A new test based on a “three-gene signature” can detect acute rejection of kidney allografts well before diagnosis by biopsy, according to a report in the New England Journal of Medicine.

In prospective, blinded fashion, the researchers developed the test using 4300 urine samples from 485 kidney allograft recipients, collected from 3 days through 12 months after transplantation. The goal was to identify messenger RNA (mRNA) levels in urinary cells that were correlated with the presence of acute graft rejection.

Normalized for 18S ribosomal RNA (rRNA) level, the combination of CD3ε mRNA, IFN-inducible protein 10 (IP-10) mRNA, and 18S rRNA provided a three-gene signature capable of differentiating between the presence and absence of rejection on allograft biopsy specimens. On receiver operating characteristic curve analysis, the area under the curve was 0.85 in the development set and 0.74 in an independent validation set.

The three-gene signature distinguished acute cellular rejection from acute antibody-mediated and borderline rejection. It also permitted diagnosis of acute cellular rejection in patients receiving anti–IL-2 antibodies versus T cell–depleting antibodies. Test performance was unaffected by the presence of urinary tract infection.

The average trajectory of the three-gene signature increased significantly in the weeks before the diagnosis of acute rejection could be made in biopsy specimens. By contrast, in patients without rejection, the level remained below the diagnostic threshold.

A molecular signature consisting of CD3ε mRNA, IP-10 mRNA, and 18S rRNA levels detected in urinary cells provides a promising, noninvasive test for acute rejection after kidney allograft transplantation. The three-gene signature “may provide a direct measure of risk…and a means of assessing immune status with repeated assessments,” the investigators said. With further evaluation, the test could be useful in the earlier identification of acute rejection, permitting individualized immunosuppressive therapy (Suthanthiran M, et al. Urinary-cell mRNA profile and acute cellular rejection in kidney allografts. N Engl J Med 2013; 369:20–31).

Renal bile casts are common in patients with severe hepatic dysfunction, and they may play an important role in the development of kidney injury, reports a study in Kidney International.

The clinicopathologic study included 44 patients with confirmed jaundice, identified at one university pathology department between 2004 and 2011. The presence and associations of intrarenal bile cast formation were analyzed by use of autopsy specimens in 41 cases and renal biopsy specimens in three.

Bile casts involving distal nephron segments were found in 24 of the 44 jaundiced patients. Bile cast nephropathy was considered mild in 16 cases but severe in eight, with extension to the proximal tubules. Tubular bile casts were found in 11 of 13 patients with hepatorenal syndrome and in all 10 with alcoholic cirrhosis. Jaundiced patients with bile casts had significantly increased total and direct bilirubin levels, with a trend toward increased creatinine and liver enzyme levels.

Published studies from the 1950s and 1960s reported on intrarenal bile casts as a mechanism of kidney dysfunction in patients with liver failure—previously termed “cholemic nephrosis” or “bile nephrosis.” However, in recent years it... Continued on page 14