gene is developmentally regulated and it is the major isoform expressed in adult rat heart. In pressure load induced hypertrophy expression of this isoform is down regulated. The mechanism of its negative regulation is virtually unknown. By promoter analysis, we have found that the sequences of α-MHC gene encompassing −600 to +420 bp cloned upstream of a chloramphenicol acetyl transferase (CAT) reporter, are sufficient to drive its muscle-specific expression in adult rat heart and in muscle cell line Sol8 but no activity was observed in non muscle cells JEG and NIH3T3. Using deletion mutant constructs, a strong negative regulatory element (NRE) was located 60 bp downstream of the transcription start site. Deletion of this region resulted in 20 fold induction of α-MHC/CAT expression in adult hearts and in Sol8 cells. This mutation also resulted in expression of α-MHC/CAT constructs in JEG cells that was otherwise inert in this cell line. Gel-shift analysis with NRE sequences showed specific interaction of nuclear factors from adult heart, Sol8 and JEG cells and each of these nuclear extracts produced different mobility DNA-protein complexes. The nucleotides required within 35 bp NRE region for factor interaction were also found different in three nuclear extracts analyzed. These data may provide in part, the mechanism for its tissue specific expression and modulation of expression in the adult rat heart (Supported by a grant from Christ Hospital Med Fund).

1045 Atherosclerosis – Mechanisms

Wednesday, March 27, 1996, 3:00 p.m.–5:00 p.m.
Orange County Convention Center, Hall E
Presentation Hour: 4:00 p.m.–5:00 p.m.

1045-15 Regression of Postprandial Lipemia After Smoking Cessation

Jörg Muntwyler, Hansruedi Schmid[1], Heinz Drexel, Dieter J. Vonderschmitt[1], Josef R. Patsch[2], Franz W. Amann. *Division of Cardiology, University Hospital, Zürich, Switzerland;[1] Institute of Clinical Chemistry, University Hospital, Zürich, Switzerland;[2] Department of Medicine, University of Innsbruck, Austria*

Several studies found a positive, independent association between postprandial lipemia and atherosclerosis. Smokers have higher fasting triglyceride (TG) levels, probably caused by decreased levels of lipoprotein lipase (LPL). In the animal model, carbon monoxide and cigarette smoke depresses clearance of chylomicron remnants. Therefore, we investigated this issue in man. Methods: Measurement of fasting lipids and postprandial lipemia in 8 healthy smokers before and 3 weeks after smoking cessation. No other change in lifestile was allowed. As a marker for postprandial lipids, 50,000 U Vitamin A/m^2 BSA was ingested with a standardized fat load. After ultracentrifugation, retinyl palmitate (RP) was measured by HPLC in the chylomicron (CM: Sf > 1000) and chylomicron remnant (CMR: Sf < 1000) fraction. Results:

Variables	Baseline Smoking	Smoking Cessation	Δ%	p-Value
AUC TG (mmol/l × 10 h)	35.7 ± 11.5	27.5 ± 7.4	−23%	0.11
AUIC total RP (μg/ml × 10 h)	41.2 ± 11.4	29.7 ± 7.1	−28%	0.05
AUC RP CM (μg/ml × 10 h)	30.7 ± 9.4	21.4 ± 5.1	−30%	0.10
AUIC RP CMR (μg/ml × 10 h)	10.6 ± 2.1	8.3 ± 2.2	−22%	0.03

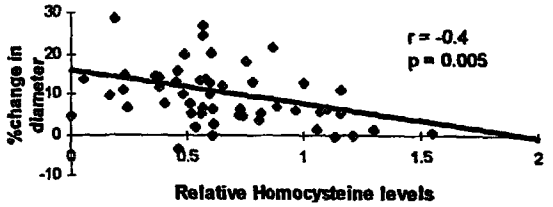
AU(I)C: Area under the (incremental) curve

After smoking cessation, fasting HDL-C and apo A-I increased and triglycerides decreased (p all < 0.05). LPL increased and was significantly (p < 0.01) correlated with the increase of HDL-C. *Conclusion:* After smoking cessation, postprandial lipemia decreases; this regression is particularly significant for the fraction containing chylomicron remnants, the potential atherogenic particles in the postprandial lipemia, and might explain a part of the increased atherosclerosis risk in smokers.

1045-16 Plasma Homocysteine Levels Predict Brachial Artery Vasoreactivity in Patients With Coronary Artery Disease

Mark R. Izzo, Marc D. Feldman, Clarence Wu, M. Zubair Jafar, Katherine Jacobs, Warren Diven, Lorna Cropcho, John George, Peter J. Counihan. *University of Pittsburgh, Pittsburgh, PA*

Plasma homocysteine has been shown *in vivo* to cause endothelial damage. The hyperemic brachial artery response to ischemia is a noninvasive test to evaluate endothelial function. Patients with CAD have been shown to have abnormal endothelial function as measured by hyperemic brachial artery response. We *hypothesized* that homocysteine may contribute to endothelial dysfunction in patients with CAD as assessed by brachial artery hyperemic response. *Methods:* Relative plasma homocysteine levels were measured at 0 and 6 hours by methionine loading in patients both at baseline and on vitamin treatment (B6 and folic acid). Brachial artery vasodilatory response to 4 minute BP cuff occlusion was measured in patients with angiographically documented CAD(n = 51). *Results:* Relative plasma homocysteine levels and hyperemic brachial artery response significantly correlated (p = 0.005) as shown below.



Conclusion: Elevated homocysteine levels are associated with an attenuated brachial artery hyperemic response. Homocysteine may contribute to endothelial dysfunction in patients with CAD.

1045-17 Effects of Conjugated Estrogens Alone and Combined With Pravastatin for Management of Hypercholesterolemia in Postmenopausal Women

M.H. Davidson, L.M. Testolin, K.C. Maki, S. von Duvillard[1], K.B. Drennan. *Chicago Center for Clinical Research, Chicago, Illinois;[1] William Patterson College, Wayne, New Jersey*

The aim of the present study was to evaluate and compare the lipid altering effects of conjugated estrogens (CE, 0.625 mg/d), pravastatin (PRAV, 20 mg/d), and combined CE + PRAV therapy among hypercholesterolemic postmenopausal women. After six weeks of following an NCEP Step I diet, 76 subjects (mean age = 61 years) were randomly assigned to receive CE, PRAV, CE + PRAV, or placebo for 16 weeks in a parallel fashion. No significant differences in demographic or lipid values were present between groups at baseline (mean LDL-C = 199 mg/dL). Sixty-seven subjects completed at least two post-randomization visits. Mean % change (SD) from baseline in lipid parameters are shown in the table (average of four samples taken at monthly intervals).

Variable	Placebo	CE	PRAV	CE + PRAV
TC	2.5 (9.7)^{2,3,4}	−6.2 (8.1)^{1,3,4}	−18.5 (7.2)^{1,2}	−15.8 (10.3)^{1,2}
LDL-C	1.8 (11.3)^{2,3,4}	−13.7 (8.1)^{1,3,4}	−25.0 (9.3)^{1,2}	−27.8 (15.2)^{1,2}
HDL-C	−2.9 (7.7)^{2,4}	25.3 (19.8)^{1,3}	4.8 (13.9)^{2,4}	22.2 (11.2)^{1,3}
TRIG	15.1 (38.5)^{3}	9.8 (38.2)^{3}	−10.9 (16.7)^{1,2}	0.6 (16.8)
LDL/HDL	5.3 (13.2)^{2,3,4}	−28.6 (11.0)^{1,4}	−27.7 (10.2)^{1,4}	−39.7 (17.2)^{1,2,3}

^{1,2,3,4}p < 0.05 vs. placebo, CE, PRAV, CE + PRAV, respectively

Both CE and PRAV improved the serum lipid profile, and the two combined were more effective at reducing the LDL-C/HDL-C ratio than either treatment alone. These data support the NCEP's recommendation to consider estrogen replacement as an initial or adjunct therapy for the management of hypercholesterolemia in postmenopausal women.

1045-18 Impaired Endothelium-dependent Vasodilator Response in Patients With High Lipoprotein(a) Levels

Tatsuaki Murakami, Sumio Mizuno, Yoshiyuki Arai, Yoshifumi Takahashi, Masateru Ohnaka. *Fukui Cardiovascular Center, Fukui, Japan*

Endothelial dysfunction is supposed to be a major factor that contributes to the atherogenic or thrombogenic processes, and lipoprotein(a):Lp(a) has been documented as an independent risk factor for atherosclerosis or myocardial infarction. In order to determine whether elevated Lp(a) levels impair endothelium-dependent vasodilator response of coronary artery, we evaluated changes in coronary blood flow dynamics assessed by quantitative coronary arteriography and intracoronary doppler-tipped guidewire (Flo Wire ™) in patients with (n = 23) high Lp(a) levels (> 33 mg/dl), and compared them to those in control patients without high Lp(a) levels (71 overall controls and 23 matched controls in age, gender, and serum total cholesterol level. We infused acetylcholine into the study coronary artery, and estimated the coronary diameter and the flow velocity. In patients with high Lp(a) levels, acetylcholine-induced maximal increases in the coronary diameter and the coronary blood flow were smaller than those in the control patients. Maximal increases in the coronary diameter were 1.6 ± 2.5% (Mean ± S.D.%) in the patients with high Lp(a) levels, 3.9 ± 3.2% in the overall control patients, and 3.7 ± 3.7% in the matched control patients (p < 0.05; patients with high Lp(a) levels vs overall and matched controls). Maximal increases in the coronary blood flow were 39.5 ± 28.4% in patients with high Lp(a) levels, 95.9 ± 81.2%