S 2. THE ROLE OF SYSTEMIC AND GLOMERULAR HYPERTENSION IN PROGRESSIVE RENAL DISEASE

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Among the most important risk factors for progression of renal disease is systemic hypertension, which may be both cause and consequence of chronic renal disease. Studies in experimental animals, and preliminary clinical observations, suggest that the efficacy of antihypertensive agents relate to their intraglomerular hemodynamic consequences, and that all antihypertensive agents may not be equally effective in slowing the progression of renal disease. The normal kidney maintains relative constancy of blood flow and glomerular capillary pressure (P_{GC}). However, in the setting of renal disease, defective autoregulation lessens the ability of the kidney to maintain normal glomerular pressures and flows in the face of changes in blood pressure. Systemic hypertension is readily transmitted into the glomerular capillary network, resulting in glomerular capillary hypertension.

Animal studies clearly indicated that reduction of systemic blood pressure does not necessarily result in a reducting in P_{GC}, and that failure to control glomerular hypertension may be associated with failure to influence disease progression. The importance of glomerular hypertension as a mechanism of injury is evidenced by numerous experimental studies showing that interventions which normalize P_{GC} slow the progression of renal disease. Most extensively studied have been angiotensin I converting enzyme inhibitors (CEI), which regularly reduce both P_{GC} and injury, particularly when started early in the disease course. CEI reduce efferent arteriolar resistance, probably by blocking angiotensin II formation, and there by lower P_{GC}. Animal studies with other antihypertensive regimens, including calcium channel blockers and vasodilator/diuretic combinations, have been much less consistent, with hemodynamic and structural protection afforded in some models, but not in others. For example, nifedipine is protective started early in non-diabetic expermental renal disease, while it is not effective in diabetic renal disease, or when started late in rats with chronic renal failure. Vasodilator/diuretic combinations have been frequently successful in animal models of diabetes, but less so in other experimental models. Multiple mechanisms appear to contribute to protective effects of the different regimens, but current explantations for the inconsistent protective effects are lacking.

Prospective controlled studies comparing different antihypertensive regimens in patients with progressive renal disease are currently in progress and should provide valuable information in the coming years. Nevertheless, preliminary clinical studies provide encouraging evidence that these experimental findings may also be true in clinical renal disease.