than infants who received both HBrv and HBIg (12.6% versus 3.6%). Notably, combined perinatal HBrv and HBIg administration markedly improved the rate of hepatitis B surface antibody seropositivity compared with HBIg administration alone (85.6% versus 68.8%).

The authors support universal neonatal immunization as the choice strategy against vertical transmission of HBV in Iran, and call for studies on prevention of horizontal transmission of the disease.

**Original article** Kabir A *et al.* (2006) Combined passive and active immunoprophylaxis for preventing perinatal transmission of the hepatitis B virus in infants born to HBsAg positive mothers in comparison with vaccine alone. *Hepatol Res* **36:** 265–271

## No evidence of neoplastic transformation after proliferation of transplanted hepatocytes

Hepatocyte transplantation is a feasible therapeutic strategy for patients with end-stage liver disease, but has poor efficacy because transplanted cells generally do not replace much of the recipient's liver. Laconi and colleagues investigated whether preconditioning of recipient animals with retrorsine (which suppresses proliferation of endogenous hepatocytes) might facilitate the clonal expansion of transplanted cells.

Rats engineered to lack CD26 expression on their hepatocytes received injections of either 30 mg/kg body weight retrorsine ($n = 16$), or saline ($n = 16$) once weekly for 2 weeks. After an additional 2 weeks, all rats received infusions of $2 \times 10^6$ $CD26^+$ hepatocytes via the portal vein (95% hepatocytes, 85–95% viable cells). After 18 months, six rats from each group were killed, the remaining rats were killed at 24 months and their livers analyzed.

There was extensive, sustained replacement of the host liver in retrorsine-treated rats killed at 18 months and 24 months ($91 \pm 7$% and $87 \pm 5$% of the host liver replaced, respectively), but no substantial proliferation of donor hepatocyte cells in control rats. Donor-derived hepatocytes were normal on histologic evaluation. Liver integrity and function were also normal in retrorsine-treated rats—demonstrated by similar levels of total proteins, alanine aminotransferase, total bilirubin, and alkaline phosphatase—compared with control rats.

Although the transplanted cells underwent multiple mitotic divisions, there was no evidence of neoplastic transformation in transplanted hepatocytes from control or retrorsine-treated rats over 2 years. These encouraging results suggest that host-liver preconditioning might improve the efficiency of hepatocyte transplantation in humans.

**Original article** Laconi S *et al.* (2006) Liver repopulation by transplanted hepatocytes and risk of hepatocellular carcinoma. *Transplantation* **82:** 1319–1323

## Pioglitazone shows promise as a treatment for NASH

In a new, proof-of-concept study, pioglitazone has been shown to lessen the metabolic and histologic abnormalities associated with non-alcoholic steatohepatitis (NASH), for which there is currently no proven pharmacologic treatment.

NASH is characterized by insulin resistance, hepatic fat accumulation and necro-inflammation (with or without centrilobular fibrosis). Belfort *et al.* randomly assigned 55 patients with biopsy-confirmed NASH and either impaired glucose tolerance or type 2 diabetes to receive a hypocaloric diet plus either pioglitazone (30 mg daily for 2 months, then 45 mg daily for the remainder of the study) or placebo for 6 months. The hypocaloric diet plus pioglitazone, as compared with the same diet plus placebo, improved glycemic control and glucose tolerance, normalized liver aminotransferase levels, decreased hepatic fat content, and increased hepatic insulin sensitivity. Compared with placebo-treated patients, pioglitazone-treated patients had improved liver histology with regard to steatosis, ballooning necrosis and inflammation. There was also a greater reduction in fibrosis in pioglitazone-treated patients, compared with placebo-treated patients, but the difference between the groups fell short of statistical significance. Fatigue and mild lower-extremity edema developed in one patient who received pioglitazone; however, fatigue also developed in one patient who received placebo. The use of pioglitazone was not associated with any other adverse events.

The authors recommend that large controlled trials of extended duration should be performed to establish the long-term safety