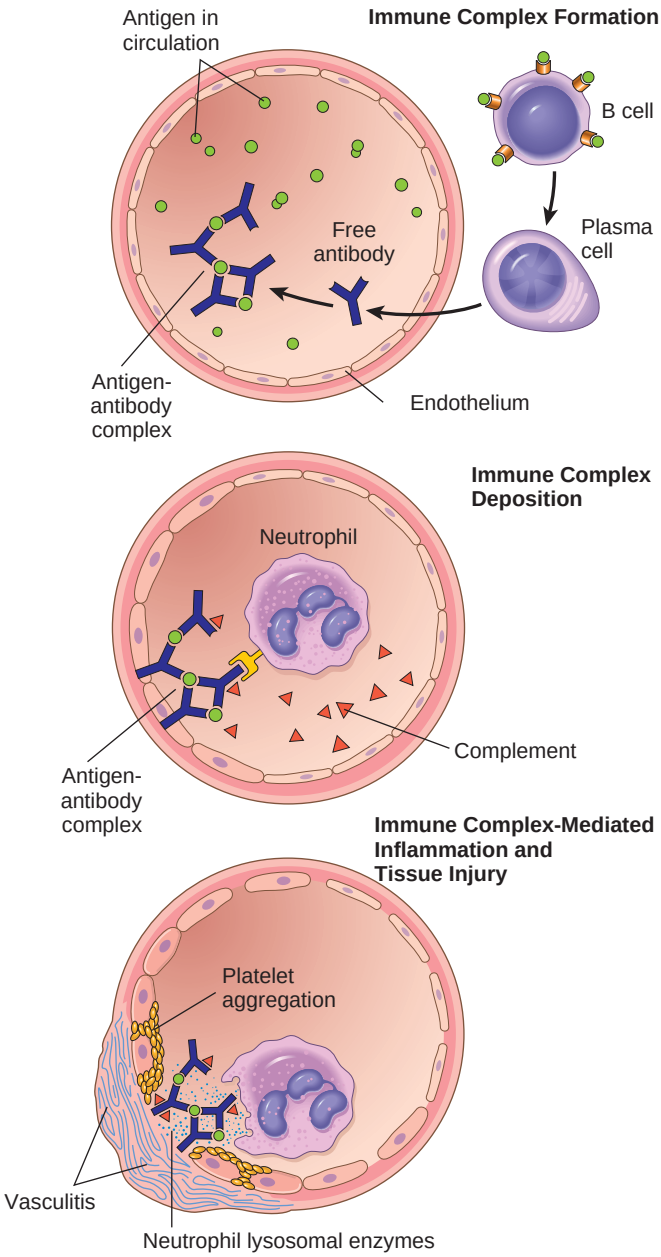

Figure 6-17 Immune complex disease. The sequential phases in the induction of systemic immune complex–mediated diseases (type III hypersensitivity).

Immune Complex–Mediated (Type III) Hypersensitivity

Antigen-antibody complexes produce tissue damage mainly by eliciting inflammation at the sites of deposition. The pathologic reaction is usually initiated when antigen combines with antibody in the circulation, creating immune complexes that typically deposit in vessel walls. Less frequently, the complexes may be formed at sites where antigen has been "planted" previously (called in situ immune complexes). The antigens that form immune complexes may be *exogenous*, such as a foreign protein that is injected or produced by an infectious microbe, or *endogenous*, if the individual produces antibody against self antigens (autoimmunity). Examples of immune complex disorders and the antigens involved are listed in Table 6-4. Immune complex–mediated diseases tend be *systemic*, but often preferentially involve the kidney (glomerulonephritis), joints (arthritis), and small blood vessels (vasculitis), all of which are common sites of immune complex deposition.

Systemic Immune Complex Disease

Acute serum sickness is the prototype of a systemic immune complex disease; it was once a frequent sequela to the administration of large amounts of foreign serum (e.g., serum from immunized horses used for protection against diphtheria). In modern times the disease is infrequent, and usually seen in individuals who receive antibodies from other individuals or species. Nevertheless, it is an informative model that has taught us a great deal about systemic immune complex disorders.

The pathogenesis of systemic immune complex disease can be divided into three phases (Fig. 6-17).

1. **Formation of immune complexes.** The introduction of a protein antigen triggers an immune response that results in the formation of antibodies, typically about a week after the injection of the protein. These antibodies are secreted into the blood, where they react with the antigen still present in the circulation and form antigen-antibody complexes.
2. **Deposition of immune complexes.** In the next phase the circulating antigen-antibody complexes are deposited in various tissues. The factors that determine whether immune complex formation will lead to tissue deposition and disease are not fully understood, but the major influences seem to be the characteristics of the complexes and local vascular alterations. In general, complexes that are of medium size, formed in slight antigen excess, are the most pathogenic. Organs where

Table 6-4 Examples of Immune Complex–Mediated Diseases

Disease	Antigen Involved	Clinicopathologic Manifestations
Systemic lupus erythematosus	Nuclear antigens (circulating or "planted" in kidney)	Nephritis, skin lesions, arthritis, others
Poststreptococcal glomerulonephritis	Streptococcal cell wall antigen(s); may be "planted" in glomerular basement membrane	Nephritis
Polyarteritis nodosa	Hepatitis B virus antigens in some cases	Systemic vasculitis
Reactive arthritis	Bacterial antigens (e.g., *Yersinia*)	Acute arthritis
Serum sickness	Various proteins, e.g., foreign serum protein (horse antithymocyte globulin)	Arthritis, vasculitis, nephritis
Arthus reaction (experimental)	Various foreign proteins	Cutaneous vasculitis