Type III Hypersensitivity

Immune Complex–Mediated (Type III) Hypersensitivity

The reaction of Ab. with Ag. generates immune complexes. Generally this complexing of Ag with Ab. facilitates the clearance of antigen by phagocytic cells.

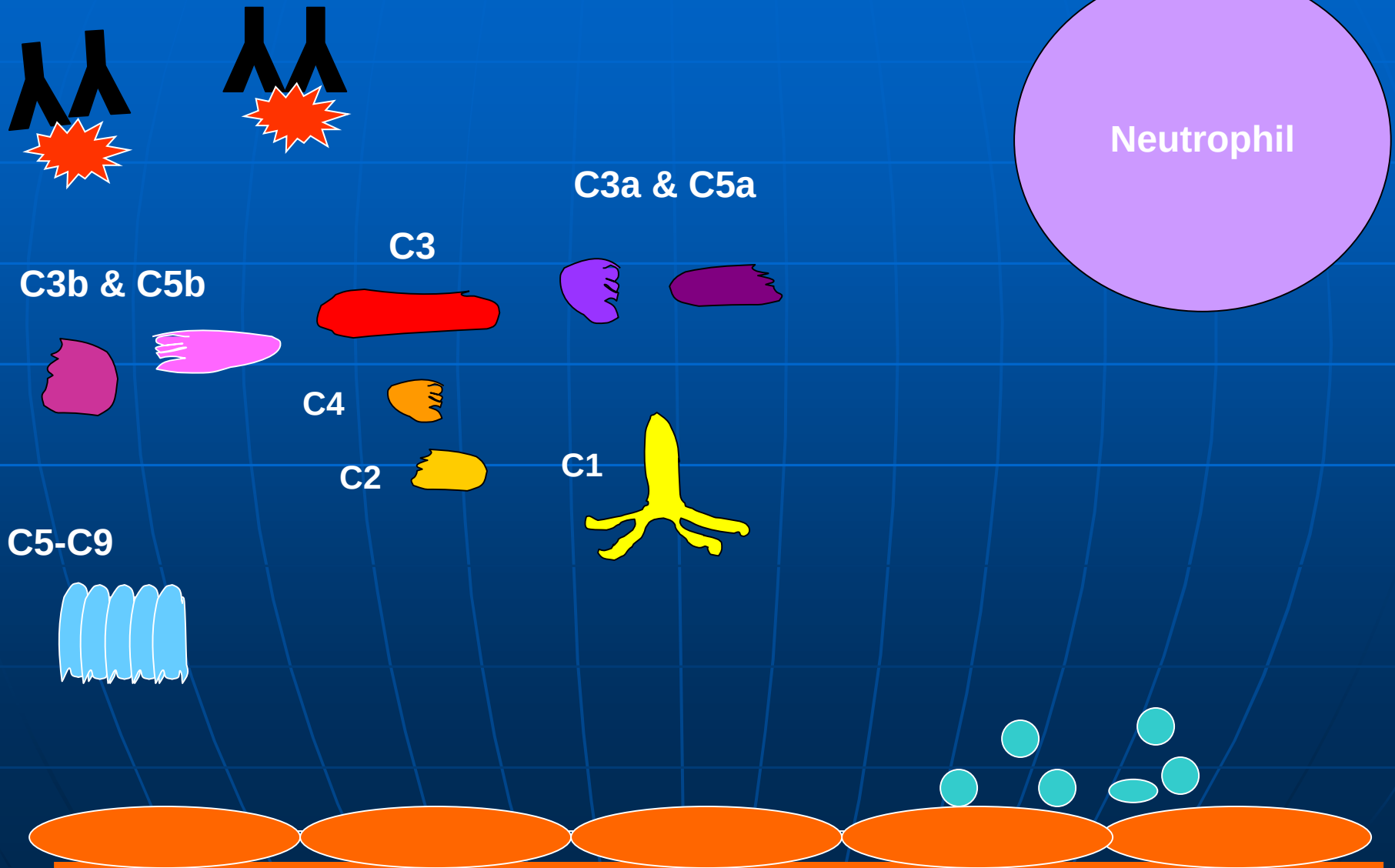
In some cases, however, large amounts of immune complexes can lead to tissue-damaging type III hypersensitive reactions.

When the complexes are deposited in tissue very near the site of antigen entry, a localized reaction develops.

Where as the complexes are formed in the blood, a reaction can develop wherever the complexes are deposited (generalized). In particular, complex deposition is frequently observed on blood-vessel walls, in the synovial membrane of joints, on the glomerular basement membrane of the kidney.

The deposition of these complexes initiates a reaction that results in the recruitment of neutrophils to the site. The tissue is injured as a consequence of granular release from the neutrophil.

Type III Hypersensitivity mechanism



Three experimental model for type III HS

- **Serum sickness**: generalized type III HS
- **Arthus reaction**: localized type III HS

Examples of IC hypersensitivity reactions

A. Arthus reaction (localized)

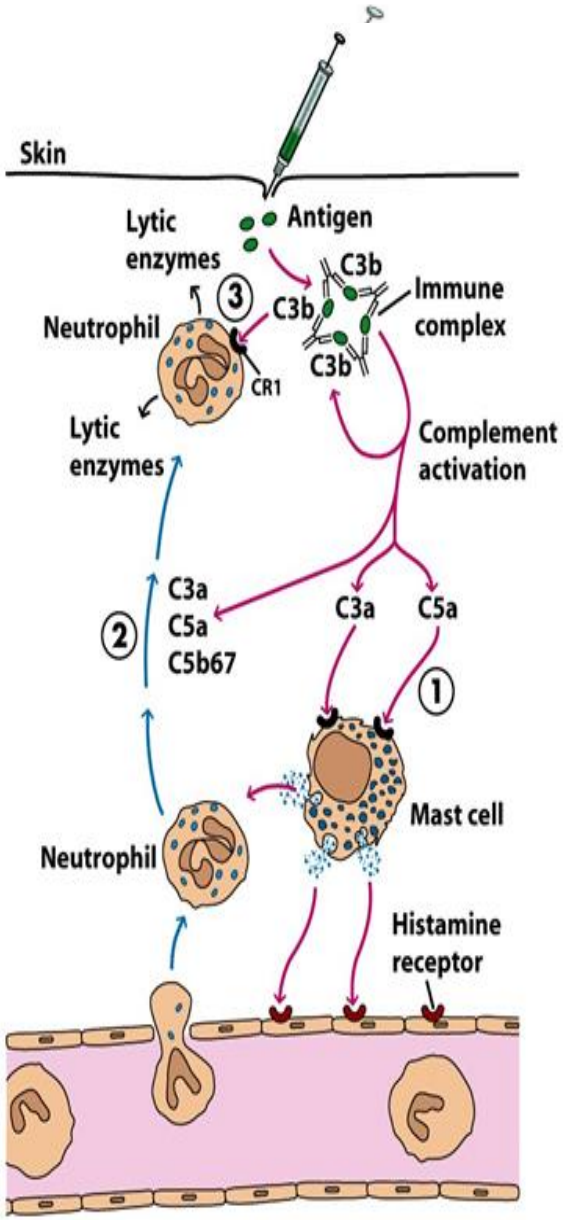
- occur in diabetics receiving repeated subcutaneous injections of insulin and after rabies vaccination.
- In such cases, repeated injections lead to formation of local immune complexes due to the reaction of antigen with its specific antibodies from the blood.
- After a number of injections, ICs are deposited in the small blood vessels leading to vasculitis, microthrombi, vascular occlusion and necrosis. These reactions are manifested by edema, erythema and necrosis.

Type III Hypersensitivity Reactions

Localized response called an Arthus reaction

Occurs when antigen is injected into an animal that has high levels of circulating antibody

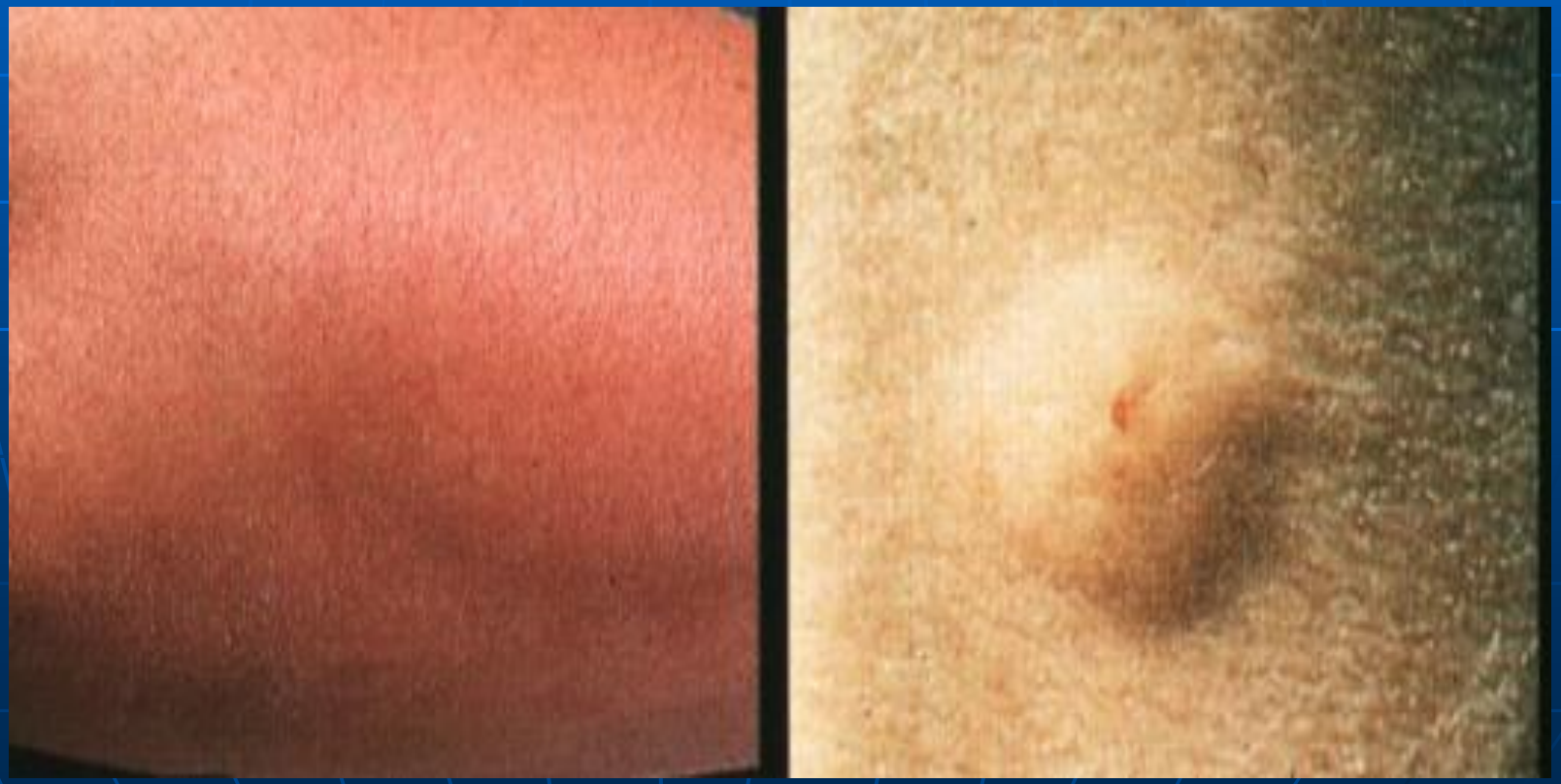
Arthus reaction is detected within 4-8 hours

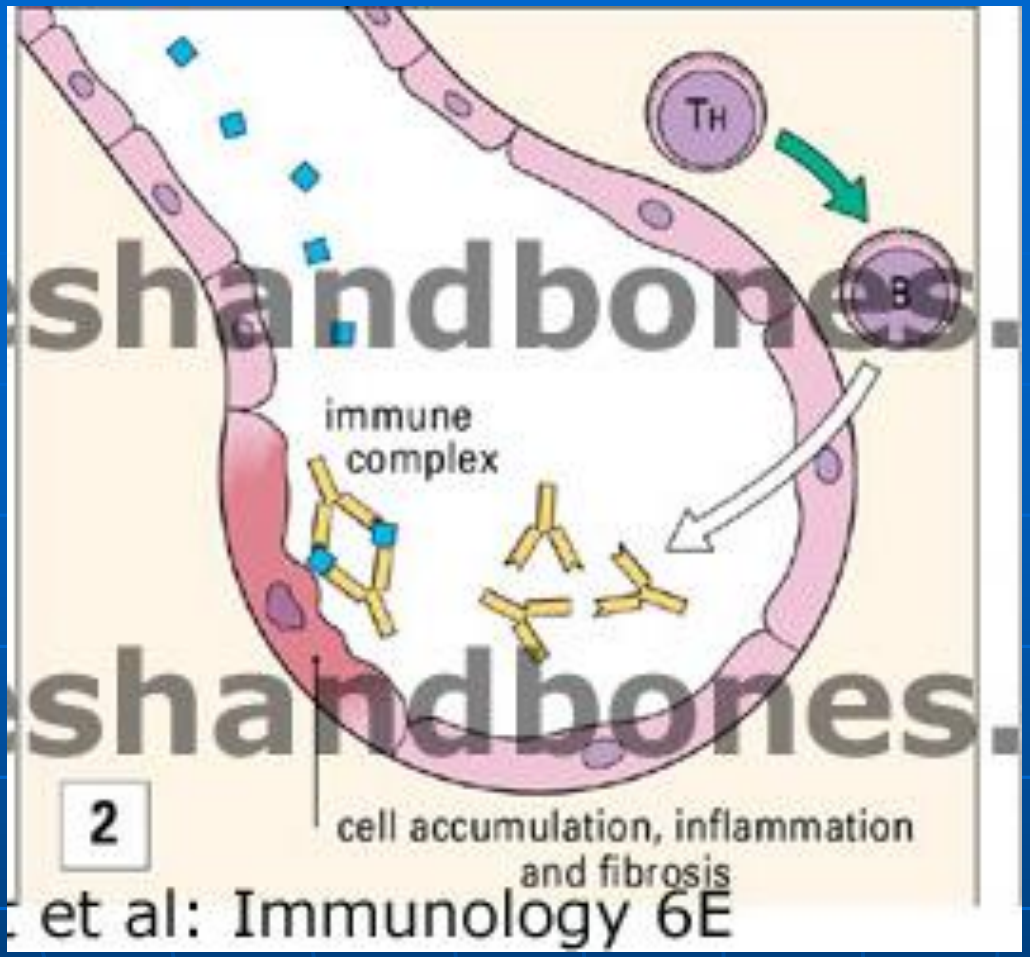


Arthus reaction

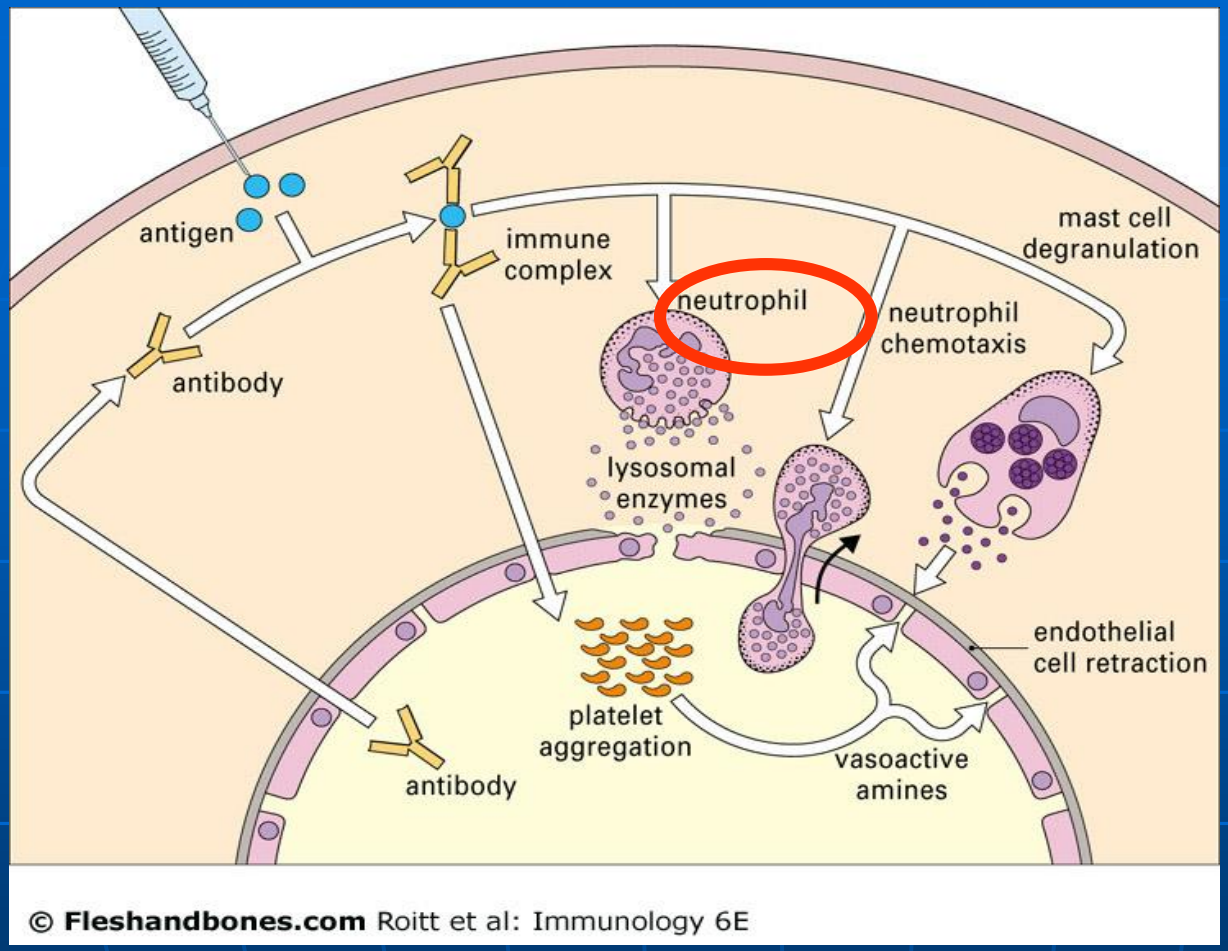
Arthus reaction
Type-II

Weal & flare reaction
Type-I





Intrapulmonary Arthus-typereactions induced by bacterial spores, fungi, or dried fecal proteins can also cause pneumonitis or alveolitis. These reactions are known by a variety of common names reflecting the source of the antigen. For example, "farmer's lung" develops after inhalation of thermophilic actinomycetes from moldy hay, and "pigeon fancier's disease" results from inhalation of a serum protein in dust derived from dried pigeon feces.

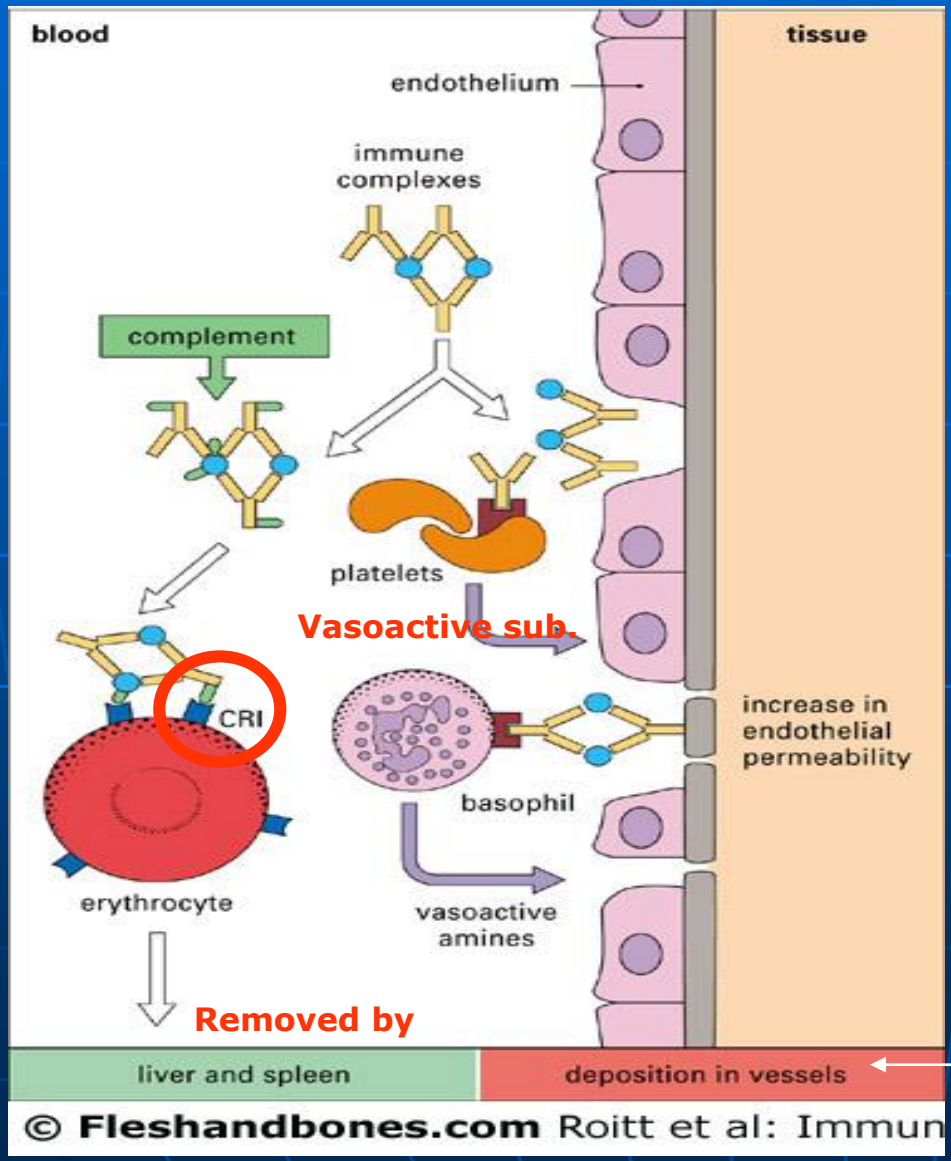


The **sequel** of Arthus Rex

Serum sickness:

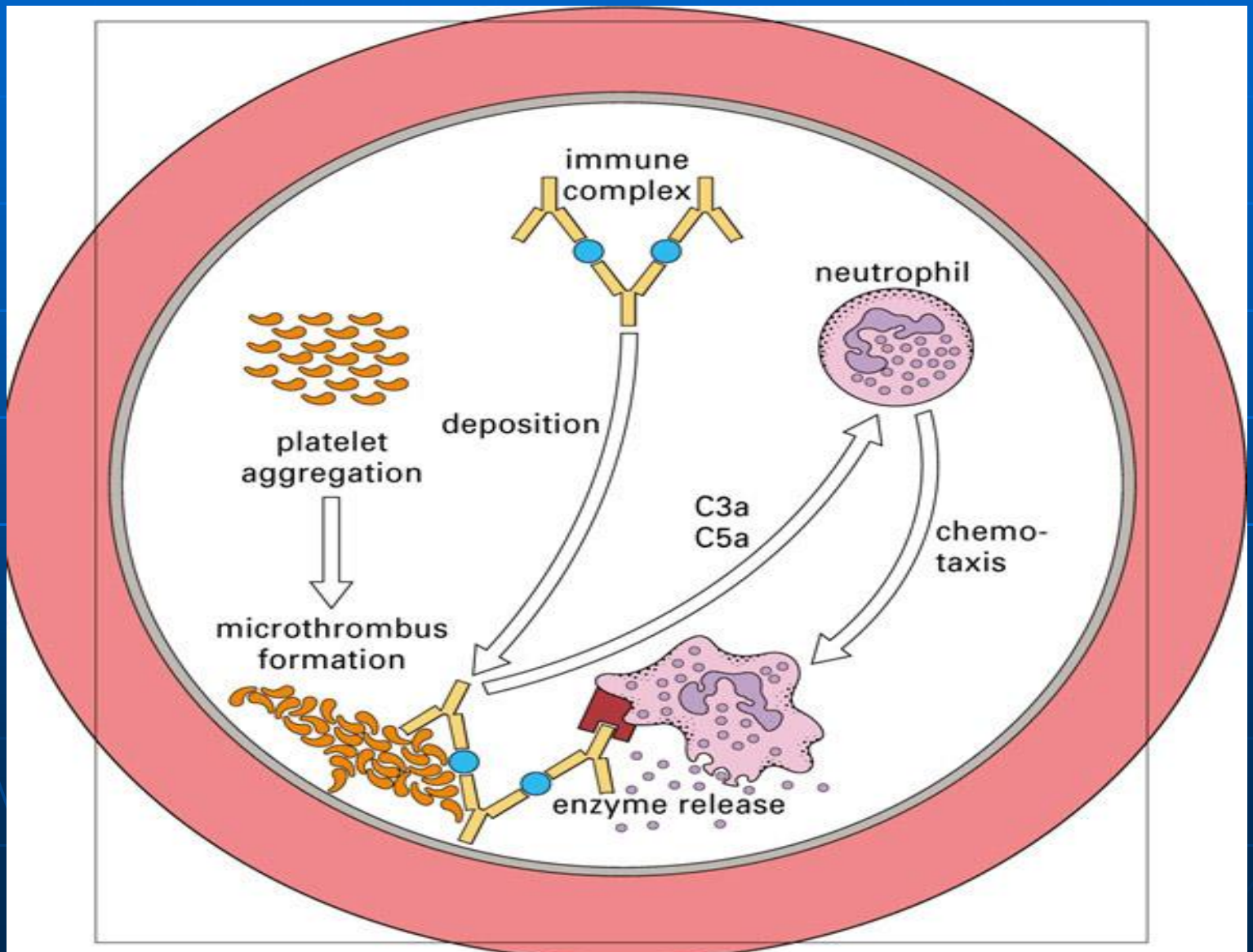
- Occurs as a **systemic inflammatory response** to the presence of immune complexes deposited in many areas of the body.
- This can occur due to injection of heterologous serum or drugs such as penicillin.
- The symptoms include: fever,uricaria,arthralgia,lymphadenopathy,splenomegaly & eosinophilia.
- These symptoms occur 7-14 days after injection of serum or drug.
- It is a self-limiting condition.

Immune complexes as a trigger for increasing vascular permeability



Mechanism in types III HS

Deposition of immune complexes in blood vessel walls



Serum Sickness

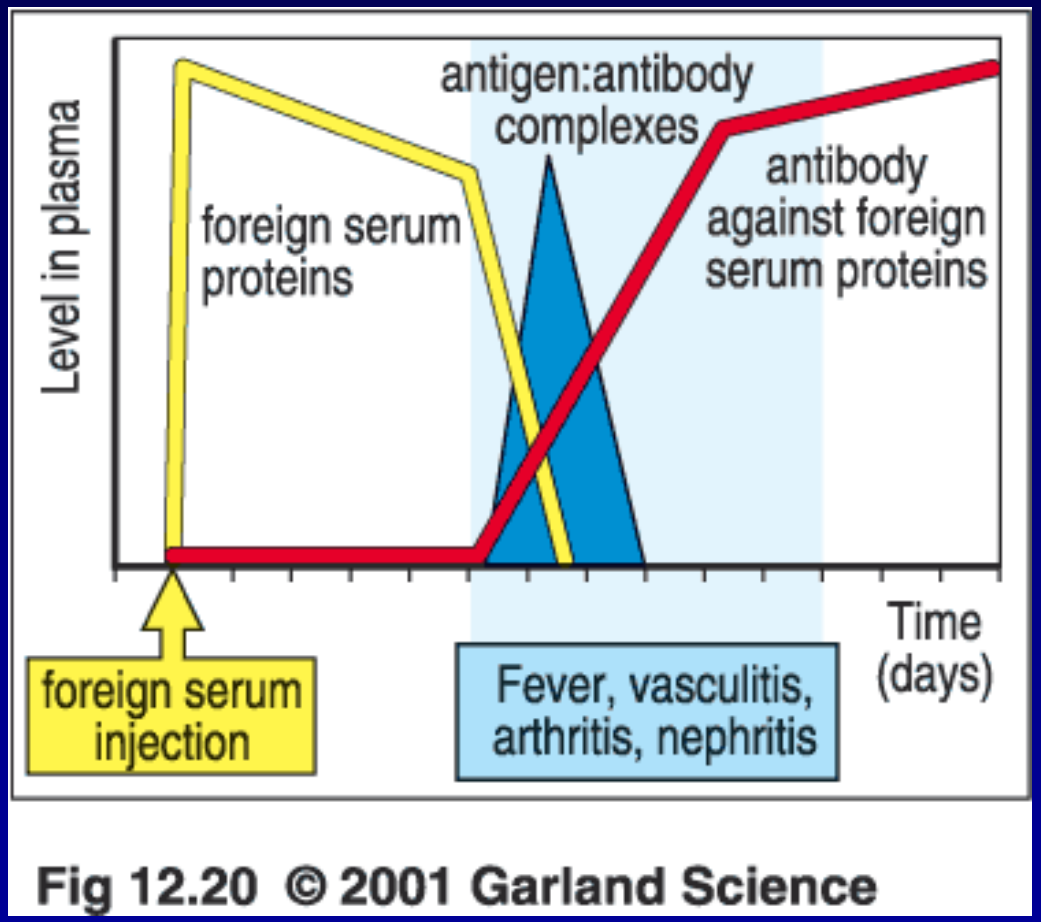


Fig 12.20 © 2001 Garland Science

- Initially described following administration of therapeutic horse serum for treatment of pneumococcal pneumonia
- Now described following certain infections, administration of penicillin and other antibiotics, vaccines, and foreign proteins
- Onset usually at 7-10 days following injection, coincides with switch to IgG, onset at 1-3 days with subsequent exposures

Serum sickness

- Serum sickness is most commonly seen today after antibiotic treatment (not due to drug allergy) and certain vaccination condition symptoms develop in 1 to 3 days on subsequent exposure to the same antigen.

- Patients who received therapeutic monoclonal antibodies from mice produced their own antibodies against foreign Abs, is a reaction called the human anti-mouse antibody response (HAMA) and develop serum sickness like symptoms.

To avoid HAMA current therapeutic Abs are humanized or genetically engineered in order to not recognized as foreign Ag.

Examples of IC hypersensitivity reactions

B. Serum sickness (Generalized)

- After IV injection of Ag, a large quantities of ICs are formed and deposited in the blood vessels, e.g:

  a-deposition within the glomeruli of the kidney (glomerulonephritis)

  b- deposition in joints leads to rheumatic arthritis

  c- binding of ICs to: RBCs causes anemia

  WBCs causes leukopenia

  Platelets cause thrombocytopenia

Immune complex diseases:

- **Rheumatoid arthritis:**It is a chronic autoimmune disease of joints,which is usually observed in young women.
- There is formation of rheumatoid factor that is an Ig G autoantibody.
- **Glomerulonephritis:** Occurs several weeks after skin infection with S.pyogenes,especially with some nephritogenic strains.
- The immune complex deposits in the glomerular basement membrane.(can occur in SLE & Hepatitis B also)

The **site** of complex deposition is dependent on the **size** of the complexes

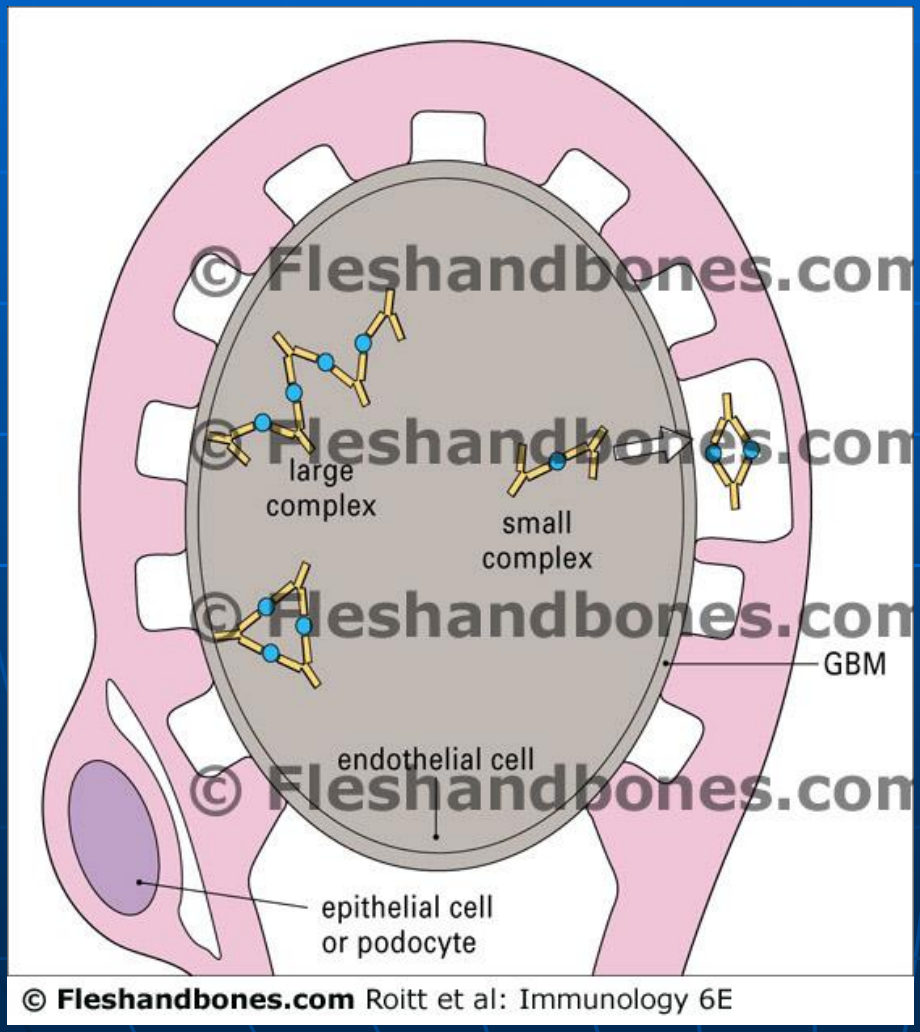
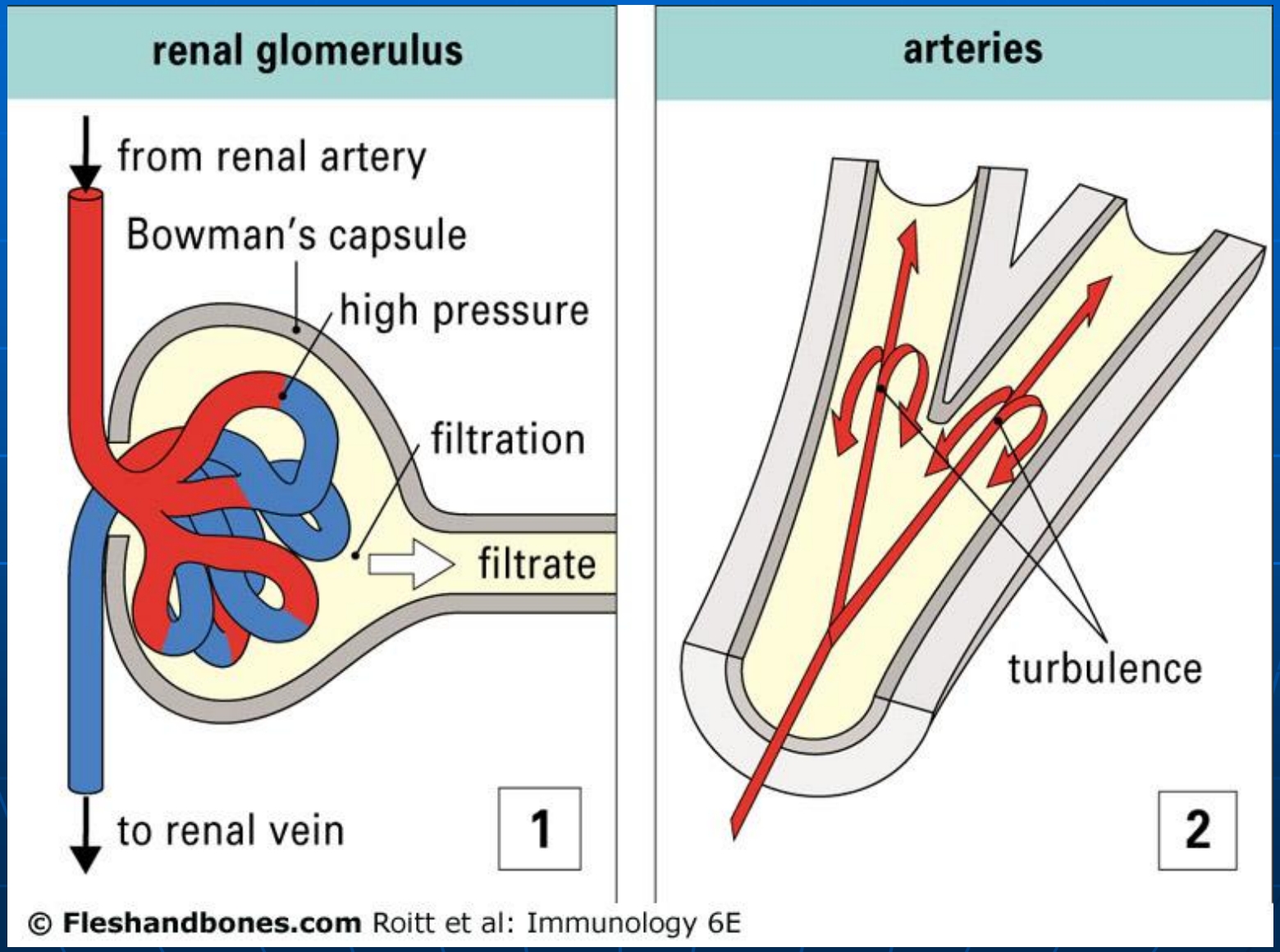


Figure shows The site of complex deposition in the kidney is dependent on the size of the complexes in the circulation. Large complexes become deposited on the glomerular basement membrane, while small complexes pass through the basement membrane and are seen on the epithelial side of the glomerulus

Heamodynamic factors affecting complex deposition



Remove of immunocomplex

Complement is helpful for complex removal