IMPAIRED ABILITY TO INCREASE CIRCULATING ATRIAL NATRIURETIC FACTOR (ANF) IN PATIENTS WITH MILD LEFT VENTRICULAR DYSFUNCTION.

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This study aimed to determine whether the ANF response to volume loading is altered in the early stage of heart failure. Thus, in 10 patients with mild left ventricular dysfunction secondary to ischemic and non-ischemic dilated cardiomyopathy (CHF) (LV end-diastolic diameter=62±3 mm, ejection fraction=40±4%, NYHA I-II) and in 8 age-matched normal controls (C) we measured immunoreactive plasma ANF levels before and during volume expansion (VE) (0.9% NaCl, .2 ml/kg/min for 2 h). VE caused the same reduction of hematocrit (7±1%) in both groups. Baseline plasma ANF levels (pg/ml) were higher in CHF (50±10) than in C (26±3, p<0.05). In response to VE ANF levels rose by 79±10% in C but did not increase in CHF (+.2±3%, p<0.001 vs. C). Reductions of plasma renin activity and aldosterone by VE were smaller in CHF (-48±3% and -23±7%, respectively) than in C (-66±3% and 51±6%) (both p<0.05). Urinary Na+ excretion rose by 133±38% in C and by 70±34% in CHF (p<0.05). In conclusion, the failure to raise endogenous ANF levels in response to increased preload is an early hallmark of heart failure. This abnormality might contribute to the reduced ability to suppress renin and aldosterone and to excrete Na+ also noted in these patients.

DOES THE LEVEL OF CIRCULATING VASOPRESSIN MODULATE ATRIAL NATRIURETIC PEPTIDE SECRETION IN RESPONSE TO VOLUME LOADING?

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Pharmacologic increases in plasma levels of arginine vasopressin (AVP) have been reported to amplify the secretion of atrial natriuretic peptide (ANP) in response to atrial stretch. To determine the effect of varying plasma AVP levels within the pathophysiologic range in man, 10 normal male subjects (25±4 years) underwent intravenous volume loading (1000 ml normal saline over 5 min). Plasma AVP and ANP levels and RA pressure were measured during AVP suppression (Low AVP) by water loading (20 ml/kg) and during elevation of plasma AVP (High AVP) by infusion of synthetic AVP (.3 U/h).

		0 Min	15 Min	60 Min
AVP	Low AVP	2.5±0.9	2.4±0.9	2.2±0.7
(pg/ml)	High AVP	33.5±14.3#	34.3±21.6#	39.5±26.0#
ANP	Low AVP	30±15	45±25	58±44*
(pg/ml)	High AVP	33±14	46±30	43±29*

*p<.05 vs 0 min; # p<.05 High vs Low AVP. RA pressure increased similarly in both groups. (Low AVP 3±1 to 11±3; High AVP 4±2 to 12±2, p<.05, for both groups).

Conclusion: Rapid volume loading produces a similar increase in plasma ANP levels in both low and high AVP states. These data suggest that the circulating level of AVP is not an important physiological modulator of secretion of ANP in response to volume loading in man.

INCREASE IN SODIUM EXCRETION BY ATRIAL NATRIURETIC PEPTIDE IN MAN IS DEPENDENT ON THE RENIN-ANGIOTENSIN SYSTEM

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The relative importance of changes in mean arterial pressure (MAP, mmHg) and the renin-angiotensin system (RAAS) on sodium excretion (UNaV, mceq/ml) and urine flow rate (UV, ml/min) during atrial natriuretic peptide (ANP) infusion to high physiologic plasma levels has not been clarified in man. Eight normal males (25±4 years) were studied supine (S) at baseline (B), during a continuous infusion of ANP while S, with prolonged head-up tilt (T) to decrease MAP, and with inhibition of the RAAS with enalaprilat (ACEI) during T and S. Each period was 45 minutes in duration. With ANP infusion, plasma levels rose from 44 p[illegible]l at baseline to 106 pg/ml with infusion (p<.05)

		[ANP INFUSION → → → → →]			
	B	S	T	T+ACEI	S+ACEI
MAP	92	93	83*	80*~	86
UNaV	267	322*	302	175#~	177#~
UV	16	17	14	8#~	7#~

p<.05: * vs B; ~ vs S; # vs T.

Conclusion: During ANP infusion, UV and UNaV are significantly reduced by interruption of the RAAS but not by moderate decreases in MAP. These data suggest that RAAS is important for increased sodium excretion with ANP infusion in man.

ATRIAL NATRIURETIC PEPTIDE IN PATIENTS WITH SEVERE CONGESTIVE HEART FAILURE IN RELATION TO M-MODE ECHOCARDIOGRAPHIC MEASUREMENTS

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In acute heart failure there is a positive linear correlation between left atrial size (LA) and plasma levels of atrial natriuretic peptide (ANP). In the CONSENSUS trial in severe chronic heart failure, an optional protocol evaluated the correlation between plasma ANP concentration and LA and the effect of treatment with enalapril or placebo in this context. Material and method: Both M-mode echocardiography and plasma ANP concentration were available at baseline in 31 patients. ANP levels were very elevated to 343 pg/ml (median). LA was 50.5 mm (mean). An inverse correlation was found between ANP-concentration and LA (r= - 0.41 p<0.005). ANP levels were significantly decreased in the enalapril treated group (from 478 ± 485 to 323 ± 345 pg/ml p<0.01) but except for one outlier did not change significantly in the placebo group. LA showed no significant changes in either group. In the enalapril group after 6 weeks there was an increase in fractional shortening % (13.3 ± 5.6 to 15.4 ± 5.8 % p<0.05) and a decrease in systolic time interval index (0.58 ± 0.14 to 0.48 ±0.14 p<0.05) were found. No significant changes in fractional shortening or systolic time interval index were found in the placebo group.

Conclusion: These findings indicate that in patients with severe chronic congestive heart failure other factors than left atrial distension are responsible for the plasma ANP level.