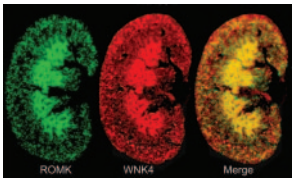
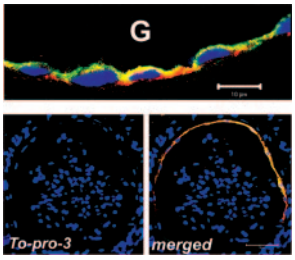
This Month's Highlights

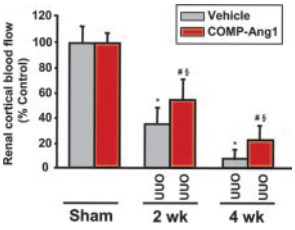
Basic Science Articles



Effects of Dietary Intake on WNK Activity and Distal Transport. Genetic studies of familial hyperkalemic hypertension (autosomal dominant, hyperkalemic hypertension with normal GFR) have linked the WNK pathways to regulation of BP and electrolyte balance. WNK4 inhibits the thiazide-sensitive NaCl co-transporter and renal outer medullary K^+ (ROMK)-mediated K^+ secretion. The long isoform of WNK1 inhibits the WNK4 effect, and the short isoform of WNK1 inhibits the inhibitory effect of WNK1-L. The major finding reported by O'Reilly *et al.* relates to the regulation of WNK1-S expression by changes in dietary K^+ and Na^+ intake, as well as separate effects of aldosterone on this regulatory system. The complexity of these pathways is just beginning to be unraveled, but potentially can explain the finely coordinated balance of distal Na^+ reabsorption between electroneutral modes and electrogenic modes, which could well provide a level of regulation of K^+ secretion in response to variations in dietary intake that has long been suspected but not clearly defined in previous studies. *See O'Reilly et al., pages 2402–2413.*

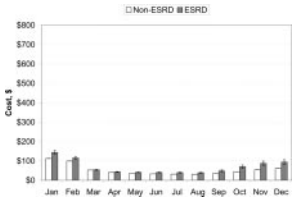


Stem Cells in Bowman's Capsule. Whether stem cells exist in the adult kidney remains a highly controversial and intensely studied question. Sagrinati and colleagues from the University of Firenze in Italy provide evidence for the existence of adult stem cells in an unexpected location, namely Bowman's capsule. They found that a subset of cells in the urinary pole of Bowman's capsule expresses two stem cell markers, CD24 and CD133. These CD24 and CD133 double-positive cells were isolated from the kidney and had two key properties of stem cells, the capacity for self-renewal and the capacity for multilineage differentiation. Importantly, these properties could be demonstrated in clones derived from a single cell. When injected into mice with acute kidney injury, the cells contributed to tubular regeneration and improved blood urea nitrogen. These exciting and provocative findings provide some of the strongest evidence for the existence of stem cells in the adult human kidney. Because they can be isolated by flow cytometry, the clinical application of the cells should be facilitated. *See Sagrinati et al., pages 2443–2456.*

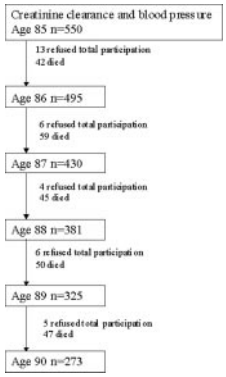


Peritubular Capillary Preservation as a Therapeutic Goal in CKD. It has long been known that loss of peritubular capillaries correlates with renal functional loss in chronic kidney disease (CKD), but whether it is a cause or a consequence of fibrosis is still debated. Kim and colleagues investigated the effects of treatment with cartilage oligomeric matrix protein–angiopoietin-1 (COMP-Ang1), a potent angiopoietin-1 variant, given *via* an adenoviral vector to mice with unilateral ureteral obstruction. Ang1 is an activating ligand for endothelial cell Tie2 receptors. Several cleaver techniques were used to follow its effects on the interstitial microcirculation, including the use of mice with green fluorescent protein–labeled endothelial cells and laser Doppler ultrasonography. Not only was COMP-Ang1 effective at preserving renal cortical blood flow (shown in the figure to the left) and interstitial capillary density, but these effects were associated with a significant reduction in TGF-β and kidney collagen levels and tubular injury. An additional benefit may an anti-inflammatory effect due to reduced endothelial cell adhesiveness as the number of interstitial macrophages was significantly reduced in the COMP-Ang1 group. *See Kim et al., pages 2474–2483.*

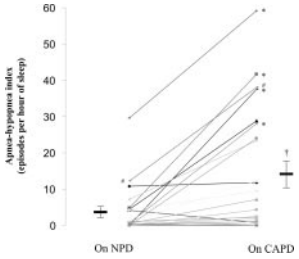
Clinical Science Articles



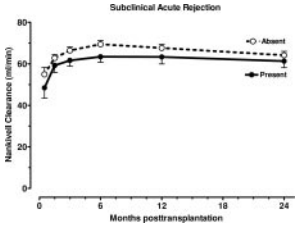
Medicare Part D. The Medicare Part D prescription drug benefit is intended to reduce medication costs among Medicare beneficiaries. A peculiarity of Part D is the variable coverage of medication costs imposed by the "doughnut hole" provision, which increases co-payments after an initial $250 deductible from 25% for the first $2250 of drug costs to 100% co-pay for the next $2850. This coverage gap is of concern to ESRD patients who have considerable drug costs. Patel *et al.* report in this issue of *JASN* that individuals with ESRD may be subject to unexpected increases in medication costs under Part D. Clinicians need to carefully monitor the impact of the new benefit to identify and deal with the effects of increased drug costs if they occur. Any adverse impacts need to be systematically documented and reported as the new benefit is rolled out, and if there is an unintended negative impact for ESRD patients, CMS and Congress must be appraised of this problem so that suitable remedies can be devised. *See Patel et al., pages 2546–2553.*



BP and the Elderly. Is renoprotective therapy that includes aggressive BP reduction to a goal of <130/85 mmHg indicated for individuals in the 9th and 10th decade of life who have otherwise asymptomatic stage 3 to 4 chronic kidney disease? The report by van Bemmel *et al.* in this issue of *JASN*, from the Leiden 85-Plus Study, suggests caution as the authors report an inverse association between BP the rate of decline of creatinine clearance. They also observed that a declining BP during follow-up was associated with increased rate of loss of kidney function. The population of elderly is growing enormously as a consequence of increased life expectancy and the demographic bulge of the postwar baby boom. The main import of these results is to remind us once again that therapeutic extrapolation to elderly populations of survivors should be done with extreme caution in the absence of evidence. *See van Bemmel et al., pages 2561–2566.*



Another Advantage of Nocturnal Peritoneal Dialysis: It Reduces Sleep Apnea. Nocturnal hemodialysis has previously been shown to improve sleep apnea compared with patients receiving conventional hemodialysis. In this issue of *JASN*, Tang *et al.* demonstrate that nocturnal peritoneal dialysis (NPD) is also effective in alleviating sleep apnea compared with continuous ambulatory peritoneal dialysis (CAPD). In this study, overnight polysomnography was compared in 46 stable NPD and CAPD patients matched for demographics and other clinical attributes. There was a highly significant difference in the prevalence of sleep apnea based on dialysis modality, defined as an apnea-hypopnea index. The investigators went on to validate these findings in a fixed sequence intervention study in which 24 incident peritoneal dialysis patients were studied during NPD and CAPD. Of note, there were greater reductions in total body water during NPD, which may have contributed to the reduction in sleep apnea symptoms. This provocative study suggests that all peritoneal dialysis may not be created equal. Increasingly, dialysis prescriptions may need to be tailored to the individual patient's needs. *See Tang et al., pages 2607–2616.*



Absence of Detectable Impact of Untreated Subclinical Rejection Found on Protocol Renal Transplant Biopsies. Protocol renal allograft biopsies are increasingly used to detect subclinical graft injury and the findings could affect prognosis and subsequent treatment strategies. The extent of cortical tubulointerstitial fibrosis detected at 6 or 12 mo posttransplant correlates with graft survival and function, but the impact of subclinical acute rejection in these biopsies remains controversial. In an observational analysis of serial protocol biopsies from 126 renal allograft recipients on calcineurin inhibitor–based immunosuppression, Scholten and colleagues noted a 31% prevalence of subclinical acute rejection at 6 mo. None of the pathologic findings were treated. In this cohort, there was no correlation between the presence of subclinical rejection at 6 mo and progressive fibrosis, proteinuria or loss of renal function over 2 yr. The data provide evidence that the majority of subclinical rejection episodes are not deleterious within this time frame, and raise questions about the need for treatment. *See Scholten et al., pages 2622–2632.*