Hypersensitivity type III, IV

By

Lecture 16

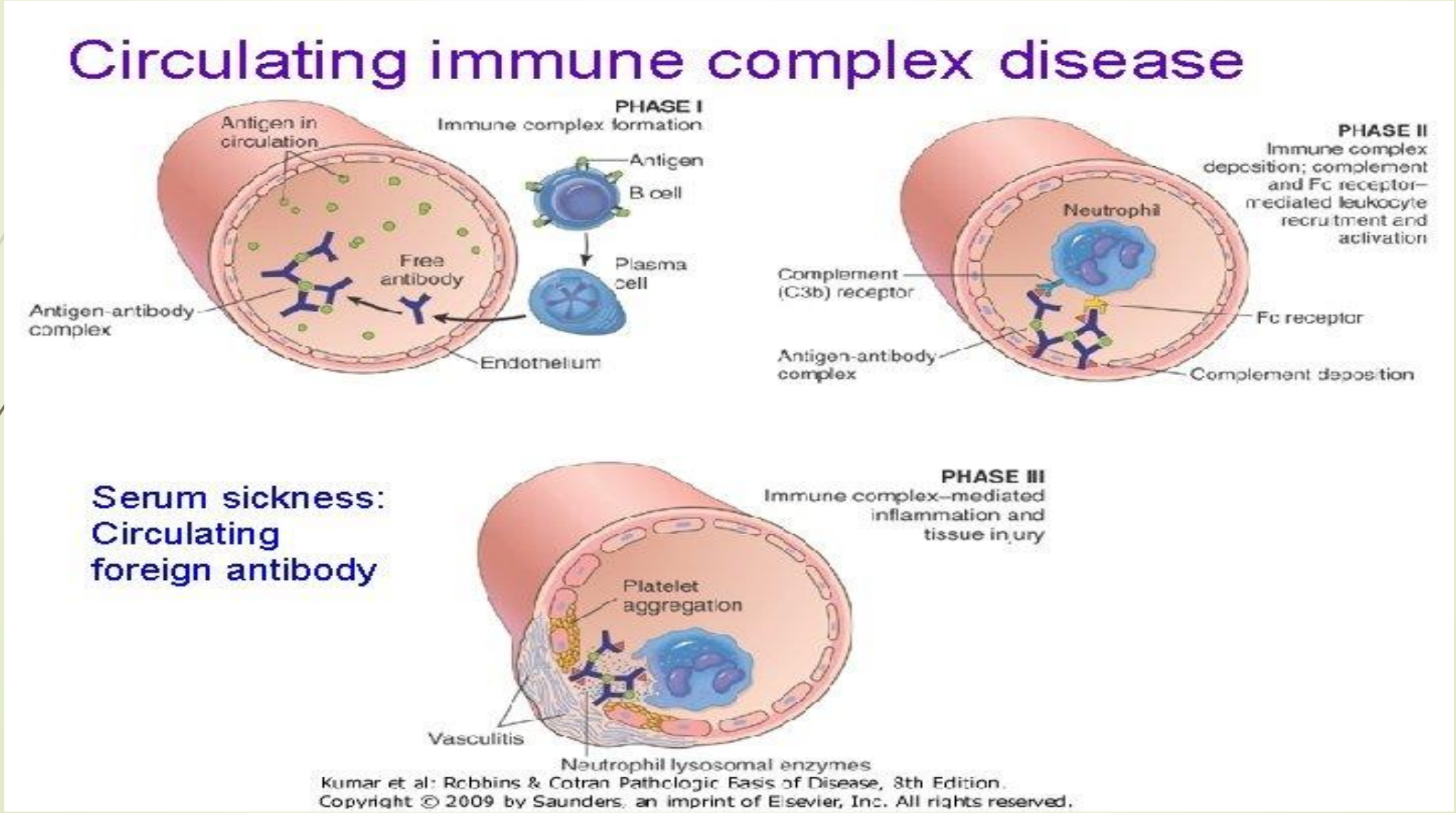
Dr. Mustafa Jawad

Type III hypersensitivity

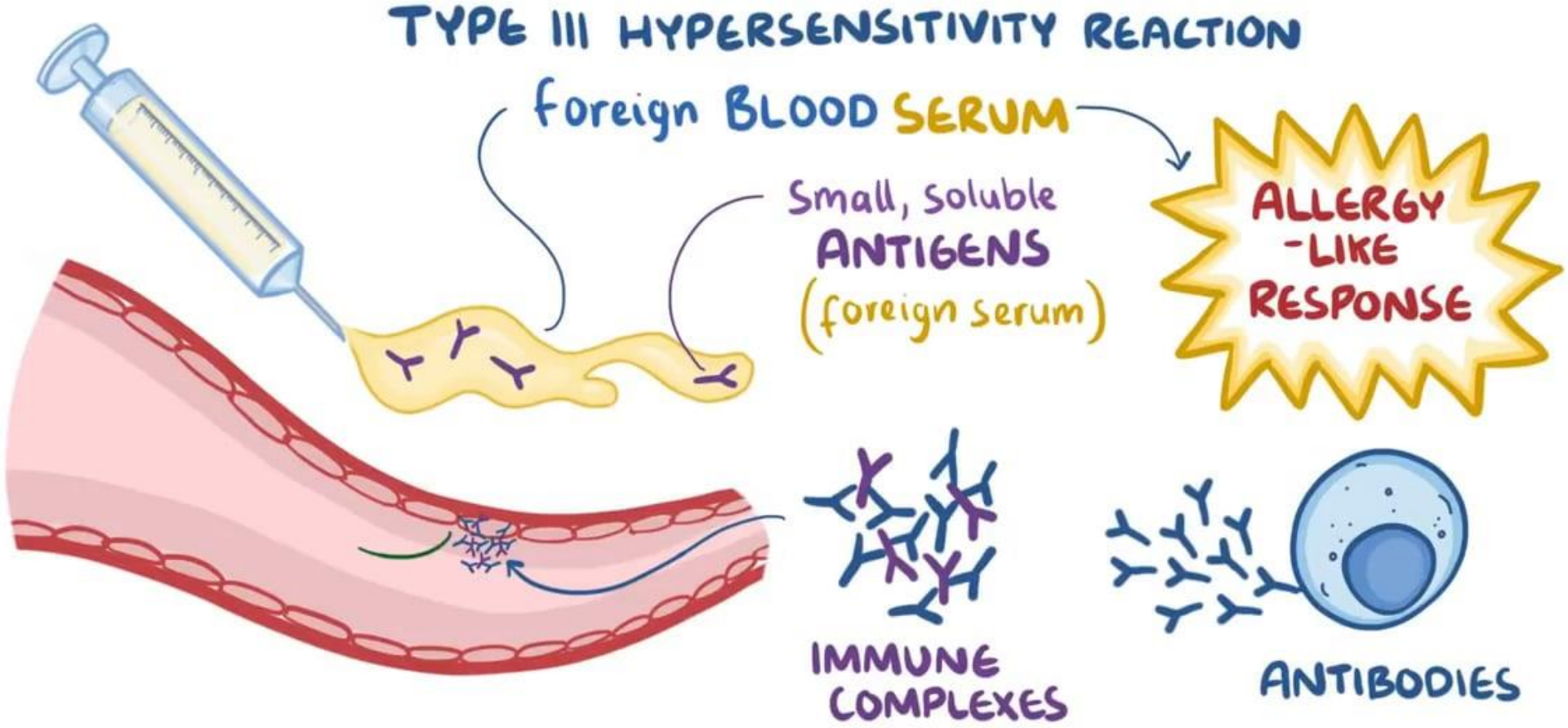
- Type III hypersensitivity occurs when **excess antigen bind antibody lead to fix complement and accumulation of immune complexes** (antigen-antibody complexes)
- **Immune complex lead to an inflammatory response** and attraction of leukocytes.
- It involves **soluble antigens** that are not bound to cell surfaces (as opposed to those in type II hypersensitivity).
- **Large immune complexes can be cleared by macrophages** but macrophages have difficulty in the disposal of small immune complexes.
- These immune complexes insert themselves into small blood vessels, joints, and glomeruli, causing symptoms.
- **Immune complex deposit in blood vessel walls** are more capable of interacting with complement ad being highly pathogenic

- **The reaction can take hours, days, or even weeks to develop, depending on whether or not there is immunological memory of the precipitating antigen**.
- Because of the nature of the antibody aggregation, tissues that are associated with blood filtration at considerable osmotic and hydrostatic bear the brunt of the damage.
- **Hence, vasculitis, glomerulonephritis and arthritis are commonly associated conditions as a result of type III hypersensitivity responses.**
- **immunofluorescence microscopy can be used to visualize the immune complexes.**
- Skin response to a hypersensitivity of this type is referred to as an **Arthus reaction**, and is **characterized by local erythema and some induration**.
- Platelet aggregation, especially in microvasculature, can cause localized clot formation, leading to blotchy hemorrhages. This typifies the response to injection of foreign antigen sufficient to lead to the condition of **serum sickness**.

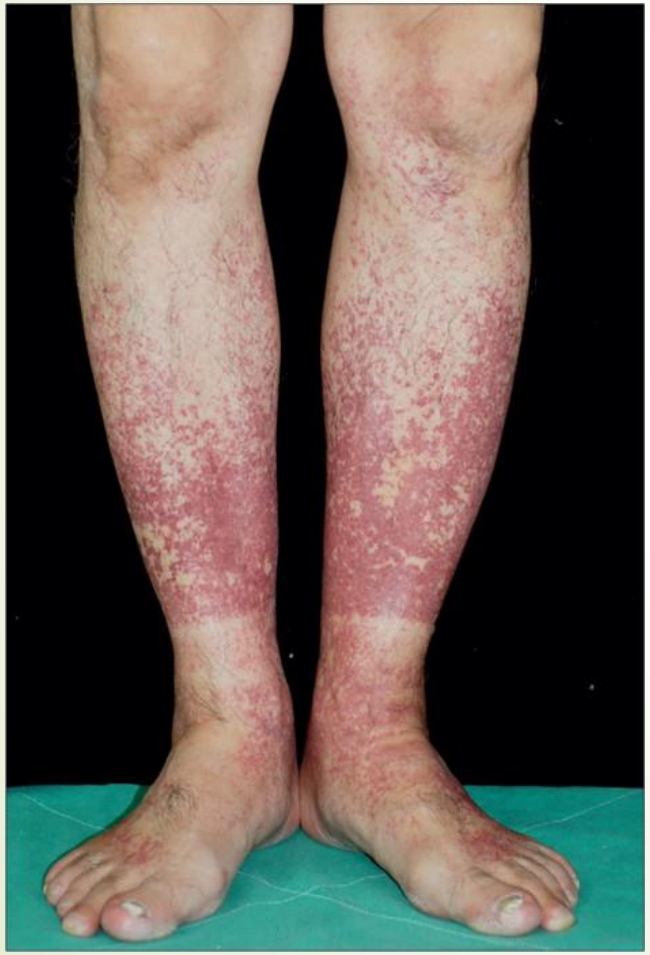
Type III hypersensitivity mechanism



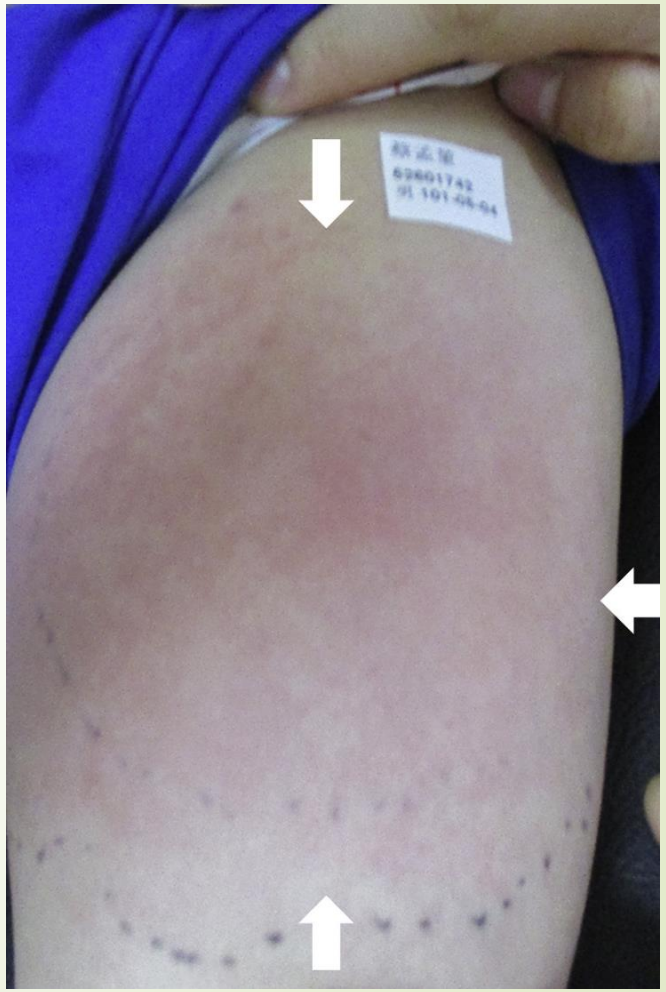
SERUM SICKNESS



Serum sickness



Arthus reaction



Disease	Target antigen	Main effects
Systemic lupus erythematosus	Nuclear antigens	•Nephritis •Skin lesions •Arthritis
Rheumatoid Arthritis	Antibody complexes: specifically IgM to IgG	•Arthritis
Post-streptococcal glomerulonephritis	Streptococcal cell wall antigens	•Nephritis
Polyarteritis nodosa	Hepatitis B virus surface antigen	•Systemic vasculitis
Reactive arthritis	Several bacterial antigens	•Acute arthritis
Serum sickness	Various	•Arthritis •Vasculitis •Nephritis
Arthus reaction	Various	•Cutaneous vasculitis
Farmer's Lung	Inhaled antigens (often mould or hay dust)	•Alveolar inflammation
Henoch–Schönlein purpura (IgA vasculitis)	Unknown, likely respiratory pathogen	•Purpura •Glomerulonephritis

Type IV hypersensitivity

- Often called **delayed type hypersensitivity** as the reaction takes several days to develop.
- **It is not antibody-mediated but rather is a type of cell-mediated response**. This response involves the **interaction of T-cells, monocytes, and macrophages.**

- This reaction is **caused when CD4+ Th1 helper T cells recognize foreign antigen in a complex with the MHC class II on the surface of antigen-presenting cells**.

- Macrophages secrete **IL-12**, which stimulates the proliferation of further CD4+ Th1 cells. **CD4+ T cells secrete IL-2 and interferon gamma (IFN-γ)**, inducing the further release of other Th1 cytokines, thus mediating the immune response.

- **Activated CD8+ T cells destroy target cells on contact, whereas activated macrophages produce hydrolytic enzymes**.

- The overreaction of the helper T cells and overproduction of cytokines **damage tissues, cause inflammation, and cell death.**

Type IV - Hypersensitivity

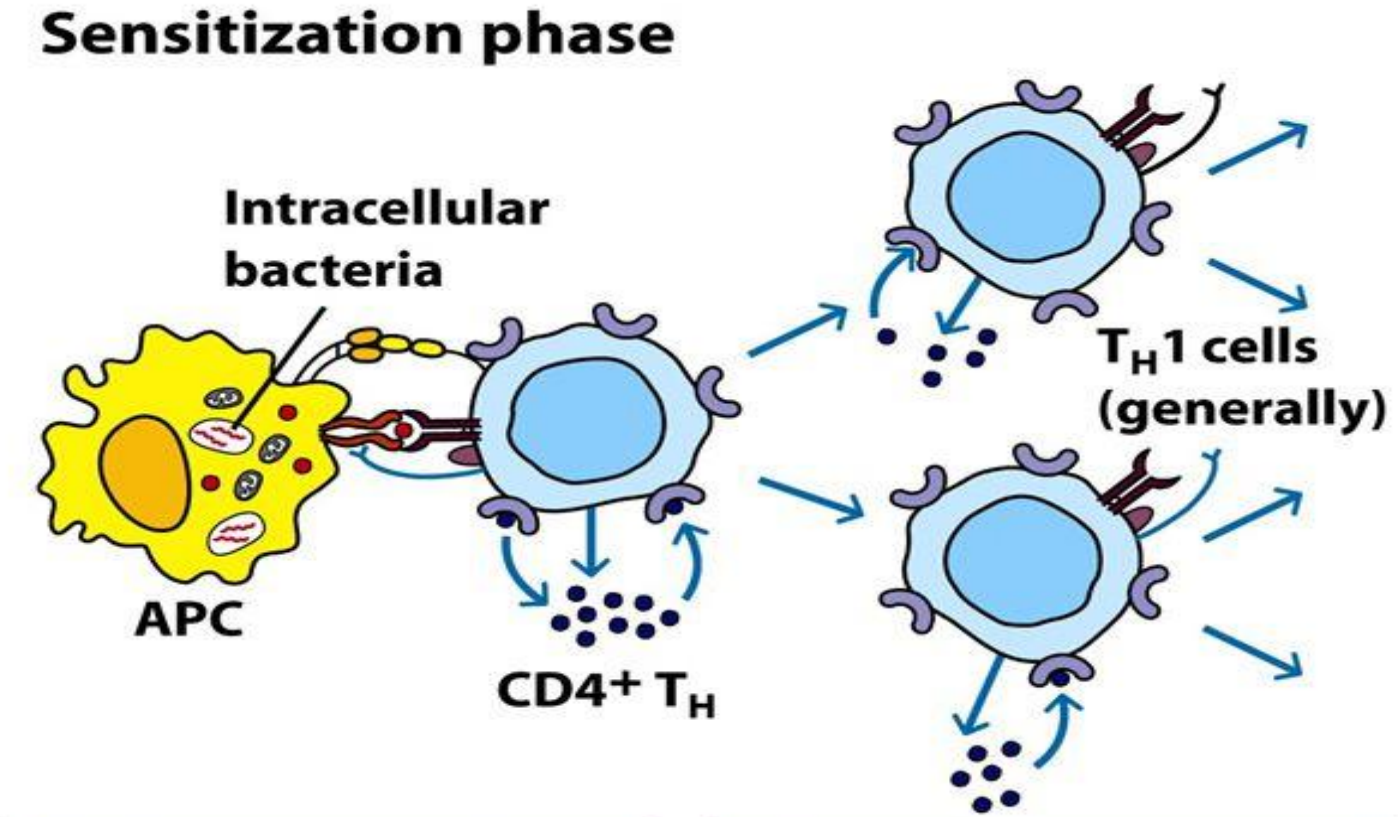
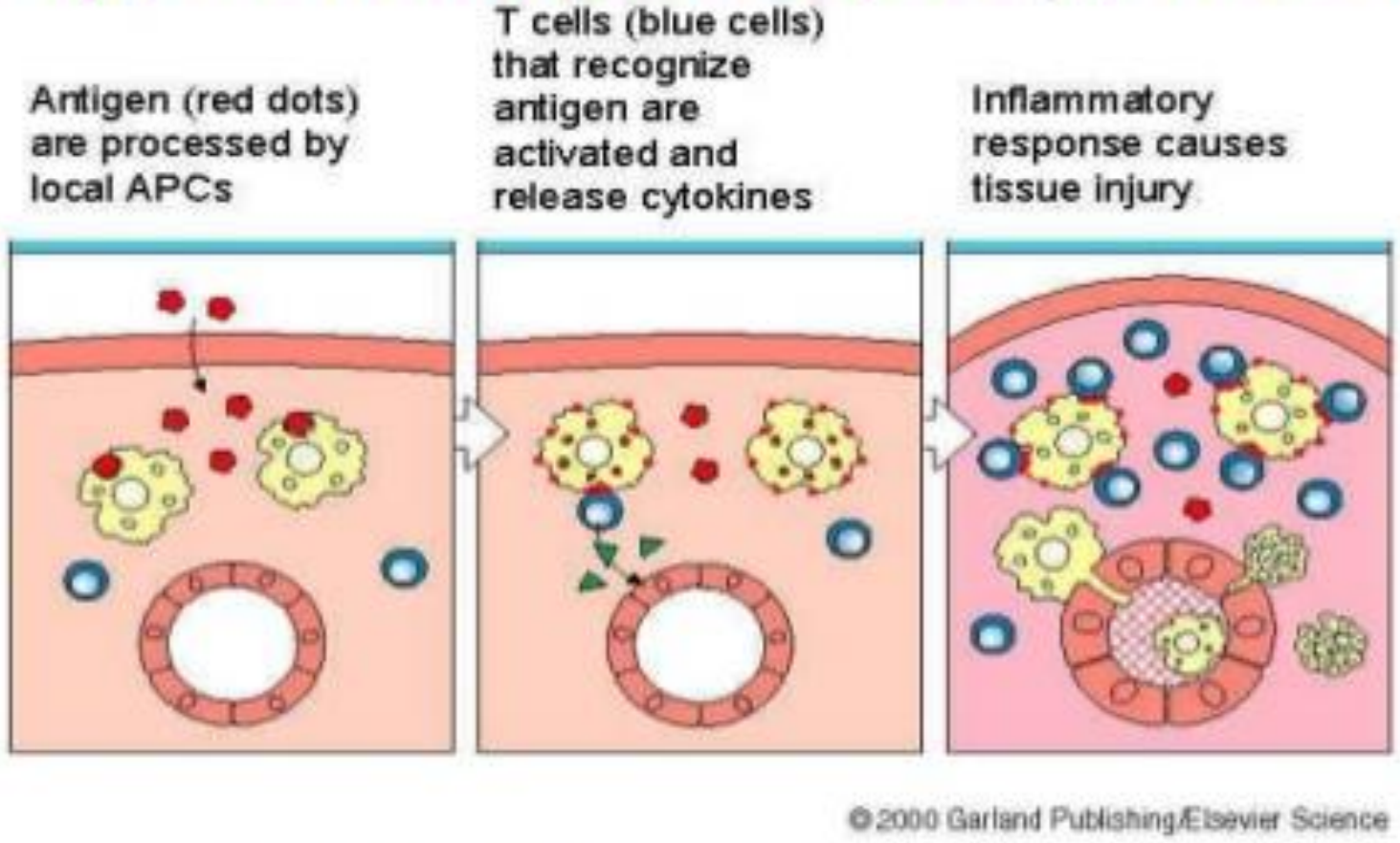


Figure 15-17a
Kuby IMMUNOLOGY, Sixth Edition

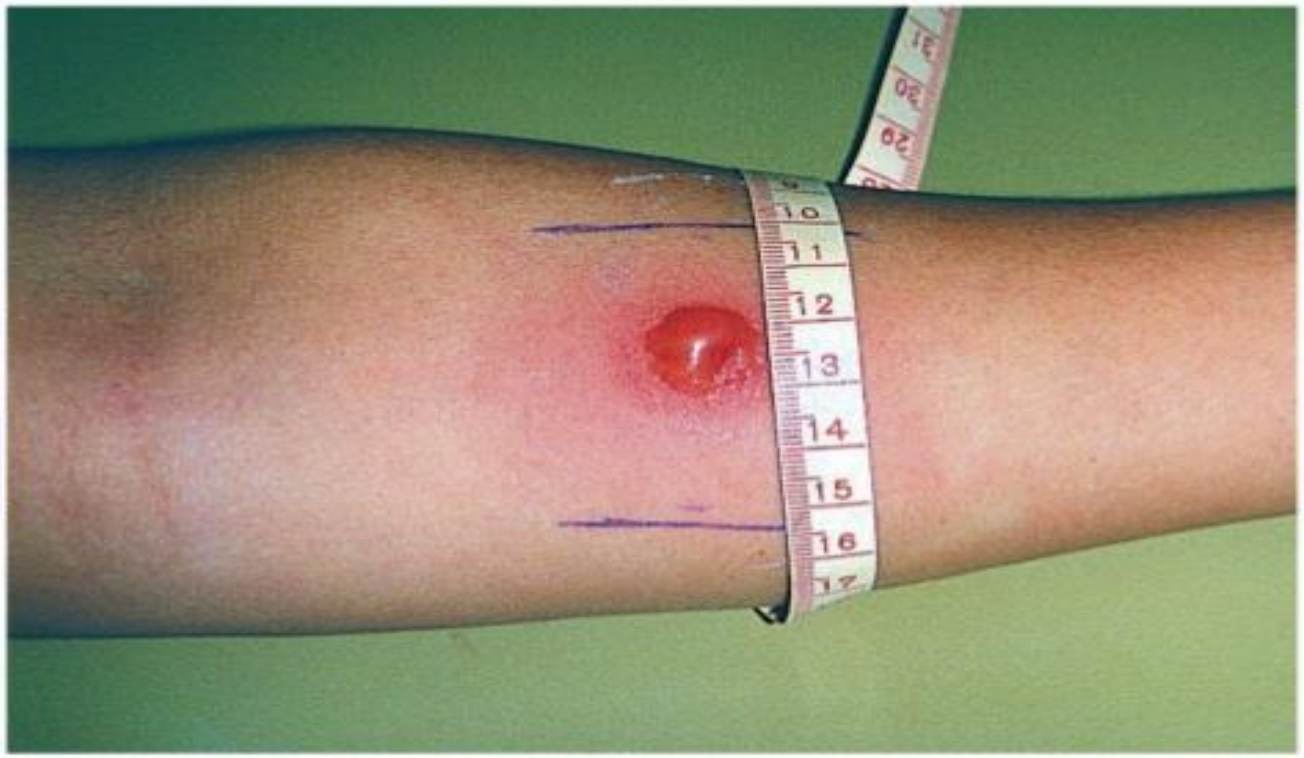
Type IV hypersensitivity – delayed-type or contact



Antigen is presented by APCs to antigen-specific memory T cells that become activated and produce chemicals that cause inflammatory cells to move into the area, leading to tissue injury. Inflammation by 2-6 hours; peaks by 24-48 hours.

Tuberculin test

A positive tuberculin test



Thank you