Results When patients with metastatic disease were compared with 5-year survivors significant increased gene expression was noted for heat shock protein (HSP-90), p=0.016 and KRAS, p=0.046. When the pattern of gene expression between those who survived less than a year (n=40) and those surviving 5 years (n=10) was compared then HSP-90 and GHRL were shown also to have altered expression. A variety of genes including TFT1, HSPD1, BCAS1, CAPDH, GHRL were globally enhanced among virtually all samples.
Conclusion HSP-90 a gene encoding a chaperone protein implicated in carcinogenesis exhibited increased expression in metastatic disease. Up-regulation of HSP-90 should help cancer cells adapt to stress conferring a survival advantage. Thus finding relative over-expression in cancers which have progressed to metastatic disease suggests a possible role as a prognostic marker. This study has identified candidate genes that could contribute to a prognostic model for gastric cancer utilising qNPA technology and demonstrates the up-regulation of HSP-90 and KRAS in advanced gastric cancer.

Competing interests None declared.

OC-096 TH17 CELLS ARE INCREASED IN *HELICOBACTER PYLORI* INFECTION AND MAY BE ASSOCIATED WITH PEPTIC ULCER DISEASE

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E Staples, R J M Ingram,* K Hussain, D P Letley, J C Atherton, K Robinson. *Univesity of Nottingham, Nottingham, UK*

Introduction *Helicobacter pylori* (*Hp*) persistently colonises the stomachs of half the world's population. The majority of hosts remain asymptomatic but 10%–15% will develop peptic ulcer disease (PUD) or gastric cancer. Disease is associated with an IFNγ-producing T-helper 1 (Th1) response. Pro-inflammatory IL-17-producing T-helper 17 (Th17) cells, which express the transcription factor RORC2, are also likely to be involved. The murine Th17 response to *Hp* has been characterised but the role of human Th17 responses remains unclear.
Aim To assess the importance of Th17 cells in *Hp*+ patients. We quantified Th17 cells in the human gastric mucosa, compared *IL17*, *RORC2* and *IFNG* transcription, and investigated correlations with PUD.
Methods Gastric biopsies were donated by patients undergoing routine upper GI endoscopy at Queen's Medical Centre in Nottingham with informed consent and ethical approval. Patient characteristics: 17 with *Hp*–associated PUD, 28 with *Hp*-associated gastritis and 17 uninfected (*Hp*–). Antral *IL17* and *RORC2* mRNA levels (all patient biopsies) and *IFNG* transcription (26 *Hp*+ and 9 *Hp*– biopsies) and were quantified by real time PCR (RT-qPCR) relative to a comparator prepared from a further 14 uninfected biopsies. Frequencies of IL-17-secreting $CD4^+$ and $CD8^+$ T-cells were assessed by flow cytometry in gastric biopsies donated by 12 *Hp*+ and 11 *Hp*– patients.
Analysis Comparisons between *Hp*+ and *Hp*– groups and patients with and without PUD used Mann–Whitney tests. Levels of mRNA expression for paired biopsies were compared with Wilcoxon signed rank tests. Spearman's rank correlation was used to analyse relationships.
Results Increased frequencies of $CD4^+IL\text{-}17^+$ Th17 (3.0-fold, p=0.001) and $CD8^+IL\text{-}17^+$ (Tc17) cells (3.3-fold, p=0.01) were present in *Hp*+ samples. RT-qPCR showed that infected patients have increased mucosal *IL17* (45.0-fold, p<0.0001) and *IFNG* expression (3.4-fold, p=0.006) and showed for the first time that *RORC2* expression was also higher (2.6-fold, p<0.0001). There was a trend towards a correlation between *IL17* and *IFNG* expression (r=0.39, p=0.051) and relative *IL17* expression was 3.1-fold higher than *IFNG* (p=0.0006). Relative *RORC2* gene expression was also 35% higher in tissue from *Hp*+ patients with PUD than in those with gastritis alone but this did not reach statistical significance (p=0.11).
Conclusion

1. The *Hp*-infected human stomach has increased frequencies of Th17 and Tc17 cells, and increased expression of *IL17*, *RORC2* and *IFNG*.
2. *IL17* expression was significantly higher than *IFNG* expression, though the sources of *IL17* have yet to be fully characterised. There was a trend for increased *RORC2* expression in PUD. Our data suggest that Th17 cell responses may influence the clinical outcome of *Hp* infection in patients.

Competing interests None declared.

OC-097 THE NOVEL GASTRIN/CCK2 RECEPTOR ANTAGONIST YF476 INDUCES CLINICAL RESPONSES AND IS WELL TOLERATED IN PATIENTS WITH TYPE I GASTRIC NEUROENDOCRINE TUMOURS

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[1]A R Moore,* [2]L Ball, [2]M Boyce, [1]A Varro, [1]D M Pritchard. *[1]Institute of Translational Medicine, University of Liverpool, Liverpool, UK; [2]Hammersmith Medicines Research, London, UK*

Introduction Autoimmune chronic atrophic gastritis causes loss of gastric parietal cells and results in achlorhydria, increased antral gastrin production and hypergastrinaemia. In some patients this hypergastrinaemia induces hyperplasia of enterochromaffin-like (ECL) cells and leads to type I gastric neuroendocrine (carcinoid) tumour (NET) development. Most type I gastric NETs behave in an indolent fashion, but a small proportion (<1%) grow more rapidly and metastasise. Surgical antrectomy has been shown to lead to resolution of hypergastrinaemia and regression of tumours in some patients. We therefore hypothesised that pharmacological inhibition of the gastrin/CCK-2 receptor using the novel orally bioavailable competitive antagonist YF476 would also lead to clinical regression of type I gastric NETs. The aims of this study were to assess (1) whether YF476 is an effective medical treatment for type I gastric neuroendocrine tumours; (2) the safety and tolerability of YF476 treatment and (3) the effects of YF476 on biomarkers of ECL cell activity.
Methods Following ethical committee and MHRA approval, six patients with small type I NETs secondary to autoimmune chronic atrophic gastritis and hypergastrinaemia have received a 12-week course of 50 mg/day YF476. Clinical responses were monitored by six weekly upper GI endoscopy with biopsy and three weekly measurement of fasting serum gastrin and chromogranin A (CgA) concentrations. Drug tolerability has been assessed by monitoring clinical adverse events and by assessing haematological, renal and hepatic blood parameters.
Results In all six patients the number and size of NETs decreased following 12 weeks of therapy (mean reduction in size of largest tumour = 39%, mean reduction in tumour number = 40%). However no patient showed complete tumour regression after 12 weeks' therapy. Serum CgA concentrations decreased in all subjects while receiving YF476, but increased to pre-treatment levels in the three subjects in whom measurements have to date been performed 12 weeks after completing therapy. Fasting serum gastrin concentrations did not significantly change while patients received YF476. YF476 was well tolerated in all patients; no serious adverse effects were reported and there was no evidence of haematological, renal or hepatic toxicity.

Conclusion YF476 is a promising new medical treatment for type I gastric neuroendocrine tumours. It appears to be well tolerated with no observed toxicity. Further trials of YF476 involving more prolonged treatment regimes are therefore warranted in this condition.

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OC-098 HOW COMMONLY IS GASTRIC CANCER MISSED AT ENDOSCOPY: A UK PRIMARY CARE BASED STUDY

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[1]S Menon,* [2]A Dhar, [3]J Hoare, [4]N Trudgill. [1]*Department of Gastroenterology, New Cross Hospital, Wolverhampton, UK;* [2]*Department of Gastroenterology, Bishop Auckland Hospital and Darlington Memorial Hospital, Darlington, UK;* [3]*Department of Gastroenterology, St.Mary's Hospital, London, UK;* [4]*Department of Gastroenterology, Sandwell General Hospital, West Bromwich, UK*

Introduction Meta-analysis of published single hospital series including 1977 subjects suggests that 14% of gastric cancer (GC) subjects have had an upper gastrointestinal endoscopy (OGD) up to 3 years previously that failed to diagnose their GC (50% in the 12 months before diagnosis and 50% 1–3 years before diagnosis).
Methods All patients with GC in the THIN general practice database covering 5 million UK subjects were examined. A nested case-control study was performed with cases subjects who underwent OGD 1–5 years prior to their OGD that diagnosed GC and controls subjects who did not undergo OGD 1–5 years prior to their diagnostic OGD.
Results 5473 GC were available for analysis (3402 males (62%), mean age 71 years), with follow-up of 46 779 subject years. 169 (3.1%, 98 males (58%), mean age 71 years) had an OGD which failed to diagnose GC between 1 and 5 years prior to diagnosis of GC, out of whom 128 (2.3%) had OGD between 1 and 3 years before and 41 (0.7%) had an OGD between 3 and 5 years before diagnosis. There were 56 primary care consultations with symptoms pertaining to oesophago-gastric cancer between 1 and 5 years prior to diagnosis of GC (dyspepsia (n) 51, anaemia 9, weight loss 12, dysphagia 3), of which all underwent OGD. No subject who had an OGD that did not diagnose cancer was on proton pump inhibitor (PPI) therapy in the year prior to OGD and 49 (0.9%) of subjects were on PPI therapy in the year prior to being diagnosed with GC. Logistic regression analysis of subjects who had an OGD that failed to diagnose cancer and those that did not, failed to identify any specific predictive factors (age 1.0 (0.99–1.01), p=0.99), sex 0.84 (0.61–1.14), p=0.26), related to an OGD that failed to diagnose GC.
Conclusion Missing GC at OGD is, reassuringly, less than half as common as previous much smaller studies in secondary care have suggested. PPI therapy does not contribute to missing GC at OGD. Advances in endoscopy and selection bias in previous studies may account for these differences.

Competing interests None declared.

OC-099 INCREASED AT RISK SCREENING AND RECOGNITION OF ATYPICAL PRESENTATION DOES NOT FULLY EXPLAIN THE 6.5-FOLD INCREASE IN PAEDIATRIC COELIAC DISEASE (CD) INCIDENCE IN THE LAST 20 YEARS IN SE SCOTLAND

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[1]V Merrick,* [2]L White, [2]E Bannerman, [1]R K Russell, [1]D Basude, [1]P Henderson, [3]D C Wilson, [1]P M Gillett. [1]*Paediatric Gastroenterology and Nutrition, Royal Hospital for Sick Children, UK;* [2]*Dietetics, Nutrition and Biological Health Sciences, Queen Margaret University, UK;* [3]*Child Life and Health, University of Edinburgh, Edinburgh, UK*

Introduction Current diagnostic practice for paediatric CD in the UK includes increased screening of family members and at- risk groups for example, diabetes mellitus.
Aims To identify all incident cases of CD in SE Scotland over the 20-year period of 1990–2009 to assess trends in incidence, symptomatology, age at diagnosis and the impact of active screening of at-risk groups. Utility of routine laboratory tests at diagnosis was also evaluated (2005–2009 diagnoses only).
Methods A retrospective review of case notes, pathology databases, endoscopy and patient records was performed for all children diagnosed with CD <16 years from 1990 to 2009 on duodenal biopsy in SE Scotland (at-risk population group of 233 000 aged <16 years). Data were age-sex standardised and analysed in 5-year epochs, with Poisson regression models used to calculate changes in incidence over time.
Results 266 biopsy positive children were diagnosed from 1990 to 2009 with an increase in incidence from 1.8 (95% CI 1.1 to 2.7) to 11.7 (95% CI 9.8 to 13.9) per 100 000 children aged <16 years during the 1990–1994 and 2005–2009 epochs respectively (p=0.001). The median age (IQR) at diagnosis also increased significantly from 29 (16–53) months to 90 (53–132) between these epochs (p<0.0001), and non-classical presentation (children with a mono-symptomatic presentation and those with extra-intestinal symptoms for example, fatigue, pallor, irritability) increased significantly from 5% to 21% respectively (p=0.008). Additionally, 7% of children were diagnosed through targeted screening in 1990–1994 compared to 23% in 2005–2009 (p=0.002). When cases identified via active screening or with non-classical symptoms were removed, a significant rise from 1.51 (95% CI 0.91 to 2.38) in 1990–1994 to 6.59 (95% CI 5.17 to 8.28) in 2005–2009 (p=0.006) remained. Routine blood investigations demonstrated that over 25% were anaemic and over 50% were iron deficient at presentation in 2005–2009.
Conclusion The incidence of paediatric CD has increased 6.5-fold over the last 20 years in SE Scotland. Children are older at diagnosis, presenting with fewer classical and more varied symptoms, and with iron deficiency anaemia the commonest laboratory abnormality. We show that both increased screening of at-risk groups and a lower threshold for serological screening (as a result of greater clinician awareness of the condition's heterogeneic nature) do not fully explain the overall rise in incidence.

Competing interests None declared.

OC-100 THE CLONAL ORIGINS OF GASTRIC ADENOCARCINOMA

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[1]T Ventayol Garcia,* [2]M Rodriguez-Justo, [3]T Graham, [2]M Novelli, [1]N Wright, [1]S McDonald. [1]*Deparment of Digestive Diseases, Blizard Institute, Barts and the London school of Medicine and Dentistry, QMUL, UK;* [2]*Deparment of Histopathology, University College London, London, UK;* [3]*Deparment of Histopathology, Cancer Research UK, London, UK*

Introduction We have previously shown that entire fields of dysplasia in the human stomach are derived from a single mutated, metaplastic gland.[1] This suggests that intestinal metaplasia (IM) can be considered a field defect among which dysplasia can arise and this would indicate that adenocarcinomas derived from such dysplasia would also be clonal. Recent work published by our laboratory has indicated that familial adenomatous polyposis–associated colorectal adenomas as well as some sporadic lesions[2] and dysplasia within Barrett's oesophagus[3] are polyclonal. There is therefore a need to ascertain the clonality of gastric adenocarcinomas (GA).