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Presentation Title: A Novel Role for Cytokines in Fluid Regulation in Heart Failure Mice

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Abstract Body: Neurohumoral excitation is the hall mark of congestive heart failure (CHF). Recently, we demonstrated that cytokines are activated in the brain after myocardial infarction (MI) in rats. In this study, we demonstrate a novel role for cytokines in fluid regulation in heart failure (HF) mice. **Method:** Cytokine knock-out mice and their corresponding controls were adapted to metabolic cages for 2 weeks. After collecting baseline, salt intake, water intake, urine volume, and urinary sodium, mice underwent MI or Sham MI and the extent of myocardial injury was confirmed using echocardiography. Subsequently, daily metabolic samples were collected for 21 days. **Results** are tabulated. Water intake was not different among groups at all time points measured. At the end of the 21 days, mice were sacrificed and their hypothalamic cytokines and AT1 receptor expression was measured using RT-PCR. **Conclusion:** 1) Hypothalamic cytokines and AT-1R contribute to impaired fluid regulation in HF mice. 2) In IL-6^{-/-} and TNF- α ^{-/-} mice with MI, fluid impairment were restored, suggesting these cytokines directly contribute to altered volume regulation. 3) This improvement in fluid regulation is due to the absence of AT1 receptor activation in the hypothalamus of cytokine knock-out mice with MI. 4) Cytokine and angiotensin interaction might contribute to altered fluid regulation in HF. * p<0.05 vs baseline and # vs MI group

Group	Salt Intake (ml/day)			Urine Volume (ml/day)			Urinary Sodium (mEq/day)		
	Pre	Day 2	Day 21	Pre	Day 2	Day 21	Pre	Day 2	Day 21
SHAM (n=5)	0.25±0.03	0.23±0.03	0.23±0.03	2.94±0.09	2.88±0.06	2.9±0.08	0.47±0.02	0.42±0.04	0.46±0.03
MI (n=5)	0.25±0.03	2.0±0.24*	1.7±0.16*	2.98±0.14	1.78±0.15*	1.94±0.12*	0.44±0.04	0.30±0.03*	0.32±0.02*
TNF- α ^{-/-}	0.26±0.02	0.24±0.02#	0.3±0.07#	3.0±0.11	2.58±0.24*,#	2.96±0.19#	0.46±0.02	0.40±0.02#	0.43±0.03#

+ MI (n =5)									
IL- 6 ^{-/-} + MI (n =5)	0.28± 0.04	0.38±0. 05*,#	0.3±0 .08#	3.04± 0.25	2.3±0.2 *,#	2.72±0 .37#	0.44± 0.03	0.39±0. 02*,#	0.42±0 .05#

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