

Title: CONTROL OF CIRCULATORY VOLUME AND SODIUM EXCRETION DURING CARDIAC SURGERY BY ATRIAL NATRIUETIC FACTOR

Authors: Margaret Wood, M.D., J. Bullington, M.D., J. W. Hammon, M.D., T. Imada, Ph.D. and T. Inagami, Ph.D.

Affiliation: Departments of Anesthesiology, Cardiac and Thoracic Surgery and Biochemistry, Vanderbilt University School of Medicine, Nashville, Tennessee 37232

INTRODUCTION. Atrial natriuretic factor (ANF) has been shown to have natriuretic, diuretic and vasorelaxant effects, suggesting that it may play an important role in the regulation of circulatory volume. Acute volume expansion resulting in an increase in atrial pressure has been shown to produce an increase in ANF levels and increased urinary sodium excretion. We postulated that the acute increase in atrial pressure produced by volume loading during termination of cardiopulmonary bypass would increase circulating ANF in patients undergoing cardiac surgery, and in addition, induce a natriuresis. The purpose of the present study, therefore, was to investigate the role of ANF during cardiac surgery, with special reference to the control of circulatory volume and sodium excretion.

METHODS. 19 patients undergoing cardiac surgery were studied. Anesthesia was with fentanyl (50 mcg/kg), diazepam (5.0-7.5mg) and pancuronium. Arterial blood samples were drawn for measurement of ANF and hemodynamic measurements made when the patient was awake (control), 10 mins post induction, 5 mins before the start of bypass, 5, 15 and 45 mins after the start of bypass, 5 mins after the start of rewarming, and immediately after the termination of bypass. To determine the response to increases in intravascular volume and atrial stretch, fluid boluses of 200cc from the pump were administered approximately 8 mins apart, CVP recorded and blood samples for ANF drawn at each time interval, until the aortic cannula was removed. Blood samples were then drawn 30, 60 mins and 4 hrs post bypass, and the morning of the first four postoperative days. 24 hour urine collections were made the day of surgery and for the next three post operative days. Plasma and urine sodium and creatinine concentrations were measured, and urinary sodium excretion, the fractional excretion of filtered sodium (FE_{Na}) and creatinine clearances calculated. Fractional excretion of filtered sodium (FE_{Na}) is calculated as urine/plasma Na divided by urine/plasma creatinine \times 100. In 4 of the 19 patients, FE_{Na} was calculated for the following time periods: (1) induction to bypass (2) bypass to rewarming (3) rewarming to termination of bypass (4) four hour period post-bypass. Plasma ANF was measured by radioimmunoassay. Statistical analysis was by analysis of variance followed by Student's t-test or linear regression as appropriate; $p < 0.05$ was taken as the minimal level of significance. Informed consent and institutional approval were obtained.

RESULTS. Mean plasma ANF levels were more than two fold higher during rewarming and after the termination of cardiopulmonary bypass but had returned to control values by the first postoperative day (POD) (Table 1). During the period of volume loading after bypass, neither ANF nor increase in ANF from control values correlated significantly with CVP (Fig 1). Urinary sodium excretion was significantly higher the day of surgery than during the postoperative period (Table 2). For the 4 patients, in whom detailed sodium excretion studies were performed during cardiac surgery there was a significant relationship between FE_{Na} and ANF ($r = 0.84$, $p < 0.001$) (Fig 2). Creatinine clearances were within the normal range on all study days.

TABLE 1: MEAN PLASMA ANF (pg/ml \pm SEM) (n=19)

Awake	10 min post Induction	Pre-Bypass	5 min - Bypass
379.9	341.7	322.4	392.6
± 88.3	± 80.9	± 58.6	± 65.9
15 min Bypass	45 min Bypass	Rewarming Bypass	Max Post-Bypass
386.4	403.2	850.7*	895.2*
± 70.6	± 149.3	± 173.7	± 173.7
POD 1	POD 2	POD 3	POD 4
305.0	384.6	490.2	395.2
± 77.4	± 71.8	± 141.6	± 170.8

* $p < 0.05$ compared to awake

FIG 1: RELATIONSHIP BETWEEN CVP AND ANF

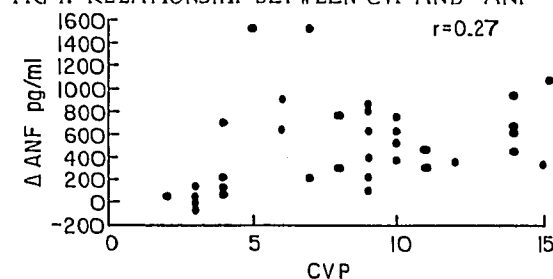
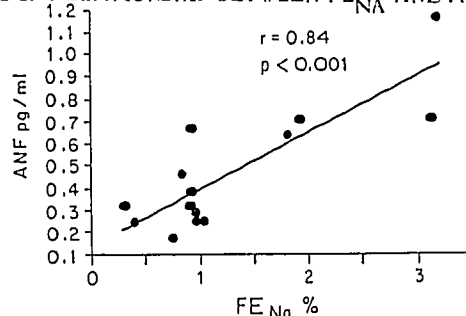


TABLE 2: URINARY SODIUM EXCRETION (n= 19 \pm SEM)

	Surgery	POD 1	POD 2	POD 3
FE_{Na} %	1.3	0.62*	0.36*	0.35*
	± 0.21	± 0.12	± 0.15	± 0.13
Sodium Excretion ($U_{Na}V$ Meq/day)	152.74	82.17	57.00*	35.32*
	± 22.45	± 18.79	± 19.37	± 12.55

* $p < 0.05$ compared to the day of surgery.

FIG 2: RELATIONSHIP BETWEEN FE_{Na} AND ANF



DISCUSSION. Rewarming and the termination of bypass appear to be potent stimuli for ANF release. Although cessation of bypass is associated with an acute increase in cardiac filling pressures and high ANF concentrations, ANF levels and CVP were not significantly correlated. However, the increased levels of ANF during cardiac surgery are associated with increased fractional urinary sodium excretion, suggesting that the elevated levels of ANF found during rewarming bypass and immediately post bypass may be responsible for the natriuresis and diuresis that occurs during this period.