Subtle Renal Injury as a Pathogenic Mechanism for Essential Hypertension

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Renal transplant studies in experimental animals and man have demonstrated that the kidney is the source of essential hypertension. Most studies have confirmed the hypothesis of Guyton that the physiological defect is a relative impairment in sodium excretion, such that higher pressures are required to excrete a sodium load. While genetic factors clearly have an important role in the pathogenesis of the renal defect, studies in identical twins have shown only a 60% concordance rate for blood pressure elevation. This suggests that other nongenetic mechanisms are likely involved. Recently we have revisited the hypothesis that subtle renal injury underlies the pathogenesis of salt-sensitivity. We have found that a variety of mechanisms can induce renal injury that then causes salt-sensitivity, including transient administration of catecholamines, angiotensin II, inhibitors of nitric oxide synthesis, and cyclosporine. In all of these models renal injury develops and is characterized by the development of preglomerular arteriolosclerosis and tubulointerstitial inflammation. Our studies in the angiotensin II infusion model have further shown that the arteriolar lesion is associated with vasoconstriction that persists after stopping the angiotensin II, leading to a fall in glomerular plasma flow.

There is also an infiltration of monocytes and T cells, some of which are expressing angiotensin II and oxidants. Prevention or treatment of the interstitial inflammation and microvascular disease will prevent or ameliorate the salt-sensitive hypertension. Thus, our studies suggest that subtle renal injury may be a major mechanism for the development of hypertension. We further show how this hypothesis engages all of the current proposed mechanisms of the pathogenesis of hypertension into one unified pathway.