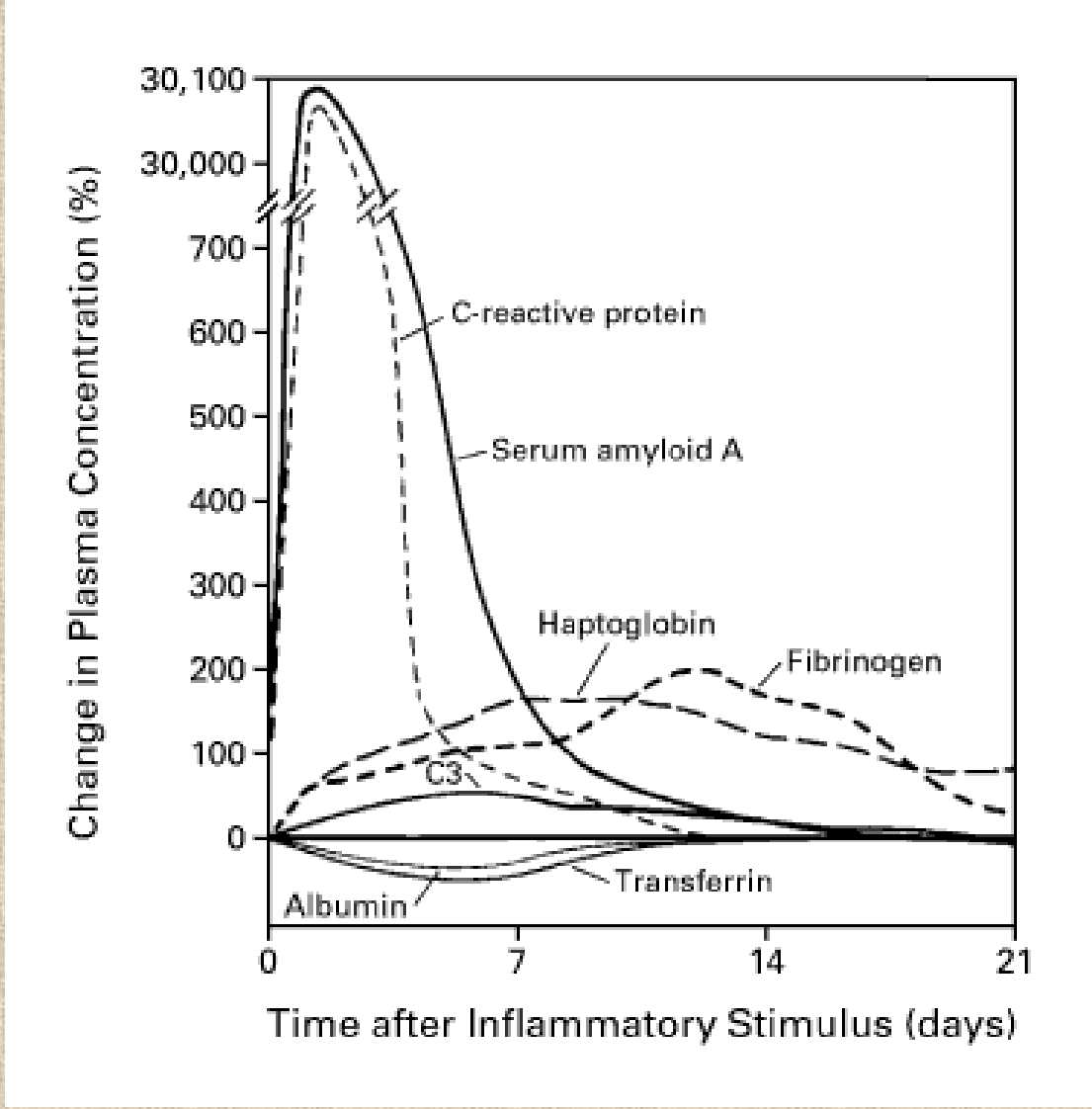


UNDER THE INFLUENCE OF IL-6 THE LIVER PRODUCES A BUNCH OF ACUTE-PHASE PROTEINS

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



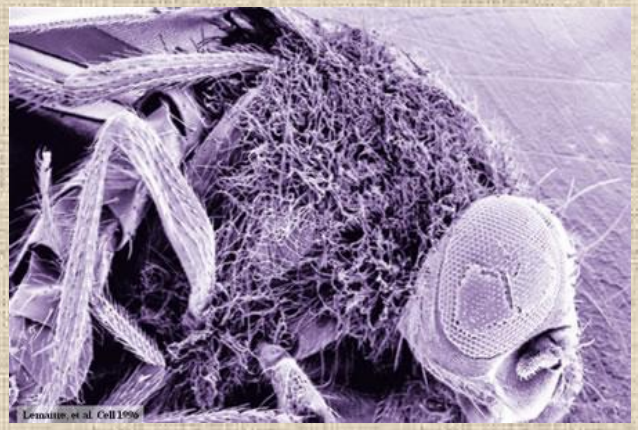
Causes of Chronic Inflammation

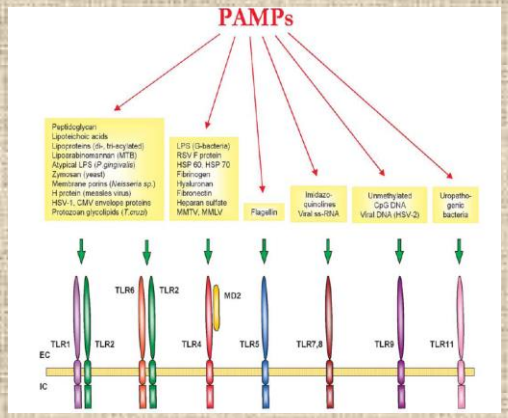
Unlike acute inflammation showing redness, swelling and pain, chronic inflammation can be invisible

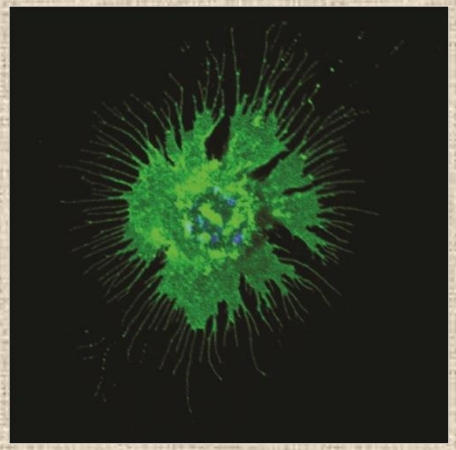
Causes

- 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

Nobel Laureates in 2011 for medicine and physiology

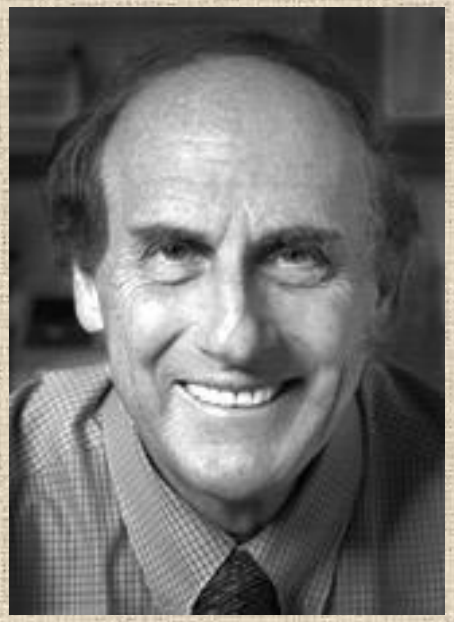






Jules A. Hoffmann

Bruce A. Beutler



Ralph M. Steinmann