(+)). With high-resolution ultrasound, we measured the diameter of brachial arteries at baseline, during reactive hyperemia (endothelium dependent vasodilatation caused by increased flow), and after sublingual nitroglycerin (an endothelium-independent dilatation).

*Results:* Flow-mediated dilation was observed in FH (−) group, but was significantly impaired or absent in FH (+) group (8.3 ± 1.9% and 5.1 ± 2.4%, respectively; P = 0.00237). Nitroglycerin caused a similar vasodilation in both groups (18.6 ± 5.8% in FH (−) group and 17.2 ± 4.9% in FH (+) group; P = NS). Baseline vessel diameter, blood flow, and degree of reactive hyperemia (Doppler estimated) were similar in both groups. Thus endothelial dysfunction is already present in normotensive adults with family history of essential hypertension.

*Conclusion:* This early endothelial dysfunction might lead to the future development of hypertension.

## 1104-49 Abnormal Capillary Permeability in Uncomplicated Hypertensive Subjects and Normotensive Atherosclerotic Patients

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*Background:* Human endothelial function has been studied in several clinical conditions, including essential hypertension and atherosclerotic vascular disease, mainly by evaluating the regional vasorelaxation induced by endothelium-dependent vasodilators. Still, local vasodilatation reflects the responsiveness of an arteriolar segment while scarce information is available on the capillary network which contains most of the endothelial cells.

*Material & Methods: (means ± SD):* The study was performed in 12 Mild-moderate Uncomplicated Essential Hypertensives (EH, $ABPM_{24\text{-}hr}$: 148 ± 10/88 ± 6 mmHg, age: 55 ± 0.9 yrs, BMI: 26.6 ± 2.8 Kg/m$^2$) and 16 normotensive ($ABPM_{24\text{-}hr}$: 118 ± 8/68 ± 9 mmHg) Patients With Atherosclerotic Peripheral Vascular Disease (ATH, 57 ± 0.9 yrs, BMI: 25.4 ± 0.2.2 Kg/m$^2$). All subjects were males, non diabetic, never treated or untreated for at least two weeks. 8 Normal Males (NOR, 59 ± 11 yrs, $ABPM_{24\text{-}hr}$: 121 ± 7/73 ± 4 mmHg, BMI: 25.4 ± 0.2.2 Kg/m$^2$) were the controls. Evaluation variables were *1.* Transcapillary albumin escape rate ($TER_{alb}$, %/hr, the one-hour decline rate of i.v. $^{125}$I-albumin), a measure of macromolecular permeability of capillary endothelium and *2.* Forearm blood flow (FBF, venous plethysmography) response (drug/baseline ratio) to i.a. acetylcholine (ACH, 7.5, 15, 30 μg/min), an endothelium-dependent vasodilator. Total cholesterol (ATH: 239 ± 33 vs EH: 181 ± 24 & NOR: 206 ± 45 mg/dl) and triglycerides (ATH: 193 ± 100 vs EH: 121 ± 78 & NOR: 117 ± 69 mg/dl) were higher ($p < 0.01$) in ATH.

*Results:* $TER_{ALB}$ was comparable between ATH and EH (10.3 ± 2.8 vs 10.4 ± 3.2%/hr) and higher ($p < 0.004$) than in NOR (7.1 ± 1.5%/hr). Forearm vasodilatation to ACH (EH: 3.2 ± 1.5, 5.1 ± 2.3, 6.9 ± 2.4 vs NOR: 3.3 ± 1.8, 5.3 ± 3.2, 6.5 ± 2.3) was preserved in EH and reduced in ATH (ACH: 3.2 ± 1.6, 3.9 ± 1.5, 5 ± 1.9 $p < 0.05$ vs NOR). Individual $TER_{ALB}$ values and maximum vasodilating responses to ACH were unrelated.

*Conclusions:* $TER_{ALB}$ is abnormal in EH and normotensive ATH indicating a systemic capillary dysfunction independent of BP levels. Independence of $TER_{ALB}$ from ACH arteriolar responsiveness suggests that involvement of different mechanisms of dysfunction at the capillary and arteriolar level.

## 1104-50 Nitric Oxide-mediated Vasodilation (tolerance) to Hypertensive Effects of Ethanol

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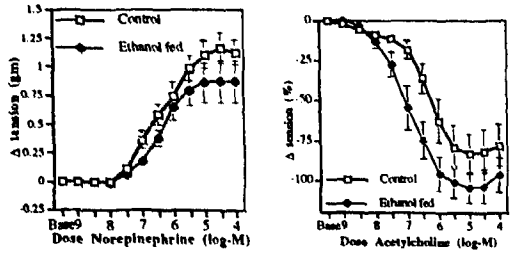
*Background:* Chronic heavy ethanol ingestion causes hypertension.

*Methods:* To measure changes in vascular reactivity induced by chronic ethanol, we studied aortae from control rats and from rats fed 36% ethanol as drinking water for 1 year. Ring segments were contracted with norepinephrine (NE), phenylephrine (Phe), and KCl. Following incubation with the nitric oxide inhibitor ʷnitro-L-arginine methyl ester (L-NAME), or mechanical denudation (DN), rings were contracted again. Phe precontracted rings were relaxed by acetylcholine (ACh) and nitroglycerin (NTG).




*Results:* Ethanol reduced maximal contraction to Phe ($p = 0.04$) and to NE ($p = 0.03$). L-NAME andDNabolished differences in NE-induced tension. There was no difference in KCl-induced constriction. Maximal ACh-induced relaxation was greater for ethanol fed rats ($p < 0.05$. NTG-induced relaxation was similar. Blood pressure was greater for ethanol rats ($p = 0.01$).

*Conclusions:* Chronic high dose ethanol causes 1) hypertension, 2) reduced adrenoceptor-mediated contraction that is endothelium-dependent and 3) increased endothelium-dependent relaxation. Increased endothelial nitric oxide may constitute an adaptive vasodilatory mechanism to chronic adrenergic centrally-mediated hypertensive effects of ethanol.

## 1104-51 L-Arginine Improves Endothelial Function in Newly Diagnosed Hypertensives

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We have shown that oral L-Arginine supplementation reduces blood pressure in untreated hypertensives possibly by restoring endothelial function. In order to test this hypothesis, we studied flow-mediated vasodilation of the brachial artery (FMV) in 14 untreated hypertensive pts (mean age 56 ± 8 years, 9 women). Using high resolution ultrasound, the diameter of the brachial artery was measured at rest, during reactive hyperemia (FMV) and in response to nitroglycerine. After baseline evaluation pts were randomised to receive either oral L-Arginine (2 g, tds) or matching placebo for 1 week according to a cross-over double-blind protocol. Resting systolic blood pressure was significantly reduced by L-Arginine but not by placebo (165 ± 20 vs 148 ± 18 mmHg, L-Arginine vs Baseline, $p < 0.05$; 164 ± 22 vs 158 ± 28 mmHg, Baseline vs Placebo, p = NS). FMV was not affected by placebo administration (1.7 ± 2.3% vs. 2.1 ± 2.6%, p = NS) while increased significantly after oral L-Arginine (1.8 ± 2.1% vs. 5.4 ± 2.8%, $p < 0.05$). No difference in GTN-induced vasodilation was noted after either L-Arginine or Placebo (16.6 ± 7.5%, 15.6 ± 5.5%, 18.2 ± 6.7%).

In conclusion L-Arginine restores impaired endothelium dependent vasodilation in newly diagnosed borderline hypertensives. This effect may explain the hypotensive effect of L-Arginine

## 1104-52 Improved Endothelium-dependent Vasodilation After Blockade of Endothelin Receptors in Patients With Essential Hypertension

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Hypertensive patients (HTs) have impaired nitric oxide (NO) activity, but the mechanism underlying this abnormality is unknown. We have recently observed an increased endothelin (ET) vasoconstrictor tone in HTs related to increased production of the peptide. In the present study, we investigated whether the increased ET activity of HTs could contribute to their impaired NO-dependent vasodilator function. To this end, the vasodilator responses to acetylcholine (ACh; 7.5, 15, and 30 μg/min), an endothelium-dependent vasodilator, and sodium nitroprusside (SNP; 0.8, 1.6, and 3.2 μg/min), an exogenous NO donor, were assessed before and after nonselective blockade of $ET_A$ and $ET_B$ receptors by combined infusion of BQ-123 ($ET_A$ blocker; 100 nmol/min) and BQ-788 ($ET_B$ blocker; 50 nmol/min) for 60 min in 6 HTs. Drugs were infused into the brachial artery and forearm blood flow (FBF) was measured by strain-gauge plethysmography. The increases in FBF from baseline induced by the 3 doses of ACh were significantly potentiated by nonselective blockade of ET receptors (0.47 ± 0.21 [mean ± SEM], 2.73 ± 2.08, and 4.71 ± 2.48 mL/min/dL before vs 3.38 ± 1.41, 6.06 ± 2.56, and 8.67 ± 3.06 mL/min/dL after ET antagonism; P = 0.01). In contrast, ET receptor blockade did not significantly modify vascular responsiveness to the 3 doses of SNP (2.85 ± 0.95, 4.76 ± 1.47, and 7.18 ± 2.27 mL/min/dL before vs 3.28 ± 1.01, 4.94 ± 1.48, and 6.5 ± 1.84 mL/min/dL after ET antagonism; P = 0.97). These findings indicate that endothelial vasodilator function in HTs improves after blockade of ET receptors, suggesting that an increased ET activity may be involved in the pathophysiology of their endothelial dysfunction.

TUESDAY POSTER