clinic within 7 days of the referral. Previously the referral to diagnosis/treatment time was around 30 weeks, with patients waiting up to 18 weeks to be seen in secondary care. Initially the faecal calprotectin on the referral pathway was set at 50µg/g. Following triage by the IBD nurse the patients referred with a faecal calprotectin between 50–100µg/g (N=100) were asked to repeat the stool sample.

Results The patients were reviewed and sent for investigation within 6 weeks of consultation with 56.5% of patients having endoscopic evaluation and only 28% of those patients received any diagnosis. When the faecal calprotectin cut off was raised to 100µg/g the result then increased to 32% for IBD, with a further 17% with a differential diagnosis. The differentials included 3 colorectal cancers (not on 2WW), gynaecological problems, mesenteric panniculitis and 12.5% had microscopic colitis.

Conclusions The referral to diagnosis time was reduced from 30 weeks to on average 9 weeks. There were around 25 new referrals a month with patients being seen within 7 days. The IBD nurse is perfectly placed to triage and review suspected new patients improving patient experience as the waiting times are reduced and the IBD nurse was capable of identifying and managing differential diagnoses.

The challenge has been finding an optimum cut off for the faecal calprotectin so to eliminate low sensitivity and specificity for aiding diagnosis of IBD but also engaging with primary care colleagues to support the referral pathway.

It is recommended that the referral pathway is a suitable method for suspected IBD patients to be seen but that more education within primary care is required to improve patient experience and increase appropriate patient referrals.

PTH-080 CLOSTRIDIUM DIFFICILE INFECTION IN PRE-EXISTING INFLAMMATORY BOWEL DISEASE: A CASE SERIES

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Introduction Inflammatory bowel disease (IBD) is a risk factor for clostridium difficile infection (CDI), and It is known that CDI in an IBD patient is associated with higher morbidity and mortality. It is thought that factors including alterations in the gut microbiome, mucosal disruption and immunosuppression provide a synergistic environment for CDI to complicate an IBD flare, yet there is no agreed consensus on best management of these patients.

Our aim is to examine a series of recent cases to assess our own practice and subsequent outcomes.

Methods A retrospective analysis was carried out of all cases of CDI in IBD patients in NHS GG&C during 2018. Patients were identified via the regional CDI database; those with co-existing IBD were extrapolated.

Data collected included demographics, IBD subtype, and presence of other CDI risk factors. Severity of symptoms was assessed using Truelove & Witts Criteria. Initial management, and any changes following the diagnosis of CDI were noted. Outcomes were measured by length of stay, survival to discharge and whether surgical intervention was required.

Results 14 patients in total were identified. 10 had a diagnosis of ulcerative colitis, 3 of Crohn's disease and 1 IBD unclassified. 11 of the 14 were on immunosuppressive therapy at the time of CDI (2 anti TNF; 1 thiopurine; 1 steroid; 7 5ASA) –

Abstract PTH-080 Table 1

Patient	Initial	Change 1	Change 2
1 – 3	Metronidazole 400 mg TDS		
4 – 5	Vancomycin 125 mg QDS		
6 – 8	Metronidazole 400 mg TDS	→ Vancomycin 125 mg QDS	
9	Vancomycin 125 mg QDS	+ IV Metronidazole 500 mg TDS	
10	Vancomycin 125 mg QDS	Vancomycin to 500 mg QDS	+ Metronidazole 500 mg TDS
11	Vancomycin 125 mg QDS	→ Fidaxomicin 200 mg BD	
12	Metronidazole 400 mg TDS	→ Vancomycin 125 mg QDS	
13	Metronidazole 400 mg TDS	→ Vancomycin 125 mg QDS	Vancomycin to 500 mg QDS
14	Metronidazole 400 mg TDS	→ Vancomycin 500 mg QDS	

this was continued in all cases. 9 of the patients presented with acute severe colitis based on Truelove & Witts Criteria.

Once the diagnosis of CDI was established metronidazole was given in 9 cases, and vancomycin in 5 (doses and any subsequent alterations shown in table 1).

Assessment with Travis criteria on day 3 indicated high chance of colectomy in 7 patients however none required surgical intervention. No patients received rescue biologics or faecal transplant. Median length of stay was 19 days (range 3–169). One patient did not survive to discharge. Since index admission 4 were readmitted, and 6 have subsequently had their IBD therapy escalated.

Conclusions Managing CDI in those with co-existing IBD is clinically challenging. This case series highlights the lack of consensus on how this should be approached, even within a single health board. This suggests that a wider body of work is required to establish guidance and provide better outcomes.

PTH-081 USTEKINUMAB TREATMENT STRATEGIES IN REFRACTORY CROHN'S DISEASE: REAL-WORLD EFFECTIVENESS DATA FROM A UK IBD CENTRE

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Introduction Ustekinumab (UST) is a human IgG1 kappa mAb to the shared p40 subunit of IL-12 and IL-23 which are involved in TH1 and TH17 mediated pathways of Crohn's disease (CD) pathogenesis. NICE approved UST for CD in April 2017, but there is limited UK data on real-world effectiveness. We present clinical effectiveness, safety and drug persistence data from a complex UK cohort.

Methods This was a retrospective observation cohort study of all CD patients treated with UST outside clinical trials in a single UK IBD centre. Physician's global assessment (PGA) was recorded at baseline, post induction and 1 year. Primary

outcome was clinical response defined by a fall in PGA. Secondary outcomes were drug persistence and fall in CRP or faecal calprotectin (FC). Statistical analysis was performed by Wilcoxon signed rank test in R v.3.4.4.

Results 84 patients (mean age 42 years, sd 14.7, mean disease duration 12.3 years, sd 8.9) were treated to December 2018. 82 (98%) had previous exposure to anti-TNF therapy, 35 (42%) to both anti-integrin and anti-TNF and 2 were naïve to biologics. 39 (46.4%) were on immunodulator co-therapy and 6 (7%) on steroids. Post-induction treatment was 12 weekly (9), 8 weekly (74) or 6 weekly (1).

Post-induction (median 14.7 weeks, IQR 8.03) and 1 year (median 44.4 weeks, IQR 13.4) reviews were available for 72 and 47 patients respectively. Post-induction clinical response occurred in 38 (53%) and remission in 5 (7%). At 1 year response occurred in 34 (72%) and remission in 7 (15%). Of 15 non-responders post induction left on UST, 9 responded by 1 year. Steroid-free response occurred in 35 (48%) post-induction and 31 (65%) at 1 year.

By 1 year 8 patients stopped UST (median 256 days, range 62–329); 1 cutaneous reaction, and 7 primary non-response or secondary loss of response. Only 1 of 8 given a second intravenous dose in an attempt to recapture response had a sustained benefit.

For those with an elevated biomarker at baseline (CRP >10 or FC >250) and repeat measurement post induction, mean CRP improved from 37 (11–96) to 28 (3.8–116) ($p=0.074$) and FC 2260 (292–6000) to 1152 (24–5084) ($p=0.089$). For paired results at baseline and 1 year mean CRP improved from 29 (11–96) to 19 (3–77) ($p=0.045$) and mean FC 2019 (823–6000) to 1070 (42–5528) ($p=0.011$). There was no significant change in normal baseline biomarkers.

Conclusions UST was well tolerated in a complex UK CD cohort and demonstrated benefit in terms of clinical response, improvement of biomarkers and in some full clinical remission. Due to delayed response continuation beyond 3 months is justifiable in some non-responders. Reloading to recapture response as described elsewhere was of limited benefit.

PTH-082 DYSREGULATION OF A NOVEL AXIS OF EPITHELIAL-T-CELL INTERACTION IS EVIDENT IN IBD

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Introduction Although epithelial dysfunction is an early initiating factor in inflammatory bowel disease (IBD), the role of the specialised intraepithelial immune compartment in this process remains unknown. Our research group has previously demonstrated that a subset of intraepithelial T cells expressing the $\gamma\delta$ T cell receptor are selectively regulated by self-encoded molecules restricted to the epithelium known as Butyrophilin-like (BTNL) proteins (Di Marco Barros et al Cell 2016). Here we investigate whether this selective regulation of human $\gamma\delta$ T cells is perturbed in the dysregulated epithelium of IBD and the factors which may contribute to this.

Methods A short-term whole gut explant culture was used to isolate $\gamma\delta$ T cells from colonic biopsies obtained at endoscopy from donors, facilitating flow-cytometric phenotyping and functional studies.

Results In the majority of non-IBD controls, co-culture of colonic lymphocytes with HEK293T cells co-transduced with intestine specific BTNL3+BTNL8 proteins, resulted in profound TCR down-regulation in a subset of $\gamma\delta$ T cells (specifically those expressing the V γ 2/3/4 chains). $\alpha_E\beta_7$ is a lymphocyte marker of epithelial residence present on the vast majority of $\gamma\delta$ T cells in health. $\alpha_E\beta_7$ + $\gamma\delta$ T cells make TCR down-regulation responses to BTNL3+8, whereas the subset of $\gamma\delta$ T cell $\alpha_E\beta_7$ - cells, which are in the minority, had grossly attenuated or absent assay responses. In many IBD patients, there is significantly reduced $\alpha_E\beta_7$ expression on $\gamma\delta$ T cells, and a severe attenuation or loss of BTNL-dependent TCR down-regulation. To assess whether the inflammatory milieu of IBD contributes to this dysregulation; addition of pro-inflammatory cytokines IL-12 and IL-18 (but not IL-1 β and IL-23) to an organ culture system lead to down regulation of $\alpha_E\beta_7$ on $\gamma\delta$ T cells and a consequent attenuation of response to BTNLs. This clearly implicates specific cytokines in the disruption of the $\gamma\delta$ -BTNL axis which is evident in disease. Further characterisation of $\alpha_E\beta_7$ - $\gamma\delta$ T cells demonstrated an activated pro-inflammatory phenotype in comparison to more quiescent $\alpha_E\beta_7$ + $\gamma\delta$ T cells.

Conclusion The BTNL- $\gamma\delta$ T cell axis, is a novel and important mechanism by which epithelial cells and a specific subset of the intraepithelial $\gamma\delta$ T cell compartment communicate, and is often dysregulated in IBD. While our data suggests that IL-12 blockade may help to restore this axis, IL-23 may be redundant in this setting, with implications for emerging therapeutic strategies. $\alpha_E\beta_7$ is a current target of therapeutic blockade, which has the potential to disrupt this axis and ultimately may exacerbate disease given the pro-inflammatory nature of $\alpha_E\beta_7$ - $\gamma\delta$ T cells.

PTH-083 FROM PARIS TO MONTREAL: EVOLUTION OF CROHN'S DISEASE LOCATION AND BEHAVIOUR FROM CHILDHOOD TO ADULTHOOD

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Introduction Crohn's disease (CD) is a progressive disorder but the natural history among paediatric onset CD appears different to that of adult onset CD. The long term disease evolution among paediatric onset CD beyond the childhood years is not well characterised. We conducted a single centre cohort study of all paediatric CD patients transitioned to adult care to assess the long term evolution of CD.

Method We conducted a retrospective observational, study of all CD patients diagnosed in childhood who were subsequently transferred to the care of an adult gastroenterology unit and had a minimum follow up of 2 years. We examined the case notes for evolution of disease location and behaviour. Disease location and behaviour was characterised using Paris classification at diagnosis and Montreal classification at last follow-up. In addition, we examined variables associated with the need for CD related intestinal resection. We used a paired McNemar's test to compare disease location and behaviour at diagnosis and most recent follow-up.