Methods Cases of cholangiocarcinoma were identified in Norwich (years 2004–2010) and Leicester (year 2007) from multi-disciplinary team meeting clinical databases. Inclusion required diagnostic evidence from CT scans and/or histology. Controls were patients, of similar ages and gender, with basal cell carcinomas treated in the dermatology departments at each hospital. The case notes of all subjects were reviewed to obtain confirmatory clinical information on cholangiocarcinoma and type 2 diabetes. Data were analysed using unconditional logistic regression to calculate ORs with 95% CIs, adjusted for age at diagnosis and gender.

Results A total of 80 cases of cholangiocarcinoma (median age at diagnosis = 76 yrs, range 41–96 years, 51% men) and 411 controls were identified. All patients had radiological evidence of cancer, with 86% involving the extrahepatic biliary system. The median survival of cases was 158 days (range 2–1092 days). There was a statistically significant increase in the odds of developing cholangiocarcinoma for those with type 2 diabetes (OR=3.00, 95% CI 1.44 to 6.25), but not for type 1 (OR=1.62, 95% CI 0.165 to 16.08). When the effect of type 2 diabetes was adjusted for use of oral hypoglycaemics, the associations were maintained (metformin OR=3.60, 95% CI 1.26 to 10.25 and sulphonylureas, OR=6.31, 95% CI 2.31 to 17.18).

Conclusion This epidemiological data supports the biological evidence for type 2 diabetes promoting the development of cholangiocarcinoma. Type 2 diabetes should be considered as a potential risk factor for cholangiocarcinoma in future aetiological studies.

Competing interests None declared.

PTU-091 PERCUTANEOUS TRANSHEPATIC CHOLANGIOGRAPHY (PTC); ARE WE HITTING THE TARGET?

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N J Taylor,* G Diana, M W James. *Nottingham Digestive Diseases Biomedical Research Unit, Nottingham University Hospitals, Nottingham, UK*

Introduction Percutaneous transhepatic cholangiography (PTC) is a procedure used to access the biliary tree for diagnostic purposes in obstructive jaundice, and to facilitate palliative stenting across biliary strictures. A previous study has shown a 19.8% in-patient mortality and significant morbidity for PTC.[1] Our aim was to audit local practice in order to identify risk factors for complications and death and to identify ways of reducing patient exposure to PTC.

Methods Retrospective Audit of all patients presenting to Nottingham University Hospitals from 1 October 2010 to 31 December 2010. Patient demographics, indication for PTC, co-morbidities, previous ERCP procedures performed, length of stay, PTC procedural details, morbidity and 30-day mortality was documented from electronic and paper records.

Results 44 patients underwent 72 procedures with a median of 1.5 procedures per patient. Median age was 67 years (IQR 62–77), 42% were female and malignant disease was seen in 91% of patients undergoing PTC. In 68% of procedures the patients had one or more co-morbid conditions. 47% of procedures were for 1st PTC and 53% were for 2nd or subsequent PTC. Overall, failed ERCP was the indication in 36% of procedures, reasons for ERCP failure were; failed cannulation (50%); inability to cross stricture (25%); hilar stricture (11%). Median length of stay was 10 days for all procedures, two patients went home the day of procedure. Frequencies for each indication for PTC were; 38% distal; 27% mid-CBD/CHD stricture; 8% hilar stricture; 7% multiple strictures; 20% other. Intended drainage was achieved in all but one patient and the stricture was crossed in 93% procedures. Median pre-procedural bilirubin was 184 μmol/l (IQR 78–271) with a delta bilirubin at 72 h post PTC of 33 μmol/l (2–89). Overall complications were seen in 41% patients; 17% minor complications (pain and biliary sepsis) and 24% suffered major complications including severe sepsis and renal failure. 30-day mortality was 18% with 13% being secondary to complications. Median survival overall was 182 days (IQR 81–321). Association with early death were Age*, ≥1 co-morbidities*, 72 h post-procedural creatinine*, complications, hilar stricture** and pre-procedural eGFR** (*p<0.05, **p<0.01).

Conclusion PTC is associated with a high incidence of complications and 30-day mortality. Risk factors for poor outcome include patient age; co-morbidity and renal function. Outcomes will likely be improved by better patient selection and pre-procedural optimisation. MRCP as part of the diagnostic pathway may identify strictures that should proceed directly to PTC and those where definitive stenting with cytology can be offered as a single-step procedure.

Competing interests None declared.

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Inflammatory bowel disease II

PTU-092 CROHN'S DISEASE ASSOCIATED NOD2 VARIANTS SHOW DIFFERENTIAL ACTIVATION OF NF-κB IN RESPONSE TO AUTO-SIGNALLING AND MURAMYL DIPEPTIDE

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[1,2,3]J Van Limbergen,* [4]F Soares, [5]R K Russell, [4]S Girardin, [2]A Griffiths, [3]D Philpott. *[1]Child Life and Health, University of Edinburgh, Edinburgh, UK; [2]Division of Gastroenterology, Hepatology and Nutrition, Toronto Sick Kids, Toronto, Canada; [3]Department of Immunology, University of Toronto, Toronto, Canada; [4]Laboratory Medicine and Pathobiology, University of Toronto, Toronto, Canada; [5]Department of Paediatric Gastroenterology, Yorkhill Children's Hospital, Glasgow, UK*

Introduction Single nucleotide polymorphisms (SNPs) located of the NOD2/CARD15 gene (nucleotide-binding oligomerization domain containing 2/caspase recruitment domain family, member 15) are associated with increased susceptibility to Crohn's disease (CD). These SNPs are thought to disrupt the sensing of bacterial muramyl dipeptide (MDP) at the C-terminus of the NOD2 protein. The precise contribution of each of these SNPs (SNP5, 8, 12 and 13) to NF-κB activation by means of NOD2-auto-signalling and stimulation with MDP has not been investigated at low levels of NOD2 expression. Data regarding the linkage disequilibrium (LD) between these CD-associated SNPs are scarce.

Methods NOD2 variant constructs (rs2066842 (SNP5), rs2066844 (SNP8), rs2066845 (SNP12) and rs2066847 (SNP13), SNP5+8, SNP5 +12 and SNP5+13) were created by site-directed mutagenesis of a pCMV plasmid containing wild-type N-terminal FLAG-NOD2. NF-κB luciferase assays were performed on HEK293 cells following transient transfection (20 h) with wildtype (WT) and NOD2 variant constructs, titrating NOD2 from 1 to 100 ng/well. The NF-κB luciferase response of NOD2 (1 ng)-transfected HEK293 cells to MDP (10 μg/well) was measured. Two-way ANOVA and unpaired t-tests were used. By means of Haploview-analysis of sequencing data of the exons and exon-intron boundaries in 24 paediatric Caucasian Crohn's disease patients, we assessed the LD between SNP5 and SNP8, 12 and 13.

Results Two-way ANOVA demonstrated an effect of NOD2 genotype and concentration on auto-signalling at low levels of expression (p<0.0001). This was due to the significant difference of auto-activation between WT and SNP5, SNP8 and SNP12 (p<0.001). At low levels of NOD2 expression (1–2 ng), the presence of SNP5 modified the auto-activating potential of SNP12 (p<0.01). Based on these titration experiments, a low NOD2 transfection of 1 ng/well was chosen for the MDP-stimulation experiment. MDP stimulation

led to a significant increase of NF-κB luciferase activity in WT and all NOD2 variant constructs, except SNP13 and SNP5+13 ($p<0.0001$). Haplotype analysis of 11 NOD2 SNPs, identified through direct sequencing in 24 children with CD, showed that LD between SNP5 and the other CD-associated variants is low ($r^2<0.1$), in spite of close physical proximity (D' 1.0).

Conclusion Our combined genetic and functional analyses demonstrate that the association of SNP5 with Crohn's disease is unlikely due to LD with other SNPs. At low levels of NOD2 expression, NOD2 variant constructs differ from WT in their auto-signalling and MDP-stimulated activation of NF-κB.

Competing interests None declared.

PTU-093 INAPPROPRIATE INFLAMMATORY RESPONSES IN THE ILEUM OF ULCERATIVE COLITIS PATIENTS

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[1]J Landy,* [2]H O Al-Hassi, [1]S T Peake, [2]N English, [3]P J Ciclitira, [4]R J Nicholls, [5]S K Clark, [2]S C Knight, [1]A L Hart. *[1]IBD Unit, St Mark's Hospital, London, UK; [2]Antigen Presentation Research Group, Imperial College, London, UK; [3]Gastroenterology, St Thomas' Hospital, London, UK; [4]Department of Biosurgery and Surgical Technology, Imperial College, London, UK; [5]Colorectal Surgery, St Mark's Hospital, London, UK*

Introduction Inflammation in ulcerative colitis (UC) is restricted to the colon. However, up to 50% of UC patients develop inflammation of the small bowel following restorative proctocolectomy (RPC). We hypothesised that in UC patients, ileal lamina propria dendritic cells would have a more "stimulatory" phenotype than in normal controls predisposing UC patients to pouch inflammation following RPC.

Methods Mucosal biopsy samples were taken from the ileum of UC patients undergoing RPC and from healthy controls undergoing colonoscopy. Lamina propria dendritic cells were isolated from biopsy tissue by collagenase digestion. DCs were identified as an HLA DR+, lineage- (CD3-, CD14-, CD16-, CD19-, CD34-, CD56-) population and expression of Toll-like receptors (TLRs), homing markers and co-stimulatory markers were measured by multicolour flow cytometry. T-tests were performed for statistical analysis.

Results There were no differences between the percentage of dendritic cells expressing TLR 2 (30.5±11.5% vs 32.5±8.8%) or TLR 4 (38.6±5.8% vs 38.8±7.2%) in the UC and healthy control ileum. A significantly greater percentage of lamina propria dendritic cells expressed the gut homing marker β7 in the normal ileum (33.8±9.6%) compared with the UC ileum (6.4±3.2%, p=0.007) as well as the co-stimulatory marker CD40 (80±2.9% vs 48.6±5.7%, p=0.001).

Conclusion Contrary to our expectations, lamina propria dendritic cells in the ileum of UC patients appear to have a less "stimulatory" phenotype than in normal controls. There may therefore be an absence of appropriate effector responses and reduced regulation by T-cells in the UC ileum. Further work is necessary to assess the T-cell responses to dendritic cell stimulation in the ileum of UC and in healthy controls.

Competing interests None declared.

PTU-094 IMMUNISATION OF IBD PATIENTS ON BIOLOGIC THERAPY: AN ENGLISH DISTRICT HOSPITAL EXPERIENCE

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[1,2]J Kayani,* [2]A Piotrowicz. *[1]East Midlands South Deanery, Leicester, UK; [2]East Kent Hospitals University NHS Foundation Trust, Margate, UK*

Introduction Patients with IBD remain at risk of preventable infections due to immunomodulatory drugs. The European Crohns and Colitis Organisation (ECCO) Consensus document[1] recommends immunising all such patients to Human Papilloma Virus (HPV-in females under 18 years), Influenza, Pneumococcus and Hepatitis B (in seronegative patients). We investigated our practice over the last 5 years.

Methods All 29 patients contactable on our Biologics' Register agreed to take part. Twenty-six remained on maintainance biologics. All had received at least one immunomodulatory drug prior to their commencement. Patients were asked if they had been immunised or offered it prior to or during their biologic therapy.

Results Responses in Abstract PTU-094 table 1. While 83% were offered influenza immunisation—28% declined all invitations and a similar number declined yearly offers of the immunisation. This was despite a number of pandemic flu scares. All patients reported that influenza and pneumococcal vaccination occurred at the instigation of Primary Carers. All those who received Hepatitis B immunisation did so as a result of Occupational or Travel requirement and those who were offered HPV did so as part of other national recommendations.

Abstract PTU-094 Table 1

Vaccination	Potential recipients	Immunised (%)	Immunisation declined (%)	Not offered immunisation
HPV	2	1 (50)	1 (50)	0
Influenza	29	16 (55)	8 (28)	5 (17)
Pneumococcus	29	4 (14)	0	25 (86)
Hepatitis B	29	6 (21)	0	23 (79)

Conclusion A recent survey of Australian Gastroenterologists found 30%—55% had never recommended such immunisations.[2] Others have found that most Gastroenterologists feel that Primary carers are responsible.[3] Primary carers however use National guidelines[4] that have no specific recommendations for Hepatitis B and HPV in patients on immunosurpressants. Gastroenterologists therefore need to promote awareness of ECCO guidelines to ensure best coverage for patients as well as advocating standardisation in National and Professional guidelines.

Competing interests None declared.

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PTU-095 A QUALITATIVE EXPLORATION OF INFLAMMATORY BOWEL DISEASE PATIENT PERCEPTIONS OF PRIMARY CARE IN THE UK

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[1]K Kemp,* [1]J Griffiths, [2]S Campbell, [1]K Lovell. *[1]School of Nursing, University of Manchester, Manchester, UK; [2]Gastroenterology, Manchester Royal Infirmary, Manchester, UK*

Introduction Many patients with IBD in the UK are managed primarily in secondary care with minimal General Practitioner (GP) involvement or within a restricted shared care protocol. As UK NHS hospitals face mounting financial and workforce pressures,