

FOREFRONTS IN NEPHROLOGY: EVOLVING BASIC CONCEPTS IN ISCHEMIC INJURY

Evolving basic concepts in ischemic injury

In this Forefronts in Nephrology, held in Antwerp, Belgium, September 20–21, 2002, the most recent aspects of ischemia/reperfusion of the kidney and, to a certain extent, other organs were discussed.

In their contribution, Bonventre and Zuk emphasize the contribution of endothelial injury, leukocyte infiltration, and generation of inflammatory mediators by the tubular cells. The protective effects of ischemic preconditioning and the ability of surviving epithelium to engage regenerative mechanisms are discussed.

The next two papers discuss more in detail the role of inflammatory cells (Friedewald and Rabb) and T cells (Ysebaert et al) in ischemia/reperfusion of kidney and other tissues.

Experiments focusing on the neutrophils have led to a modest expectation of its role in acute renal failure. Recent studies looking at blocking T-cell function and interactions provided renal protection in experimental ischemia/reperfusion. Little is known about the role of the macrophages.

A more specific role in the initial phase of ischemia/reperfusion has been discovered demonstrating the adhesion of T cells to B7-1 expressed by the endothelial cells of the ascending vasa recta, generating the more than 150 years described medullary vascular congestion of the kidney soon after ischemic injury.

About the extension phase of ischemia/reperfusion, there is a role for the vascular endothelial cell in maintaining reduction of renal perfusion, ongoing hypoxia, and inflammatory processes as demonstrated in the contribution of Molitoris and Sutton.

Kaushal, Basnakian, Shah, and Dagher discuss the growing importance of the role of apoptosis in the generation and regulation of acute tubular injury. Guanosine triphosphate (GTP) depletion and activation of p53 seems to be major inducers of apoptotic cell death

after ischemic renal injury. Inhibition of apoptosis seems potentially useful in preventing injury to the ischemic kidney.

In a nice report, Price, Megyesi, and Safirstein discuss the process of regeneration and recovery shortly after injury. They have collected arguments that renal injury and recovery are part of the same responses, and that these processes depend on proper coordination of the cell cycle machinery. Jassem and Heaton discuss the critical role of mitochondria in the complex cascade of events, including loss of energy, derangement of ionic homeostasis, production of reactive oxygen species, and cell death observed after ischemia/reperfusion.

Rookmaaker, Verhaar, van Zonneveld, and Rabelink discuss the role of progenitor cells and transdifferentiation in renal maintenance and repair after acute ischemic injury. The potential clinical implications of these findings are emphasized.

The paper by Güler, Gwinner, Schwarz, and Haller deals with the long-term effects of acute ischemia/reperfusion injury.

Finally, Taylor presents a recent paradigm of the association of hypoxia and chronic inflammation. In the intestine, microvascular disruption ischemia due to chronic inflammation may contribute significantly to the pathogenesis of inflammatory bowel disease.

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