Oxidative stress and kidney injury

Reactive oxygen species

Free radicals are chemical species with a single unpaired electron on an outer orbital. Such chemical states are highly unstable and result in cell injury. Reactive oxygen species (ROS) are a type of oxygen derived free radical. ROS are produced normally in small amounts in all cells during the reduction-oxidation (redox) reactions that occur during mitochondrial respiration and energy generation. In this process, molecular oxygen is sequentially reduced in mitochondria by the addition of four electrons to generate water/ during this reaction ROS and other intermediates are formed, including superoxide anion. Superoxide dismutase (SOD) converts superoxide anion to hydrogen peroxide. Hydrogen peroxide is much more stable than superoxide anion. ROS are produced in phagocytic leukocytes, mainly neutrophils and macrophages, to destroy ingested microbes and other substances during inflammation and host defense. ROS in leukocytes are generated in a process called respiratory burst. In this process, a phagosome membrane enzyme catalyses the generation of superoxide, which is converted to hydrogen peroxide. Hydrogen peroxide is then converted to a highly reactive compound hypochlorite by the enzyme myeloperoxidase.

Cells have developed many mechanisms to remove free radicals and thereby minimize injury; SOD reactivity increases rate of decay of superoxide, glutathione peroxidases breakdown hydrogen peroxidase to oxidised glutathione and water, catalase catalyze the breakdown of hydrogen peroxide to water and oxygen, and endogenous and exogenous antioxidants either block the formation of free radicals or scavenge them once they have formed. In addition, free radicals are inherently unstable and decay spontaneously.

The generation of free radicals is increased and the activity of protective endogenous antioxidant enzymes decreases, in several situations; the absorption of radiant energy (such as UV light or X-ray), the enzymatic metabolism of exogenous chemicals (such as drugs), inflammation, and in diabetes. These situations result in high amounts of superoxide anion being produced, overwhelming antioxidant enzyme capabilities, thus hydrogen peroxide is converted to the highly reactive hydroxyl radical, instead of being broken down.

ROS, such as hydroxyl radicals, cause cell injury by three mechanisms; lipid peroxidation of membranes, double bonds in membrane polyunsaturated lipids are vulnerable to attack by ROS, the lipid radical interactions yield peroxidases, which are themselves unstable; cross-linking and other changes in proteins, free radicals promote sulfhydryl-mediated protein cross-linking, resulting in degradation or loss of enzymatic activity; DNA damage, free radical reactions with thymine in DNA produce single-strand breaks.

The kidney

The most superficial region of the kidney is the renal cortex. Deep to the cortex is the renal inner medulla. The cortex is composed of nephrons. The medulla exhibits renal pyramids. The pyramids are formed of parallel bundles of urine collecting tubules and capillaries. The pyramids apex are the renal papilla to drain urine from the collecting ducts via papillary ducts into the minor calyx. Nephrons are the structural and functional units of the kidneys. The nephron regulates excretion by; filtration, glomerular filtration takes place at the