

**Table 1** Baseline characteristics of liver transplant recipients with ursodeoxycholic acid (UDCA) therapy and controls

| Characteristic                   | UDCA group (n = 14) | Placebo group (n = 12) | p Value*       |
|----------------------------------|---------------------|------------------------|----------------|
| Age (y)                          | 56.3 (12.6)         | 50.7 (15.7)            | 0.3            |
| Sex (M:F)                        | 7:7                 | 6:6                    | NS             |
| OLT indications (%)              |                     |                        |                |
| Cryptogenic                      | 7                   | 25                     |                |
| Cholestatic                      | 36                  | 8                      |                |
| Alcoholic                        | 36                  | 8                      |                |
| Autoimmune                       | 14                  | 17                     |                |
| Miscellaneous                    | 7                   | 42                     |                |
| No of previous rejections        | 0 (1)               | 0 (1)                  | NS             |
| Time since OLT (months)          | 51.8 (12.8)         | 60.2 (29.2)            | 0.3            |
| Biochemistry                     |                     |                        |                |
| ALT (U/l)                        | 18.8 (8.7)          | 29.9 (29.5)            | 0.1 (4–26)     |
| AST (U/l)                        | 23.8 (9.5)          | 32.8 (20.3)            | 0.1 (5–27)     |
| ALK PH (U/l)                     | 93.1 (25.2)         | 123 (50.6)             | 0.08 (16–98)   |
| Bilirubin ( $\mu\text{mol/l}$ )  | 12.4 (4.5)          | 15.2 (6.6)             | 0.2 (3.4–17.1) |
| Creatinine ( $\mu\text{mol/l}$ ) | 144.1 (55.7)        | 163.6 (60.3)           | 0.3 (71–168)   |
| Immunosuppression                |                     |                        |                |
| CyA dose (mg twice daily)        | 128 (42.6)          | 139.58                 | 0.6            |
| CyA level (ng/ml)                | 130.3 (68)          | 172.5 (50)             | 0.1            |
| Regimens                         |                     |                        | NS             |
| CyA+Aza                          | n = 8               | n = 6                  |                |
| CyA+prednisone                   | n = 2               | n = 3                  |                |
| CyA alone                        | n = 4               | n = 3                  |                |

Data are expressed as mean (SD).

ALK PH, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; Aza, azathioprine; CyA, ciclosporin; OLT, orthotopic liver transplantation.

\*t test or Fisher's exact test as appropriate.

- 7 **Calmus Y, Guechot J, Podevin P, et al.** Differential effects of chenodeoxycholic acid and ursodeoxycholic acids on interleukin 1, interleukin and tumor necrosis factor alpha production by monocytes. *Hepatology* 1992;16:719–23.
- 8 **Gonzalez A, Czaja A, Carpenter H, et al.** Recurrent autoimmune hepatitis after orthotopic liver transplantation. *Liver Transpl* 2001;7:302–10.
- 9 **Pageaux GP, Bismuth M, Perney P, et al.** Alcohol relapse after liver transplantation for alcoholic liver disease: does it matter? *J Hepatol* 2003;38:629–34.

## Hepatitis C virus RNA quantitation and degradation studies in whole blood samples in vitro

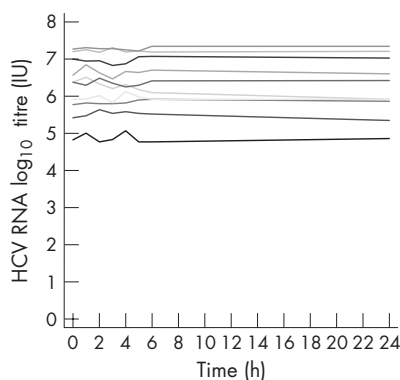
Hepatitis C virus (HCV) qualitative and quantitative polymerase chain reaction (PCR) tests have evolved from specialist research tools into tests that are widely used in routine clinical practice. Clinical therapeutic decisions are based on HCV RNA titre; hence if the result is inaccurate, patients may be given, or alternatively denied, treatment inappropriately. Little data exist on the effect of environmental conditions on HCV RNA titre after blood has been taken from the patient.<sup>1–3</sup>

We therefore decided to evaluate the variation in HCV RNA titre after whole blood samples were taken from patients, to determine whether time at room temperature, temperature variation and blood collection systems affect the result obtained by the clinician.

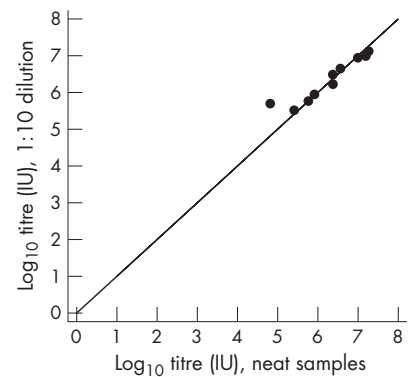
Patients were recruited to the study from the liver clinic at the John Hunter Hospital in Newcastle, New South Wales, Australia. From each of 10 patients who were known to be HCV RNA positive from previous HCV qualitative PCR testing, 24 ml blood was collected in EDTA tubes. Immediately after each sample was taken, it was transported to the laboratory. Serial plasma samples were tested using the Roche Amplicor (Roche Laboratories, Sydney,

Australia) HCV quantitative PCR kits to assess HCV RNA titres. Samples were tested for HCV RNA titre after standing between 0 and 24 h at room temperature (24°C). Comparisons of HCV RNA titre were also made after one freeze–thaw cycle, after collection in serum or EDTA tubes, and after 1:10 dilution of the 0-h samples.

HCV RNA titre was stable at room temperature for >24 h (fig 1). It was also stable over one freeze–thaw cycle, and no difference was seen in HCV RNA titre between blood collected in EDTA and that collected in serum tubes. Some patients had high HCV RNA levels, above the recommended upper limit for accuracy of the Roche Amplicor kit, but a 1:10 dilution of these samples and subsequent comparison with the neat samples revealed a high correlation coefficient of 0.91 (fig 2), indicating that the kit may still provide accurate HCV quantitation above the recommended upper limit.



**Figure 1** Hepatitis C virus (HCV) RNA degradation assays for samples at 0–24 h (individual patients shown).



**Figure 2** Hepatitis C virus RNA degradation assays, comparison of neat samples with 1:10 dilution.

Covariance analysis of the variability of the  $\log_{10}$  RNA titre in two separate tests on the same frozen plasma samples showed covariance levels to be similar to those reported by Roche Laboratories (Sydney, Australia) in their reproducibility data.<sup>4</sup>

Hence, from this study, we can conclude that HCV RNA is stable within the parameters tested, at least for the highly conserved 244 base target sequence in the 5' untranslated region of the HCV genome, which is used during the reverse transcription-PCR amplification stage in the Roche Amplicor kit.<sup>4</sup> It is possible that the long single strand HCV RNA molecule may fragment during the first 24 h after collection such that the virus is no longer viable for infection, but this theory cannot be tested within the limits of this study.

If HCV RNA does not fragment, the results of this study suggest that it may remain viable for at least 24 h at room temperature, which has public health implications for transmission of the virus through needle sharing, razors and household contact. Education of patients and their close contacts should emphasise that the virus may remain viable for at least 24 h at room temperature with little or no RNA degradation, hence care should be exercised with all potential body fluid contact.

## Acknowledgements

We thank Sister Tracey Jones, CNC, John Hunter Hepatitis C service, and Sister Liz Ianna, Education and Treatment nurse, John Hunter Hepatitis C service, for the invaluable help and support in patient counselling, recruitment, and specimen collection and transportation. We also thank the scientific staff of the Division of Microbiology, Hunter Area Pathology service, for their performance of the assays.

### J Watson

John Hunter Hospital, Newcastle, New South Wales, Australia; Faculty of Health, University of Newcastle, Newcastle, New South Wales, Australia; Barwon Health Service, Geelong, Victoria, Australia

### S Graves

Faculty of Health, University of Newcastle, Newcastle, New South Wales, Australia; Hunter Area Pathology Service, John Hunter Hospital, Newcastle, New South Wales, Australia

### J Ferguson

John Hunter Hospital, Newcastle, New South Wales, Australia; Faculty of Health, University of Newcastle, Newcastle, New South Wales, Australia; Hunter Area Pathology Service, John Hunter Hospital, Newcastle, New South Wales, Australia

**C D'Este**

Faculty of Health, Centre for Clinical Epidemiology and Biostatistics, University of Newcastle, Newcastle, New South Wales, Australia

**R Batey**

John Hunter Hospital, Newcastle, New South Wales, Australia; Faculty of Health, University of Newcastle, Newcastle, New South Wales, Australia; Drug and Alcohol Services, Hunter New England Health Service, Newcastle, New South Wales, Australia

Correspondence to: Dr J Watson, Barwon Health Service, 16 Park Street, Geelong, Vic 3220, Australia; tingewik@bigpond.net.au

doi: 10.1136/gut.2006.108860

Competing interests: None.

**References**

- 1 **Kessler H**, Stelzl E, Raggam R, *et al*. Effects of storage and type of blood collection tubes on hepatitis C virus level in whole blood samples. *J Clin Microbiol* 2001;**39**:1788–90.
- 2 **Grant P**, Kitchen A, Barbara J, *et al*. Effects of handling and storage of blood on the stability of hepatitis C virus RNA: implications for NAT testing in transfusion practice. *Vox Sang* 2000;**78**:137–42.
- 3 **Schmid P**, Tong M, Conrad A, *et al*. Analysis of the viability of freezer stored serum samples for hepatitis C virus RNA analysis by the superquant method: results of a 16 year retrospective study. *J Viral Methods* 1999;**82**:201–6.
- 4 **Lee SC**, Antony A, Lee N, *et al*. Improved version 2.0 qualitative and quantitative AMPLICOR reverse transcription-PCR tests for hepatitis C virus RNA: calibration to international units, enhanced genotype reactivity, and performance characteristics. *J Clin Microbiol* 2000;**38**:4171–9.

## Outpatient liver biopsy: a prospective evaluation of 500 cases

Percutaneous core liver biopsy plays an important role in the management of parenchymal liver disease in establishing diagnosis, evaluating prognosis and monitoring the effect of therapy. Despite the first biopsy been carried out over 100 years ago, debate surrounds best practice.

Day case liver biopsy has become increasingly popular and has not been shown to be associated with increased complications.<sup>1,2</sup> Under most day case regimens, patients are observed for up to six hours post biopsy but the majority of complications occur within the first hour post procedure and studies have suggested that the observation period may be reduced from the standard 4–6 h.<sup>3–5</sup>

Our study prospectively evaluated short stay (1 hour observation) liver biopsy over a 3 year period. Patients referred for non-focal core ultrasound guided liver biopsy were recruited. Patients were excluded if platelet counts were <50 000/mm<sup>3</sup> or prothrombin time >3 s and also if they suffered from severe ascites or intrahepatic biliary dilatation. Patients were required to have a responsible adult to accompany them for the first 24 hours after the procedure. Ultrasound guided biopsies (Bardâ Biopty-Cutâ 18G cutting needle) were usually taken from the right lobe of the liver using an intercostal approach.

Patients were observed for 1 h within the ultrasound department, receiving analgesia as required. The radiologist who had performed the procedure reassessed the patient prior to discharge. No other departments within our

hospital were involved in the management of the patient.

In total, 500 patients (291 males and 209 females) underwent core liver biopsy. Mean patient age was 43 years (range 18–76). In 495 (99%) patients, a definitive or indicative pathological diagnosis was obtained from the biopsy.

A total of 110 (22%) patients experienced pain at the time of or within 1 h of the procedure and of these, 15 (3%) required analgesia; 496 patients were discharged after 1 h of observation. Three patients were kept under observation for a further 1 h due to pain. One patient (0.2%) required admission for a haemorrhagic complication. There were no recorded delayed complications or deaths at follow up.

Our study has shown that outpatient percutaneous liver biopsy may be performed within a 2 h total time period and that almost all patients are safely discharged within 1 h of observation following the procedure. Most guidelines for day case percutaneous liver biopsy recommend an observation period of 4–6 h.<sup>3</sup> This is based primarily on studies showing that only 60% of complications occur within 2 h of the procedure but we feel that our study, together with recent investigations, suggest that this observation period is too long and that most patients can safely be discharged within 1 h.<sup>4–7</sup>

In patients who have the procedure carried out with ultrasound, the reported complication rate is low, generally significantly less than 1% for major complications.<sup>8,9</sup> However, in a review of clinical practice among physicians in the USA, only 76% used ultrasound.<sup>10</sup> We believe that the low complication rate that we recorded was related to the use of ultrasound during the procedure and that short stay liver biopsy should always be coupled with imaging guidance. In many institutions, a day ward is used for procedures such as liver biopsies. By performing the procedure on an outpatient (short observation) basis, significant cost savings may be accrued.

In conclusion outpatient liver biopsy is safe when performed on carefully selected patients in a setting that provides close observation for 1 h after biopsy. Major complications after outpatient liver biopsy are rare and manifest early. We propose that short stay liver biopsy is a safe and feasible technique.

**P Beddy**

Department of Radiology, The Adelaide and Meath Hospital, Dublin, Ireland

**I L Lyburn**

The Cheltenham Imaging Centre, Cheltenham, UK

**T Geoghegan**

Department of Abdominal Imaging and Gastroenterology, Vancouver General Hospital, Vancouver, Canada

**O Buckley**

Department of Radiology, The Adelaide and Meath Hospital, Dublin, Ireland

**A R Buckley**

Department of Abdominal Imaging and Gastroenterology, Vancouver General Hospital, Vancouver, Canada

**W C Torreggiani**

Department of Radiology, Adelaide and Meath Hospital, Dublin, Ireland

Correspondence to: Dr William C Torreggiani, Department of Radiology, Adelaide and Meath Hospital, Tallaght, Dublin 24, Ireland; william.torreggiani@amnch.ie

doi: 10.1136/gut.2006.110460

Competing interests: None.

**References**

- 1 **Younossi ZM**, Teran JC, Ganiats TG, *et al*. Ultrasound-guided liver biopsy for parenchymal liver disease: an economic analysis. *Dig Dis Sci* 1998;**43**:46–50.
- 2 **Douds AC**, Joseph AE, Finlayson C, *et al*. Is day case liver biopsy underutilised? *Gut* 1995;**37**:574–5.
- 3 **Grant A**, Neuberger J. Guidelines on the use of liver biopsy in clinical practice. *Gut* 1999;**45**(Suppl 4):IV1–V11.
- 4 **Firipi RJ**, Soldevila-Pico C, Abdelmalek MF, *et al*. Short recovery time after percutaneous liver biopsy: should we change our current practices? *Clin Gastroenterol Hepatol* 2005;**3**:926–9.
- 5 **Pokorny CS**, Waterland M. Short-stay, out-of-hospital, radiologically guided liver biopsy. *Med J Aust* 2002;**176**:67–9.
- 6 **Piccinino F**, Sagnelli E, Pasquale G, *et al*. Complications following percutaneous liver biopsy. A multicentre retrospective study on 68,276 biopsies. *J Hepatol* 1986;**2**:165–73.
- 7 **Bicknell SG**, Richenberg J, Cooperberg PL, *et al*. Early discharge after core liver biopsy: is it safe and cost-effective? *Can Assoc Radiol J* 2002;**53**:205–9.
- 8 **Caturelli E**, Giacobbe A, Facciorusso D, *et al*. Percutaneous biopsy in diffuse liver disease: increasing diagnostic yield and decreasing complication rate by routine ultrasound assessment of puncture site. *Am J Gastroenterol* 1996;**91**:1318–21.
- 9 **Vautier G**, Scott B, Jenkins D. Liver biopsy: blind or guided? *BMJ* 1994;**309**:1455–6.
- 10 **Angtuaco TL**, Lal SK, Banaad-Omiotek GD, *et al*. Current liver biopsy practices for suspected parenchymal liver disease in the United States: The evolving role of radiologists. *Am J Gastroenterol* 2002;**97**:1468–71.

## Inflammatory syndrome with liver adenomatosis: the beneficial effects of surgical management

We report a case of a patient with an inflammatory syndrome cured after resection of an adenoma. A 33-year-old woman was admitted to the department of internal medicine in May 2004 for invalidating pain in the spinal cord in the context of an inflammatory syndrome. The patient had been on oral contraceptives (Adepal) for the past 16 years. The inflammatory syndrome involved fever (37.4–38°C), anaemia, C reactive protein 90 mg/l, fibrinogen 7 g/l, sedimentation rate 106 mm and haptoglobin 2.9 g/l. Investigations for infectious, viral, systemic, hormonal and haematological disorders were all negative.

Liver function tests showed abnormally high levels of alkaline phosphatase ( $\times 3N$ ),  $\gamma$ -glutamyltransferase ( $\times 2N$ ), and alanine aminotransferase ( $\times 1.5N$ ). Liver ultrasound scan showed two nodules in the right lobe (12 and 4 cm across), which was confirmed by magnetic resonance imaging (MRI), and three additional 1-cm-nodules in the same lobe. A right hepatectomy was performed in November 2004. In March 2005, the inflammatory syndrome had normalised: the red blood cell count was 4.4 T/l, haemoglobin 12.7 g/dl, hematocrite 39.2%, mean globular volume 93  $\mu\text{m}^3$ , C reactive protein 3 mg/l, sedimentation rate 6 mm, and liver tests had returned to normal