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The renin-angiotensin system traditionally has been conceived as a neuroendocrine system functioning in the circulation. Recent research has confirmed the existence of autocrine/paracrine tissue renin-angiotensin systems present and functioning at multiple sites, including cardiac, vascular, and renal tissues, which contain the majority of angiotensin-converting enzyme in the body. It appears that the circulating renin-angiotensin system is activated acutely to maintain homeostasis and is then turned off at cardiovascular compensation, while the tissue renin-angiotensin systems exert long-term actions that affect cardiovascular function and structure, which may play a pathophysiological role in congestive heart failure, hypertension, and vascular disease and influence the response to therapy with angiotensin-converting enzyme-inhibiting agents.