Inflammation is an all encompassing term for a complex process that entails multiple cellular, hormonal and biochemical alterations that are both systemic and organ-specific. A panoply of acute and chronic infections as well as many exogenous and intrinsic sources of inflammation is associated with an increased risk for ischemic stroke. The molecular mediators of these processes are the focus of enormous research interest in both vascular and neurobiology and encompass investigatory areas including atherogenesis, vascular autoregulation, endothelial function, hemostasis, leukocyte and bone marrow activation and intrinsic neuroinflammatory mechanisms.

Atherosclerosis affecting precerebral as well as intrinsic brain arteries and arterioles plays a key role in the pathogenesis of stroke. Atherosclerosis producing focal carotid stenosis localized to the carotid bulb and proximal internal carotid artery is a principal cause of atheroembolic ischemic stroke in North America. The development of the atherosclerotic lesion is usually a gradual one taking place over a time scale measured in years and is characterized by chronic inflammation within the vessel wall in a response to the deposition of oxidized LDL cholesterol components. During acute atherothrombosis there is an abrupt transition from a chronic indolent inflammatory process to one that is far more fulminating and giving rise to the so-called hot or active plaque. This response entails increased leukocytosis within the atheroma, activation of the regional vascular endothelium that promotes further recruitment of leukocytes as well as digestion of the fibrous cap by the expression of tissue matrix metalloproteinases (MMPs) that ultimately cause plaque rupture and exposure of subendothelial tissue factor to the hemostatic components of blood. The exact triggers and related mechanistic events that switch an atheroma from one that is silent to one that is active remains incompletely understood. However, being able to accurately distinguish between these 2 states for a given atheromatous plaque in the carotid artery is very important because the clinical disposition of hot plaques is to produce stroke and transient ischemic attack (TIA). In this section, Dr David Saloner discusses the emerging application of high-resolution MRI to characterize carotid plaque morphology.

During the course of brain ischemia, inflammatory mechanisms both intrinsic to brain as well as blood are among the important mediators of focal cerebral injury. With the onset of focal brain ischemia, microglia become activated within the penumbra and thereby facilitate further local neuronal injury via pathways that include poly(ADP-ribose) polymerase-1 activation and activation of multiple MMPs. The activation of MMPs disrupts the blood-brain barrier, alters microvascular endothelial function and impairs the functional integrity of the neurovascular unit. These events promote the entry of peripheral leukocytes into brain and expose “protected” cerebral elements to peripheral immune surveillance systems. These processes are exquisitely detailed in the following discussions of Drs Swanson and del Zoppo. Finally, although the fundamental neurobiology of the inflammatory cascade that occurs during brain ischemia is being worked out in animal models of stroke, Dr Sebastian Jander discusses evolving MRI techniques that may allow many aspects of these processes to be studied in human stroke.
Inflammation and Stroke: Introduction
Bruce M. Coull

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