

a positive FOBT result are referred for colonoscopy, which puts great pressure on already stretched resources. As 80% of positive FOBT results are false, CT colonography (CTC) has been suggested as a less invasive alternative to colonoscopy.

To assess the value of CTC as a replacement test for colonoscopy in patients with a positive FOBT result, Walleser *et al.* performed a systematic review of five eligible studies to compare CTC with colonoscopy for sensitivity and specificity and to assess the cost-effectiveness of the two procedures. CTC detected 63% of lesions 10 mm or larger in diameter, but colonoscopy was significantly more sensitive, detecting 95% of such lesions. The specificity of colonoscopy was also higher at 99.8%, compared with 95% for CTC. Colonoscopy was more sensitive (96%) and more specific (99.7%) than CTC (89% and 96%, respectively) for detecting the presence of any cancerous lesion.

Taking costs into account, the authors conclude that CTC is, overall, less effective, less accurate and more costly than colonoscopy in patients with a positive FOBT, primarily owing to better accuracy with colonoscopy. They suggest, however, that the use of CTC has future potential as the technology is evolving and accuracy might improve.

Original article Walleser S *et al.* (2007) What is the value of computerized tomography colonography in patients screening positive for fecal occult blood? A systematic review and economic evaluation. *Clin Gastroenterol Hepatol* 5: 1439–1446

Repeat liver transplantation is possible in cases of aggressive HCV infection

Patients who develop recurring cholestatic HCV infection after liver transplantation often experience graft failure. Most transplant centers exclude such patients from repeat transplants because of their extremely poor prognosis; however, in this report, Kwo *et al.* describe two patients with an aggressive HCV infection whose second liver transplant proved successful due to the administration of interferon therapy during the course of surgery.

Both patients had developed a clinically aggressive HCV infection after the initial liver transplants. Infection in the first patient

developed when standard interferon and ribavirin therapy were discontinued due to non-response. The second patient developed HCV recurrence with cholestasis 2 months after an apparently successful graft. In both patients, after therapy with interferon α -2b and ribavirin, HCV was undetectable and repeat orthotopic liver transplantation was performed. Interferon α -2b was administered intravenously in both patients from the first incision to the end of surgery (4 h). This approach was intended to produce high serum interferon levels to prevent any possibility of HCV re-infection in the new graft. Both patients recovered well, and no evidence of recurrent viremia was reported at 36 and 24 months, respectively.

The authors conclude that aggressive therapy with interferon and ribavirin can achieve HCV RNA clearance in patients with cholestatic post-transplant HCV infection, enabling a successful repeat transplant. They recommend further investigation of the anhepatic administration of interferon to liver transplant patients at high risk of HCV recurrence who can clear virus before repeat transplantation.

Original article Kwo PY *et al.* (2007) Intravenous interferon during the anhepatic phase of liver retransplantation and prevention of recurrence of cholestatic hepatitis C virus. *Liver Transpl* 13: 1710–1713

Passive immunotherapy as a vaccine against hepatitis C

The diversity of HCV makes immunotherapy or vaccine design very difficult. Law *et al.* have identified broadly neutralizing antibodies from a human with hepatitis C and demonstrated their HCV-targeting activity in mice with a chimeric human–mouse liver.

Human monoclonal antibodies (mAbs), which showed binding specificity to three different antigenic regions on HCV E2 glycoprotein, were isolated. So-called antigenic region 3 (AR3)-specific antibodies were found to target more different strains of HCV *in vitro* than antibodies specific for antigenic regions 1 and 2. This observation suggests that AR3 is a highly conserved region, making it an ideal target for passive immunotherapy. To determine whether or not the AR3-specific antibodies could protect against HCV infection *in vivo*, they were given to mice genetically engineered to support a large population of human liver cells. Nine

mice received AR3-specific antibodies and four control mice received IgG1 antibodies to HIV1 before all mice were inoculated with HCV-infected human serum. The serum viral load in the four control mice was maintained at >10,000 RNA copies/ml throughout the duration of the study. HCV was detected immediately after inoculation in five of the nine mice that received mAbs, but had cleared by 6 days after inoculation. Five mice were still protected by week 6, by which time the serum level of the mAbs would have decayed to <10% of the initial level.

The authors conclude that AR3 could be a favorable target for vaccine design.

Original article Law M *et al.* (2008) Broadly neutralizing antibodies protect against hepatitis C virus quasiespecies challenge. *Nat Med* **298**: 25–27

Fish oil protects against some, but not all, types of fatty liver

Fish oil is thought to be protective against fatty liver disease, the incidence of which is increasing as a result of diets high in sucrose and fat. However, it is unclear whether fish oil is protective against all kinds of fatty liver. Yamazaki *et al.* investigated the effect of fish oil supplementation on ddY mice fed a diet high in either sucrose or safflower oil.

Compared with mice fed a high-starch diet, mice on diets high in sucrose or safflower oil accumulated much higher concentrations of liver triglycerides. Mice fed on high-starch or high-sucrose diets containing 10% (dietary energy) fish oil were protected against liver triglyceride accumulation; however, for mice on a high-safflower-oil diet, fish oil exacerbated the triglyceride accumulation. In a second experiment, a diet high in butter led to greater liver triglyceride accumulation than one high in safflower oil; however, although fish oil exacerbated fat accumulation in safflower-fed mice, it had neither a positive nor negative effect in butter-fed mice.

Fish oil led to reduced expression of the transcription factor SREBP-1c and its target SCD1 (stearoyl-CoA desaturase 1) in starch-fed and sucrose-fed mice, but increased expression of these proteins in safflower-oil-fed mice. Fish oil caused increased expression of PPAR γ (peroxisome proliferator-activated receptor γ) in safflower-oil-fed mice, but not in other mice.

The authors conclude that the effect of fish oil on fatty liver differs according to the cause of the disease.

Original article Yamazaki T *et al.* (2007) Fish oil prevents sucrose-induced fatty liver but exacerbates high-safflower oil-induced fatty liver in ddY mice. *Hepatology* **46**: 1779–1790

Could changes in intestinal function and morphology underlie chronic heart failure?

Chronic heart failure (CHF) is a state of chronic inflammation, but the origins of the inflammatory state are unclear. One parameter that might be involved in the generation of this state is lipopolysaccharide, also called endotoxin. This cell-wall component of Gram-negative bacteria can cross the gut wall and enter the general circulation if normal barrier function is impaired. It has been suggested that an enhanced intestinal bacterial biofilm in patients with CHF might additionally contribute to elevated plasma concentrations of lipopolysaccharide. This rise in lipopolysaccharide levels might then activate monocytes and macrophages to release proinflammatory mediators and, thus, stimulate inflammation.

To test this theory, Sandek *et al.* evaluated 22 patients with CHF and compared the function and morphology of their guts with those of 22 controls. Patients with CHF had significantly thicker bowel walls in the terminal ileum, the ascending, transverse and descending colon, and in the sigmoid, than did controls. In addition, patients with CHF showed increased intestinal permeability and decreased D-xylose absorption, which strongly suggested bowel ischemia. Furthermore, the mucus of patients with CHF contained larger numbers of adherent bacteria than did that of control individuals, indicating the presence of an augmented biofilm.

The authors recognize that further investigation is warranted, but suggest that increased permeability of the intestine in patients with CHF, and the presence of an augmented bacterial biofilm, could contribute to the chronic inflammatory state and the malnutrition long observed in patients with CHF.

Original article Sandek A *et al.* (2007) Altered intestinal function in patients with chronic heart failure. *J Am Coll Cardiol* **50**: 1561–1569