non-synonymous polymorphism in exon 4 of the *Tapasin* gene causing an arginine to threonine change that could affect tapasin function. We have investigated the effect of this SNP in resolving hepatitis C virus (HCV) infection in a cohort of 336 patients from the UK.

Aim We have investigated the effect of the SNP rs2071888 in resolving hepatitis C virus (HCV) infection in a cohort of 336 patients from the UK.

Method Genomic DNA from 216 chronically infected individuals and 120 spontaneous resolvers of HCV was genotyped with an allele specific PCR designed to identify the G/C SNP in exon 4 of the *Tapasin* gene. Individuals were also typed for HLA-A, -B and -C. Results were analysed for association with hepatitis C outcome.

Results Overall the G allele of tapasin was associated with protection against chronic HCV infection (p=0.018, OR=1.99, 95% CI 1.14 to 3.46). Interestingly, in combination with heterozygosity at the HLA-B locus, heterozygosity at the tapasin locus was also protective (Abstract OP04 figure 1, p trend =0.005). Furthermore, we identified specific HLA-B alleles associated with protection in the context of the Tapasin G, but not Tapasin C allele. Specifically the G allele was most protective in the context of B*0702 (p=0.029, OR=4.56, 95% CI 1.2 to 17.27), and B*5701 (p=0.029, OR=12, 95% CI 1.2 to 120). Tapasin has been shown to bind specifically to amino acids 114 and 116 of HLA class I. Consistent with this functional interaction we found that aspartate at position 114 and serine at 116 were most beneficial in the context of both the G allele (D114/TapG, p<0.0001, OR=3.3, 95% CI 1.83 to 5.98; S116/TapG, p<0.0001, OR=2.73, 95% CI 1.57 to 4.76).

Conclusion The G allele of tapasin was associated with protection from chronic HCV infection, both alone and in combination with specific HLA class I alleles. Individuals who are heterozygous for both tapasin and HLA-B are relatively protected from chronic HCV infection. This heterozygosity may allow them to present a broader range of peptides to CTL and thus mount a more effective anti-HCV immune response.

Transplant

OP05 THE IMPACT OF COMORBIDITIES ON OUTCOME OF PATIENTS ASSESSED FOR LIVER TRANSPLANTATION, WAITING LIST MORTALITY AND POST LIVER TRANSPLANTATION SURVIVAL USING THE CHARLSON COMORBIDITY INDEX

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Introduction Severity of liver disease determines accurately the outcome of patients on liver transplant (LT) waiting list (WL). Comorbidities are known to affect post-LT outcomes but their effect on outcome of transplant assessment (TA) or WL mortality have not been fully explored in previous studies.

Aim To study the impact of comorbidities on TA, WL mortality and post LT survival.

Method Retrospective study of all patients assessed for LT at our centre between 1 January 2000 and 31 December 2007 (n=1484). Patients with acute liver failure (175), amyloid (43), those assessed for re-LT (149) and 24 with incomplete information were also excluded. Nine comorbidities (Charlson Comorbidity Index - CCI) were prospectively defined according to Volk *et al* (*Liver Transplant* 2007;**13**:1515–20). Kaplan–Meier analysis was performed to determine impact of comorbidity on outcome. Cox regression hazard analysis was used to determine predictors of outcome and presented as (OR, 95% CI, p value).

Results We analysed 1093 patients. Median age was 54 years (17–84), 67.5% were men (738). There were 192 (17.6%) patients with hepatocellular carcinoma (HCC). Patients with ≥1 comorbidity were 499 (46.6%) with most common comorbidities being diabetes (23.2%) and renal dysfunction (12.1%). Of 1093 assessed patients, 826 (75.6%) were listed. Patients with ≥1 comorbidity had significantly decreased LT free survival (log rank =33.586, p<0.001). Multivariate analysis showed CCI (1.79, 1.52 to 2.11, p<0.001), age (1.03, 1.00 to 1.05, p=0.035), Na (0.93, 0.89 to 0.97, p=0.001), MELD (1.10, 1.06 to 1.14, p<0.001) as being predictive. Of those listed for LT (826), 600 (72.6%) were transplanted, 161 (19.5%) died on WL and 65 (7.9%) were delisted. Listed patients with ≥1 comorbidity had significantly decreased LT free survival (log rank =9.045, p=0.003). Multivariate analysis showed CCI (1.79, 1.52 to 2.11, p<0.001), age (1.02, 1.01 to 1.03, p=0.006), pre-LT Hb level (0.87, 0.80 to 0.95, p=0.003), Na (0.96, 0.93 to 0.99, p=0.014) and MELD (1.14, 1.11 to 1.18, p<0.001) were predictors of listing outcome. Transplanted patients with ≥1 comorbidity had significantly decreased post LT survival (Log rank =7.645, p=0.006). Multivariate analysis showed that only CCI (1.36, 1.13 to 1.64, p=0.001) and HCC (1.74, CI 1.21–2.51, p=0.003) were independently associated with post-LT mortality. Similar post LT survival results seen when CCI was divided into 0, 1 and ≥2 comorbidities (Log rank =11.342, p=0.003).

Conclusion We demonstrate that comorbidities significantly impact on the outcome of patients with chronic liver disease at TA, on wait-list and post LT survival. Adding CCI to known liver prognostic models may improve their prediction ability.

Basic science

OP06 MATERNAL OBESITY PROGRAMS OFFSPRING INNATE IMMUNE DYSREGULATION IN NON-ALCOHOLIC FATTY LIVER DISEASE

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Introduction Obesity induced, non-alcoholic fatty liver disease (NAFLD), is the major cause of chronic liver dysfunction. In tandem, obesity and NAFLD rates in reproductive age women are rising. We have previously reported increased susceptibility to NAFLD in offspring exposed to maternal obesity via programming.

Aim Our aim is to investigate the effects of maternal obesity on hepatic innate immune function in a more physiologically relevant model of NAFLD.

Method Female mice were fed standard or obesogenic chow, before, throughout pregnancy and in lactation. Offspring were then weaned onto either standard or obesogenic chow and studied at 3, 6 and 12 months. Read-outs included biochemical and histological indicators of NAFLD and fibrosis, hepatic triglycerides, gene expression analysis of pro-fibrotic pathways, FACS analysis of liver innate immune cells and flow cytometric detection of ROS.

Results Offspring only exposed to a post-weaning hyper-calorific diet (Group 2) exhibited raised leptin, ALT and hepatic triglyceride content compared to controls (Group 1) (p<0.001). Moreover, hepatic gene expression of injury and fibrogenic markers were increased (Abstract OP06 table 1, p<0.01). As expected, a more robust phenotype was observed at 12 compared to 3 months. Additionally, offspring exposed to maternal obesity plus a post-weaning hyper-calorific diet (Group 3), displayed a more profound NAFLD phenotype with development of fibrosis and a NAFLD Activity Score >5. Mechanistically, we observed increased Kupffer cell numbers with impaired phagocytic function and raised ROS production, alongside reduced NKT cell numbers, in Group 3 compared to Group 1 (p<0.01).

Abstract OP06 Table 1 Gene expression analysis of hepatic injury and fibrogenic markers

	3 Months Postpartum			12 Months Postpartum		
Gene	Group 1	Group 2	Group 3	Group 1	Group 2	Group 3
IL-6	1.00±0.21	1.44±0.41	2.01±0.45	0.38±0.48	1.53±0.37	9.65±2.31
TNF-α	1.00±0.30	1.32±0.79	2.13±0.33	1.14±0.36	4.59±0.98	8.65±1.12
α-SMA	1.00±0.24	3.06±0.98	2.86±0.28	0.87±0.22	1.96±0.87	23.86±8.5
Collagen	1.00±0.36	3.45±0.69	3.05±0.53	0.37±0.15	4.96±2.42	6.62±3.23

Conclusion Maternal obesity programs development of offspring NAFLD with progression to fibrosis in the context of a post-weaning hyper-calorific diet. Innate immune dysfunction may be responsible for the observed programmed phenotype.

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OP07 PHENOTYPIC DESCRIPTION OF A LARGE COHORT OF PSC PATIENTS IN THE UK

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Introduction Primary Sclerosing cholangitis (PSC), a chronic cholestatic liver disease of unknown aetiology or pathogenesis, remains an area for active research.
Aim The demographic and phenotypic characteristics of a UK cohort of 1194 patients with PSC are described.
Method All patients were recruited as part of an ongoing national collaborative effort (PSC-UK) between October 2008 and May 2011. The diagnosis of PSC was confirmed on the basis of characteristic ERCP, MRCP or histology. Patients with small-duct PSC were also included. All patients completed a descriptive phenotypic questionnaire sent at recruitment. Demographic, phenotypic data and family history were extracted from the participant questionnaires.
Results 1194 patients have returned completed questionnaires. Median age at recruitment was 59 years and 63% were male (male to female ratio =1.7:1). 64% of patients were lifelong non-smokers and only 4.3% were smoking at recruitment. 63.5% reported inflammatory bowel disease, split into 87% with Ulcerative colitis and 13% with Crohn's disease. 1.5% had a sibling with PSC and 14% had a sibling with inflammatory bowel disease. Further, 0.5% had one or more children with PSC and 4.6% had children with inflammatory bowel disease. 24% were asymptomatic, but over 50% reported itching and fatigue as the presenting symptom. Jaundice was present in 35%. The most common associated autoimmune disease was thyroid disease, present in 9% followed by Coeliac disease in 2.1% and type 1 diabetes mellitus in 1.8%. 16% of patients reported pan-procto or sub-total colectomy and 12.2% had undergone cholecystectomy. 2.7% of patients reported a history of colon cancer and 1.25% patients had a history of skin cancer.
Conclusion This is the largest reported demographic and phenotypic description of a single cohort of PSC patients. PSC is more common in young, non-smoking male patients. The frequency of associated inflammatory bowel disease is similar to that reported in other studies. It is plausible that siblings of patients with PSC have an increased risk of not only PSC but also inflammatory bowel disease. These data are consistent with increasing evidence pointing to a role of genetic factors in the pathogenesis of PSC.

OP08 NAFLD RELATED HCC IS RISING DRAMATICALLY IN THE NORTH OF ENGLAND

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Introduction A reported increase in hepatocellular cancer (HCC) in western nations has been attributed to the rising prevalence of predisposing hepatitis C (HCV) related chronic liver disease. In parallel, however, the prevalence of the metabolic syndrome has risen markedly, and both a raised BMI and type 2 diabetes, characteristic features of the syndrome, are independently associated with an increased risk of HCC development.
Aim We have assessed the prevalence of the metabolic syndrome in our patients with HCC.
Method 686 consecutive patients with HCC, diagnosed as per EASL guidelines, referred to our unit over a 10-year period (2000 and 2010), have been studied and demographic, laboratory, radiological variables, treatments and survival recorded.
Results The numbers of patients referred from our catchment population of 3.5 million has increased more than 10-fold in 10 years, reaching 133 in 2010. While numbers with underlying hepatitis B, haemochromatosis, autoimmune or cryptogenic cirrhosis have remained constant, those with underlying HCV or ALD have increased fivefold up to 10 and 35 per year respectively. The most dramatic increase, however, has been in those patients with NAFLD, increasing from 1 or 2 to over 30 per year in 2009 and 2010. There has also been an increase in HCC arising in individuals without chronic liver disease, 40 and 65% of which had diabetes and the metabolic syndrome respectively. Patients with NAFLD related HCC were significantly older (median age of 72 yrs vs 65 and 61 for ALD and HCV respectively. While NAFLD HCC cases were less likely to be detected by surveillance, they were more likely to be detected incidentally. Survival was determined by stage at presentation for all etiologies, and was not adversely affected by advanced age in the NAFLD population.
Conclusion NAFLD related HCC now equals that related to ALD in Northern England. The median age at presentation was higher for NAFLD HCC patients, but this did not adversely affect their survival. While relatively few NAFLD HCC cases were detected by surveillance, and the prognosis was particularly poor for those presenting with symptomatic disease (median 8.14 months), this was offset by an increase in incidental HCC detection, largely in diabetic follow-up clinics. The median survival of incidental patients (median 21.2 months) was similar to that of detected by surveillance (18.68 months). A raised awareness of the risk of HCC in older diabetic patients may reduce the numbers of those presenting with advanced symptomatic disease.

OP09 TIPS OUTCOMES FOR REFRACTORY ASCITES: A SINGLE CENTRE EXPERIENCE

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Introduction Transjugular intrahepatic portosystemic shunt (TIPS) insertion is established as an important intervention in the