# ABSTRACTS – ORAL

## 701 Coronary Vascular Physiology: Basic I

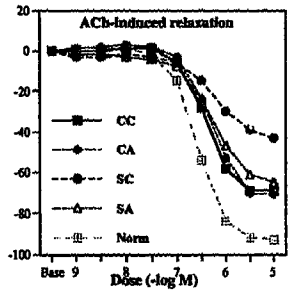
Monday, March 25, 1996, 10:30 a.m.–Noon
Orange County Convention Center, Room 314

10:30

### 701-1 L-Arginine Restores Normal Endothelium-Mediated Relaxation in Hypercholesterolemic Rabbits Exposed to Tobacco Smoke

Stuart J. Hutchison, Michael Ibarra, Tony M. Chou, Richard E. Sievers, Kanu Chatterjee, Stanton A. Glantz, Prakash C. Deedwania, William W. Parmley. *University of California, San Francisco, CA*

Hypercholesterolemia (HC) and tobacco smoke are associated with impaired endothelium-mediated relaxation. L-Arginine (L-Arg) has been shown to protect against endothelial dysfunction secondary to HC. We sought to investigate whether L-Arg would protect against endothelial dysfunction secondary to environmental tobacco smoke-exposure (ETS) in an animal model of atherosclerosis. Aortic rings of male New Zealand white rabbits were studied in organ baths and isometric tension recorded. Rings were precontracted with norepinephrin to EC50, then exposed to acetylcholine [$10^{-9}$ to $10^{-4}$ M]. 32 rabbits were rendered HC by diet; half were randomized to L-Arg (10 weeks of 2.25% in drinking water) and half to ETS for 10 weeks in a 2 × 2 design. HC rabbits received ETS and L-Arg (SA group, n = 8), received ETS and no L-Arg (SC group, n = 8), received no ETS and L-Arg (CA group, n = 8), and received no ETS and no L-Arg (CC group, n = 8). 8 normal non-HC rabbits served as controls. Maximal relaxation of SC, SA, CC, CA (−46 ± 8, −78 ± 5, −70 ± 3, −75 ± 3) was less ($p < 0.05$) than of normals (−93 ± 3; $P < 0.05$). Maximal relaxation of SC was less than SA ($p < 0.05$), and CC was less than CA ($p < 0.05$).




ETS exposure results in significantly impaired endothelium-mediated relaxation. L-Arg restores normal endothelium-mediated vasorelaxation in ETS/HC and HC rabbits.



11:00

### 701-3 Vitamin E Restores Impaired Acetylcholine-Mediated Vasodilatation Secondary to Environmental Tobacco Smoke

Tony M. Chou, Stuart J. Hutchison, Severin P. Schwarzacher, Krishnankutty Sudhir, Prakash C. Deedwania, William W. Parmley. *University of California, San Francisco, CA*

Environmental tobacco smoke (ETS) impairs endothelium-dependent vasodilation in vitro. This study investigated effects of ETS on acetylcholine (Ach)-mediated blood pressure (BP) changes in vivo. 17 New Zealand white rabbits were fed a cholesterol diet (0.3%) for 10 weeks (Chol). 7 animals served as diet controls (nonETS) and 10 (ETS) were exposed to ETS for 6 hours/day. In addition, 4 nonETS and 3 ETS animals received vitamin E for 8 weeks prior and during their Chol-diet (Vit and nonVit). 5 rabbits served as healthy controls (nonChol). BP was measured before and after 3 min with incremental IV doses of norepinephrine (NE, 1, 4, 20 μg/kg), Ach (3.3, 10, 30 μg/kg) and nitroglycerine (NTG, 1, 10, 40 μg/kg). *Results:* Following NE, the nonChol had a higher BP response compared to Chol (+74.3 ± 5% vs +58.9 ± 4%, p = 0.04). Max BP response to Ach was attenuated in Chol compared to controls (−79.5 ± 1.6% vs −44.3 ± 7.3%; p = 0.0002) and in ETS vs nonETS (−65 ± 4.5% vs −29.8 ± 9.7%; p = 0.006). Ach max BP response was improved in the Vit compared to nonVit (−60.0 ± 9.3% vs −33.3 ± 9.3%; p = 0.06). NTG caused greater BP change in nonChol compared to Chol (−70.0 ± 7.7% vs −33.8 ± 3.8%; p + 0.01) with a trend towards greater change in nonETS vs ETS (−41.2 ± 2.5% vs 27.4 ± 5.9%; p = 0.07). *Conclusions:* Both ETS and hypercholesterolemia independently impair Ach and NTG-mediated BP responses. Vitamin E appears to attenuate this ETS effect and partially restores response to Ach. The antioxidant effect of vitamin E may be protective against vascular damage from tobacco smoke.

11:15

### 701-4 Importance of Ischemia for Myocardial Angiogenesis: Effect of Basic Fibroblast Growth Factor on Well Developed Collaterals

Matie Shou, Venugopal Thirumurti, Sharmini Rajanayagam, Daisy F. Lazarous, Everett Hodge, Stephen E. Epstein, Ellis F. Unger. *Cardiology Branch, NHLBI, Bethesda, MD*

Basic fibroblast growth factor (bFGF), an angiogenic growth factor, is currently the subject of a Phase I trial in pts with ischemic heart disease. The efficacy of bFGF is well established in animal models of myocardial ischemia; however, the importance of myocardial ischemia as a primer for coronary angiogenesis is unknown. This study was designed to evaluate the potential of bFGF to enhance coronary collateral perfusion in the absence of myocardial ischemia. A secondary goal was to ascertain whether the effects of brief bFGF treatment would be detectable in the very long term (6 months). Thirty dogs were subjected to ameroid-induced occlusion of the left circumflex coronary artery and randomized *twice* to treatment: 10 and 183 days post ameroid placement. bFGF (1.74 mg/d × 7 d) or vehicle were injected via the left atrium, a regimen proven efficacious in previous studies. Collateral perfusion was evaluated during maximal vasodilation as the ischemic/normal zone ratio (IZ/NZ) prior to the second treatment and again 19 days later.

| Day 10–16 | IZ/NZ (day 182) | day 183–189 | IZ/NZ (day 201) |
|---|---|---|---|
| bFGF | 0.51 ± 0.03 | bFGF | 0.50 ± 0.02 |
| | 0.51 ± 0.03 | vehicle | 0.57 ± 0.04 |
| Vehicle | 0.48 ± 0.01 | bFGF | 0.49 ± 0.01 |
| | 0.48 ± 0.01 | vehicle | 0.47 ± 0.02 |