Prevalence of Intimal CRP in Unstable Angina
Atheroma: Modification by Statin Therapy
Gerhard Bauersfeld, René Andrit, Dirk Skovasch, Peter Braun, Thomas M. Schiele, Thomas Grunder, University of Borken, Germany.

Background: Inflammation is basically involved in progression and/or complication of atherosclerosis. Though C-reactive protein (CRP) is an independent serum marker strongly predicting major adverse coronary events, the intimal prevalence of CRP in advanced target lesions that determine different clinical settings, and its modification by statin therapy, are unknown.

Methods: Coronary atheroma samples retrieved from 48 primary target lesions of patients suffering either unstable angina (UA; n=32) or stable angina (SA; n=16) were examined by immunohistochemistry using the APAAP technique. Presence of CRP, plaque localization, and prevalence in either group were studied.

Results: Immunohistochemical examination demonstrated signals for CRP in 27 of 48 (56%) coronary target lesions vs. none of 20 undiseased control samples. As the central finding, immunoreactive CRP was detected in 23 of 32 (72%) UA lesions, and only in 4 of 16 (26%) SA lesions (p<0.01). Lesional CRP-positive cells correlated strongly with plaque areas exhibiting ruptures and fissures (r=0.86, p<0.001), with a local expression up to 70%, and were identified as macrophages/foam cells by double immunostaining for CRP and CD68. When categorizing all lesions into those with and without statin therapy, CRP was found consistently decreased in lesions from patients with statin medication (30 vs. 75%; p<0.01). The more with UA lesions. Conclusions: Intimal CRP shows a strong prevalence in clinical instability, indicating an important stimulus for foam cell formation and plaque rupture. Beyond lipid lowering, plaque stabilization via reduction of intimal CRP may be a new important therapeutic effect of statins preventing plaque rupture.

Enhanced Expression of Lectin-Like Oxidized Low Density Lipoprotein Receptor (LOX-1) at Sites of the Culprit Lesion in Patients With Acute Coronary Syndromes
Yuki Sato, Takahiro Naka, Katsuaki Hara, Masatoshi Otsuka, Akino Itoh, Masayuki Ochiai, Yoshio Ikura, Masahito Chikanae, Masako Ueda, Osaka City General Hospital, Osaka, Japan.

Background: Experimental studies have shown that oxidized low density lipoprotein (ox-LDL) plays an important role in the progression of atherosclerosis. Recently, we have demonstrated that ox-LDL plays a pivotal role in the genesis of coronary plaque instability and development of acute coronary syndromes. (Shishido S et al. J Am Coll Cardiol 1995-1996, 201:556-560). Lectin-like oxidized low-density lipoprotein receptor (LOX-1) is also considered to play a key role in atherogenesis, and recent in vitro studies have demonstrated that LOX-1 binds to activated platelets. Thus far, we are unaware of any studies that have looked into the potential role of LOX-1 in patients with acute coronary syndromes.

For this reason, we have studied the expression of LOX-1 in various types of human coronary atheroma plaques including ruptured and eroded plaques. Methods: Frozen sections of normal coronary artery segments (Normal, n=21), and coronary atherosclerotic segments (n=71) with early atherosclerotic plaques [early AP], advanced atherosclerotic plaques (advanced AP), ruptured plaques (RP), and eroded plaques (EP) were stained with antibodies against smooth muscle cells (SMC), macrophages (MAC), endothelial cells (EC), platelets (GPⅡb/Ⅲa), and LOX-1. We used computer-aided planimetry which quantified the immunoreactivity of LOX-1 and MAC. For the identification of cell hypertrophy which express LOX-1, immunostaining for double staining was also used. Results: In Normal, there was no expression of LOX-1. In early AP, LOX-1 expression was found in EC and SMC at the plaque site. In advanced AP, LOX-1 expression was found in accumulated macrophages and also EC of intimal microvessels. In RP and EP, LOX-1 was strongly expressed not only on EC, but also on MAC and also on platelet thrombi, and EC of intimal microvessels. The percentage of LOX-1 positive area within the intima was significantly higher in EP (p<0.01) and RP (p<0.004) than in normal advanced AP. Conclusions: These findings strongly suggest a role for LOX-1 in macrophage infiltration and thrombosis with activated platelets, which may be integral parts of inflammatory response related to plaque rupture and erosion in human coronary atherosclerotic lesions.

Carotid Atherosclerotic Plaque Instability in Patients With Acute Myocardial Infarction
Andrea Rossi, Lorenzo Franceschini, Massimiliano Fusaro, Giorgio Golia, Piero Zardini, Andrea Rossi. Lorenzo Franceschini, Massimiliano Fusaro, Giorgio Golia, Piero Zardini, Andrea Rossi. Department of Cardiology, Heart Center, Duleburg, Germany.

The instability of the atherosclerotic plaque (PL) is primarily determined by local factors, but additional vascular risk factors predicted the presence of unstable carotid PL (4.5; 95% C.I.: 2.1-9.3; p<0.0001). Conclusion: Patients with ACE had frequently unstable PL in other arterial sites such as carotid arteries. This findings supports the hypothesis that PL instability might partly reflect a systemic process.

Enhanced Expression of the Inflammatory Protein LOX-1 at Sites of the Culprit Lesion in Patients With Acute Coronary Syndromes
Yuki Sato, Takahiro Naka, Katsuaki Hara, Masatoshi Otsuka, Akino Itoh, Masayuki Ochiai, Yoshio Ikura, Masahito Chikanae, Masako Ueda, Osaka City General Hospital, Osaka, Japan.

Background: Experimental studies have shown that oxidized low density lipoprotein (ox-LDL) plays an important role in the progression of atherosclerosis. Recently, we have demonstrated that ox-LDL plays a pivotal role in the genesis of coronary plaque instability and development of acute coronary syndromes. (Shishido S et al. J Am Coll Cardiol 1995-1996, 201:556-560). Lectin-like oxidized low-density lipoprotein receptor (LOX-1) is also considered to play a key role in atherogenesis, and recent in vitro studies have demonstrated that LOX-1 binds to activated platelets. Thus far, we are unaware of any studies that have looked into the potential role of LOX-1 in patients with acute coronary syndromes.

For this reason, we have studied the expression of LOX-1 in various types of human coronary atheroma plaques including ruptured and eroded plaques. Methods: Frozen sections of normal coronary artery segments (Normal, n=21), and coronary atherosclerotic segments (n=71) with early atherosclerotic plaques (early AP), advanced atherosclerotic plaques (advanced AP), ruptured plaques (RP), and eroded plaques (EP) were stained with antibodies against smooth muscle cells (SMC), macrophages (MAC), endothelial cells (EC), platelets (GPⅡb/Ⅲa), and LOX-1. We used computer-aided planimetry which quantified the immunoreactivity of LOX-1 and MAC. For the identification of cell hypertrophy which express LOX-1, immunostaining for double staining was also used. Results: In Normal, there was no expression of LOX-1. In early AP, LOX-1 expression was found in EC and SMC at the plaque site. In advanced AP, LOX-1 expression was found in accumulated macrophages and also EC of intimal microvessels. In RP and EP, LOX-1 was strongly expressed not only on EC, but also on MAC and also on platelet thrombi, and EC of intimal microvessels. The percentage of LOX-1 positive area within the intima was significantly higher in EP (p<0.01) and RP (p<0.004) than in normal advanced AP. Conclusions: These findings strongly suggest a role for LOX-1 in macrophage infiltration and thrombosis with activated platelets, which may be integral parts of inflammatory response related to plaque rupture and erosion in human coronary atherosclerotic lesions.

Carotid Atherosclerotic Plaque Instability in Patients With Acute Myocardial Infarction
Andrea Rossi, Lorenzo Franceschini, Massimiliano Fusaro, Giorgio Golia, Piero Zardini, Andrea Rossi. Lorenzo Franceschini, Massimiliano Fusaro, Giorgio Golia, Piero Zardini, Andrea Rossi. Department of Cardiology, Heart Center, Duleburg, Germany.

The instability of the atherosclerotic plaque (PL) is primarily determined by local factors, but systemic factors such as infection, inflammation, autoimmunity or genes might also be important. We aimed to analyze whether patients with acute coronary artery event (ACE) such as myocardial infarction (AMI) might have a higher proportion of unstable PL of culprit arteries compared with patients with stable coronary artery disease (CAD). Methods: 68 consecutive patients with AMI (Group 1) and 95 patients without ACE (Group 2) had carotid arteries duplex ultrasound. Carotid atherosclerosis has been quantified by: number of carotid atherosclerotic segments (n=71), number of carotid plaques (2.5±1 vs 3.2±2, p=0.02), degree of stenosis [50±21% vs 38±38%], stenosis thickness and degree of maximal stenosis. According their morphology, PL were divided in stable (fibrocalcific) and unstable (soft and or not-homogeneous). Results: The two groups did not differ for age (66±8 vs 67±19; p=0.3), sex (9% vs 22%; p=0.3), number of carotid PL (2.6±1 vs 2.5±2; p=0.2), degree of stenosis (50±19% vs 42±6%; p=0.4), but group 1 had more frequently unstable carotid PL than group 2 (43% vs 15%; p=0.004), a higher number of carotid unstable PL (0.5±0.6 vs 0.1±0.4; p=0.001). In the overall population, logistic regression analysis showed that presence of ACE, adjusted for traditional vascular risk factors predicted the presence of unstable carotid PL (4.5; 95% C.I.: