several antigens including HBV core (HBc). Generating a strong T-cell response to this antigen to counter immunotolerant mechanisms in chronic HBV is an attractive therapeutic strategy. We have previously shown that lentiviral vaccines (LV) encoding antigen can generate potent CD8 and CD4 responses and these can be dramatically enhanced by co-expression of viral FLICE-like inhibitory protein (vFLIP) from Kaposi sarcoma-associated herpes virus. vFLIP is a potent stimulator of the NFKB pathway which matures and activates dendritic cells, enhancing expression of costimulatory molecules (including CD80, CD86 and ICAM1) and increasing IL-12 secretion.

Aim In this study we aimed to assess CD8 T-cell and antibody responses in HLA-A2 transgenic mice vaccinated with LV co-expressing vFLIP and HBc (A), expressing HBc alone (B) or HBc with an inactive vFLIP mutant (vFLIPa57l) (C).

Method HLA-A2 transgenic mice were vaccinated with LV 12 days before sacrifice and harvest of splenocytes. These were restimulated overnight with an HLA-A2 restricted HBc peptide (18—27) and/or overlapping HBc peptides. IFN? responses were measured by intracellular cytokine staining and by ELIspot. Antibody responses were assessed by ELISA on serum obtained at sacrifice.

Results Vaccination with LV co-expressing vFLIP and HBc (A) results in enhanced CD8-T-cell responses compared with mice vaccinated with LV expressing HBc alone (B) or HBc with an inactive vFLIP mutant (vFLIPa57l) (C). This was demonstrated on intracellular cytokine staining for IFN? of CD8+ve splenocytes re-stimulated overnight with HLA-A2 restricted peptide HBc 18—27 (A:B:C=5.35% :1.44% :0.84%). IFN? Elispot demonstrated twofold greater CD8 T-cell responses after restimulation with overlapping HBc peptides in splenocytes from mice vaccinated 12 days previously with LV co-expressing vFLIP and HBc compared with mice vaccinated with LV encoding HBc alone (p=0.006). LV expressing HBc also generated a strong antibody response comparable to vaccination with recombinant protein HBc virus-like particles (VLP). This was despite the presumed endogenous HBc antigen expression in transduced cells and no known mechanism of HBc secretion. LV encoding a mutant HBc p138g which does not multimerise into VLPs failed to raise an antibody response.

Conclusion LV encoding HBc are a potential means of generating both therapeutic CD8 T-cell and antibody responses in chronic HBV. Our data suggest that an intact VLP structure is essential for the generation of an antibody responses to HBc delivered with a lentiviral platform. We are now using this system to explore potential synergy between T-cell and B-cell responses to HBc in HBV infection.

P77 AN ANTI-VIRAL ROLE FOR CD4+ T CELLS IS OBSERVED IN ONLY A MINORITY OF PATIENTS SUCCESSFULLY TREATED FOR HEPATITIS C VIRUS

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Introduction CD4+ T cells are thought to play an important role in the control and elimination of non-cytopathic viral infections such as HCV. However their role in patients being treated with type I IFNs is not clear.

Aim To assess the role of HCV-specific CD4+ T cells in patients being treated for HCV infection.

Method 33 consecutive viraemic patients undergoing treatment had ex vivo (IFNg-producing) and cultured anti-viral CD4+ T cells intensively measured at multiple time points along with viral loads, alanine transaminase and serum cytokines (IL-2, -4, -5, -6, IL-10, TNFa and IFNg).

Results The patients could be divided almost equally into four groups depending on long term virus eradication or treatment failure and the magnitude of CD4+ cell responses: group 1: treatment failure, group 2—4 treatment success with group 2: no T cell responses, group 3: extremely weak transient T cell responses and group 4: strong robust responses. Early proliferation but not an ex vivo response was associated with rapid (k1 > 2 day-1) initial viral clearance and patients with robust early proliferation demonstrated reduced serum IL-10 compared to group 1 (p<0.0002). However the majority of successfully treated patients (groups 2 and 3) demonstrated variable rate of viral clearance, increased levels of IL-10 and a paucity of CD4+ T cell responses.

Conclusion Anti-viral CD4+ T cells may only have a role in a selected small group of patients in controlling viraemia, and in most patients the mechanisms of viral elimination awaits further studies.

P78 PREVALENCE OF VIRAL HEPATITIS IN PATIENTS UNDERGOING ANTI-TUBERCULOSIS THERAPY IN WEST LONDON

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Introduction Tuberculosis (TB) is prevalent in over a third of the world's population, with Asia (31%) and Africa (55%) accounting for most cases. The rising UK incidence of TB is partly due to increasing immigration from these regions. The UK prevalence of Hepatitis B virus (HBV) is estimated at 0.1% and the prevalence of Hepatitis C Virus (HCV) at 0.4%. HBV & HCV are treatable, but are largely asymptomatic until advanced liver disease has occurred. Therefore, HBV and HCV screening are recommended in high risk groups. Patients with TB do not currently undergo routine screening for these viruses, but are offered screening for HIV. HBV & HCV share similar epidemiological hotspots with TB and studies from Asia suggest HBV/HCV are significantly associated with TB infection and Drug-Induced Liver Injury (DILI) from anti-TB therapy. Currently, no studies have investigated the prevalence of viral hepatitis in TB patients in Western Europe, and the risk this poses to DILI.

Aim To assess (1) the prevalence of viral hepatitis in patients undergoing anti-TB therapy in West London; (2) if patients with serological evidence of viral hepatitis are at increased risk of DILI.

Method This was a prospective study of 245 newly diagnosed active (n=167) and latent (n=78) TB patients embarking on anti-TB therapy. Liver Function Tests (LFTs) were performed prior to & 2 weeks after initiation of anti-TB therapy. Patients were offered both HIV and viral hepatitis screening. All patients were tested for viral markers, including HBsAg, HBeAg, HBcAg, anti-HBc, seropositivity to HCV, and to HIV. DILI was defined as ALT elevated twice above the upper limit of normal (2x >ULN (40 IU/L)) any time following normal pre-treatment LFTs.

Results 149 (61%) TB patients were from the Asian Subcontinent and Sub-Saharan Africa, while only 15 (6%) were from the UK, mimicking global TB prevalence. 49 (20%) patients had serological markers for HBV or HCV, of whom 7 (3%) were HBsAg positive (one patient was Asian, two South East Asian and four Sub-Saharan African). 37 patients (15%) had isolated antibody to HBcAg. Five (2.0%) patients were HCV positive (one Asian, two Sub-Saharan African and two UK Caucasian). 17% of those with viral markers had raised pre-treatment ALT. 2.6% of patients tested for HIV were positive for viral hepatitis. 18% of active TB patients and 23% of latent TB patients had markers for viral hepatitis. Ten (5.4%) patients were diagnosed with DILI, of whom only 1 (0.5%) had

markers for viral hepatitis. Four (2.2%) patients required treatment interruption due to elevated LFTs, none of whom had serological markers of viral hepatitis.

Conclusion In our West London cohort, TB patients are a high risk group for HBV and HCV carriage. We found no increased risk of DILI in patients with markers of viral hepatitis undergoing anti-TB therapy. Screening for viral hepatitis in high risk groups is advocated by several international associations. However, testing for HBV and HCV in TB patients is not routine practice in the UK. Larger studies are required to identify the highest risk groups within TB populations. Until then, we recommend that screening for viral hepatitis is considered in all patients with TB.

P79 HEPATITIS E VIRUS IS HIGHLY ENDEMIC IN SOUTH WEST FRANCE

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Introduction Locally acquired hepatitis E virus (HEV) infection is an emerging infection in developed countries. South West France has a high incidence of HEV and has reported a large number of chronic cases of HEV infection. We previously estimated the HEV seroprevalence in blood donors in Midi-Pyrénées to be 16.6%, very much higher than the rate seen in Northern France (3.2%). However, comparison between seroprevalence studies is difficult. There is no gold-standard for measuring HEV antibodies and commercial assays vary in performance. A recent study has suggested poor sensitivity in a commonly used HEV IgG assay, which underestimates seroprevalence by a factor of 4.5[1]. Since this assay was used in our previous study of HEV seroprevalence in Midi-Pyrénées, we repeated the study using a more sensitive assay previously validated against sera from cases of HEV genotype 3 infection.

Aim To re-examine the seroprevalence of anti-HEV IgG using a sensitive, validated assay.

Method Sera from 512 blood donors (aged 18–65 yrs) and 50 children (aged 2–4 yrs) were tested for anti-HEV IgG (Wantai, Beijing, China). Demographic data and putative risk factors for HEV acquisition were collected using a structured questionnaire.

Results The HEV seroprevalence in blood donors was 52.5%. 63.1% of donors from rural areas and 42.9% of donors from urban ones were positive for anti-HEV IgG ($p<0.01$). The HEV seroprevalence increased gradually with the age from 32.8% in donors aged 18–27 years to 70% in donors aged 58–65 years ($p<0.01$). The prevalence of anti-HEV in men (51.4%) and women (54.7%) was similar. In children aged 2–4 years the HEV seroprevalence was 2%, suggesting that the high seroprevalence seen in the blood donors was not due to cross-reacting antibodies. Multivariate analysis identified age, rural residence, contact with cats and hunting as the factors independently associated with anti-HEV IgG positivity.

Conclusion HEV is highly endemic in South West France, and the seroprevalence approaches that found in many developing countries where HEV is endemic. Seroepidemiological studies of hepatitis E which use less sensitive assays may not produce a valid assessment of the relevant risk factors.

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P80 ANTIVIRAL THERAPY IN HCV CIRRHOTIC PATIENTS: EARLY ON-TREATMENT HAEMATOLOGICAL PARAMETERS AND GENOTYPE PREDICT RESPONSE

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Introduction Pegylated interferon-a (Peg-IFN)+ribavirin (Riba) is standard of care for treatment of chronic hepatitis C (CH-C). Antiviral therapy is recommended in those with compensated disease and lower rates of treatment responses are noted with little data on predictors of outcome in this "difficult to treat" group.

Aim To assess pre-treatment, on treatment haematological, biochemical and clinical characteristics of patients with CH-C cirrhosis and response to antiviral therapy in a single centre cohort.

Method 66 patients with CH-C infection and cirrhosis (96% Child-Pugh A, median MELD 13 and UKELD 44), median age 51 years (range 21–70), 50 males; treated with Peg-IFN 2a and weight based Riba (13 mg/kg/day) according to their genotype (24–72 weeks) between July 2006 and December 2009. Patients were divided into 3 groups by response: sustained responders (SVR) n=20 (30%), relapsers (Rel) n=24 (37%) and non-responders (NR) n=22 (33%). Virological, biochemical and haematological parameters (HCV RNA viral load, HCV genotype (G), sodium, bilirubin, creatinine and albumin levels, prothrombin time, haemoglobin (Hb) levels and neutrophil (ANC), platelets (PLT) counts were assessed at baseline (W0) and at different timepoints: treatment week 4 (TW4), TW8, TW12, TW24 (G1&4) and at the end of therapy (EOT). Child-Pugh, MELD and UKELD scores were assessed and compared with outcome.

Results Baseline HCV RNA viral load was similar in SVR, Rel and NR. SVR was significantly lower (13% vs 54%, $p<0.01$) in G1&4 patients. No differences in Child-Pugh (median 5, range 5–12), MELD (median 13, range 10–16) and UKELD (median 44, range 39–50) scores at any point were detected. Baseline ANC and PLT (both $\times 10\hat{}9$/ml) were lower in NR than SVR and Rel (median ANC: 2.43 vs 3.67 and 3.21, $p=0.04$ and median PLT: 122 vs 142 and 156, $p=0.05$). Baseline Hb levels (g/dl) were similar in all patients, but decreased significantly during therapy at TW4, TW8 and TW12 in SVR than in NR and Rel (TW4: 1.9 vs 1 vs 1.2, $p=0.03$; TW8: 2.6 vs 1.9 and 2.2, $p=0.03$ and TW12: 3.5 vs 2.8 vs3, $p=0.04$). There was no difference in dose reductions of Peg-IFN and Riba and use of haematological growth factors between groups.

Conclusion Antiviral therapy in our population was safe. Early decrease in Hb at W12 (perhaps reflecting inter-individual ribavirin concentration); HCV genotype, higher baseline ANC and PLT counts were associated with response.

P81 PSYCHIATRIC SIDE EFFECTS OF ANTIVIRAL THERAPY WITH PEGYLATED INTERFERON AND RIBAVIRIN ARE ASSOCIATED WITH POOR RESPONSE IN CHILDREN WITH CHRONIC HEPATITIS C

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Introduction Chronic hepatitis C (CHC), a mild disease in childhood, can progress to cirrhosis in young adulthood. Successful Peg-IFN+ribavirin therapy prevents progression, but has, among others, neuropsychiatric (NP) side effects (SE) that might impact on response.

Aim To study the influence of Peg-IFN+ribavirin-related NPSE on treatment response in paediatric CHC using novel age-adapted questionnaires.