**C-REACTIVE PROTEIN-MEDIATED ENDOTHELIAL DYSFUNCTION AND ACUTE CORONARY ARTERY DISEASE**

**J.G. Filep**

Maisonneuve-Rosemont Hospital, University of Montreal, Montreal, QC, Canada

Acute coronary artery disease (CAD) is associated with endothelial dysfunction and enhanced neutrophil influx into culprit lesions. Epidemiological studies have shown consistent relationship between markers of inflammation, such as C-reactive protein (CRP) and risk prediction of acute CAD. However, the role of CRP as a regulator of endothelial function is not fully understood. Indeed, CRP exists in conformationally distinct forms, which exhibit distinct activities on the endothelium. Native pentameric CRP rapidly dissociates into its subunits monomeric CRP (mCRP) on activated or apoptotic cells. Using CRP isomer-selective antibodies, we detected mCRP, but not native CRP in fatty streak lesions and fibro-fatty plaques in human coronary arteries. More pronounced mCRP staining was detected in advanced lesions where mCRP frequently co-localized with neutrophils, monocytes/macrophages or platelets. Conformational rearrangement in native CRP was associated with upregulation of ICAM-1, VCAM-1 and E-selectin expression and production of IL-8 and MCP-1 in cultured human coronary artery cells (HCAEC), leading to enhanced neutrophil adhesion. These activities were under the control of the intrasubunit disulfide bond, functioning as a redox switch. In HCAEC, the actions of mCRP were mediated through unlocking the lipid raft interaction motif and the IgG receptor FcgammaRIII (CD16). By contrast, mCRP affected neutrophil function through CD16. These data suggest that endothelial cell activation may facilitate mCRP formation, which in turn, may aggravate endothelial dysfunction and promote neutrophil recruitment, ultimately leading to plaque destabilization and acute CAD.

(Grant support: MOP-94851 and MOP-102619 from the CIHR).