≥33–62 μmol/l. As the bilirubin concentration increased, there was a considerable increase in the proportion of patients with a difference of ≥3 MELD points according to the assay used.

The authors conclude that the differences among results obtained with the various assays could unjustly influence the prioritization of patients for transplantation, particularly if they had marked jaundice; the particular assay used should, therefore, be taken into account when calculating MELD scores.

Original article Cholongitas E *et al.* (2007) Different methods of creatinine measurement significantly affect MELD scores. *Liver Transpl* **13:** 523–529

Hydroxyzine improved sleep in patients with cirrhosis and minimal hepatic encephalopathy

Patients with cirrhosis and minimal hepatic encephalopathy often experience sleep difficulties, but treatment with benzodiazepines is frequently ineffective and can have serious side effects. Dysregulated histaminergic neurotransmission has been associated with sleepiness through alterations in sleep–wake cycles in these patients; interestingly, regulation of these cycles has been shown to be partially restored by histamine H1 blockers in animal models of cirrhosis. In a double-blind, randomized, controlled trial, therefore, Spahr *et al.* investigated the potential of the histamine H1 blocker hydroxyzine to improve sleep in patients with cirrhosis and minimal hepatic encephalopathy.

All 35 patients (mean age 56 years [range 36–69 years]) studied had biopsy-proven cirrhosis (mean Pugh's score 9 [range 7–12]) and long-standing sleep difficulties. Exclusion factors were depression, active alcohol consumption or benzodiazepine use. Patients were randomly assigned hydroxyzine 25 mg at bedtime ($n = 17$) or placebo ($n = 18$). Sleep quality was assessed at baseline and at 10 days. Forty percent of hydroxyzine-treated patients indicated improved sleep quality in subjective neuropsychological tests, compared with no patients in the placebo group. Actigraphy showed a fall in night-time activity, leading to increased sleep efficiency in 65% of hydroxyzine-treated patients, compared with only 25% of patients in the placebo group.

The authors conclude that hydroxyzine treatment improved sleep in patients with cirrhosis and minimal hepatic encephalopathy, but recommend caution as treatment with histamine H1 blockers carries a risk for the development of overt hepatic encephalopathy.

Original article Spahr L *et al.* (2007) Histamine H1 blocker hydroxyzine improves sleep in patients with cirrhosis and minimal hepatic encephalopathy: a randomized controlled pilot trial. *Am J Gastroenterol* **102:** 744–753

New genetic risk factors identified for Crohn's disease

Although the precise cause of Crohn's disease is unknown, genetic predisposition is known to be an important risk factor; so far, three genes (*CARD15*, *IL23R* and *ATG16L1*) have been associated with disease development. Furthermore, there is evidence that gut microflora are involved in triggering and maintaining the disease state. Rioux and colleagues performed a genome-wide association study to identify other genes associated with Crohn's disease, and characterize their roles.

The data generated included 304,413 single nucleotide polymorphisms (SNPs) from 946 patients with ileal Crohn's disease and 977 healthy controls. There were four new SNPs that were associated with Crohn's disease. The first mapped to *ATG16L1* (ATG16 autophagy-related 16-like 1), a gene previously suspected to be involved in autophagy. The second SNP mapped to a noncoding region on chromosome 10. The third was located in *PHOX2B* (paired-like homeobox 2B), a gene coding for a transcription factor that is predominantly expressed in differentiating neurons. The fourth locus mapped to a region that contains *NCF4*, which encodes a protein involved in NADPH oxidase activity and production of reactive oxygen species during phagocytosis.

The authors also found that, in cells in which *ATG16L1* was silenced, autophagy of intracellular bacteria was less efficient than in control cells expressing *ATG16L1*. This demonstrates a role for ATG16L1 in autophagy in humans, and suggests that *ATG16L1* variants in patients with Crohn's disease might alter their immune response to pathogens, which in turn could trigger disease.

Original article Rioux JD *et al.* (2007) Genome-wide association study identifies new susceptibility loci for Crohn disease and implicates autophagy in disease pathogenesis. *Nat Genet* **39:** 596–604