Aim To assess the utility of BRUM1 as a first-line molecular investigation for patients with neonatal cholestasis in whom an inherited causes is suspected.
Method DNA from 95 infants with neonatal cholestasis in whom an inherited cause was suspected was amplified by PCR and hybridised to BRUM1 (validated against reference sequencing with 98.9% agreement (CI 0.97 to >0.99)) for simultaneous sequencing of the main causes of inherited disease in this group which included ATP8B1, ABCB11, ABCB4, VPS33B, VIPAR, NPC1 and NPC2. Children with known α-1 antitrypsin deficiency or Alagille syndrome were not included.
Results 30 infants had pathogenic mutations, which cause neonatal cholestasis. 23 of the mutations were novel.

Abstract P03 Table 1 Results

Gene	Total number of mutations	Novel mutations
ATP8B1	6	1
ABCB11	11	10
ABCB4	2	1
VPS33B	5	4
VIPAR	2	2
NPC1	17	4
NPC2	1	1

In this cohort of patients, 30.5% of infants with neonatal cholestasis had a genetic diagnosis confirmed by BRUM1. The average time to diagnosis was 5–25 days.
Conclusion A specific and rapid genetic diagnosis in infants with a phenotype of neonatal cholestasis can be made using a single resequencing microarray, to optimise clinical management and facilitate appropriate counselling of families.

P04 ADMISSION SERUM LACTATE IS A STRONG PREDICTOR OF OUTCOME IN CIRRHOTICS ADMITTED TO INTENSIVE CARE UNIT, AND WHEN ADDED TO THE LIVER-SPECIFIC SCORES OF MODEL FOR END-STAGE LIVER DISEASE OR UK MODEL FOR END-STAGE LIVER DISEASE, IMPROVES THEIR RESPECTIVE PREDICTIVE VALUE

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Introduction Accurate prognostic indicators of patient survival in an intensive care unit (ICU) help guide clinical decision-making. Factors known to portend poor prognosis in acutely ill cirrhotics in ICU include the need for mechanical ventilation, development of shock, renal failure and sequential increase in the number of failing organs. While serum lactate is now an established marker of survival and/or the need for transplantation in fulminant liver failure, its impact on critically ill cirrhotics is less well known.
Method We retrospectively studied 133 consecutive acutely ill cirrhotics admitted to the ICU between 2005 and 2008 at the Royal Free Hospital, a tertiary referral centre in liver diseases and transplantation. Data were collected on demographic variables, aetiology of liver disease, liver-specific prognostic scores (Child–Turcotte–Pugh (CTP), model for end-stage liver disease (MELD), UK model for end-stage liver disease (UKELD)), and acute illness scores (acute physiological score and chronic health point (APACHE II), sequential organ failure assessment score (SOFA)). In addition, serum lactate levels at 0, 24 and 48 h were also recorded. Multivariable logistic regression analysis was performed, and the discrimination ability of each of the above-mentioned scoring models in predicting ICU and hospital survival of these patients was evaluated using the area under the receiver operating characteristic (ROC) curve.
Results The ICU and hospital non-survivors—43/133 (32.3%) and 57/133 (43.4%) respectively—had similar demographic features as the survivors, but had significantly higher mean admission MELD, UKELD, SOFA and APACHE II scores, as well serum lactate levels on admission. Serum lactate at admission and particularly at 24 h had a better discriminative accuracy for mortality (AUC=0.737 and 0.764) compared with liver-specific prognostic scores, MELD (AUC=0.732 and 0.720), MELD-Na (AUC=0.338 and 0.554) and UKELD (AUC=0.698 and 0.695). Acute illness scores exhibited a rather poorer predictive power, both APACHE II (AUC=0.632 and 0.571) and SOFA (AUC=0.688 and 0.716). Adding lactate to MELD and UKELD scores further improved their outcome prediction potential (AUC MELD-lactate=0.737 and UKELD-lactate=0.717).
Conclusion Serum lactate is a powerful independent tool in predicting survival of acutely ill cirrhotics on ICU. Persistent hyperlactataemia after aggressive resuscitation for 24 h may reflect native liver's inability to metabolise it. In that case, should lactate not be incorporated in the liver function scoring models such as CTP, MELD or UKELD?

P05 B-CELL EPITOPE MAPPING OF ANTI-RO-52 RESPONSES IN PATIENTS WITH PRIMARY BILIARY CIRRHOSIS

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Introduction Up to 40% of patients with primary biliary cirrhosis (PBC) show reactivity against Ro-52 (*Hepatology* 2009), a Sjögren's syndrome (SS)-associated autoantibody. Previous studies have shown that anti-Ro-52 in SS targets the central, coiled-coil sequence of the 475-aa of the antigen. No study has dissected anti-Ro-52 reactivity in PBC.
Aim To investigate anti-Ro-52 B-cell responses in patients with PBC and compare them with those obtained in patients with SS.
Method Human recombinant full-length Ro-52 and 3 constructs spanning the whole protein were expressed in *E. coli* and tested for reactivity by a line immunoassay. Construct 1 (C1: aa1–129) contained the RING finger and the B-Box domains, construct 2 (C2: aa125–268) contained the coiled-coil domain and construct 3 (C3:aa 268–475) contained the B30.2/SPRY domain. Twenty-three 18-mer peptides overlapping by 12aa were synthesised and tested by an in house ELISA to better define the core epitopes within the highly immunogenic C2 region. Overall, 122 serum samples (68 from Ro-52 positive PBC patients, 39 from Ro-52 positive SS patients without liver disease and 15 from Ro-52 negative healthy blood donors) were tested.
Results Reactivity to the C2 construct of Ro-52 was present in all Ro-52 positive sera from PBC and SS patients and in none of the controls ($p<0.001$). Reactivity to the C3 construct was virtually absent in PBC (3%) and SS (0%) while reactivity to C1 was equally present in PBC (15%) and SS (10%). Within the immunodominant C2 sequence, 2 novel epitopic regions were identified using peptide mapping: the first sequence (aa 175–192: 1 peptide) was recognised by the great majority of patients with PBC (86%) and SS (69%), the second sequence (aa235–258: two overlapping peptides) was recognised by 35% PBC and 54% SS patients (p=NS, for both).
Conclusion This is the first systematic B-cell mapping approach of anti-Ro-52 responses in PBC patients showing that the antigenicity