**CHRONIC STRESS CONVERTS ATHEROSCLEROTIC LESIONS FROM A STABLE TO A MORE VULNERABLE PHENOTYPE**

**A.H. Najafi**, N. Aghili, J.U. Tilan, J.A. Andrews, X. Peng, R. Virmani, Z. Zukowska,

S.E. Epstein, M.S. Burnett

Cardiovascular Research Institute, Washington, DC, USA

Aims: The purpose of these studies was to determine the effects of chronic stress on atherosclerotic plaque characteristics commonly associated, in humans, with “vulnerability to rupture”.

Methods and Results: Lard-fed, male ApoE -/- mice were subjected to chronic cold stress (standing in 1cm iced water 1hr/day/4wks) prior to sacrifice at 16, 20 or 40 weeks, or left unstressed. H&E and Movat’s pentachrome, and Ter119, CD31, Mac3, and neuropeptide Y (NPY) staining was performed on brachiocephalic arteries. At 20 weeks, lesions in the brachiocephalic arteries of stressed vs. non-stressed mice had larger necrotic cores, thinner fibrous caps (p=0.05), greater inflammation (p=0.02), and more intraplaque hemorrhage/neovascularization (p=0.03) than non-stressed mice. NPY immunoreactivity increased in lesions following stress exposure (p=0.03). Neuropeptide Y was elevated in platelet-rich plasma and corticosterone concentration was greater in the urine of mice exposed to chronic stress.

Conclusions: ApoE -/- mice exposed to chronic stress develop complex lesions with large necrotic core, thin fibrous cap, a high degree of inflammation and intraplaque hemorrhage/neovascularization--a phenotype that, in humans, is usually considered characteristic of plaques with increased vulnerability to rupture.