Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney Int Suppl 3:5, 2013.)

The dispiriting term *end-stage renal disease* represents a stage of CKD where the accumulation of toxins, fluid, and electrolytes normally excreted by the kidneys leads to death unless the toxins are removed by renal replacement therapy, using dialysis or kidney transplantation. These interventions are discussed in **Chaps. 312** and **313**. End-stage renal disease will be supplanted in this chapter by the term stage 5 CKD.

■ PATHOPHYSIOLOGY OF CKD

The pathophysiology of CKD involves two broad mechanisms of damage: (1) specific initiating mechanisms particular to the underlying etiology (e.g., genetic abnormalities in kidney development, immune complex deposition, and inflammation in certain types of glomerulonephritis, or toxin exposure in certain diseases of the renal tubules and interstitium), and (2) nonspecific mechanisms involving hyperfiltration and hypertrophy of the remaining viable nephrons, which are common consequences of long-term reduction of renal mass, irrespective of underlying etiology. The responses to reduction in nephron number are mediated by vasoactive hormones, cytokines, and growth factors. Eventually, the short-term adaptations of hyperfiltration and hypertrophy to maintain GFR become maladaptive as the increased pressure and flow within the nephron predisposes to distortion of glomerular architecture, abnormal podocyte function, and disruption of the filtration barrier, leading to sclerosis and dropout of the remaining nephrons **(Fig. 311-2)**. Increased intrarenal activity of the renin-angiotensin system (RAS) appears to contribute both to the initial compensatory hyperfiltration and to the subsequent maladaptive hypertrophy and sclerosis. This process explains why a reduction in renal mass from an isolated insult may lead to a progressive decline in renal function over many years and the efficacy of pharmacologic approaches that attenuate this response **(Fig. 311-3)**.