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OXIDATIVE STRESS IN FETAL AND NEONATAL BRAIN DEVELOPMENT

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Free radicals (FRs) are normally generated as by-products of aerobic respiration and various metabolic processes. Oxidative stress (OS) occurs when the production of FRs exceeds the capacity of antioxidant defenses. Nevertheless, a certain amount of OS is required to allow for the normal progression of embryonic and fetal growth. OS has been implicated in the regulation of reproductive processes in both animal and human, such as follicular development, ovulation, fertilization, embryogenesis, placental differentiation and growth. In contrast OS has emerged as a likely promoter of several pregnancy-related disorders, such as spontaneous abortions, embryopathies, preeclampsia, fetal growth restriction, preterm labor and low birth weight. Clinical studies suggest a link between maternal and fetal infection/inflammation and brain damage. The most common view is that intrauterine infection causes a fetal systemic inflammatory response resulting in injury to cerebral white matter. At birth, newborn is exposed to a relatively hyperoxic environment and additional FRs sources such as inflammation, hypoxia, ischemia-reperfusion, glutamate and non protein bound iron (NPBI) release may enhance OS. The susceptibility of the developing brain in extreme low gestational age newborn is due to the intrinsic vascular derangements in the autoregulation of cerebral blood flow and the local metabolic vulnerability, furthermore asphyxia causes an increase in NPBI, that significantly correlates with neurodevelopmental outcome. As matter of fact, a positive correlation exists between the development of IVH and NPBI levels in cord blood suggesting the dangerous potential of NPBI on oligodendrocytes. Brain injury is a leading cause of mortality and disability. The improvement in understanding the pathophysiological mechanisms involved in perinatal brain lesions will allow to identify new neuroprotective strategies.