Conclusions: RH, a physiological vasodilator response to ischemia, is associated with an immediate, dose-related and selective t-PA release from endothelial cells. Thus, a general relationship seems to exist between local vasomotion and fibrinolytic control in man, possibly as a result of stimulation by endogenous agonists produced in response to blood flow reduction, although vasodilatation per se may also contribute by increasing shear stress.

Key Words: Tissue plasminogen activator; endothelium; atherosclerosis; hypertension; reactive hyperemia

F019
CHARACTERISATION OF ET-1 PRODUCTION OF CULTURED ENDOTHELIAL CELLS ISOLATED FROM HUMAN BRAIN MICROVESSEL—EFFECT OF CYTOKINES, AND LIPOPROTEIN(a)
M. Tóth, M. Vastag, I. SkopáI, M. Pék, I. Karádi, R. deChatel, and Z. Nagy. 1st Dept. of Medicine, Semmelweis University Medical School, Budapest, Hungary

Brain tissue was obtained from human cadavers, with approval of the Ethical Committee of Health and Research Council. Microvessel endothelial cells were isolated by enzymatic digestion, followed by gradient centrifugation. ET-1 was measured from the supernatant by RIA developed at our laboratory, using an antibody purchased from Peninsula (sensitivity 0.8 pg/tube, 90% intercept 18.2 pg/tube). Basal level of ET-1 in the supernatant increased with time (3 hrs: 18.3 ± 4.3 pg/ml; 6 hrs: 31.3 ± 1.1 pg/ml; 24 hrs: 88.0 ± 5.7 pg/ml; 48 hrs: 86.3 ± 11.2 pg/ml; MEAN ± STDEV). TNF-α (270 U/ml) increased ET-1 concentration (3 hrs: 190 ± 64%; 24 hrs: 217 ± 39%; 48 hrs: 207 ± 5%; values are relative changes to control, run parallel to the stimulated wells). A lower dose of TNF-α (210 U/ml) revealed dose dependence of the effect (3 hrs: 137%; 24 hrs: 170%; 48 hrs: 212%). IL-1-α also increased ET-1 dose dependently (IL-1-α 38,8 U/ml: 3 hrs: 129%; 24 hrs: 161%; 48 hrs: 212%; IL-1-α 1,4 U/ml: 3 hrs: 116%; 24 hrs: 122%; 48 hrs: 180%). Lipoprotein(a) (Lp(a)) was prepared from human plasma by gradient centrifugation. Lp(a) had a dual effect on ET-1, increasing ET-1 in the first three hours, but reducing it by the end of the 48 hour observation period. This effect was not dose dependent in the concentration range tested (Lp(a) 450 μg/ml: 3 hrs: 188%; 24 hrs: 91%; 48 hrs: 85%; Lp(a) 360 μg/ml: 3 hrs: 180%; 24 hrs: 94%; 48 hrs: 52%). Lp(a) reduced the stimulatory effect of cytokines on ET-1. Maximal values at 48 hrs were: TNF-α: 207%; TNF-α + Lp(a): 91%; IL-1-α: 212%, IL-1-α + Lp(a): 64%. Characterization of ET-1-like immunoreactivity by HPLC revealed that the total ET-1 like immunoreactivity coeluted with the synthetic human ET-1 standard. A cell culture of human brain microvessels was established for studying the regulation of ET-1 release. The cells secrete intact ET-1 to the supernatant. TNF-α and IL-1-α increased ET-1 concentration of the supernatant, whereas Lp(a) alone had a dual effect on it. When given together Lp(a) reduces the effect of cytokines on ET-1.

Key Words: Human endothelial cells; endothelin; lipoprotein(a)

F020
EFFECT OF LOSARTAN AND BENAZEPRIL ON MESENTERIC ARTERIES IN SPONTANEOUSLY HYPERTENSION RATS
Shang-hua Xu, Liang-di Xie*, Ke-gui Wu, and Chang-Shen Xu. Hypertension Division, First Affiliated Hospital, Fujian Medical College, Fuzhou, P.R. China

The aim of this study is to investigate the effect of losartan, benazepril on vasoemotion function of mesenteric arteries in spontaneously hypertensive rats. 16 wks male SHR were treated for 16 weeks with losartan (10 mg·kg⁻¹·d⁻¹), benazepril (10 mg·kg⁻¹·d⁻¹) and the combination of these two agents (10 mg·kg⁻¹·d⁻¹ losartan, 10 mg·kg⁻¹·d⁻¹ benazepril), respectively. Sex- and age-matched SHR and WKY served as controls. Vascular reactivity to vasoactive substances was studied with isolated rings of mesenteric arteries from rats. SHR was characterized by a decreased endothelium-dependent relaxation in response to ACh. Both concomitant and alone treatment of losartan, benazepril increased the relaxation sensitivity to ACh. Effect of concomitant treatment on relaxation sensitivity to ACh was similar to that in losartan group, and was more significant than benazepril alone (pD₂: SHR-L: 7.28 ± 0.26, SHR-BL: 7.48 ± 0.70 VS SHR-B: 6.32 ± 0.62 P < 0.05). ACh also caused remarked endothelium-dependent contraction in SHR mesenteric arteries compared with WKY, which was augmented by inhibitors of NO-synthases L-NAME. At the present of L-NAME, ACh-induced endothelium-dependent contraction was similarly inhibited by the three therapies (Cmax: SHR-BL: 2.00 ± 0.49, SHR-B: 2.42 ± 1.64, SHR-L: 2.67 ± 1.94 VS SHR-C: 6.18 ± 1.12 P < 0.05). SNP-induced endothelium-independent relaxation was impaired, which was completely normalized by the treatment of either losartan, benazepril or their concomitant. These results indicate that the treatment of losartan and benazepril had effects on mitigated the endothelial dysfunction in mesenteric arteries rings from SHR. The effect of concomitant treatment is more effective or equivalent to the treatment of each alone.

Key Words: Inbred SHR; hypertension; Losartan; Benazepril; endothelial function

F021
LEAD CAUSES COMPENSATORY UP-REGULATION OF NITRIC OXIDE (NO) SYSTEM IN CULTURED ENDOTHELIAL CELLS—ROLE OF SUPEROXIDE
N.D. Vaziri*, and Y. Ding. Division of Nephrology and Hypertension, UC Irvine, Irvine, California

Chronic exposure to low levels of lead causes hypertension (HTN) in humans and animals. We have previously shown increased reactive oxygen species leading to enhanced NO inactivation, depressed NO bioavailability and compensatory up-regulation of NO synthases (NOS) in rats with lead-induced HTN. In this study we tested the effect of lead (medium containing lead acetate, 1 PPM) on endothelial NOS expression and NO production in cultured human coronary endothelial cells. To discern the role of oxidative stress lead-treated and control cells were treated for 24 hrs with a superoxide dismutase (SOD)—mimetic agent, tempol, and a potent antioxidant compound, lazaroaid (both at