**CLASSES OF ANTIHYPERTENSIVE AGENTS USED IN TREATMENT OF CHRONIC RENAL DISEASE**

- **Diuretics:**
  - Thiazide class
  - Loop diuretics
  - Potassium-sparing agents

- **Adrenergic inhibitors**
  - Peripheral agents, e.g., guanethidine
  - Central α-agonists, e.g., clonidine, methyldopa, and guanfacine
  - α-Blocking agents, e.g., doxazosin
  - Combined α-β blocking agents, e.g., labetalol

- **Vasodilators**
  - Hydralazine
  - Minoxidil

- **Classes of calcium-channel blocking agents**
  - Verapamil
  - Diltiazem
  - Dihydropyridine

- **Angiotensin-converting enzyme inhibitors**

- **Angiotensin receptor blockers**

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**FIGURE 2-25**

The current classification of agents applied for chronic treatment of hypertension as summarized in the report by the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure [23]. Attention must be given to drug accumulation and limitations of individual drug efficacy as glomerular filtration rates decrease in chronic renal disease. Potassium levels may increase during administration of potassium-sparing agents and medications that inhibit the renin-angiotensin system, especially in patients with impaired renal function [24].

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**FIGURE 2-26**

Strict blood pressure control and progression of hypertensive nephrosclerosis. Whether vigorous blood pressure reduction reduces progression of early parenchymal renal disease in blacks with nephrosclerosis is not yet certain. A and B, A randomized prospective trial comparing strict (panel A) blood pressure control (defined as diastolic blood pressure [DBP] <80 mm Hg) with conventional (panel B) levels of diastolic control between 85 and 95 mm Hg for more than 3 years could not identify a reduction in rates of disease progression [25]. Of patients, 68 of 87 were black. Rates of progression in these patients were low. It should be emphasized that entry criteria excluded patients with diabetes and massive proteinuria. Initial studies from the African American Study of Kidney Disease trial confirm that biopsy findings in most patients with clinical features of hypertension were considered consistent with primary hypertensive disease [26]. Whether lower than normal levels of blood pressure in these patients will prevent progression to end-stage renal disease over longer time periods remains to be determined. GFR—glomerular filtration rate. (From Toto and coworkers [25]; with permission.)
Angiotensin-converting enzyme (ACE) inhibitors and chronic renal disease. Progression of type I diabetic nephropathy to renal failure was reduced in the ACE inhibitor arm of a trial comparing conventional antihypertensive therapy with a regimen containing the ACE inhibitor captopril. All patients in this trial had significant proteinuria (>500 mg/dl). The most striking effect of the ACE inhibitor regimen was seen in patients with higher serum creatinine levels (>1.5 mg/dL) as shown in the top two lines. It should be noted that calcium channel blocking drugs were excluded from this trial and the ACE inhibitor arm had somewhat lower arterial pressures during treatment. These data offer support to the concept that ACE inhibition lowers intraglomerular pressures, reduces proteinuria, and delays the progression of diabetic nephropathy by more mechanisms than can be explained by pressure reduction alone. (Data from Lewis and coworkers [27].)

Angiotensin-converting enzyme (ACE) inhibition in nondiabetic renal disease. A and B, Shown here are serum creatinine levels from the 12-month (panel A) and 36-month (panel B) cohorts followed in the benazepril trial. In this trial, 583 patients were randomized to therapy with or without benazepril [28]. Slight reductions in the rates of increase in creatinine and of stop points in the ACE inhibitor group occurred; however, these reductions were modest. Whereas these data support a role for ACE inhibition, the results are considerably less convincing than are those for diabetic nephropathy. These results argue that some groups may not experience major benefit from ACE inhibition over the short term. Preliminary reports from recent studies limited to patients with proteinuria suggest that rates of progression were substantially reduced by treatment with ramipril [29]. (From Maschio and coworkers [28]; with permission.)
1. Hypertension may result from renal disease that reduces functioning nephrons.
2. Evidence shows a clear relationship between high blood pressure and end-stage renal disease.
3. Blood pressure should be controlled to ≤130/85 mm Hg (<125/75 mm Hg) in patients with proteinuria in excess of 1 g/24 h.
4. Angiotensin-converting enzyme inhibitors work well to lower blood pressure and slow progression of renal failure.