Novel ALG9 Mutations and Kidney Cysts
Dominantly inherited polycystic kidney and liver phenotypes occur when polycystin-1 functional dosage is reduced in epithelial cells in these organs. Besse et al. identified heterozygous loss-of-function mutations in ALG9 in a cohort of genetically unresolved polycystic liver and kidney disease and show that Alg9 inactivation in vitro results in impaired polycystin-1 maturation. They then ascertained ALG9 mutation carriers in a large cohort of exome-sequenced individuals, finding 718 (88%) of those over age 50 had multiple kidney cysts. These findings identify ALG9 as a novel human polycystic kidney and liver disease gene and support the utility of a genotype-driven approach. See Besse et al., pages 2091–2102. Also see related editorial by Sandford, pages 2037–2039.

Oral Inhibitor of Sodium-Phosphate Cotransporter
Treatment options for hyperphosphatemia in patients with CKD are limited to dietary phosphate restriction and oral phosphate binders. Thomas et al. demonstrate in mice that pharmacologic inhibition of sodium-phosphate cotransporter Npt2a, which mediates much of phosphate reabsorption in the kidney, causes a dose-dependent phosphaturia, reductions in plasma phosphate levels, and suppression of parathyroid hormone. It also increases urinary excretion of sodium, chloride, and calcium, without affecting urinary potassium excretion, flow rate, or pH. The results show for the first time that a novel Npt2a inhibitor has potential as a treatment for kidney disease–related hyperphosphatemia. See Thomas et al., pages 2128–2139. Also see related editorial by Lederer, pages 2039–2040.

Bladder Cell Transcriptome
To understand the cellular origins of bladder diseases, it is essential to have a comprehensive map of the cellular anatomy of the normal human bladder. Using single-cell RNA sequencing, Yu et al. created a single-cell transcriptomic map of human bladder cells and a similar map of the mouse bladder. Comparisons of human and mouse bladder cells showed many cell types with cross-species similarities. They also discovered a new human bladder cell type that may play a role in allergic reactions and nerve conduction, and a second type that may play a role in bladder emptying. These findings may be helpful in studies of the relationship between bladder cell types and diseases. See Yu et al., pages 2159–2176.

Arteriovenous Fistula Maturation and Interventions
Endovascular or surgical interventions are often used to assist clinical maturation of arteriovenous fistulas (AVFs) before use in dialysis, but the effect of such assisted maturation on long-term AVF outcomes is poorly studied. In this retrospective analysis, Lee et al. identified elderly patients who underwent AVF creation after initiation of hemodialysis, and whose AVF was used successfully for dialysis with or without assisted maturation. They found a positive association between the number of prematuration interventions and the likelihood of primary patency loss and frequency of interventions after maturation. These findings highlight the burden of costly interventions to assist clinical maturation for successful AVF use. See Lee et al., pages 2209–2218, and related editorial by Lok, pages 2040–2042.

Serious Illness Treatment Preferences for Older Adults with Advanced CDK
Although effective advance care planning is a national priority for nephrologists, a number of barriers hinder communication between patients and clinicians about treatment goals and patient preferences. Baddour et al. found that a question eliciting patients’ treatment preference when confronted with a serious illness associated with two validated tools measuring health outcome priorities and acceptability of end-of-life scenarios, including chronic dialysis. Their findings suggest that this question about serious illness and treatment preference can provide a point of entry for communication about goals of care and trade-offs of aggressive treatments such as dialysis, taking into account patients’ essential priorities. See Baddour et al, pages 2252–2261.

Tracking Anti-HLA Antibodies in Kidney Waitlist Patients
To reduce organ rejection risk, patients on kidney transplant waiting lists are regularly monitored for changes in HLA antibody status. A new retrospective analysis of the dynamics of anti-HLA antibodies over time in such patients finds that the kinetics of alloimmunity do not appear to correlate with the interval between measurements, whereas the magnitude of alloimmune status change increased significantly in patients with a previous transplant versus those without such a history. This suggests that an individualized strategy for monitoring waitlisted patients, based on their alloimmunization history, might be preferable to regular monitoring as currently advised. See Togninalli et al., pages 2262–2274, and related editorial by Jackson and Manook, pages 2042–2044.

This Month’s Highlights