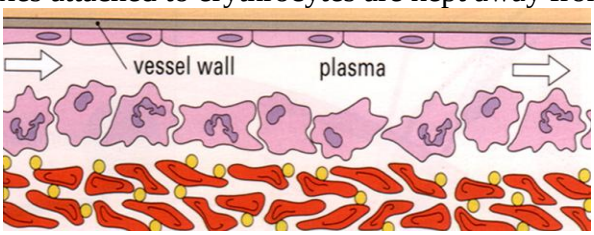
- **Type III (immune complex-mediated) hypersensitivity reaction:**
  - The immune complexes that cause disease may either involve self or foreign antigens bound to antibodies.
  - These immune complexes are filtered out of the circulation in the small vasculature, so their sites of ultimate damage do not reflect their sites of origin.
  - These diseases tend to be systemic, with little tissue or organ specificity.
  - **Summary: type III hypersensitivity is characterized by:**
    - ✓ Systemic damage.
    - ✓ Immune complexes activate complement.
    - ✓ Self or foreign antigens.
  - **Examples of type III hypersensitivity reactions:**

Disease	Antigen involved	Clinical manifestations
Systemic Lupus Erythematosus (SLE)	Double-stranded DNA, Sm and other nucleoproteins	Nephritis, arthritis, vasculitis and butterfly facial rash
Post-streptococcal glomerulonephritis	Streptococcal cell wall antigens (may be planted in glomerular basement membrane)	Nephritis and "lumpy bumpy deposits"
Arthus reaction	Any injected protein	Local pain and edema at site of injection
Serum sickness	Various proteins	Arthritis, vasculitis and nephritis (confused with SLE!)
Polyarteritis nodosa	Hepatitis B virus antigen	Systemic vasculitis

- **Immune complex disease:**
  - **Immune complexes are composed of:**
    - ✓ Antigen.
    - ✓ Antibody.
    - ✓ Complement.
  - **Normal clearance of immune complexes:**
    - ✓ They bind to erythrocytes and transported to the liver where they are removed by hepatic macrophages.
    - ✓ Immune complexes which are released from erythrocytes are taken up by cells bearing receptors for Fc and complement (e.g. macrophages).
    - ✓ Complement solubalization of large complexes produces small soluble complexes which may be taken up directly by tissue macrophages.
  - **Role of erythrocytes in immune complex disease:**
    - ✓ Immune complexes attached to erythrocytes are kept away from vessel walls



  - **Complex clearance by mononuclear phagocytes:**
    - ✓ Large immune complexes are cleared most quickly than small immune complexes (why?):
      - ❖ Because they present an IgG-Fc lattice to reticuloendothelial cells (macrophages) with Fc-receptors, permitting higher avidity binding to these cells.
      - ❖ They also fix complement better than small complexes.
  - **Hemodynamic factors affecting complex deposition:**
    - ✓ High blood pressure.
    - ✓ Turbulence at bifurcations of arteries (favoring deposition of immune complexes).

- **Biological effects of C5a:**
  - ✓ Activation of neutrophils.
  - ✓ Neutrophil adhesion.
  - ✓ Neutrophil emigration and chemotaxis.
  - ✓ Activation of monocytes.
  - ✓ Mast cell degranulation resulting in smooth muscle contraction and increased vascular permeability.
- **Opsonization and phagocytosis**: C3b or C4b complement will bind to a bacterium enhancing phagocytosis via macrophages which express complement-receptors on their surfaces.
- **Deposition of immune complexes in blood vessel walls:**

Deposition of immune complexes in blood vessel walls – I

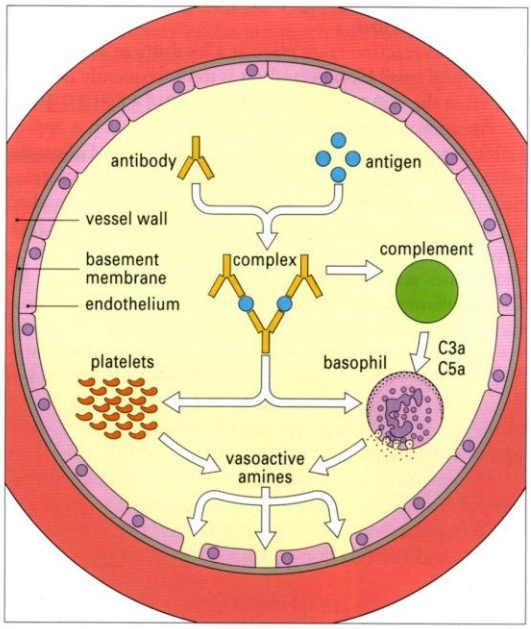


Fig. 25.5 Immune complexes act on complement to generate C3a and C5a, which in turn stimulate basophils to release vasoactive amines. The complexes also act directly on basophils and platelets (in humans) to produce vasoactive amine release. The amines released (e.g. histamine, 5-hydroxytryptamine) cause endothelial cell retraction and thus increase vascular permeability.

Deposition of immune complexes in blood vessel walls – II

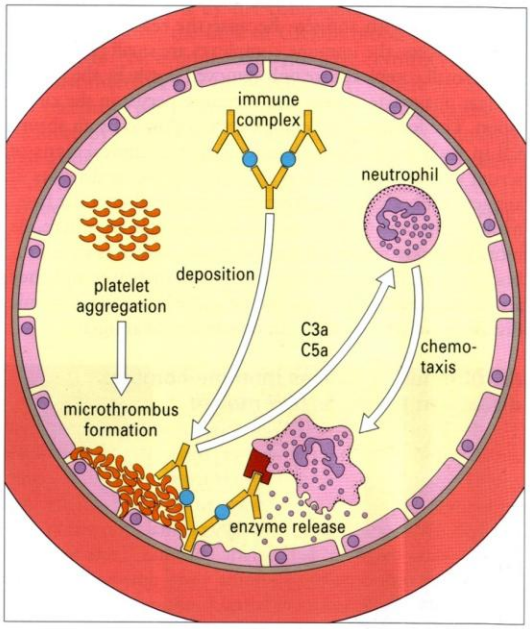


Fig. 25.6 Increased vascular permeability allows immune complexes to be deposited in the blood vessel wall. This induces platelet aggregation and complement activation. The aggregated platelets form microthrombi on the exposed collagen of the basement membrane of the endothelium. Neutrophils are attracted to the site by complement products, but cannot ingest the complexes. They therefore exocytose their lysosomal enzymes, causing further damage to the vessel wall.

- **Immune complex deposition in the kidney (depending on the size):**
  - ✓ Large complexes become deposited on the glomerular basement membrane.
  - ✓ Small complexes pass through the basement membrane and are seen on the epithelial side of the glomerulus (subepithelial).