

P009 Reactive species augment blood-mediated inflammatory response

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Emerging evidence suggests that blood is a central determinant for the involvement of reactive species (ROS) as signaling molecules for the propagation of coronary heart disease (CHD). We conducted a series of studies to identify key inflammatory pathways targeted by ROS and their implications in the pathogenesis of CHD. We at first demonstrated using an *ex vivo* model of blood recirculation that there is a greater imbalance between antioxidant capacity and the production of ROS in CHD patients as compared with healthy subjects. We also demonstrated an increasing pro-oxidant activity at different levels of disease progression from stable to unstable angina and impaired left ventricular function. Immunohistochemistry of myocardial biopsies demonstrated a significant differential distribution of apoptotic cell-death and an extensive infiltration of blood-derived monocytes into the vessel wall in patients with stable angina, unstable angina and impaired left ventricular function with greater levels in the latter two stages, a process that was significantly related to peroxynitrite-mediated nuclear factor kappa B (NF-kappaB) activation. Further *in vitro* investigations suggested that peroxynitrite regulated the production of inflammatory cytokines by monocytes via both canonical and non-canonical pathways of NF-kappaB activation and that NOS-derived endogenous nitric oxide acts as the major regulator of inflammatory pathways in isolated leukocytes from CHD subjects with or without diabetes mellitus.