glutamine levels ($r=0.78$, $p=0.002$). Myo-inositol concentration decreased significantly by 0.7 ($\pm 0.7$) mMol/l between scans and this correlated with the mean difference in ADC ($r=0.59$, $p<0.04$).

**Conclusion** These results show that hyperammonia can be derived from nitrogenous substrates in the colon and can directly drive changes in brain water distribution as a mechanism for cerebral oedema development. Since cerebral astrocytes contain glutamine synthetase, our MRS data suggests intracerebral formation of glutamine from ammonia. Development in therapy for hepatic encephalopathy need to focus on amelioration of colonic ammonia formation.

**REFERENCES**

**P12** MEASURING THE EFFECTIVENESS OF A MULTIDISCIPLINARY NASH CLINIC

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1C M Peake, 2J F L Cobb-old, 3Q M Anstee, 4M Yee, 5M R Thursz. 1Imperial College, London, UK; 2Hepatology and Gastroenterology Section, Department of Medicine, Imperial College, London, UK; 3Institute of Cellular Medicine, Newcastle University, Newcastle-Upon-Tyne, UK; 4Division of Diabetes, Endocrinology and Metabolism, Department of Medicine, Imperial College, London, UK

**Introduction** Non-alcoholic fatty liver disease (NAFLD) and specifically non-alcoholic steatohepatitis (NASH) are associated with both increased liver-related and cardiovascular morbidity and mortality. A multi-disciplinary, individualised approach targeting the complex pathogenesis of the disease has been employed in a tertiary/secondary care setting. The aims of this study were (1) to investigate the effectiveness of a multi-disciplinary NASH clinic by assessing the change in liver disease markers and risk factors for liver-related and cardiovascular mortality over time, and (2) to identify factors that influence patient response to treatment.

**Method** This was a retrospective survey of current clinical practice. NASH/NASHLD was defined histologically or NAFLD by echogenic liver on ultrasound with raised aminotransferase values in absence of a significant alcohol history or other hepatic co-morbidities. Interventions included: lifestyle advice; dietetic input; exercise classes; pharmacological therapy; bariatric surgery. Clinical and anthropometric data were collected including serum ALT, BMI, HBA1c, systolic blood pressure, total and HDL cholesterol values and analysed for the cohort overall and for patients who were obese, diabetic, hypertensive and dyslipidaemic respectively. Responders to treatment were defined as those with a >10% decrease in ALT overall over the study period. Univariate and multivariate analysis were conducted to analyse baseline factors influencing patient response.

**Results** 145 patients were included with median follow-up of 12.5 months (range 3–44 months). Overall improvement was seen in ALT ($-15\%$, $p=7\times10^{-6}$), BMI ($-1.5\%$, $p=6\times10^{-5}$) and total cholesterol ($-4.1\%$, $p=0.006$). BMI improved by $>10\%$ in $8\%$, by $>7\%$ in $16\%$ and by $>5\%$ in $25\%$ of patients. Patients categorised by abnormal baseline ALT, baseline obesity, baseline hypertension and baseline dyslipidaemia had improvements in ALT ($-19\%$, $p=1\times10^{-6}$), BMI ($-2.4\%$, $p=0.001$), systolic BP ($-5.4\%$, $p=5\times10^{-5}$) and total cholesterol ($-5.5\%$, $p=0.002$) respectively. Patients with type 2 diabetes made up a higher proportion of those who did not respond or who progressed compared to those who responded on univariate analysis ($p=0.02$), but this was not significant on multivariate analysis. Moreover, patients with diabetes did not have a significant decrease in ALT ($-8\%$, $p=0.06$).

**Conclusion** The management framework adopted by the multi-disciplinary NASH clinic is effective at reducing ALT overall. Cardiovascular risk factors were improved overall. Diabetic patients had a poor ALT response. These data support the use of a multidisciplinary NASH clinic, but long-term outcome data are awaited.

**P13** THE PERFORMANCE VALIDITY OF BREATH SAMPLE ANALYSIS IN THE DIAGNOSIS OF HEPATIC ENCEPHALOPATHY IN PATIENTS WITH CIRRHOSIS
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1H Halliday, 2S Stevens, 3M Stubbs, 4R Morris, 5M Morgan. 1Centre for Hepatology, University College London Medical School, London, UK; 2Centre for Research in Analytical, Materials and Sensor Science, University of the West of England, Bristol, UK; 3Research Department of Primary Care and Population Health, University College London, London, UK

**Introduction** Hepatic encephalopathy (HE) has a detrimental effect on patients’ health-related quality of life and a significant negative impact on survival. Nevertheless, there is no diagnostic gold standard so the condition is often poorly diagnosed and managed.

**Aim** The aim of this study was to evaluate the performance validity of breath sample analysis for volatile organic compounds (VOCs) in the diagnosis of hepatic encephalopathy (HE) in patients with cirrhosis.

**Method** The patient population comprised 26 individuals (17 men, 9 women) of mean (range) age 60 (45 to 75) years, with biopsy-proven cirrhosis secondary to alcohol (n=21), or non-alcoholic steatosis, hepatitis C, autoimmune hepatitis, haemochromatosis or cryptogenic cirrhosis. Responders to treatment were defined as those with a >10% decrease in ALT overall over the study period. Univariate and multivariate analysis were conducted to analyse baseline factors influencing patient response. 145 patients were included with median follow-up of 12.5 months (range 3–44 months). Overall improvement was seen in ALT ($-15\%$, $p=7\times10^{-6}$), BMI ($-1.5\%$, $p=6\times10^{-5}$) and total cholesterol ($-4.1\%$, $p=0.006$). BMI improved by $>10\%$ in $8\%$, by $>7\%$ in $16\%$ and by $>5\%$ in $25\%$ of patients. Patients categorised by abnormal baseline ALT, baseline obesity, baseline hypertension and baseline dyslipidaemia had improvements in ALT ($-19\%$, $p=1\times10^{-6}$), BMI ($-2.4\%$, $p=0.001$), systolic BP ($-5.4\%$, $p=5\times10^{-5}$) and total cholesterol ($-5.5\%$, $p=0.002$) respectively. Patients with type 2 diabetes made up a higher proportion of those who did not respond or who progressed compared to those who responded on univariate analysis ($p=0.02$), but this was not significant on multivariate analysis. Moreover, patients with diabetes did not have a significant decrease in ALT ($-8\%$, $p=0.06$).

**Conclusion** The management framework adopted by the multi-disciplinary NASH clinic is effective at reducing ALT overall. Cardiovascular risk factors were improved overall. Diabetic patients had a poor ALT response. These data support the use of a multidisciplinary NASH clinic, but long-term outcome data are awaited.
PHENOTYPIC AND FUNCTIONAL PROFILE OF CD4POSCD25HIGH REGULATORY T CELLS IN AUTOIMMUNE HEPATITIS/SYSTEMIC LUPUS ERYTHEMATOSUS OVERLAP SYNDROME

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M S Longhi, Y Ma, M Samyn, P Gordon, G Mielk-Vergani, D Vergani. King’s College London School of Medicine, King’s College Hospital, Denmark Hill, London, UK

Introduction Autoimmune hepatitis (AIH) is a severe inflammatory liver disorder characterised by hypergammaglobulinaemia, seropositivity for autoantibodies and interface hepatitis on histology. Though the mechanisms leading to immune-tolerance breakdown have not been fully elucidated, a numerical and functional defect of circulating CD4posCD25high regulatory T-cells (T-regs) plays a key role in permitting effector lymphocytes to attack hepatocytes. We have identified a cohort of children with concomitant AIH and systemic lupus erythematosus (SLE), a multi-system autoimmune disease in the context of which most studies have reported numerical and functional T-reg impairment.

Aim To define the phenotypic and functional profile of T-regs in children with AIH and SLE (AIH/SLE).

Method 9 AIH/SLE patients (8 females; median age: 13.9 years), 16 AIH patients (15 females; median age: 13.3 years) and 9 healthy subjects (HS, 6 females; median age: 54 years) were studied. T-reg phenotype was determined by flow cytometry after cell incubation with anti-CD4, CD25 and CD127 monoclonal antibodies. Frequency of FOXP3pos and IFNy, IL-4, IL-17 and IL-9-producing cells was assessed by intracellular staining. T-reg suppressor function was evaluated as reduction of cell proliferation, measured by 3H-thymidine incorporation.

Results The number of T-regs in AIH/SLE patients (7.0±1.1) tended to be higher than in AIH (4.8±1.1; p=0.01) and was similar to HS (7.0±1.6). While the proportion of FOXP3pos cells within T-regs did not differ, that of CD4posCD25highCD127pos cells was higher in AIH/SLE (2.4±0.99) than in AIH (0.46±0.2; p=0.019) and HS (0.63±0.3; p=0.05). The frequency of IFNy-producing cells within T-regs was higher in AIH/SLE (6.75±1.7) than in AIH (4.8±1.9; p=0.019) and HS (5.5±0.82; p=0.05); conversely that of IL-4-producing cells within T-regs was lower in AIH/SLE (0.2±0.47) than in AIH (0.86±0.3; p=0.02) and HS (0.9±0.47; p=0.06). The frequency of IL-17 and IL-9-producing cells was negligible and did not differ among the groups. Addition of CD127posT-regs, while decreasing CD25pos cell proliferation by 51.6% in HS (p=0.02) and by 12.5% (p=0.056) in AIH, did not affect the proliferation of CD25neg cells isolated from AIH/SLE patients.

Conclusion Compared to AIH and HS, T-regs from AIH/SLE are more activated, are skewed towards a Th1 cytokine profile and are functionally defective. These data suggest that more severe alteration of T-reg phenotype and function may predispose to autoimmune manifestations.