11

Future perspectives

The ultimate aim of all studies on the pathophysiology of I/R injury would be to gain insight into the processes which directly cause I/R injury in patients. When the sequence of events and mechanisms involved in I/R injury become more clear, a specific, more targeted therapy may be within reach. However, current treatment is still supportive and simultaneous with mechanistic studies, others focus on experimental therapies that alleviate I/R injury.

The first moment of intervention is already prior to transplantation. Before the actual transplantation the graft has already been exposed to various noxious events, including potential donor brain death and cold preservation. These non-immunological factors such as donor health and the duration of the ischemic period probably have substantial impact on short and long term graft function. Consequently, interventions in the donor aimed at minimizing pre-transplantation graft injury, may potentially have large effects in preventing acute and long term graft dysfunction. In chapter 11.1 the successes of donor pretreatment are discussed.

Next, during transplantation, I/R injury may be limited by modulation of the inflammatory response. Various anti-inflammatory drugs have been tested in animal experiments and human trials. Unfortunately they generally had more side-effects than wanted effects on I/R injury. From this perspective, mesenchymal stromal cells (MSCs) are under extensive investigation, since MSCs are able to exert immune regulatory and reparative effects. These versatile cells have been shown to migrate to sites of injury and to enhance repair by paracrine mechanisms instead of by differentiating and replacing the injured cells. In chapter 11.2 various preclinical studies and the first clinical study are discussed demonstrating the beneficial effects of MSC's.