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MECHANISM OF ANP SECRETION AND ITS CLINICAL SIGNIFICANCE

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The heart is an endocrine organ secreting atrial natriuretic peptide (ANP) involved in the regulation of body fluid and blood pressure. ANP is a polypeptide hormone synthesized and stored mainly in atrial cardiomyocytes, and secreted into the blood stream by various stimuli. The natriuretic peptide family also includes brain natriuretic peptide (BNP), C-type natriuretic peptide (CNP), Dendroaspis natriuretic peptide (DNP), and urodilatin. BNP is originally isolated in porcine brain but most abundant in the cardiac ventricles and is described as a ventricular hormone because of a rapid and marked expression in several cardiac diseases and a local regulator of ventricular remodeling. CNP is principally found in porcine brain and later on in vascular endothelial cells, and acts as a local hormone because of low plasma level. DNP is a recently isolated *Dendroaspos augusticeps* snake and urodilatin is a natriuretic peptide originated from the kidney. The natriuretic peptides share a 17-amino acid disulfide ring structure with a highly conserved sequence. However, they are genetically distinct peptides that exert diverse actions on cardiovascular, renal, and endocrine functions. The major important stimulator of ANP secretion is atrial stretch. Endothelin and protein kinase C activator also are the potent stimuli of ANP secretion. However, whether vasoconstrictors such as angiotensin II and vasopressin have a direct positive or negative effect on ANP secretion has not been determined with certainty. Several recent studies have helped to define the cellular mechanism contributing to regulation of ANP secretion including stretch-activated ion channels, prostaglandins, and intracellular calcium. A number of steps in the cellular transduction of the ANP signal remain to be resolved. The release of ANP in disease states such as myocardial infarction and heart failure appears to be related to both mechanical and cellular events. Under chronic hemodynamic overload, increases in cardiac synthesis and secretion of ANP and BNP are regarded as a cardioprotective mechanism, given the beneficial effects of ANF and BNP on cardiac preload, afterload and cardiovascular growth. At the clinical aspects, the elevation of circulating ANF and BNP in heart failure or following acute coronary syndromes has been shown to have diagnostic and prognostic implications. Moreover, these peptides themselves hold promise as therapeutic agents in the treatment of heart failure, hypertension, bronchospasm and in tissue remodeling following acute myocardial infarction. (Supported by a grant of KOSEF, R01-2006-000-10554-0)