families of the children. European and Afro-Caribbean children have genotype A, Oriental children only had genotype B, while the majority of South Asian children had genotype D. Genotype C was uncommon in any of these ethnic groups.

Overall response to treatment was better in children with genotypes A 10/18 (55%) and D 19/39 (49%) compared to those with B and C for all forms of treatment.

Although the response to Interferon alone was better in children with genotype A (50%) compared to D (36%), prednisolone priming improved the response in both genotypes to 67% & 70% respectively.

Abstract P86 Table 1 Results: Seroconversion by treatment and genotype

	Number	A (%)	B (%)	C (%)	D (%)
Trial 1					
Pred/IFN	19	4/6 (67)	0/2	0/1	7/10 (70)
IFN	20	2/4 (50)	0/5	0	4/11 (36)
Trial 2					
Lamivudine	22	2/5 (40)	0/1	0/1	8/15 (53)
Trial 3					
Adefovir	7	2/3 (67)	0	0/1	0/3

**Conclusion** Pre-treatment assessment of genotype in children may provide a guide to potential response and improve information and choice for families.

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PERIPHERAL MARKERS OF IMMUNE ACTIVATION ARE NOT ASSOCIATED WITH DEPRESSION AND COGNITIVE IMPAIRMENT BEFORE AND DURING ANTIVIRAL THERAPY IN CHRONIC HEPATITIS C INFECTION

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Introduction Cognitive impairment (CI) and depression are associated with chronic HCV infection and its treatment with alphainterferon (IFN). Chronic immune activation may predispose susceptible individuals to IFN-induced CNS effects. Neopterin (Neo) and beta-2-microglobulin (ß2m) are both IFN-induced markers of cellular immune activation. Raised serum Neo concentrations have been linked with CI in a number of inflammatory states.

**Aim** We hypothesised that peripheral markers of immune activation might identify/predict patients who develop CNS effects on IFN. **Method** 42 HCV-infected patients (RNA+ve, HIV-ve) with mild liver disease and no significant comorbidities were compared to 20 matched controls. Subjects completed depression questionnaires (HADS-D) and cognitive testing on a computerised battery (United BioSource, UK) after appropriate training, at baseline, week 4 (W4) and W12. Serum Neo was measured by ELISA, ß2m nephelometrically.

**Results** At baseline 28% of patients showed significant deficits in tests of attention, 12% had depressive symptoms (HADS-D>8). Neo and ß2m levels were significantly greater in HCV patients compared to controls (mean 8.3 SD (2.1) vs 6.6 (2.6) and 2.4 (0.4) vs 1.7 (0.6), p<0.002) but this was not associated with depression or CI. On treatment, Neo and ß2m levels increased significantly at W4 (mean change ( $\Delta$ ) 5.3 and 0.8 respectively, p<0.001). ß2m increased further at W12. Neo and ß2m correlated closely at all time points (p<0.001). Rates of significant depressive symptoms increased on treatment to 43% by W12 (p=0.003). Baseline values and  $\Delta$  Neo and  $\Delta$  ß2m did not predict incidence of depression. Mean HADS-D scores increased from 3.5 (3.5) at baseline to 7.1 (5.1) at W12

(p<0.001).  $\Delta$  HADS-D was not associated with  $\Delta$  Neo or  $\Delta$  ß2m. Performance in the attention test deteriorated from 1166 (127) ms at baseline to 1216 (148) ms at W12 (p=0.001). 33% of patients had impairments >1SD compared to baseline performance, which were not associated with  $\Delta$  HADS-D,  $\Delta$  Neo or  $\Delta$  ß2m. Neither baseline performance nor baseline Neo or ß2m were predictive of significant on-treatment CI. There were improvements in "speed of memory" on treatment from 3452 (641) ms at baseline to 3330 (630) ms at W12 (p=0.006) which had no statistical associations.

**Conclusion** We confirm the high incidence of IFN- induced depression and CI. The improvements in memory are unexplained but may be due to a learning effect on the battery. The lack of an association with Neo and ß2m suggests that CNS effects of IFN are unrelated to peripheral immune activation. Emerging evidence of HCV infection of the brain and microglial activation may represent a central susceptibility to IFN-induced CNS symptoms.

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## FOLLOW-UP OF HCV PATIENTS REFERRED TO SPECIALIST SERVICES—WHERE DO THEY ALL GO?

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**Introduction** The Liver Service provides assessment and treatment for patients with Hepatitis C Virus (HCV) infection. Referrals are accepted irrespective of patient's co-morbid disease, route of infection, current or past use of illicit substances. After referral, an outpatient appointment is posted with one further appointment offered if the first appointment is not attended. Patients who attend are asked to arrange follow-up appointments with reception staff immediately after the consultation. Those who fail to attend on two consecutive occasions are not offered another appointment unless they make contact or are re-referred.

**Aim** The aims of this study were:

- ▶ Determine the number of new hepatitis C positive patients referred, seen and still under review at the clinic within a 1 year time frame.
- ► Identify patients no longer under follow-up and the reason for this
- ▶ Determine the number of patients who were commenced on antiviral therapy.

**Method** Information for referral and attendance at clinics between April 2008 and March 2009 was obtained from the Health Intelligence Department. HCV status was confirmed by the laboratory computer system and follow-up status of patients was obtained from the patient administration system (PAS). The medical records of patients with no planned follow-up were reviewed to determine the reason for this. Information on patients who had commenced HCV antiviral therapy was obtained from the Grampian Hepatitis C database

Results In total 137 HCV antibody positive patients were referred to the service. 130 (95%) were HCV RNA positive, 5 (4%) were HCV RNA negative and in 2 (1%) the HCV RNA status was unknown. The median age of the HCV RNA positive patients was 34 (IQR 11.6, range 19-62), and 84 (65%) were male. Of the HCV RNA positive patients, 28 (22%) patients were never seen due to non-attendance, 102 (78%) were seen at least once and 59 (45%) are still under follow-up. The first appointment offered was attended by 56 (55%) patients. A higher proportion of males attended at least one clinic appointment 87% (73/84) compared to 63% (29/46) of females, (p=0.003). There was no statistical difference between the age of those seen and not seen. There were 43 patients no longer under continued review following their initial attendance with 31 as a result of failing to attend on more than one occasion, 1 deceased and 1 relocated. There is no documented explanation why the remaining 10 patients do not have follow-up arranged.

Of the 102 patients who attended clinic at least once, 44 (43%) were commenced onto antiviral therapy between 2008 and 2010.

**Conclusion** Our clinic policy resulted in almost 80% of patients being assessed whereas only 55% would have been seen had we not offered another appointment for those who failed to attend on the first occasion. Almost half of those seen were commenced onto antiviral therapy. The reasons for failure to attend among females require further examination. Patients without a review appointment with no apparent reason will be offered a further appointment.

Only 45% of patients in this cohort are under continued review. The service is currently undergoing redesign with the aim of improving the proportion of patients attending.

## **Transplant**

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TRANSARTERIAL CHEMOEMBOLIZATION AS NEO-ADJUVANT THERAPY PRE-TRANSPLANTATION IN PATIENTS WITH HEPATOCELLULAR CARCINOMA

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**Introduction** Hepatocellular carcinoma (HCC) is the main indication for 15% of liver transplants. Currently the criteria used for listing patients are the Milan criteria. However, as waiting time is increasing, patients may fall out these criteria while on the waiting list.

**Aim** We retrospectively evaluated the effect of neo-adjuvant transarterial chemoembolization (TACE) in consecutive patients transplanted for HCC.

**Method** We analysed data from consecutive patients who were transplanted for HCC between 1990 and 2010 as main indication in our unit. Laboratory, epidemiological, radiological and histological data were analysed. Survival was evaluated using multiple regression analysis.

**Results** In total 148 patients were transplanted for HCC, of which 74 had TACE as neo-adjuvant therapy. Mean follow-up post-transplant was  $31\pm29$  months (range 1-145). Patients had a mean of  $1.6\pm0.9$  (range 1-5) TACE sessions and had a mean waiting list time of  $2.5\pm2.4$  months (range 0.5-12.3). TACE response was evaluated in explanted livers as follow: no response in 10 (16%), partial tumour necrosis in 35 (55%) and complete tumour necrosis in 19 (30%). Tumour recurred in 21 (14%) patients in a mean time of  $5.1\pm14$  months. Recurrence happened in 2/10 patients who did not respond to TACE, 1/35 who had a partial response and 0/19 who had a complete response (p=0.040). TACE as neo-adjuvant therapy was associated with less recurrence irrespective of histological response (18.3% recurrence in patients who did not have TACE vs 5.6% in patients who had, p=0.037). No serious adverse effects of TACE were noted.

**Conclusion** TACE is an effective neo-adjuvant therapy in patients listed for liver transplantation, as it is associated with significantly less post-transplantation tumour recurrences. As waiting lists are getting longer, its use as a standard neo-adjuvant therapy should be further explored.

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OUTCOMES OF CADAVERIC SPLIT LIVER TRANSPLANTATION FOR HEPATITIS C INFECTED PATIENTS. A SINGLE CENTRE COHORT

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**Introduction** Concern exist as to the outcome of patients with liver cirrhosis secondary to hepatitis C virus (HCV) infection who receive split liver transplantation (SLT).

**Aim** To determine the graft and patient outcomes following SLT and to identify factors that influence outcome.

**Method** Retrospective study of all adults transplanted for HCV cirrhosis at our centre from 2000 to 2008.

Results Of 1284 patients, 242 were transplanted for HCV. 19 were excluded because of re-transplantation and 11 excluded as they received living donor grafts. Of the remaining 212, 21 received cadaveric SLT and 191 received whole liver grafts (WLT). Median age was 52 years (IQR 47-59). Men comprised 80%. No significant difference found in age, gender, serum Na and HCC between SLT and WLT groups (p=NS). However, there was significant difference in median transplant MELD between SLT, 11 (IQR 5.8) and WLT 14 (IQR 6.7, p=0.047). Virological and/or histological recurrence in graft (any fibrosis) was confirmed in 18/21 (86%). There was no significant difference in post-LT RNA between SLT & WLT (p=0.117) within 6 months of transplant. Median ICU stay was 3 days (IQR 2-5) and median hospital stay was 20 days (IQR 14-33). There was no significant difference in ICU or hospital stay between groups (p=NS). Kaplan-Meier analysis showed no significant difference in patient (Log rank=1.74, p=0.187) or graft (Log rank=2.47, p=0.12) survival in SLT vs WLT with median follow-up of 3.28 years (IQR 1.17-6.05). Univariate analysis revealed that recipient gender, donor risk index >1.7, donor age, height, BMI>25, cold ischaemia time (CIT) >10 h and graft steatosis were significant factors in relation to outcome. On multivariate analysis, only recipient gender (HR 0.142, p=0.001), donor age (HR 0.944, p=0.008), donor BMI >25 (HR 0.276, p=0.015) and CIT >10 hours (HR 0.218, p=0.004) remained significant. There was no significant difference in patient survival for SLT in HCV +/HCV- patients. However, graft survival was significantly improved in HCV+ patients (Log rank 4.12, p=0.042). Recipient gender (male 82% of HCV+, p=0.0001), HCC (54% of HCV+, p=0.0001) and mean MELD (HCV+ 11, HCV- 14, p=0.006) were significantly different. Donor variables were not significantly

**Conclusion** In our cohort, SLT for HCV+ patients provides a good alternative to WLT with comparable outcomes. Recipient selection accounted for improved graft outcomes for HCV+ group.

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NITISINONE TREATMENT REDUCES THE NEED FOR LIVER TRANSPLANTATION IN CHILDREN WITH TYROSINAEMIA TYPE 1 AND IS ASSOCIATED WITH IMPROVED POST-TRANSPLANT RENAL TUBULAR FUNCTION

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**Introduction** Tyrosinaemia Type 1 (TT1) is a disorder of tyrosine metabolism which may lead to liver failure and a high risk of hepatocellular carcinoma (HCC). Treatment previously consisted of dietary restriction and orthotopic liver transplantation (OLT) but was transformed by the introduction of Nitisinone in 1992. Here we report how Nitisione has altered the outcome of and need for OLT in patients with TT1 in our centre.

**Method** A retrospective analysis was performed of patients treated for TT1 at Birmingham Children's Hospital from 1989 to 2009.

**Results** 38 patients were treated with no significant difference in the annual number of patients seen before and after 1992 (p=0.47). 6/7 (85.7%) seen prior to 1992 and 7/31 (22.6%) initially treated with Nitisinone underwent OLT. The primary indication for OLT prior to 1992 was hepatic dysplasia in all with rising  $\alpha$ -fetoprotein in 4. Post 1992 indications were suspected/high risk of HCC in five patients, proven HCC in 1 and failure to