Kent has a catchment population of 655 000 and a local viral hepatitis service.

Aim We wished to assess the management of Hepatitis B infection within West Kent following the introduction of these guidelines and audit local compliance.

Method We identified all patients who tested positive for Hepatitis B surface Antigen (HBsAg) over a 2-year period (January 2006 until December 2007) from microbiology records. We examined the referral source, and whether basic demographic, biochemical, and virological parameters had been recorded. In addition, we examined whether the patient was referred to the viral hepatitis service. The referral source was grouped into six categories: Primary Care, Obstetrics, Genito-Urinary Medicine, Occupational Health, General Medicine and "Other".

Results 21 366 screening tests for Hepatitis B were performed during the 2-year period. Obstetrics accounted for 8299/21 366 (38.8%) of requests, followed by Genito-Urinary Medicine 6998/21 366 (32.8%), Primary Care 4284/21 366 (20.1%), and "Other" with 1128/21 366 (5.2%). Occupational Health (329/21 366) and General medicine (328/21 366) accounted for 1.5% of all screening requests. 89/21 366 (0.4%) of tests were positive for HBsAg. The median age of patients testing positive for HBsAg was 34 years. Ethnicity data were missing in 60% (53/89) of positive results. 59% (52/89) of positive results had been requested in Primary Care, followed by 21% (19/89) in General Medicine, and 11% (10/89) in Genito-Urinary Medicine. 57% (41/89) of patients testing positive for HBsAg had liver function tests checked within 6 months. 44% (39/89) of patients were referred on to specialist hepatology services. 28% (25/89) had radiological imaging following the positive HBsAg result. 6% (5/89) patients met the diagnosis criteria for acute hepatitis B but only two of these patients were referred on to specialist services.

Conclusion During the 2-year study period, 3.3% of the population in West Kent was tested for Hepatitis B infection. The majority of positive cases were in samples referred from primary care. However, less than half the patients with a positive HBsAg result were referred to specialist services. This contravenes HPA guidelines and leaves patients at risk of developing the sequelae of untreated Hepatitis B infection. Our experience shows that the HPA standards are yet to fully penetrate into routine clinical practice. With thanks to the Department of Microbiology, Maidstone Hospital.

P19 SERUM CREATININE UNDERESTIMATES RENAL FUNCTION IN PATIENTS WITH CIRRHOSIS AS COMPARED TO PATIENTS WITH ORGANIC RENAL DISEASE

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Introduction Although serum creatinine is a well-recognised marker of prognosis in cirrhosis, it is only an indirect marker of renal function as it is affected by various extra-renal factors. The measurement of glomerular filtration rate (GFR) by the plasma clearance Cr-EDTA is an acceptable substitute of the gold standard of inulin clearance. We assessed the correlations of serum creatinine with GFR measured by Cr-EDTA in patients with cirrhosis in comparison with patients with renal disease.

Method We analysed data from 298 consecutive patients who underwent GFR assessment by Cr-EDTA as part of their liver transplant work-up. We collected similar data on 187 consecutive non-cirrhotic patients who attended the renal outpatient clinic. GFR was assessed by bolus infusion of Cr-EDTA and single or serial serum measurements after 2, 4, 6 and 24 h. Spearman test was used to correlate serum creatinine and GFR in renal and liver patients. The significance of the difference between the correlations from the two groups was calculated by transforming the Spearman's r to Fischer's z-score, estimating the SE of difference between the two correlations and finally dividing the differences between the two z-scores by the SE. If the result was 1.96 or higher, then the difference in the correlation was considered significant in the 0.05 level.

Results Serum creatinine significantly and inversely correlated with GFR in patients with cirrhosis ($r=-0.702$, $p<0.001$) and renal disease ($r=-0.856$, $p<0.001$), however the difference of the correlation was significant between patients with renal disease and patients with cirrhosis ($p<0.05$). When analysis was performed according to gender, there were significant correlations of serum creatinine and GFR in patients with cirrhosis (males $r=-0.806$ and females $r=-0.699$) and renal disease (males $r=-0.877$ and females $r=-0.890$). Moreover, the difference of the correlation was again significant among male and female patients with renal disease and cirrhosis and notably in male compared to female patients with cirrhosis ($p<0.05$). Therefore, for a given GFR, patients with cirrhosis have lower serum creatinine values than patients with renal disease. Moreover, female patients with cirrhosis have lower serum creatinine values than male patients with the same GFR.

Conclusion Serum creatinine underestimates renal function in patients with cirrhosis compared to patients with renal disease. Serum creatinine cut-offs used to define renal failure in the general population are not applicable to patients with cirrhosis and should be re-evaluated as they systematically underestimate renal function.

P20 FUNCTIONAL CAPACITY IS SIGNIFICANTLY IMPAIRED IN PRIMARY BILIARY CIRRHOSIS AND RELATED TO ORTHOSTATIC SYMPTOMS

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Introduction Primary biliary cirrhosis (PBC) is associated with a significant and diverse symptom burden independent of conventional markers of disease severity. It is unclear how this symptom load impacts upon function in day to day living and, if functional impairment is present, which symptom(s) are predominantly responsible.

Aim We assessed patient-reported functional ability and its interrelationship with symptoms in PBC.

Method 81% (75/93) of the PBC symptom study cohort, originally derived in 2005, consisting of all PBC patients resident within the geographical area defined by zip codes NE1-NE25 (Newcastle-upon-Tyne and surrounding suburbs) completed a further set of postal-return symptom assessment tools in 2009. This included the disease specific symptom assessment tool the PBC-40, a marker of autonomic symptom burden, the Orthostatic Grading Scale (OGS), and the patient reported outcome measure health assessment questionnaires (PROMIS HAQ), that assesses functional ability (which was also completed by a liver disease control group (primary sclerosing cholangitis n=31 (PSC) and matched controls (n=55)).

Results Over 4 yrs of follow-up, total symptom burden, assessed using the cumulative PBC-40 domain scores, increased significantly ($p=0.03$). The predominant factor was a significant rise in Cognitive domain scores indicating worsening cognitive symptoms ($p<0.0001$). Functional impairment (PROMIS HAQ) was substantial in the PBC patients and exceeded that seen in the PSC controls. When the individual functional domains of the PROMIS HAQ were

considered, we found that the PBC group had significant impairment in arising, eating, walking, reach and grip activity but not in dressing or hygiene. Functional impairment correlated positively with greater PBC-40 Fatigue, Cognitive and Social & Emotional domain scores and higher autonomic symptom burden determined by OGS score. Change in the PBC-40 Cognitive and Social & Emotional domain scores between 2005 and 2009 strongly predicted functional ability in 2009 Multivariate analysis confirmed that total PROMIS HAQ scores were predicted independently by PBC-40 Social & Emotional domain scores ($p=0.02$; $\beta=0.3$) and orthostatic symptoms ($p=0.04$; $\beta=0.3$).

Conclusion PBC is associated with a substantial impairment of functional capacity to a greater degree than has previously been appreciated. The distribution of symptoms of PBC evolves over time, with cognitive symptoms making an ever-greater contribution to the overall burden. The major determinant responsible for both functional impairment and the specific symptoms contributing to it appears to be autonomic dysfunction which is potentially modifiable by treatment.

P21 THE EVALUATION OF SERUM FERRITIN AND TRASFERRIN SATURATION IN THE DIAGNOSIS OF HAEMOCHROMATOSIS IN AN ETHNICALLY DIVERSE POPULATION

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Introduction Hereditary haemochromatosis (HH) is the most common genetic abnormality in populations of Northern European ancestry. There are limited data on the frequency of HFE in populations from the Indian subcontinent. Elevated serum ferritin (Fe) and transferrin saturation (TSAT) are often used as the basis for referral for HFE gene analysis.

Aim We undertook this study to evaluate the performance of elevated Fe and TSAT in the diagnostic algorithm of HH in a Caucasian population and how it compared when applied to an Indian population.

Method Data on all patients referred from the gastroenterology service for HFE gene analysis between 2001 and 2009 were evaluated. Serum Fe and TSAT were recorded where available to assess their utility in predicting HFE gene mutations and subsequent requirement for venesection. An estimation of the prevalence of iron overload due to HFE gene mutations in our large Indian population was sought.

Results 307 patients with elevated Fe levels underwent HFE genetic analysis. 146/307 (48%) patients had a TSAT performed at the time of referral. 34/307 (11%) were homozygotes for C282Y mutation, while 18 (6%) were compound heterozygotes. Almost half of those tested 147/307 (48%) had no genetic mutation.

Abstract P21 Table 1 Results Median serum Fe and TSAT values for different HFE genotypes

	Ferritin (μmol/l)	TSAT (%)
WT/WT*	472	33.5
WT/H63D or C282Y	424	37
H63D/H63D	484	41
Hd3D/C282Y	684.5	52.5
C282Y/C282Y	871	82

WT*; wild type.

A TSAT >45% was found in 42/146 tested patients. All C282Y/C282Y patients tested had a TSAT >45%, almost a quarter of whom (23.5%) had a TSAT <55%. All WT/WT patients with a TSAT >45% had alcoholic liver disease. The positive predictive value of a TSAT >45% in detecting a C282Y/C282Y or C282Y/H63D mutation was 54.7% compared to 14.5% for ferritin. The negative predictive value of a TSAT >45% in excluding a C282Y/C282Y or C282Y/H63D mutation was 96.2%. 32/307 (10.4%) patients from the Indian sub-continent underwent HFE genetic testing. The mean Fe was 421 with a mean TSAT of 40.3% compared to 564 and 47.7%, respectively, for the Caucasian population ($p<0.05$.) In this subgroup, there was one H63D/H63D mutation and 6 (19%) H63D/WT heterozygotes. None had a C282Y mutation. TSAT had a NPV of 100% in excluding clinically significant HH.

Conclusion TSAT has an excellent NPV and should be an integral part of the diagnostic algorithm for HH, where a cut-off value of 45% detects all C282Y homozygotes, while a higher cut-off value may miss some patients. This translates well into Indian populations. HFE gene mutations are extremely rare in patients of Indian descent and other aetiologies for elevated Fe/TSAT should be sought.

P22 DERANGEMENTS IN ENERGY, AMINO-ACID AND GUT MICROBIAL METABOLISM IN HEPATIC ENCEPHALOPATHY: A METABOLOMIC APPROACH

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Introduction Hepatic encephalopathy (HE) pathogenesis is related to gut microbial products, which lead to deranged cerebral bioenergetics. Biofluid MR spectroscopy (MRS) can be used to determine changes in bioenergetics, gut microbial products, amino acid and lipid metabolites. Lactulose is used as a first-line HE Rx despite a poor evidence basis.

Aim To evaluate the clinical and metabolic consequences of lactulose withdrawal in HE.

Method Patients with cirrhosis on lactulose for precipitated HE underwent cognitive testing with inhibitory control (ICT), urine and serum collection for MRS and inflammatory markers while on lactulose. Lactulose was then withdrawn and patients followed for 30 days with visits at day 2, 14 and 30; ICT, serum and urine testing were repeated at every visit. Relapse of HE was defined clinically. Multivariate analysis of urine and serum metabolites involved principal components analysis (PCA) and partial least squares discriminant analysis (PLS-DA). Univariate analysis was applied to hypothesis-driven metabolites, multivariate-driven metabolites and inflammatory marker concentrations.

Results 7 cirrhotic men (age 53±7 years, 5 HCV, 2 alcohol) on lactulose for 6±5 months for precipitated HE (5 GI bleed, 2 infections) were included. Three patients clinically relapsed 38±6 days post-withdrawal; all 3 had >15 ICT lures while on lactulose. None of those who scored <15 ICT lures on lactulose relapsed. Lure increase OR, 2.5 (CI: 1.7 to 3.6) predicted relapse. Using ICT lures >15 as a cut-off for HE relapse, MRS distinguished with a sensitivity and specificity of 70.0%/63.6% using urine and 100%/100% using serum on PLS-DA. Urine PLS-DA: In relapsers, urine TMAO was reduced indicating altered gut bacterial metabolism while malonic acid and citrate were higher demonstrating impaired energetics. Glycine and phenylalanine, associated with false neuro-transmitters, were also increased in relapsers along with creatinine. Serum PLS-DA: Relapsers had higher choline and its metabolite, dimethylglycine levels which is associated with extrusion of choline after astrocyte swelling in HE as well as higher levels of lipids. Univariate analysis confirmed that relapsers had lower TMAO ($p=0.00280$) and higher choline ($p=0.0414$), LDL (0.0265) and creatinine ($p=0.00970$). Inflammation was depressed in relapsers compared to others evidenced by decreased endotoxin ($p=0.03$), IFN-γ ($p=0.045$), IL-4 (0.0002) and TNF-α