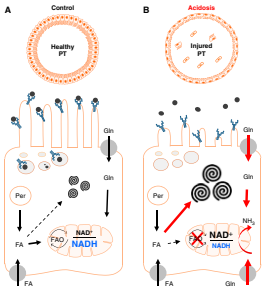
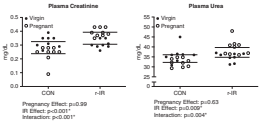
This Month's Highlights

NAD, Lipid Metabolism, and Acidosis-Induced AKI



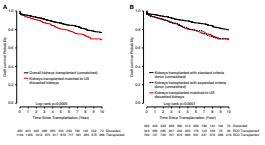
Clinical studies have suggested that metabolic acidosis aggravates tubular damage in patients with either AKI and CKD, but the mechanisms have been unknown. Using intravital live cell imaging and other complementary techniques, the authors demonstrated in the mouse kidney that metabolic acidosis induces acute changes in the mitochondrial NAD redox state, respiratory chain function, and lipid metabolism, which collectively lead to tubular cell damage. Intravenous injection of bicarbonate increases blood pH and improves tubular function, whereas pretreatment with an NAD precursor is highly protective. Thus, changes in cell metabolism explain the harmful effects of metabolic acidosis on kidney tubules. There are viable strategies to ameliorate these effects in patients. *See Bugarski et al., pages 342–356.*

Model of Pregnancy-Associated AKI



Increasing evidence suggests that patients have lingering subclinical damage after AKI, despite clinical recovery as defined by serum creatinine levels. Recent findings indicate that women with a history of AKI have poorer maternal and fetal outcomes in pregnancy, suggesting that subclinical injury impairs the renal response. The authors demonstrated that after female Sprague Dawley rats experienced biochemical resolution of surgically induced renal ischemia-reperfusion injury, they subsequently developed renal insufficiency during pregnancy and intrauterine growth restriction. This novel model may serve as a useful preclinical tool to address the critical gap in knowledge regarding the mechanisms by which AKI predisposes to adverse pregnancy outcomes. *See Gillis et al., pages 375–384.*

Kidney Histology and Graft Rejection Prediction



Many kidneys donated for transplantation are discarded because of abnormal histology discovered in a preimplantation biopsy. In an analysis of data from transplant centers in France and Belgium, where pretransplant biopsies are prospectively performed as standard practice but do not guide organ allocation decision-making, Reese *et al.* found that transplant histology did not improve the prediction of allograft failure beyond a baseline set of donor and recipient characteristics. They also found that kidneys transplanted in Europe that were similar to discarded donor kidneys from deceased US donors had acceptable allograft survival, suggesting lost transplant opportunities in the United States. *See Reese et al., pages 397–409.*

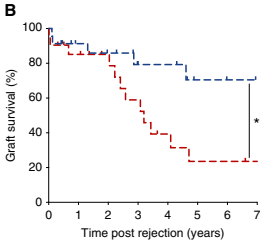
Air Pollution and CKD Risk

Minimal data exist on how exposure to high levels of an air pollutant, fine particulate matter ($PM_{2.5}$), such as in areas of mainland China, may affect CKD risk. In their analysis of data from a large survey of Chinese adults, Li *et al.* demonstrated significant associations between long-term exposure to high ambient $PM_{2.5}$ levels and an increased risk of CKD prevalence and albuminuria. These associations were significantly stronger in urban areas, among males, and among individuals <65 years and those with comorbidities. These findings offer insight for target population protection and offer evidence that policies to reduce ambient $PM_{2.5}$ pollution may lower CKD risk. *See Li et al., pages 448–458. Also see related editorial by Al-Aly and Bowe, pages 260–262.*

CKD Darbepoeitin Dosing Strategy and Transfusions

Historically, erythropoietin-stimulating agents have been titrated to achieve a predefined hemoglobin concentration when treating CKD patients with anemia. This randomized trial was designed to describe the benefits and potential risks of a new treatment strategy, using a low fixed dose of darbepoetin alfa compared with a hemoglobin-based titration-dose algorithm. The authors show that use of a low fixed dose of darbepoetin may be an alternative to a dose-titration approach to minimize red blood cell transfusions in CKD patients with anemia, and results in a smaller cumulative dose. *See Toto et al., pages 469–478.*

Antibody-Mediated Rejection



In kidney transplant recipients whose donor-specific antibodies (DSAs) do not activate complement, recruitment of innate immune effectors, particularly natural killer (NK) cells, mediates graft destruction. Combining observations from a cohort of kidney transplant recipients with antibody-mediated rejection (AMR), transcriptomic data, and use of *in vitro* models, Koenig *et al.* demonstrated that the capacity of the recipient's NK cells to sense absence of self HLA-I molecules (*i.e.,* missing self) on graft vasculature synergizes with DSA-dependent NK cell activation to worsen the outcome of complement-independent chronic AMR. Thus, screening for missing self could help to stratify risk of graft failure and guide a personalized therapeutic approach in patients with AMR. *See Koenig et al., pages 479–494. Also see related editorial by Hidalgo, pages 262–264.*