eventually clear, but others develop chronic glomerulonephritis or even rapidly progressive glomerulonephritis.

Nonstreptococcal Acute Glomerulonephritis (Postinfectious Glomerulonephritis)

A similar form of glomerulonephritis occurs sporadically in association with other infections, including those of bacterial (e.g., staphylococcal endocarditis, pneumococcal pneumonia, and meningococcemia), viral (e.g., hepatitis B, hepatitis C, mumps, HIV infection, varicella, and infectious mononucleosis), and parasitic (malaria, toxoplasmosis) origin. In these settings, granular immunofluorescent deposits and subepithelial humps characteristic of immune complex nephritis are present. Postinfectious glomerulonephritis due to staphylococcal infections differs by sometimes producing immune deposits containing IgA rather than IgG.

Rapidly Progressive (Crescentic) Glomerulonephritis

Rapidly progressive glomerulonephritis (RPGN) is a syndrome associated with severe glomerular injury, but does not denote a specific etiologic form of glomerulonephritis. It is characterized by rapid and progressive loss of renal function associated with severe oliguria and signs of nephritic syndrome; if untreated, death from renal failure occurs within weeks to months. *The most common histologic picture is the presence of crescents in most of the glomeruli (crescentic glomerulonephritis).* As discussed earlier, these are produced predominantly by the proliferation of the parietal epithelial cells lining Bowman capsule and by the infiltration of monocytes and macrophages.

Classification and Pathogenesis. RPGN may be caused by a number of different diseases, some restricted to the kidney and others systemic. Although no single mechanism can explain all cases, there is little doubt that **in most cases the glomerular injury is immunologically mediated**. A practical classification divides RPGN into three groups on the basis of immunologic findings (Table 20-6). In each group the disease may be associated with a known disorder, or it may be idiopathic. The common denominator in all types of RPGN is severe glomerular injury. Several distinct pathogenic mechanisms have been described, as follows:

- *Anti-GBM antibody-mediated disease, characterized by linear deposits of IgG and, in many cases, C3 in the GBM.* In some of these patients, the anti-GBM antibodies cross-react with pulmonary alveolar basement membranes to produce the clinical picture of pulmonary hemorrhage associated with renal failure *(Goodpasture syndrome)*. Plasmapheresis to remove the pathogenic circulating antibodies is usually part of the treatment, which also includes therapy to suppress the underlying immune response.

  The antigen common to the alveoli and GBM is a peptide within the noncollagenous portion of the α_3 chain of collagen type IV. What triggers the formation of these antibodies is unclear in most patients. Exposure to viruses or hydrocarbon solvents (found in paints and dyes) has been implicated in some patients, as have various drugs and cancers. There is a high prevalence of certain HLA subtypes and haplotypes (e.g., HLA-DRB1) in affected patients, a finding consistent with the genetic predisposition to autoimmunity.
- *Diseases caused by immune complex deposition. RPGN can be a complication of any of the immune complex nephritides, including postinfectious glomerulonephritis, lupus nephritis, IgA nephropathy, and Henoch-Schönlein purpura.* In all these cases, immunofluorescence studies reveal the granular pattern of staining characteristic of immune complex deposition. This type of RPGN frequently demonstrates cellular proliferation and influx of leukocytes within the glomerular tuft, in addition to crescent formation. These patients usually cannot be helped by plasmapheresis, and they require treatment for the underlying disease.
- *Pauci-immune RPGN, defined by the lack of detectable anti-GBM antibodies or immune complexes by immunofluorescence and electron microscopy.* Most patients with this type of RPGN have circulating *antineutrophil cytoplasmic antibodies* (ANCAs) that produce cytoplasmic (c) or perinuclear (p) staining pattern and are known to play a role in some vasculitides (Chapter 11). This type of RPGN may be a component of a systemic vasculitis such as granulomatosis with polyangiitis (formerly called *Wegener granulomatosis*) or microscopic polyangiitis. In many cases, however, pauci-immune crescentic glomerulonephritis is limited to the kidneys and hence *idiopathic*. More than 90% of such idiopathic cases have c-ANCAs or p-ANCAs in the sera. The presence of circulating ANCAs in both idiopathic crescentic glomerulonephritis and cases of crescentic glomerulonephritis that occur as a component of systemic vasculitis, and the similar pathologic features in either setting, have led to the idea that these disorders are pathogenetically related. According to this concept, all cases of crescentic glomerulonephritis of the pauci-immune type are manifestations of small-vessel vasculitis or polyangiitis, which is limited to glomerular and perhaps peritubular capillaries in cases of idiopathic crescentic glomerulonephritis. Since these entities are viewed as part of a spectrum of vasculitic disease, the clinical distinction between systemic vasculitis with pauci-immune renal involvement and idiopathic crescentic

Table 20-6 Rapidly Progressive Glomerulonephritides

Type I (Anti-GBM Antibody)
Renal limited
Goodpasture syndrome
Type II (Immune Complex)
Idiopathic
Postinfectious glomerulonephritis
Lupus nephritis
Henoch-Schönlein purpura
IgA nephropathy
Others
Type III (Pauci-Immune)
ANCA-associated
Idiopathic
Granulomatosis with polyangiitis (formerly Wegener granulomatosis)
Microscopic polyangiitis

ANCA, Antineutrophil cytoplasmic antibodies; GBM, glomerular basement membrane.