Results Both the TLR4 antagonist's (STM28 and IAXO compound) reduced the plasma liver enzymes, ammonia and creatinine to the control level. The increase in the plasma TNF-α induced by APAP (45±3.2) was attenuated following TLR4 antagonist (20±2.3) (p<0.01). This was associated with a reduction in brain water (p<0.01). Both the TLR4 antagonists significantly reduced pericentral necrosis of the liver. Both these interventions showed an improvement in the survival as using the log rank test (p<0.02). TLR4 KO mice treated with APAP were protected from liver necrosis and had significantly better survival than wild type controls (p<0.002).

Conclusion These data provides evidence for an important of TLR4 in APAP induced ALF and provide the rationale for a clinical trial of this strategy in ALF.

Competing interests None declared.

OC-067 | **THE BALANCE BETWEEN T HELPER 17 AND FOXP3+ T REGULATORY CELLS IN PATIENTS WITH CHRONIC HEPATITIS C: RELATION TO DISEASE ACTIVITY AND HEPATIC FIBROSIS**

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Introduction T helper (Th)17 cells, a newly identified subset of Th cells, are major mediators of inflammation-associated disease and have a reciprocal developmental relationship with the immuno-suppressive T regulatory (Treg) cells, which actively restrain the inflammatory response. The present work was designed to study the balance between Th17 cells and Treg cells in patients with chronic hepatitis C (CHC) in relation to disease activity and severity of hepatic fibrosis.

Methods Twenty patients with treatment-naive CHC and 20 healthy subjects were included in the study. The Th cells, Th17 cells and Treg cell subsets in fresh whole blood samples were identified as $CD3^+CD4^+$, $CD4^+IL17A^+$ and $CD4^+CD25^+FoxP3^+$ cells respectively using flow cytometry and expressed as percentages of total lymphocytic count. Serum IL17 levels were measured using solid phase sandwich enzyme linked immunosorbant assay kit. Liver biopsies from patients with CHC were examined to assess histological activity grade and fibrosis stage according to METAVIR scoring system. Liver-infiltrating $CD4^+$ (Th cells), $IL17A^+$ cells (Th17 cells) and $FoxP3^+$ cells (Treg cells) were detected by immunohistochemical staining and their proportions were determined as ratios of infiltrating $CD4^+$ Th cells.

Results Patients with CHC showed significant increases in the percentage of Th17 cells, Th17 cells/$FoxP3^+$Treg cells ratio in peripheral blood and serum IL17 levels and a significant decrease in the percentage of circulating $FoxP3^+$Treg cells compared with healthy subjects (p<0.01). The percentages of peripheral blood $CD4^+$ Th cells were not statistically different between the two groups (p=0.284). The proportions of liver-infiltrating $IL17A^+$ cells and $FoxP3^+$ cells of the total intrahepatic $CD4^+$ cell population were inversely correlated and showed positive correlations with the percentages of circulating Th17 cells and $FoxP3^+$ Treg cells respectively in patients with CHC (p<0.05). The METAVIR necroinflammation grade and fibrosis stage [but not serum HCV RNA levels] were directly correlated with the proportion of intrahepatic $IL17A^+$ cells and $IL17A^+$ cells/$FoxP3^+$ cells ratio and serum IL17 levels and were inversely correlated with the proportion of liver-infiltrating $FoxP3^+$ cells (p<0.05).

Conclusion In patients with CHC, the $CD4^+$ Th cell phenotype is skewed towards the IL17 producing-Th phenotype. The imbalance between Th17 and $Foxp3^+$ Treg cells plays an important role in disease progression and hepatic fibrosis in CHC.

Competing interests None declared.

OC-068 | **ALBUMIN IS CENTRAL IN MEDIATING THE CARDIO-RENAL DYSFUNCTION OF CIRRHOSIS: A STUDY IN ANALBUMINAEMIC RATS**

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Introduction Albumin is a multifunctional protein which is reduced in concentration and function in liver disease. Albumin infusion prevents and improves renal dysfunction in patients with advanced liver failure but the mechanisms of its beneficial properties are unclear. We hypothesised that albumin is central in the maintenance of cardio-renal function in cirrhosis and albumin impairment worsens outcome. In order to answer this question we investigated analbuminaemic rats, characterised by lack of albumin but with normal protein concentration, following induction of cirrhosis with bile duct ligation (BDL).

Methods Male Sprague-Dawley (SD) and Nagase analbuminaemic (NAR) rats were studied 6 weeks after BDL or sham surgery (n=6 sham-SD, 8 sham-NAR, 7 SD-BDL, 7 NAR-BDL). Rats underwent systemic mean arterial pressure (MAP) and portal pressure (PP) assessment under terminal anaesthesia. Plasma and urine were collected for measurements of renal function and protein profile. Plasma renin activity (PRA) was measured as a marker of cardio-renal dysfunction. Urinary neopterin, a marker of macrophage activation was assessed.

Results NARs showed plasma total protein concentration similar to SD despite lack of albumin before (72±15 vs 82±8) and after BDL (67±7 vs 75±22). After BDL both groups of animals showed histological evidence of severe liver damage, though the NARs showed a significantly worse systemic haemodynamics with lower MAP (p=0.01), evidence of renal dysfunction indicated by higher plasma creatinine and higher PRA (p<0.05) compared with SD (Abstract OC-068 figure 1). There was a significant inflammatory response following BDL in both groups showed by an increase in urinary neopterin which was found to correlate with PRA (r=0.59, p<0.01).
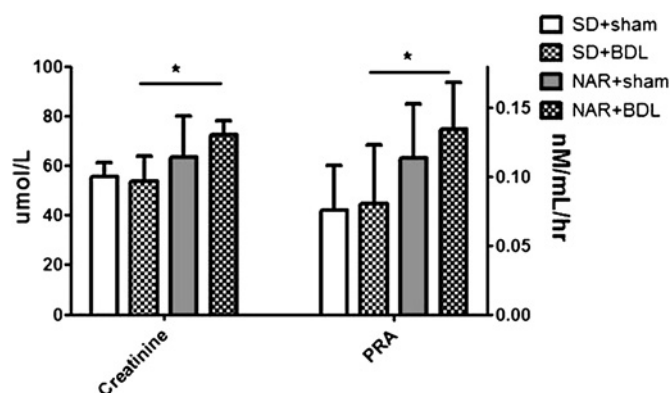
Abstract OC-068 Figure 1 Plasma creatinine concentration and plasma renin activity in the different groups of animals

Conclusion A lack of albumin was associated with a raised PRA and a marked deterioration in systemic haemodynamics and renal function after liver injury (BDL), despite normal total plasma protein concentration. This worsened outcome in the absence of albumin strongly supports the central role of albumin in

maintenance of cardio-renal function in liver failure and may indicate that albumin plays a crucial role in moderating inflammation.

Competing interests None declared.

OC-069 ROTATIONAL THROMBOELASTOMETRY IN CIRRHOSIS: HYPERCOAGULABLE AND HYPERFIBRINOLYTIC

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Introduction Cirrhotics have complex acquired derangements of haemostasis. Routine coagulation tests suggest a hypocoagulable profile, resulting in frequent administration of blood components for prophylaxis and treatment of bleeding. Rotational thromboelastography (ROTEM®), unlike standard coagulation tests, provides a real-time measurement of clot formation, strength and stability in whole blood and may more accurately reflect in vivo coagulation. We aimed to (1) identify the key derangements in the haemostatic pathways in patients with cirrhosis; (2) determine the prevalence of overt hyperfibrinolysis and whether this could be improved with anti-fibrinolytics.

Methods We used ROTEM® to investigate: (1) Clotting time (CT) and maximum clot firmness (MCF) in stable, non-bleeding cirrhotics compared to healthy volunteers; (2) The presence of overt hyperfibrinolysis and whether this could be reversed by spiking blood samples ex vivo with the antifibrinolytic aprotinin (APTEM test). Overt hyperfibrinolysis was defined by a maximum lysis (ML) of $>15\%$ and by comparing the clot lysis index at 60 min between EXTEM and APTEM parameters.

Results 106 adult cirrhotics and 28 healthy volunteers were enrolled after informed consent. Median EXTEM CT was shorter in cirrhotics than controls (51s vs 58s, $p<0.01$) and the clotting time shortened as Child-Pugh score increased in severity (52s Child A, 49s, Child B, 47s Child C). In cirrhotics there was strong correlation between EXTEM MCF with both platelet count ($r=0.801$, $p<0.0001$) and fibrinogen levels ($r=0.653$, $p<0.0001$), as well as fibrinogen and FIBTEM MCF ($r=0.641$, $p<0.0001$). 25% (26/106) of cirrhotics had evidence of overt hyperfibrinolysis. After spiking samples from cirrhotics with aprotinin, hyperfibrinolysis was completely reversed (ML$<15\%$) in 50% (13/26) cases and partially reversed in 50% (13/26) cases. There was a significant reduction in the median ML between EXTEM and APTEM clot profiles (13 vs 11, $p<0.001$). D-dimer levels increased with increasing disease severity (Child A-894, Child B-1835, Child C-5281).

Conclusion Cirrhotics have a hypercoagulable clotting time, despite prolonged PT, APTT and thrombocytopenia supporting the concept of re-balanced haemostasis. Use of ROTEM® may avoid unnecessary and potentially harmful transfusion of pro-coagulant blood components in cirrhotics. The high prevalence of overt hyperfibrinolysis in cirrhosis requires further elucidation and clinical studies to investigate the potential role of anti-fibrinolytics in the prophylaxis of variceal bleeding.

Competing interests None declared.

BAPEN symposium: "original communications"

OC-070 SYSTEMATIC REVIEW ON THE PREVALENCE OF MALNUTRITION IN GENERAL PRACTICE

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Introduction Information on the prevalence of malnutrition in general practice is very limited. This review was undertaken to establish the overall prevalence of malnutrition among adult patients registered with General Practitioners (GP), and also in specific patient groups.

Methods A literature search was undertaken using standard systematic review methodology on 22 August 2011 using Pub Med (1948−2011), Embase (1980−2011) Cochrane Collaboration (2011), and also by cross referencing. Studies were included if they involved adults ≥18 years, registered at a GP in any country provided they reported the prevalence of malnutrition. They were excluded if the populations were not linked to GP or involved pregnant or lactating women.

Results Of 54 studies initially identified, only seven met the inclusion criteria (five from the UK). Five set out to establish the prevalence of malnutrition (group 1) but another two reported prevalence (group 2). In group 1 studies the prevalence of malnutrition ranged widely, 0%−12%, with up to 38% being at risk of malnutrition. They involved different methodologies (consecutive patients, random sampling, subjects from larger studies, GP databases) and heterogeneous populations, varying in age (≥18 years (n=2 studies), ≥65 years (n=2), and >90 years (n=1)) and diagnosis/clinical status (Diabetes (n=1), chronic diseases including cancer and CVD (n=1), no "acute illness" (n=1), "apparent wellness" (n=1) and a mixture of health and various diseases (n=1)). They identified malnutrition using Mini Nutritional Assessment (n=2), Body Mass Index (BMI) with varying cut-offs (≤18.5 kg/m^2, n=1; <20kg/m^2, n=1), and unintentional weight loss (n=1). Among group 2 studies, one reported a prevalence of only 0.4% in people aged ≥65 years, according to entries about malnutrition in the GP notes extracted from a large randomly selected population (n=75 176) from the General Practice Research Database.[1] The other group 2 study reported a prevalence of 0% among a randomly selected group of subjects ≥75 years using mid-arm circumference, mid-upper arm muscle circumference and triceps skinfold thickness that were less than the 5th centile of reference data of a very different population group.

Conclusion This systematic review confirms that there is a lack of data on the prevalence of malnutrition in general practice, with relevant studies using different identification methods and populations, making it difficult to establish a reliable overall prevalence.

Competing interests None declared.

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OC-071 WITHDRAWN