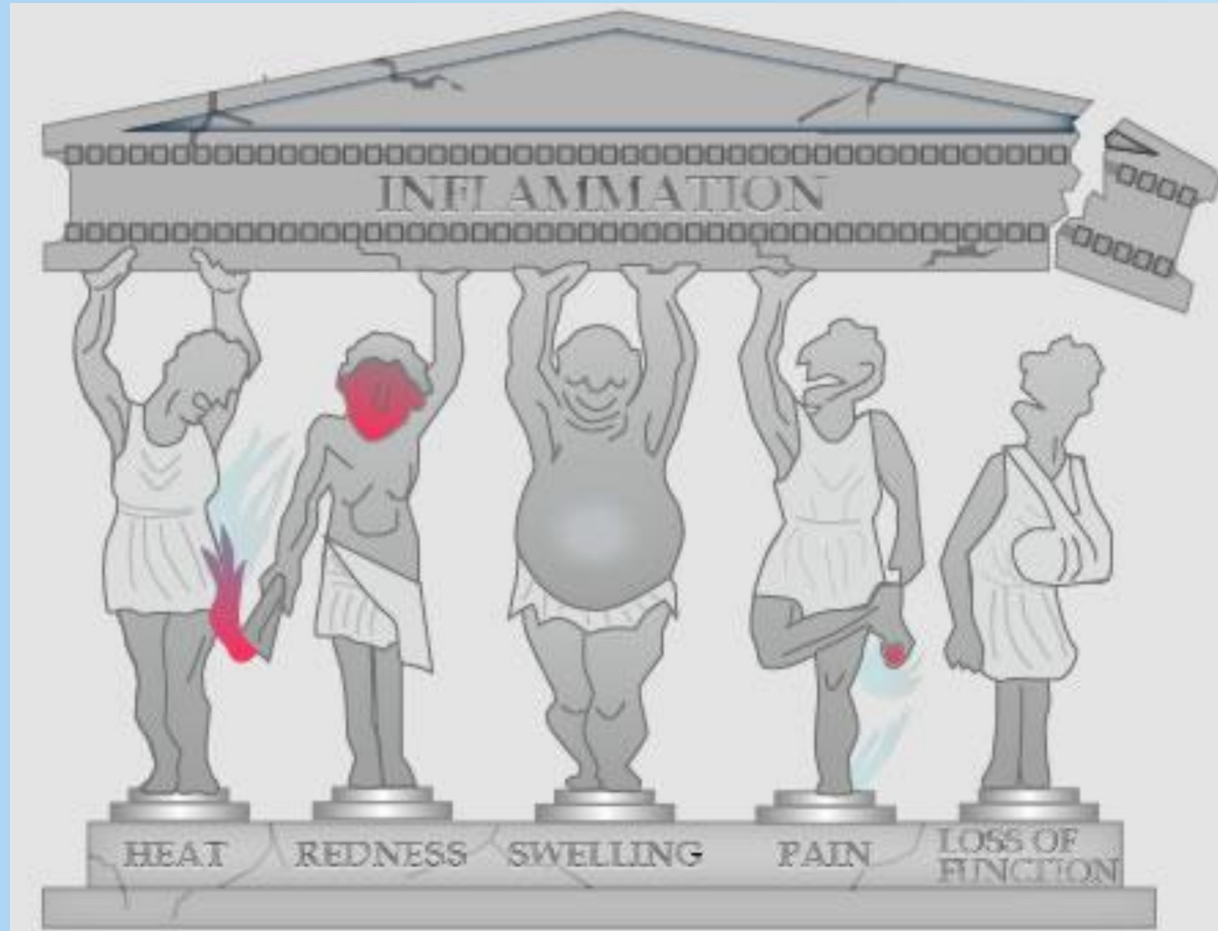


Acute Inflammation & Hypersensitivity Reactions

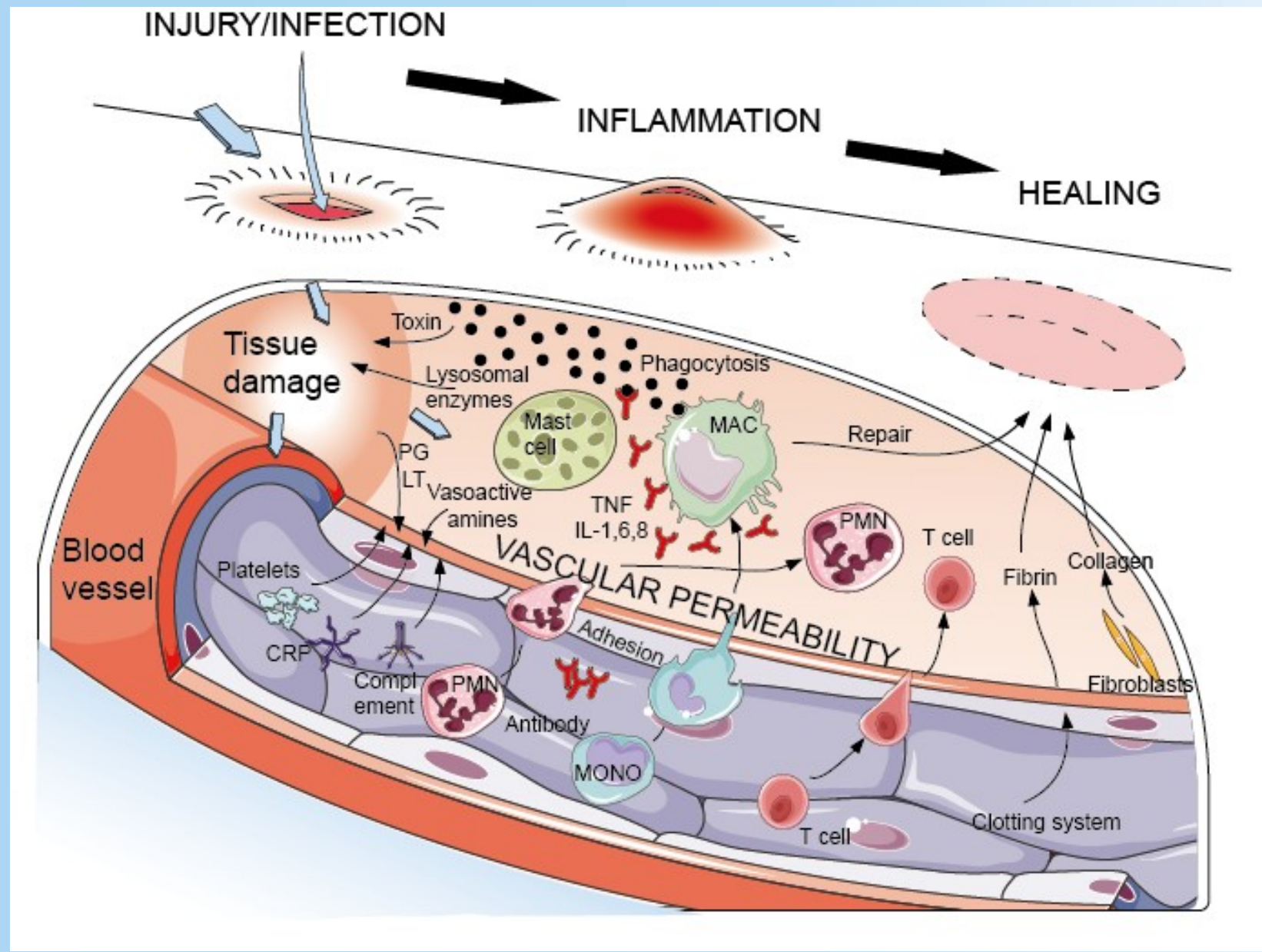
By James Melvin
MD3, B.Sc. Biochemistry

5 Cardinal Signs of Inflammation



Plasma Protein Systems

- The Kinin system
- The Clotting/Fibrinolytic System
- The Complement System



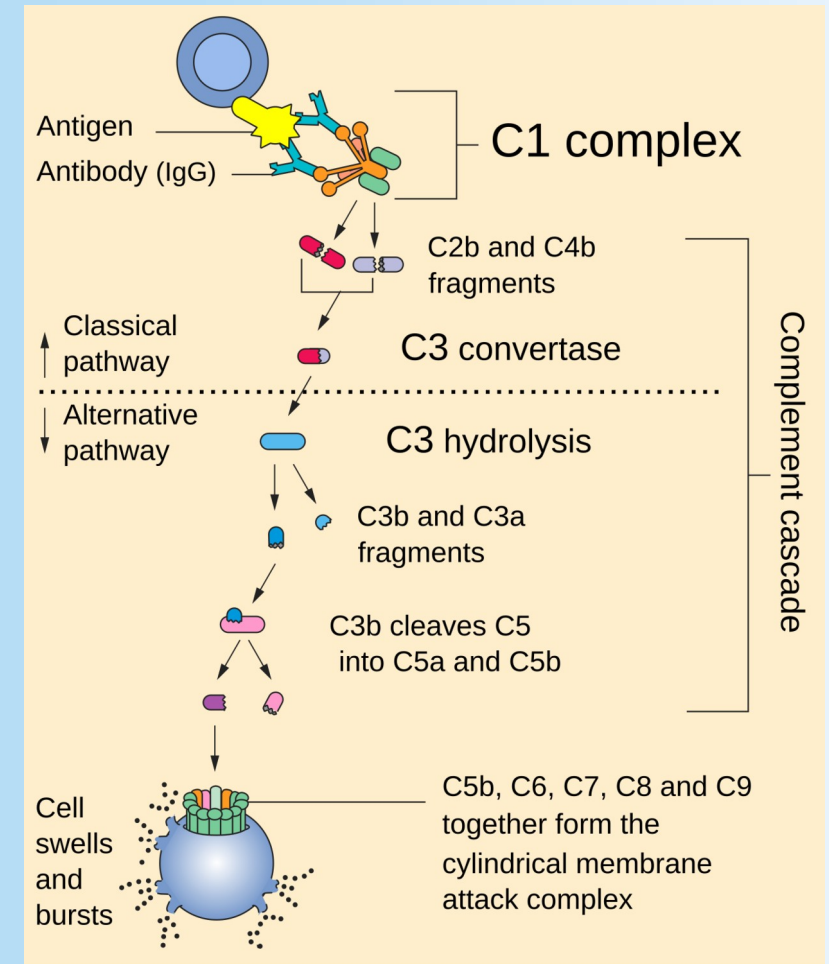
1. The Complement System

(Innate immunity & inflammation)

- Activation pathways:
- Classical (IgG/IgM)
- Alternative
- Lectin

Key functions

- C3b → opsonization
- C3a, C5a → inflammation (anaphylatoxins)
- C5b-9 (MAC) → cell lysis
- Enhances phagocytosis & microbial killing



2. The Clotting / Fibrinolytic System

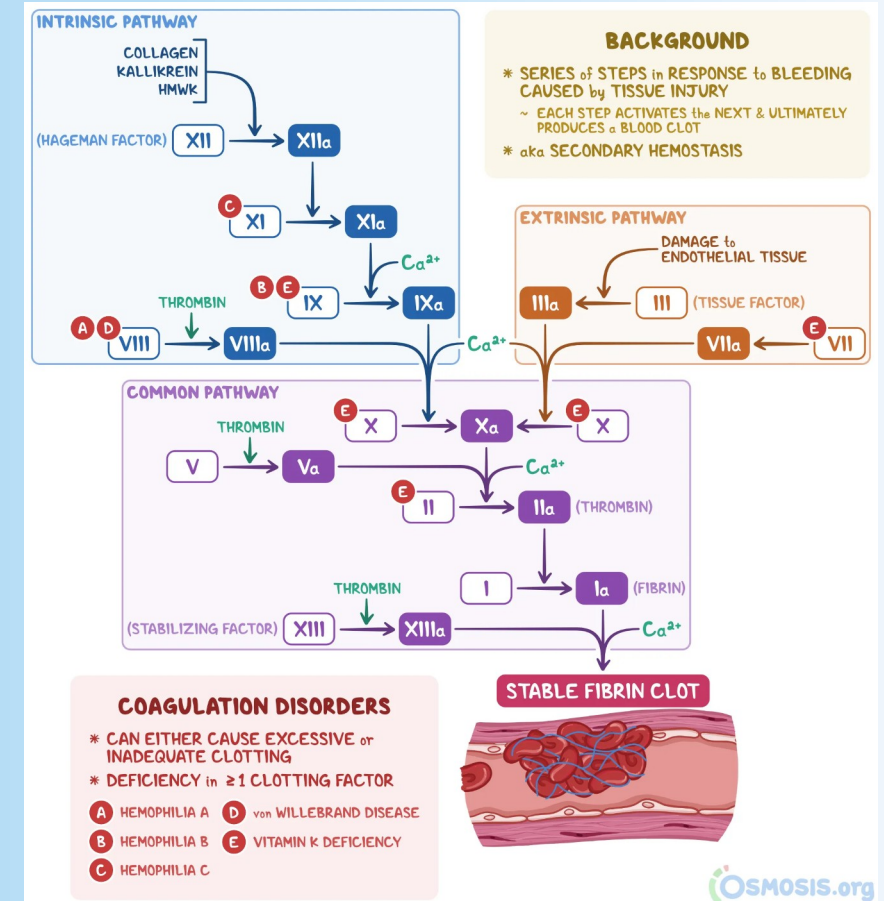
Hemostasis & clot breakdown

- Coagulation cascade → fibrin clot formation
- Thrombin
- Converts fibrinogen → fibrin
- Activates platelets

Fibrinolysis

- Plasminogen → plasmin
- Plasmin degrades fibrin (↑ D-dimer)
- Tightly regulated to prevent:
- Thrombosis
- Excess bleeding (hemophilia, ↓ Vit. K , “blood thinners”)

- Clinical link: DIC = overactivation of both clotting & fibrinolysis



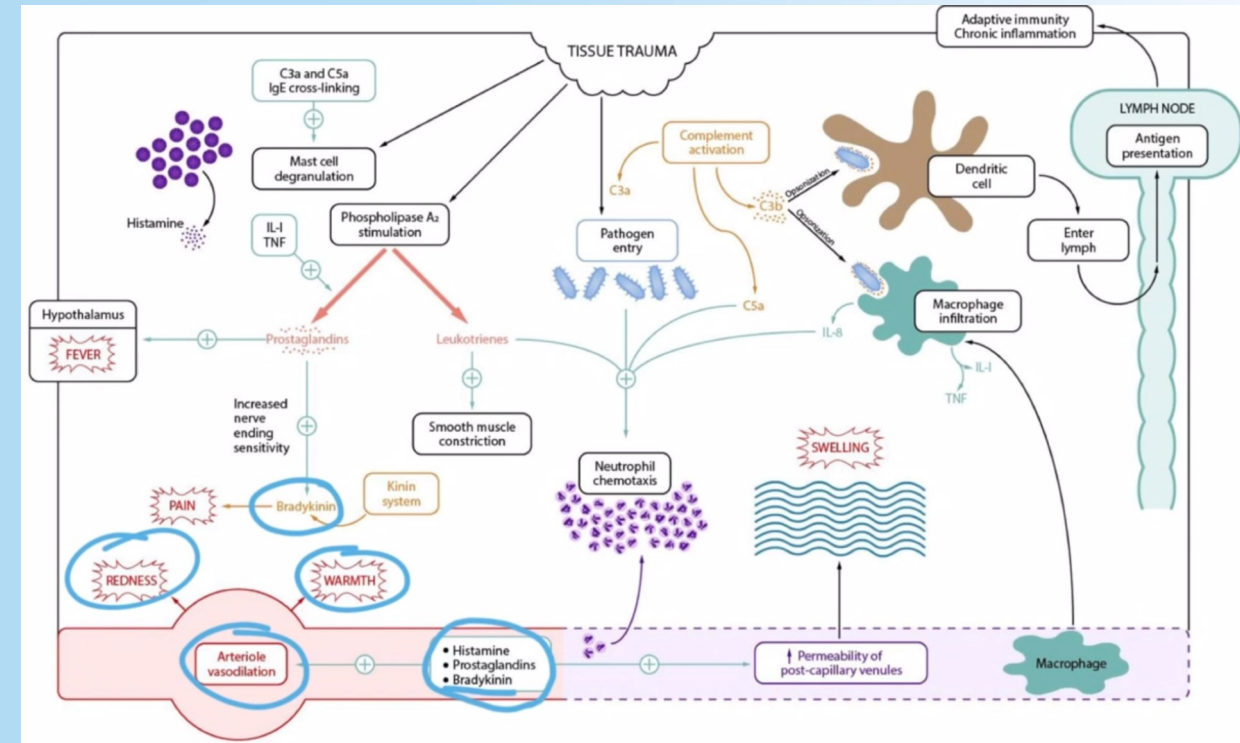
3. The Kinin System

Key mediator: Bradykinin

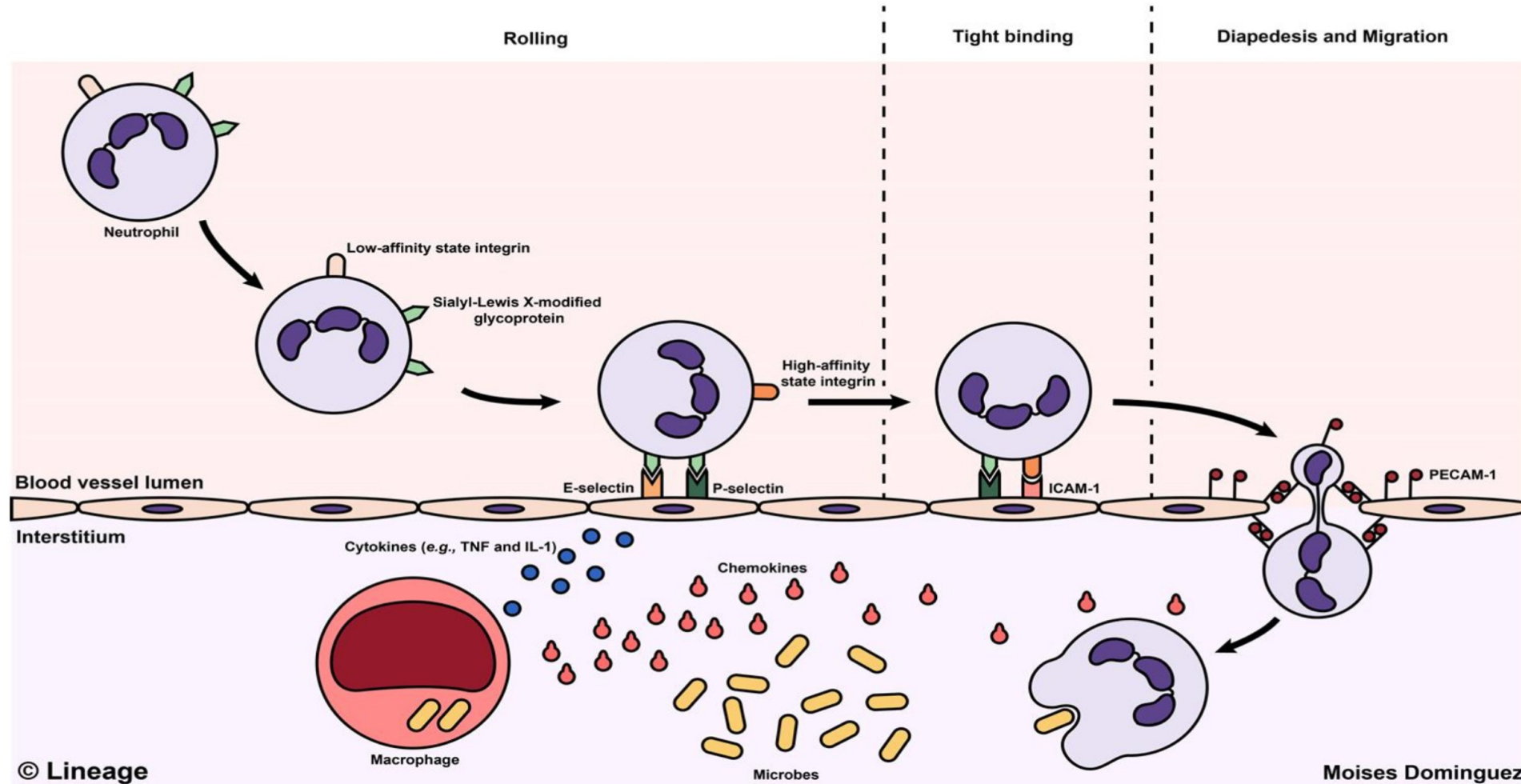
- Generated from kininogen via kallikrein

Effects:

- ↑ Vascular permeability
- Vasodilation → ↓ BP
- Pain
- Bronchoconstriction
- Inactivated by ACE
- ↑ Bradykinin → ACE inhibitor cough & angioedema
- Clinical link: Hereditary angioedema (↓ C1 esterase inhibitor)



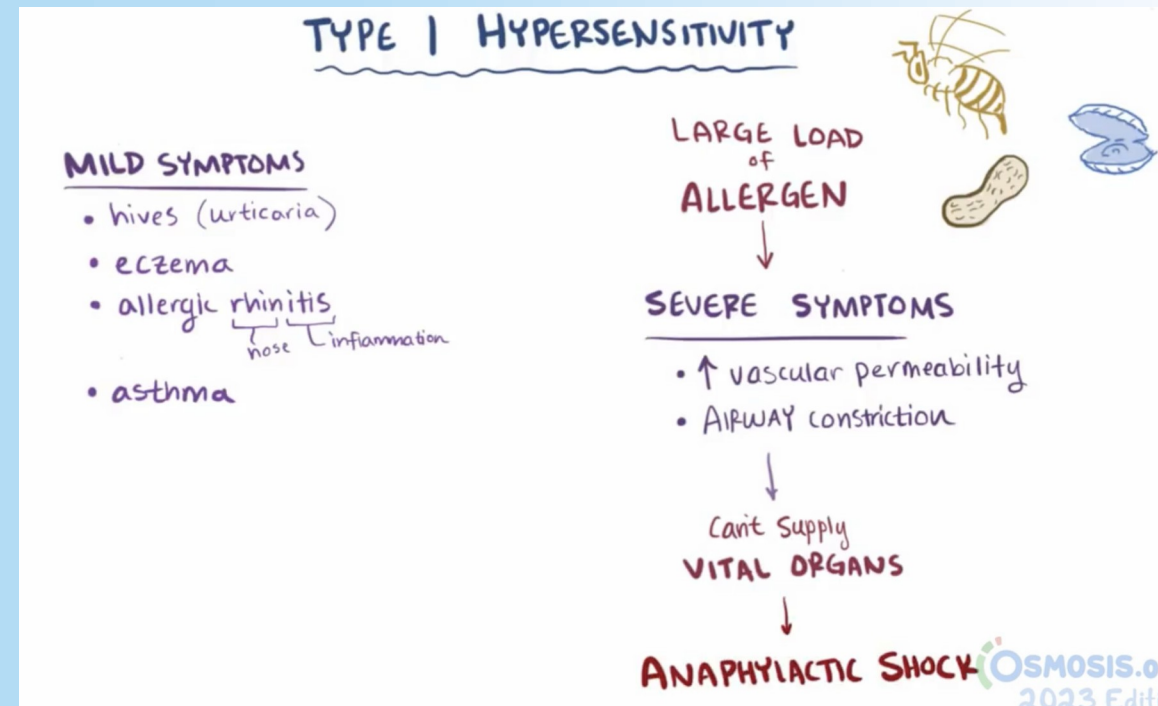
Leukocyte Extravasation



Type I Hypersensitivity (Immediate, IgE mediated)

Core Mechanism

- First exposure:
- Allergen → APC → Th2 cell activation
- Th2 cytokines:
- IL-4 & IL-13 → B-cell class switching to IgE
- IL-5 → eosinophil activation
- IgE binds FcεRI receptors on mast cells & basophils
- Re-exposure → IgE cross-linking → mast cell degranulation
- ⌚ Onset: Immediate onset. Seconds to minutes after exposure. (Also late phase rxn than can occur 4-8hr later.)

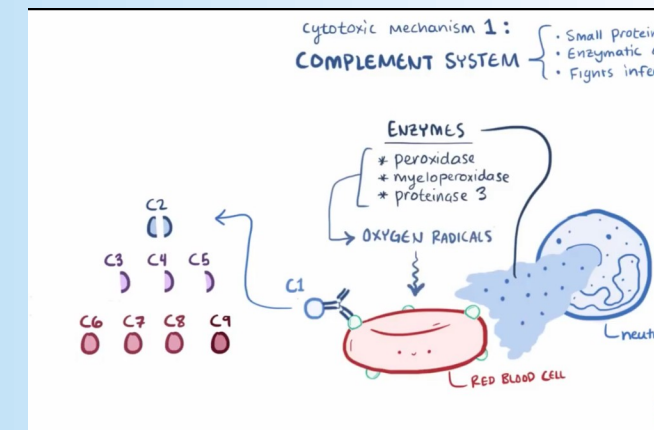
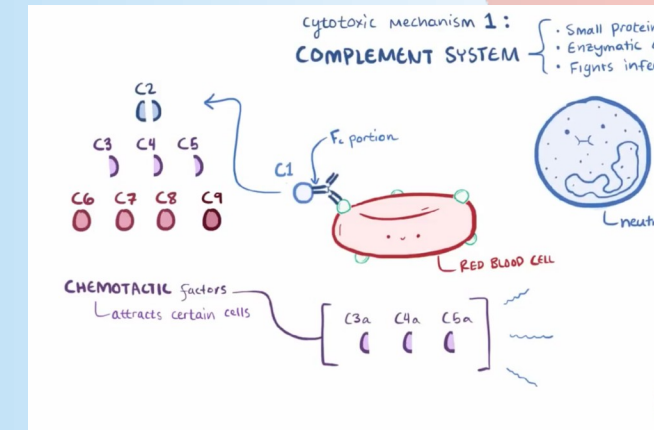
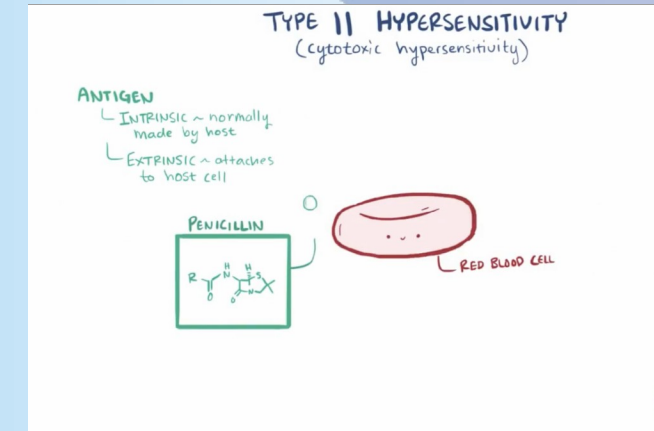


Type II Hypersensitivity (Antibody-mediated, cytotoxic (ADCC) OR receptor-mediated

Core Mechanism

- IgG or IgM antibodies bind to antigens on cell surfaces or extracellular matrix
- Leads to tissue damage or altered cell function via:
- Complement activation → cell lysis
- Opsonization → phagocytosis
- ADCC (NK cells)
- Receptor stimulation or blockade (important!)

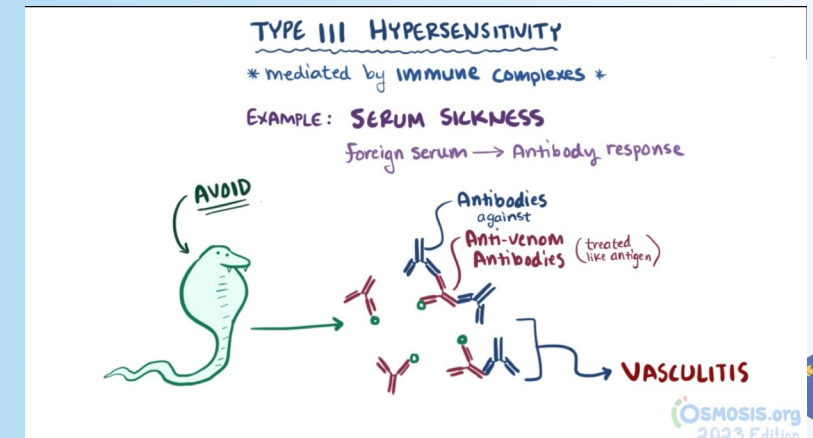
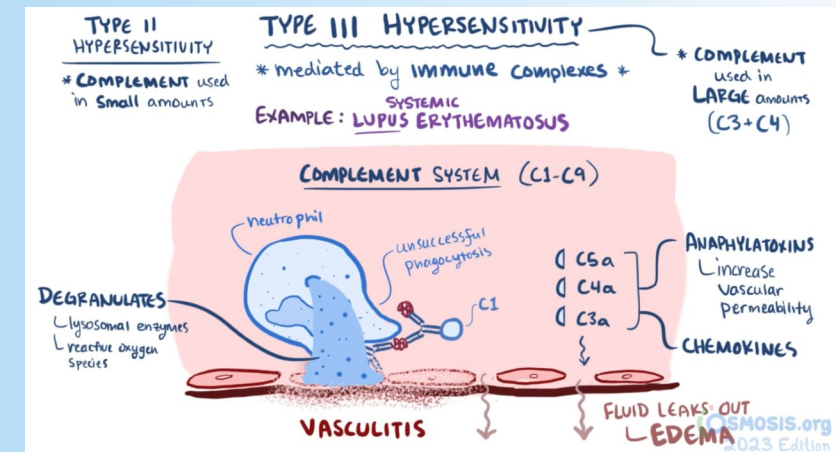
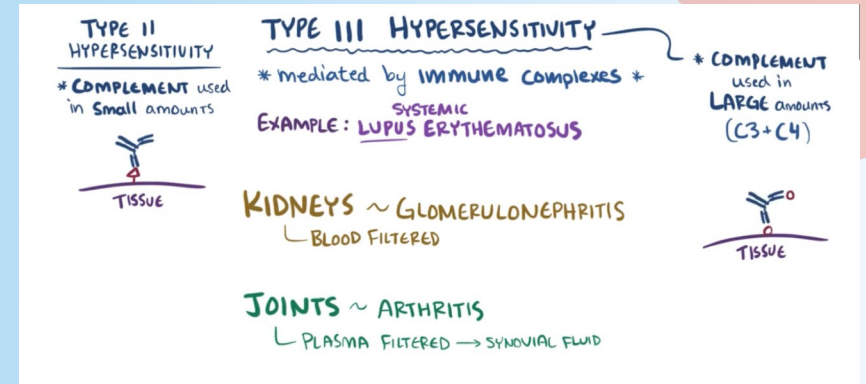
🕒 Onset: hours to days



Type III Hypersensitivity Immune complex-mediated inflammation

- Soluble antigen + IgG or IgM antibodies
- Formation of circulating immune complexes
- Deposition in tissues (vessels, kidneys, joints, skin)
- Complement activation (C3a, C5a)
- Neutrophil recruitment → enzyme + ROS release
- Tissue damage

🕒 Onset: hours to weeks



Key Difference between Type II and Type III Hypersensitivities

Type II → antibodies bind fixed antigens on cells

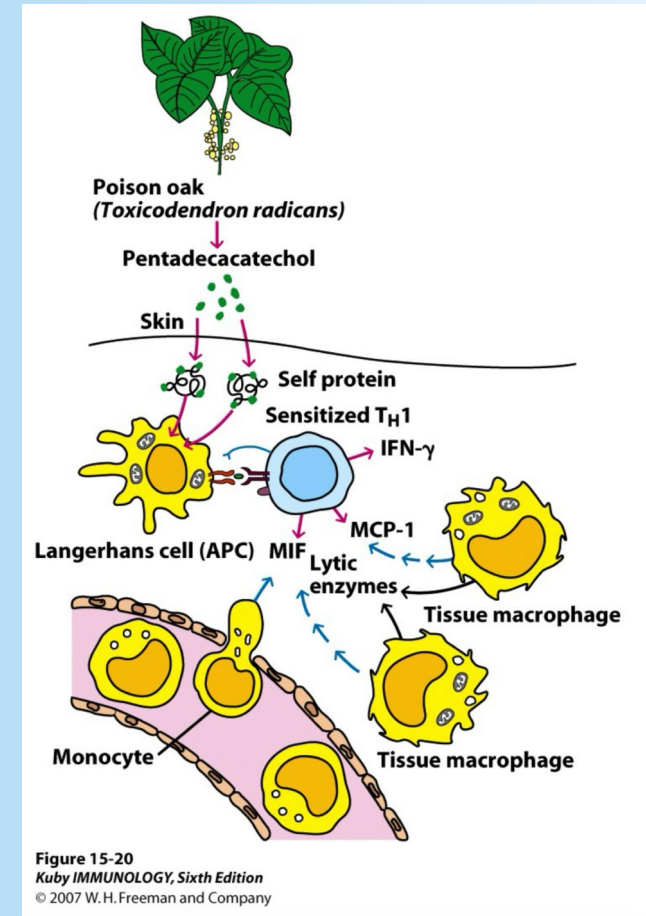
- IgG and IgM bind on cell membranes, basement membrane & ECM.
- Activate complement and Fc-mediated mechanisms
- Examples:
 - Autoimmune hemolytic anemia → IgG
 - Goodpasture syndrome → IgG
 - ABO transfusion reaction → IgM

Type III → immune complex-mediated

- IgG, IgM antibodies bind soluble antigens → form circulating immune complexes
- Complexes deposit in:
 - Blood vessel walls
 - Glomeruli
 - Synovium
- Examples:
 - SLE: anti-dsDNA, anti-Smith (IgG), ↓ C3/C4
 - Post-infectious GN: anti-streptococcal IgG (ASO, anti-DNase B), ↓ C3
 - Arthritis: IgG immune complexes (often SLE-related)

Type IV Hypersensitivity

- No antibodies involved
- Mediated by T lymphocytes
- $CD4^+$ Th1 cells → cytokine release
- $CD8^+$ cytotoxic T cells → direct cell killing
- Causes macrophage activation and tissue damage
- 🕒 Onset: 48-72 hours (delayed)



Pathophysiologic Steps (exam sequence)

Antigen presented on MHC

T-cell sensitization (first exposure)

Re-exposure → T-cell activation

Cytokines (IFN- γ , TNF- α) released

Macrophage recruitment → inflammation / granulomas

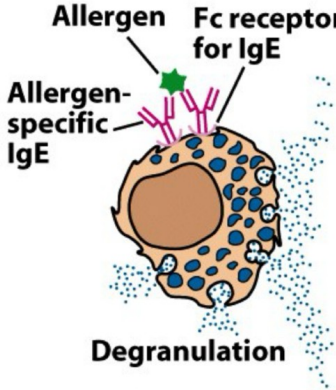
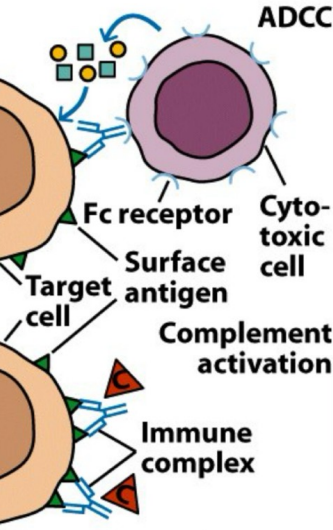
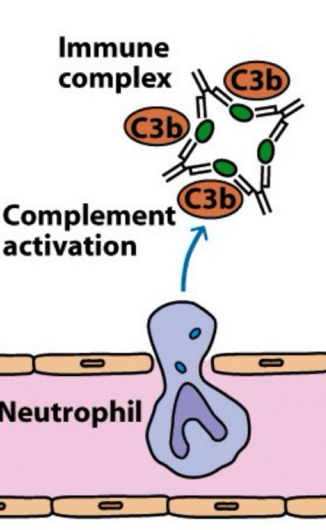
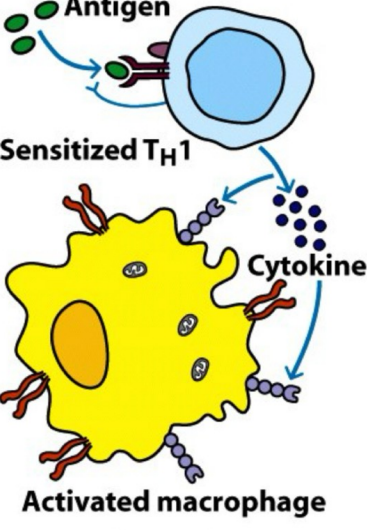
 Type I	 Type II	 Type III	 Type IV
IgE-Mediated Hypersensitivity	IgG- or IgM-Mediated Cytotoxic Hypersensitivity	Immune Complex-Mediated Hypersensitivity	Cell-Mediated Hypersensitivity
Ag induces cross-linking of IgE bound to mast cells and basophils with release of vasoactive mediators.	Ab directed against cell surface antigens mediates cell destruction via complement activation or ADCC.	Ag-Ab complexes deposited in various tissues induce complement activation and an ensuing inflammatory response mediated by massive infiltration of neutrophils.	Sensitized T_H1 cells shown above release cytokines that activate macrophages or T_C cells that mediate direct cellular damage. T_H2 cells and CTLs mediate similar responses.
Typical manifestations include systemic anaphylaxis and localized anaphylaxis such as hay fever, asthma, hives, food allergies, and eczema.	Typical manifestations include blood transfusion reactions, erythroblastosis fetalis, and autoimmune hemolytic anemia.	Typical manifestations include localized Arthus reaction and generalized reactions such as serum sickness, necrotizing vasculitis, glomerulonephritis, rheumatoid arthritis, and systemic lupus erythematosus.	Typical manifestations include contact dermatitis, tubercular lesions, and graft rejection.

Figure 15-1
Kuby IMMUNOLOGY, Sixth Edition
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Thank you for your attention!! 😊

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