were excluded. 80 (14%) subjects had past infection with HBV (HBsAg negative, HBcAb positive). Individuals with past HBV were significantly older than HBsAg positive and HBsAg, HBcAb negative subjects ($p<0.001$). The prevalence of HBsAg positivity was highest in subjects born in Vietnam (17.4%, 4/23), followed by China (11.5%, 24/157), Hong Kong (8.3%, 18/288), the UK (6.7%, 5/75) and other (6.2%, 2/32). Only 12% of subjects reported previous vaccination against HBV. To date, 25 of the HBsAg positive individuals have been seen in our clinic. 1 was HBeAg positive (immunotolerant) and 24 were HBeAg negative. Of these, 3 have active disease (including 1 cirrhotic) and have been started on treatment. 14 have inactive cHBV and 7 are undergoing observation to determine disease activity. No cases of co-infection with HCV, HIV or Delta were found.

Conclusion 1. Undiagnosed cHBV is common in the British-Chinese community of NE England, including subjects born in the UK. 2. A proportion had active cHBV requiring treatment. 3. If these results were applied to the entire UK British-Chinese population targeted screening should lead to approximately 32 250 newly diagnosed cases of cHBV. 4. These results provide evidence for a UK HBV screening and vaccination program for the British-Chinese community.

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P55 HCV QUASISPECIES ANALYSIS OF PATIENTS WITH GENOTYPE 3 HCV WHO RELAPSE SUGGEST TWO DIFFERENT MECHANISMS OF RELAPSE

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Introduction Patients persistently infected with genotype 3 HCV are more likely to have a sustained viral response (SVR) to interferon and ribavirin therapy than patients infected with genotype 1. However many patients with advanced fibrosis infected with genotype 3 HCV relapse following therapy. The mechanisms underlying relapse are not known.

Aim To examine the speed of relapse and compare quasispecies prior to and immediately following relapse.

Method 30 chronically infected patients with advanced fibrosis (fibrosis score >F3/6) were treated for 24—48 weeks with Peg IFN α 2a and ribavirin. Plasma samples were taken pre-treatment, during treatment and weekly post treatment. The HCV quasispecies in the pre-treatment sample and the first HCV-RNA positive post-treatment samples of the relapsed patients were assessed.

Results All of the patients responded with loss of virus on treatment. 18 had a sustained viral response and 12 patients relapsed post-treatment. All of the patients that relapsed did so within 4—6 weeks of treatment cessation.

HCV-RNA was extracted from the pre- and post samples of relapsed patients. 10—15 clones from both samples were successfully prepared and sequenced over the E2 region, including the HVR1, 2 and 3 regions and the PKR-eIF2α region in five patients. Construction of phylogenetic trees showed that in two patients the quasispecies that emerged post-treatment were similar to those seen pre-treatment but in three patients a dramatic shift in populations occurred.

Conclusion Relapse post therapy is very rapid and two distinct patterns of relapse were seen. These data suggest that there may be different mechanisms of relapse following treatment withdrawal in patients with genotype 3 HCV.

P56 WHAT IS THE BEST METHOD OF CASE FINDING FOR CHRONIC VIRAL HEPATITIS IN MIGRANT COMMUNITIES?

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Introduction The prevalence of chronic viral hepatitis in people born in Pakistan living in the UK is 5% (2.7% Hepatitis C Virus (HCV) and 1.8% Hepatitis B Virus (HBV). Studies from the HPA show an increased risk of end stage liver disease from HCV in people from Pakistan living in the UK. Screening migrants from high prevalence regions (>2%) for HBV is cost effective if screening of 35% of a population is achieved. Given that screening for viral hepatitis in migrants will reduce morbidity, mortality and onward transmission of chronic viral hepatitis, the outstanding question is how should this be done?

Aim The aim of this observational study was to evaluate community, and general practice (GP) based approaches to screening migrants for viral hepatitis.

Method We distributed 5000 testing cards in Mosques, following an awareness campaign, encouraging people from Pakistan to attend their GP surgery for viral hepatitis testing. In primary care practices we studied two approaches targeting registered Pakistani/British Pakistani patients: an opportunistic approach, whereby patients attending the practice were offered screening for HBV and HCV, and an 'opt out' approach, where patients were contacted by letter and invited to opt out of screening. Those who did not 'opt out' were telephoned and asked to attend screening clinics.

Results 5000 leaflets were distributed to Mosques but no patients presented to their GP for testing. In the primary care study there were 1163 Pakistani/British Pakistani patients in the 'opportunistic' arm. Of these 17 (1.5%) were screened and all were uninfected. In the 'opt out' arm there were 1134 eligible patients. It was not possible to screen 524 patients (46%) due to inadequate contact details (38%), previous screening (4%) or incorrectly recorded ethnicity (4%). Of those who could be contacted and were eligible for screening, 37% (223/600) have been screened. 75% of those who made a screening appointment were born in Pakistan, and 25% were British Pakistani patients. 1% of those screened were found to be HBsAg positive and 2.4% were HCV antibody positive.

Conclusion Community awareness campaigns and leaflets do not directly lead to testing for viral hepatitis in at risk immigrant groups. A direct screening approach is more effective than an opportunistic screening approach in primary care. Inaccurate GP records reduce the efficiency of screening but GP based testing is easy to implement, popular with patients and effective. First generation migrants are more likely to comply with screening which may improve the cost-effectiveness of this approach.

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P57 THE IL28B GENE SNP RS12979860 CC HAPLOTYPE, PREDICTOR OF RESPONSE TO TREATMENT IN CHRONIC HCV INFECTION, IS ASSOCIATED TO HIGH NUMBERS OF CD56BRIGHT NK CELLS, LOW NUMBERS OF CD3-CD56-CD16 + NK CELLS AND LOW HCV-SPECIFIC IL-10 PRODUCTION

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Introduction Single nucleotide polymorphisms (SNPs) rs12979860 and rs8099917 near the IL28B gene predict response to treatment in

chronic hepatitis C (CH-C). Control of HCV infection is linked to strong immune responses. Little is known on the association between IL28B SNPs, innate and adaptive immune responses in relation to therapy outcome in CH-C.

Aim To evaluate the relationship between rs12979860 and rs8099917, pre-treatment frequency/phenotype of natural killer (NK) cells (innate immunity), HCV-specific immune responses (adaptive immunity), and Peg-IFN/ribavirin response.

Method Patients: 19 CH-C genotype 1 patients (13 males, median age 47 years) treated with Peg-IFN/ribavirin were divided in 3 groups: 10 responders (SVR), 5 non-responders (NR) and 4 relapsers (Rel).

Methods: rs12979860 and rs8099917 were tested by direct sequencing. Baseline numbers of NK cells ($CD3^{-}CD56^{+}$), their subsets $CD56^{dim}/CD56^{bright}$, $CD3^{-}CD56^{+/-}CD16^{+/-}$, and expression of NK cell activation/inhibition (NKG2D/NKG2A) markers were investigated by flowcytometry on peripheral blood mononuclear cells (PBMC). PBMC IFN-γ and IL-10 production after exposure to HCV-core, NS3, NS4, NS5 antigens was evaluated by intracellular cytokine staining. Results are presented as medians.

Results rs12979860 haplotype CC was present in 32% of patients (40% SVR and 50% Rel), CT in 63% (60% SVR, 50% Rel and 80% NR) and TT in 5% (20% NR); rs 8099917 haplotype TT was present in 68% (80% SVR, 75% Rel and 40% NR) and GT in 32% (20% SVR, 25% Rel and 60% NR). Baseline number of NK cells was similar in all groups, but that of $CD56^{bright}$ cells was higher in SVR than Rel/NR (6.7% vs 3.3%, p=0.04). $CD3^{-}CD56^{-}CD16^{+}$ cells were more frequent in NR and Rel than SVR (14.4% vs 10.1% and 7.7%, p=0.05). The proportion of $CD56^{dim}$ cells $NKG2D^{+}$ was higher in SVR than Rel and NR (51.1% vs 37.3% and 25.2%, p=0.04). While number of HCV-specific IFN-γ producing cells was similar in all groups, IL-10 producing cells were higher in Rel and NR than SVR for HCV core ($CD4^{+}$/IL-10: 4.8% vs 3.5% vs 1.8%, p=0.05). Compared to patients with rs12979860 CT/TT haplotypes, those with CC haplotype had more $CD56^{bright}$ cells (6.8% vs 3.5%, p=0.04), but fewer $CD3^{-}CD56^{-}CD16^{+}$ NK cells (7.9% vs 14.2%, p=0.05) and HCV-core specific $CD4^{+}$/$IL\text{-}10^{+}$ cells (4.5% vs 2.1%, p=0.05). There was no association between rs8099917 haplotypes, NK-cell number/phenotype and HCV-specific immune responses.

Conclusion High numbers of $CD56^{bright}$ NK cells, low numbers of unconventional $CD3^{-}CD56^{-}CD16^{+}$ NK cells, and low HCV-specific IL-10 production at baseline are associated with IL28B gene SNP rs12979860 CC haplotype and successful antiviral treatment of CH-C genotype 1.

P58 GENETIC, VIROLOGICAL AND IMMUNOLOGICAL PRE-TREATMENT PREDICTORS OF THERAPY RESPONSE TO PEG-IFN/RIBAVIRIN IN CHILDREN WITH CHRONIC HEPATITIS C

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Introduction Vertically acquired chronic hepatitis C (CH-C) is a mild disease in childhood but may accelerate in adolescence. Effective early therapy with pegylated interferon (Peg-IFN) and ribavirin (Riba) prevents progressive liver damage. Control of HCV infection depends on both innate and adaptive immunity. Little is known about treatment predictors in children with CH-C.

Aim To assess whether single nucleotide polymorphisms (SNP) near IL28B gene rs12979860 and rs8099917, HCV genotype (G) and pre-treatment innate and adaptive immunity [frequency/phenotype of natural killer (NK) cells, HCV-specific T cell responses, frequency/phenotype of T regulatory cells (T-regs), plasma levels of IFN-γ inducible protein 10 (IP-10)] predict therapy response in children with CH-C.

Method Patients: 32 children with CH-C (19 males, median age 12 yrs, 53% G1) treated according to genotype with Peg-IFN (60 μg/m^2/week) and riba (15 mg/kg/d) were divided into responders (22, R), relapsers (4, Rel) and non-responders (6, NR).

Methods: rs12979860 and rs8099917 were tested by direct sequencing; baseline numbers of NK cells ($CD3^{-}CD56^{+}$) and their subsets $CD56^{dim}/CD56^{bright}$, $CD3^{-}CD56^{+/-}CD16^{+/-}$, of CD4+cells expressing programmed death receptor ($CD4^{+}PD1^{+}$) and of T-regs ($CD4^{+}CD25^{+}FoxP3^{+}$) by flowcytometry on peripheral blood mononuclear cells (PBMC). PBMC IFN-γ and IL-10 production after exposure to HCV-core, NS3, NS4, NS5 antigens was evaluated by intracellular cytokine staining. Baseline IP-10 plasma levels [pg/ml] were measured by ELISA. All presented as median.

Results rs12979860 haplotype CC was present in 34% (91% R and 9% NR), CT in 47% (73% R, 7% Rel and 20% NR) and TT in 19% (17% R, 50% Rel and 33% NR); rs8099917 haplotype TT was seen in 50% (88% R and 12% NR), GT in 44% (50% R, 29% Rel and 21% NR) and GG in 6% (50% R and 50% NR) patients. Non-G1 CH-C was linked with better response than G1 (53% vs 80%, p=0.02). Baseline number of $CD56^{bright}$ NK cells was higher in R than Rel & NR (3.7% vs 1.8% and 1.3%, p=0.05). Compared to R, Rel and NR had higher numbers of $CD3^{-}CD56^{-}CD16$ cells (17.4% vs 12.9% & 10.7%, p=0.05), of HCV-core-specific IL-10 producing cells ($CD4^{+}$/IL-10: 4.4% and 3.8% vs 1.7%, p=0.03), of CD4+PD1+ cells (7.1% and 6.9% vs 4.3%, p=0.03) and of T-regs (4.2% and 3.0% vs 1.4%, p=0.04). Baseline plasma IP-10 levels were higher in NR than Rel and R (85 vs 34 and 15, p<0.01). By multivariate analysis only possession of CC rs12979860 and TT rs8099917 haplotypes and low baseline IP-10 levels were associated with response to therapy.

Conclusion Possession of both major haplotypes CC rs12979860 and TT rs8099917 for IL28B gene SNPs and low baseline IP-10 levels predict successful therapy response in children with CH-C.

P59 SUBANALYSES OF THE TELAPREVIR LEAD-IN ARM IN THE REALIZE STUDY: RESPONSE AT WEEK 4 IS NOT A SUBSTITUTE FOR PRIOR NULL RESPONSE CATEGORISATION

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Introduction On treatment, a poor therapeutic response to peginterferon (P)/ribavirin (R) is defined as a <1 log10 decline in viral load at week 4. Null response (NR) to a current or prior course of PR is defined as a <2 log10 decline in HCV RNA at week 12. The FDA adopted the week 12 NR definition in its recent draft guidance. The REALIZE study uniquely enrolled classically defined prior NR, partial responders and relapsers, and included an arm with a PR lead-in (L-I) phase. This design allows a comparison of on treatment response after 4 weeks of PR with prior response categories, including a comparison of 'null response', as well as the relationship between < or −1 log10 RNA decline and SVR in response to T/PR treatment.

Method Patients in the lead-in arm (N=240) received 4 weeks of PR followed by telaprevir (T) 750 mg 8 hourly for 12 weeks combined with PR followed by 32 weeks of PR alone. Control patients (N=121) received 48 weeks of PR. All patients received pegylated interferon alfa-2a.