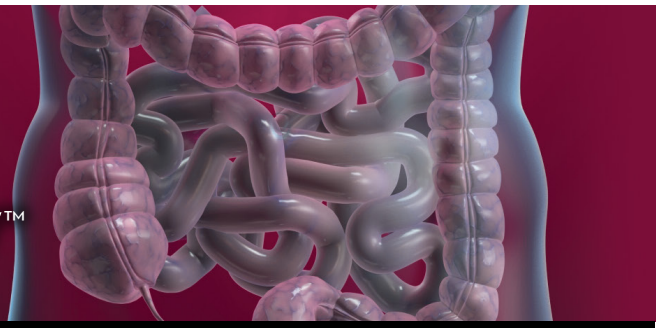
IBD RESEARCH REVIEW™



Making Education Easy

Issue 70 – 2025

In this issue:

Abbreviations used in this issue

BMI = body mass index
CD = Crohn's disease
IBD = inflammatory bowel disease
IL = interleukin
JAK = Janus kinase
MAPK = mitogen-activated protein kinase
NFkβ = Nuclear factor kappa-light-chain-enhancer of activated B cells
OR = odds ratio
STAT = signal transducer and activator of transcription 1
TB = tuberculosis
TGF = transforming growth factor
TNF = tumour necrosis factor
UC = ulcerative colitis

Welcome to Issue 70 of IBD Research Review.

We begin this issue with a study investigating hypercoagulation in patients hospitalised with acute severe UC and discover that such individuals remain prothrombotic for up to 12 weeks post discharge. Findings from a Canadian study investigating the gut microbiome and bile acids provide insight into the pathophysiology of IBD associated with primary sclerosing cholangitis and suggest possible targets for modulating the risk and course of IBD in this group of patients. Nurse Practitioner Christine Ho has reviewed two studies for this review, one investigating a risk prediction tool for diagnosis of IBD, and the other, contraception and fertility in IBD. In our Science Blog for this issue, Dr Srikantaiah Manjunatha discusses macrophage polarisation and targeted regulation in IBD.

We hope you enjoy the latest issue of IBD Research Review and welcome your comments and feedback.

Kind regards,

Professor Michael Schultz
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Dr Srikantaiah Manjunatha
manju@researchreview.co.nz

Hypercoagulation after hospital discharge in acute severe ulcerative colitis: A prospective study

Authors: Griffiths BJ et al.

Summary: This small study assessed serial thrombotic profiles in 27 patients with acute severe UC and 25 controls with quiescent UC from hospitalisation to 12 weeks post discharge. Patients with acute severe UC exhibited significantly elevated endogenous thrombin potential and maximum clot firmness versus controls, and these remained significantly ($p < 0.05$) elevated for 4 weeks and 8-12 weeks after admission, respectively. Factors that may have been responsible for changes in the global haemostatic profile included Von Willebrand (VW) factor antigen, factor VIII, Clauss fibrinogen concentration, and platelet count, which all increased from presentation to 8-12 weeks.

Comment (SM): A hypercoagulable state is associated with IBD, with increased risk of thromboembolic events. The risk is about three-fold higher than in the general population. The pathophysiology of this prothrombotic state is multifactorial including inflammation-mediated endothelial dysfunction, platelet activation, activation of coagulation pathways and impaired fibrinolysis. Guidelines recommend routine thromboembolic event prophylaxis for hospitalised patients with IBD flare. There are no definite guidelines for extending the prophylaxis post-discharge. This study aimed to characterise the serial coagulation profile in patients with acute severe UC during hospitalisation and up to 12 weeks following discharge. This is the first study to undertake an in-depth analysis of individual and global coagulation parameters. Marked elevation in individual factors at admission were seen in fibrinogen, platelets, factor VIII, VW factor with heightened levels of inhibitors of fibrinolysis plasminogen activator inhibitor-1 and thrombin activatable fibrinolysis inhibitor. The changes persisted up to 12 weeks despite adequate treatment. The global assessment was by rotational thromboelastography and thrombin generation assay, measuring various parameters of overall coagulation state. Global coagulation assays evaluate the net effect of pro- and anti-coagulant factors rather than focussing on individual factors. Enhanced thrombin generation reflects the cumulative effect of clotting factors, reduced inhibition of clotting and platelet activation. Global assays have shown shortened clotting time and increased clot strength confirming the hypercoagulable state. These advanced methods of investigation are helpful to risk stratify patients with IBD flare and select patients for extended thromboprophylaxis, especially when standard laboratory tests appear to be normal. This aids in a proactive personalised approach to prevent serious complications of thromboembolic events. Further studies are needed to clarify which patients need extended prophylaxis and to understand the impact of treatment of inflammation on the thrombotic risk. Future studies should also determine how best to integrate global assays of coagulation into routine standard of care in IBD management.

Reference: Clin Gastroenterol Hepatol. 2024;Dec 16 [Epub ahead of print]
Abstract

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Inflammatory bowel disease associated with primary sclerosing cholangitis is associated with an altered gut microbiome and bile acid profile

Authors: Leibovitzh H et al.

Summary: This study examined differences in gut microbiome composition, bile acid profile and bile acid-related microbial functions between IBD patients with (n = 54) and without (n = 62) primary sclerosing cholangitis (PSC). Faecal DNA shotgun metagenomic sequencing revealed lower microbial gene richness (p = 0.004) and compositional shifts (p = 0.03) in patients with IBD-PSC versus IBD-only. IBD-PSC was associated with altered microbial composition and function, including lower *Blautia obeum*, and greater *Veillonella atypica*, *V. dispar*, and *Clostridium scindens* (all p < 0.05) abundance, and an increase in microbial genes involved in secondary bile acid metabolism. Lower serum sulphated and higher conjugated secondary bile acids were associated with IBD-PSC and greater liver fibrosis.

INDEPENDENT COMMENTARY BY

Dr Srikantaiah Manjunatha (Manju)

BSc,MBBS,MD,FRCP,FRACP, Consultant Gastroenterologist (Retd)

Dr Srikantaiah Manjunatha (Manju) is a former Consultant Gastroenterologist for Te Whatu Ora–Southern, Dunedin and Honorary Senior Clinical Lecturer at the University of Otago. After completing his MBBS from the University of Mysore in India and MD (Medicine) from the prestigious PGIMER (Post Graduate Institute of Medical Education & Research), Chandigarh, India, he moved to the UK in 1988. He completed advanced training in medicine and gastroenterology in the UK after obtaining his MRCP (UK) in 1989. He worked as a registrar, senior registrar and consultant in medicine and gastroenterology for 25 years in the NHS, UK.

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Comment (SM): IBD phenotype associated with PSC is distinct from IBD without PSC and is characterised by a quiescent disease course, right colonic predominance and higher prevalence of colorectal cancer. These phenotypes have different gut microbiome composition and function. The gut microbiome and bile acids have a close bidirectional relationship, resulting in modulation of microbiome by bile acids and formation of secondary bile acids by bile acid metabolising microbiome. Primary bile acids are formed in the liver and secreted in bile after conjugation. The majority of primary bile acids are recirculated through enterohepatic circulation. The remainder get deconjugated to secondary bile acids by the help of the gut microbiome. This study used metagenomic sequencing and a large array of serum and stool bile acid metabolites to assess the PSC-driven differences in stool microbial composition and bile acid-related microbial functions in IBD with and without PSC. It highlights the microbial and bile acid signatures differentiating IBD with and without PSC. IBD-PSC patients had reduced microbial gene richness compared to IBD only patients. A significant shift in microbial composition revealed decreased abundance of *B. obeum* and increased abundance of Veillonella species and *C. scindens*. There was also increased abundance of microbial genes involved in secondary bile acid metabolism. Serum bile acid profile showed decreased serum sulphated bile acids and increased serum conjugated secondary bile acids, which were associated with increased liver fibrosis. No significant associations were seen in stool bile acids. In essence, there was an inverse correlation between Veillonella species and serum sulphated bile acids and a positive correlation with secondary bile acids. This study opens up the potential treatment strategies including targeting gut microbiome, bile acid metabolism and anti-fibrotic agents that may lead to enhanced surveillance and early intervention. This optimistic progress facilitates personalised medicine in addressing the challenges in this unique group of IBD-PSC patients.

Reference: J Crohns Colitis 2024;18(12):1957-1966
Abstract

Anti-integrin αvβ6 antibodies predict pouchitis in patients with ulcerative colitis after restorative proctocolectomy with ileal pouch-anal anastomosis

Authors: Nakanishi R et al.

Summary: This small study examined the association between the development of pouchitis and anti-integrin αvβ6 antibodies in 16 UC patients after restorative proctocolectomy (RPC) with ileal pouch-anal anastomosis (IPAA). Anti-integrin αvβ6 antibody levels were decreased at 3, 9, and 12 months after RPC ($p < 0.05$); however, antibody levels remained high in patients who developed pouchitis. Antibody levels at RPC were higher in those who developed pouchitis versus those who did not. Integrin αvβ6 was not expressed at the time of RPC in the terminal ileal epithelium, but expression became positive in the pouch epithelium after pouchitis developed.

Comment (SM): Recent studies have reported cumulative colectomy rates of 7% and 9.6% at 5 and 10 years after diagnosis of UC, despite advances in treatment. RPC and IPAA is a widely practiced surgical procedure in these patients and pouchitis is the most common complication. Integrin αvβ6 is a cell surface receptor that plays a crucial role in epithelial homeostasis, wound healing and tissue repair. Its dysregulation plays an important role in the pathogenesis of IBD. It primarily binds to various extracellular matrix proteins and is expressed in minimal quantities in healthy individuals. It is markedly upregulated in colonic and small bowel epithelium in IBD, particularly in the areas of active inflammation. UC patients express higher levels of integrin αvβ6 than CD patients. It is induced in response to inflammation by TNF-α, TGFβ and IL-1β. Anti-integrin αvβ6 antibodies produced in response can be a potential biomarker for UC. The levels of these antibodies come down after surgery. This study investigated the role of these antibodies in predicting the occurrence of pouchitis in patients with UC who underwent RPC with IPAA. Patients who developed pouchitis exhibited particularly elevated levels post-surgery unlike those who did not develop pouchitis. Statistical analysis demonstrated that patients with antibodies above a certain cut off level (106.5 U/mL) had a significant risk of developing pouchitis with a sensitivity of 75% and specificity of 100%. This study suggests that measuring anti-integrin αvβ6 antibodies at the time of RPC and thereafter may serve as a prognostic biomarker for predicting the risk of pouchitis. This can identify patients at higher risk, potentially guiding post-operative monitoring and management strategies.

Reference: Inflamm Bowel Dis. 2025;31(3):777-785
Abstract

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RESEARCH REVIEW VIDEO

Immune-Related Adverse Events When Using Immunotherapy to Treat Cancer

In this video Dr Rivalland discusses a wide variety of autoimmune toxicities and the potential mechanisms underlying irAEs. He also uses a patient case study to illustrate this in a real-world setting.

Dr Rivalland is a Medical Oncologist specialising in cancers of the lung, melanoma, brain and soft tissue tumours. He works at both Harbour Cancer & Wellness and Auckland City Hospital, and is involved in scientific research and clinical trials.

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Crohn's disease with latent tuberculosis infection or intestinal tuberculosis: Rapid discrimination by targeted next-generation sequencing

Authors: Ye L et al.

Summary: This prospective study examined the use of targeted next-generation sequencing (tNGS) for intestinal tuberculosis (ITB; n = 66) diagnosis and discrimination from CD with latent tuberculosis infection (LTBI; n = 34). Sensitivity, specificity, positive predictive value and negative predictive value for ITB were 83% (95% CI 72-91), 100% (95% CI 87-100), 100% (95% CI 92-100) and 76% (95% CI 60-87), and tNGS had higher diagnostic sensitivity than acid-fast bacillus (AFB) staining (15%; 95% CI 4-39; $p < 0.05$), tuberculosis polymerase chain reaction (TB-PCR; 22%; 95% CI 12-36; $p < 0.05$) or detection of caseous necrotising granulomas (17%; 95% CI 9-28; $p < 0.05$). Models combining comprehensive multi-clinical evaluation with tNGS increased sensitivity over tNGS alone (97% vs 83%). All patients with CD and LTBI were negative on tNGS.

Comment (SM): TB continues to be a major health problem especially in developing countries. The prevalence of IBD has also increased worldwide. Differentiating CD with LTB from ITB is very difficult and often leads to misdiagnosis and inappropriate treatment. The early, rapid and accurate detection of ITB in patients with undetermined intestinal ulcers but without extra intestinal manifestations of TB remains a challenge in TB endemic countries. Interferon gamma release assay like the Quantiferon Gold test is a modern alternative to tuberculin skin test, which can detect TB infection but cannot distinguish between latent and active infection. It is quite useful in screening for latent TB. Other tests like TB-PCR, demonstrating AFB, detecting caseating granulomas on biopsy etc., have high specificity but very low sensitivity. Hence there has been a need for highly specific and sensitive methods to diagnose ITB and differentiate it from CD with LTBI. Metagenomic tNGS for microbial DNA has been shown to be of high diagnostic value. This prospective study aimed to evaluate the diagnostic performance of tNGS using fresh biopsy tissue. This was compared to conventional diagnostic methods. tNGS outperformed all other methods like AFB staining, TB-PCR and demonstration of caseating granulomas. None of the patients with CD-LTB were positive for tNGS. The sensitivity of tNGS further increased (from 83% to 97%) when combined with other factors. tNGS has revolutionised the future of diagnostics and may be used as a frontline diagnostic method for ITB diagnosis and an effective method to discriminate CD with LTB. This will be particularly useful in high TB endemic countries.

Reference: Aliment Pharmacy Ther. 2025;61(7):1218-1225
Abstract

Contemporary risk of surgery in patients with ulcerative colitis and Crohn's disease: A meta-analysis of population-based cohorts

Authors: Tsai L et al.

Summary: This systematic review and meta-analysis sought to estimate the rates and trends of colectomy in UC patients, and of primary and re-resection in CD patients based on 48 studies conducted between 1955 and 2016. Overall, in UC patients, 1-, 5-, and 10-year colectomy risks were 4.0% (95% CI 3.3-5.0), 8.8% (95% CI 7.7-10.0) and 13.3% (95% CI 11.3-15.5), with a decline in risk over time ($p < 0.001$). Contemporary risks (studies conducted after 2000) were 2.8% (95% CI 2.0-3.9), 7.0% (95% CI 5.7-8.6) and 9.6% (95% CI 6.3-14.2). In CD patients, overall 1-, 5-, and 10-year risks of surgery were 18.7% (95% CI 15.0-23.0), 28.0% (95% CI 24.0-32.4) and 39.5% (95% CI 33.3-46.2), also showing a decline in risk over time ($p < 0.001$). Contemporary risks were 12.3% (95% CI 10.8-14.0), 18.0% (95% CI 15.4-21.0) and 26.2% (95% CI 23.4-29.4). In a meta-analysis of eight studies in CD patients with prior resection, cumulative risk of a second resection 5- and 10-years after the first was 17.7% (95% CI 13.5-22.9) and 31.3% (95% CI 24.1-39.6).

Comment (MS): In this review, my focus is on surgery in IBD. To start off with, I reviewed the above study to set the scene. The paper compared, primary surgery rates in UC and CD as well as re-surgery rates in patients diagnosed before 2000 and in patients diagnosed after 2000 under the assumption that the widening introduction of targeted biological medication influenced disease course. The authors identified 26 studies in UC and 22 studies in CD comprising patients diagnosed between 1955 and 2016. Analysed were the 1-, 5- and 10-year risk of surgery. Indeed, there was a significant reduction in all categories. For UC, the overall 1-, 5-, and 10-year risk of colectomy reduced from 4.0% to 2.8%, 8.8% to 7.0% and from 13.3% to 9.6%. Similarly, in CD, the overall 1-, 5-, and 10-year risk of surgery reduced from 18.7% to 12.3%, 28.0% to 18.0% and 39.5% to 26.2%. A limited number of studies looked at re-surgery risk at 5 years (17.7%) and 10 years (31.3%). No separation between historic or contemporary cohorts was given. The authors speculate that this reduction could be attributed to either earlier detection due to heightened awareness or better and more effective treatment. Given that New Zealand for many years had very limited access to advanced therapies, the question remains if this trend is seen here as well.

Reference: Clin Gastroenterol Hepatol. 2021;19(10):2031-2045.e11
Abstract

After surgically induced remission, ileal and colonic mucosa-associated microbiota predicts Crohn's disease recurrence

Authors: Hernández-Rocha C et al.

Summary: This study examined tissue-associated microbiota from 349 post-operative colonoscopies and 944 biopsy samples from 262 patients with CD. Differences in ileal and colonic mucosa-associated microbiota were accounted for by ileal inflammation. In 97 patients in surgically-induced remission who later developed endoscopic recurrence, there was lower diversity and microbial deviations versus those who remained in endoscopic remission. Depletion of Anaerostipes genus and an increase of genera from the Gammaproteobacteria class increase the risk of recurrence. The gut microbiome better predicted future recurrence better than clinical features.

Comment (MS): Tsai et al., demonstrated a 17.7-31.3% re-surgery risk for patients with CD following primary resection highlighting the fact that surgery cannot cure the disease. The task is to identify patients at risk of early recurrence. Currently, the gold standard is colonoscopy after 6-12 months to stratify patients according the Rutgeerts classification of the anastomosis into those with a good prognosis (i0-i1) and early recurrence (i2–i4). Unclear is what drives inflammation. As CD is generally seen as the result of an overly aggressive immune response toward ubiquitous bacteria, the authors hypothesised that analysis of the microbiome at time of first post-surgical endoscopy might provide an answer concerning recurrence of disease. To take it even further, the authors postulated that the post-operative scenario might give answers to the pathogenesis of CD. Patients who had undergone ileo-caecal resection (including the ileo-caecal valve) were recruited. Excluded were patients treated with metronidazole and those who had their first colonoscopy prior to 3 months or after 18 months following surgery. A total of 294 patients were recruited and data from 397 colonoscopies obtained. The authors found that postoperatively, patients with Rutgeerts score i0-i1 who display abnormal microbial patterns, developed significant inflammatory lesions when compared with patients who remained in remission. In further detail, Anaerostipes as well as Faecalibacterium, both short-chain fatty acid producers, were depleted in patients with CD who despite being in endoscopic remission experienced future recurrence. This finding is interesting as that a reduction of Faecalibacterium was seen in healthy relatives of IBD patients years before the onset of *de novo* disease. In a clinical, practical context, the changes in the microbiome predicting relapse were seen in rectal mucosal biopsies as well as in biopsies closer to the anastomosis.

Reference: Clin Gastroenterol Hepatol. 2025;23(4):612-620.e10
Abstract

INDEPENDENT COMMENTARY BY
Professor Michael Schultz
MD, PhD, FRACP

Michael studied in Erlangen-Nuremberg and trained in Manchester, London and Regensburg, Germany. He went to Chapel Hill, NC at the University of North Carolina for his postdoctoral fellowship. Michael joined the Department of Medicine at the University of Otago in 2005, taking up a joint clinical position as a Senior Lecturer and Gastroenterologist with the Southern District Health Board. **FOR FULL BIO CLICK HERE.**

Clinical predictors of early and late endoscopic recurrence following ileocolonic resection in Crohn's disease

Authors: Hernández-Rocha C et al.

Summary: This North American, multicentre, prospective study sought to identify clinical predictors of recurrence after ileocolic resection at initial and later postoperative colonoscopies in 365 patients (674 colonoscopies; median age 32 years; 51.8% male; 10.1% non-White ethnicity; 36.4% receiving anti-TNF agents; 8.2% smokers). At initial postoperative colonoscopy, 29.9% of patients were experiencing recurrence. Factors associated with recurrence were male sex (OR 1.95; 95% CI 1.12-3.40), non-White ethnicity (OR 2.48; 95% CI 1.09-5.63), longer interval before colonoscopy (OR 1.09; 95% CI 1.002-1.18), and postoperative smoking (OR 2.78; 95% CI 1.16-6.67). Risk of recurrence was lower with prophylactic anti-TNF therapy (OR 0.28; 95% CI 0.14-0.55), but was protective in anti-TNF-experienced not anti-TNF-naive patients. Among those without recurrence at initial colonoscopy, a Rutgeerts i1 score was associated with later recurrence (OR 4.43; 95% CI 1.73-11.35).

Comment (MS): Post-operative colonoscopy within 6-12 months after surgery remains the gold standard to predict recurrence. However, in the current health system environment, colonoscopies are difficult to obtain in a timely fashion. The authors aimed to predict recurrence (early or late) using clinical factors. A total of 674 colonoscopies from 365 CD patients were included in the analyses. At first endoscopy, 70.1% of patients had no disease (Rutgeerts score i0 to i1) while 29.9% showed signs of early recurrence (i2 to i4). Clinically, male gender, smoking after surgery and a longer interval between surgery and first colonoscopy were associated with an increased risk of recurrence. While usually i2 is classified as early recurrence and optimisation of therapy is recommended, in the present study, already i1 lesions were associated with recurrence to a higher degree than i0, while only anti-TNF use with or without concurrent thiopurines post-surgically was associated with a reduced risk of endoscopic recurrence. Interestingly, the protective effect of anti-TNF therapy was only seen in patients with prior anti-TNF use, but this could be due to the small sample size. Those who started anti-TNF treatment *de novo* were not protected. The authors therefore recommend continuation of anti-TNF therapy and postulate that anti-TNF prior to surgery was initiated too late to remedy the damage that had already occurred, i.e., penetrating or stenosing disease. Also interesting was the finding that there was no reduction in surgery over the 10-year study period despite better access to biological therapy.

Reference: J Crohns Colitis 2024;18(4):615-627
Abstract

Vedolizumab to prevent postoperative recurrence of Crohn's disease (REPREVIO): A multicentre, double-blind, randomised, placebo-controlled trial

Authors: D'Haens G et al.

Summary: The multinational double-blind, randomised, placebo-controlled REPREVIO trial examined the use of vedolizumab to prevent postoperative recurrence of CD in 84 patients after ileocolonic resection. The probability of a lower modified Rutgeerts score after 26 weeks on vedolizumab compared to placebo was 77.8% (95% CI 66.4-86.3; $p < 0.0001$). Severe endoscopic recurrence occurred in 10 (23.3%) vedolizumab recipients versus 23 (62.2%) placebo recipients (difference -38.9%; 95% CI -56.0 to -17.3; $p = 0.0004$). Serious adverse events occurred in 3 (7.0%) vedolizumab (bilateral tubo-ovarian abscesses, thrombosed haemorrhoids, pancreatic adenocarcinoma) and 2 (5.4%) placebo (intestinal perforation related to CD; severe abdominal pain) recipients.

Comment (MS): In the previous study, vedolizumab treatment was not associated with a decrease of post-operative recurrence; however, this might be due to the small sample size of this subgroup. In this study, 84 patients were randomised 1:1 to receive vedolizumab or placebo within 4 weeks of surgery. All patients had to have at least one risk factor for post-operative recurrence (active smoking, perforating disease, previous anti-TNF exposure, or more than one previous resection). Previous treatment with vedolizumab was excluded. Approximately 50% of patients in both groups had prior anti-TNF treatment. Ileo-colonoscopic evaluation of the anastomosis was undertaken at 6 months. At week 26, any recurrence (Rutgeerts score >i0) in the vedolizumab group occurred in 58% compared to 97.3% in the placebo group ($p < 0.0001$). In fact, only 23% versus 62% in the vedolizumab group experienced severe recurrence (>i2b; $p = 0.0004$). Clinical recurrence was similar for both groups (20.9% vedolizumab vs 21.6% placebo). The post-operative treatment with vedolizumab was safe. The authors do not mention if pre-operative treatment with anti-TNF made a difference to the outcome.

Reference: Lancet Gastroenterol Hepatol. 2025;10(1):26-33
Abstract

Development and validation of a risk prediction tool for the diagnosis of inflammatory bowel disease in patients presenting in primary care with abdominal symptoms

Authors: Umar N et al.

Summary: This UK, retrospective cohort study sought to develop and validate a risk prediction tool for IBD based on data from 2,054,530 patients in a development cohort (0.7% with IBD; 66.3% UC; 33.7% CD) and 673,320 patients in a validation cohort. Predictors used in the model (age, smoking, BMI, gastrointestinal symptoms, extraintestinal manifestations, comorbidities, family history, laboratory investigations) provided good discrimination and calibration in men (C-statistic 0.78; 95% CI 0.77-0.79) and women (C-statistic 0.78; 95% CI 0.77-0.79). In the validation cohort, the model slightly overestimated IBD risk at higher risk thresholds.

Comment (CH): This UK retrospective cohort study looking at the development and validation of a risk prediction tool for the diagnosis of IBD looks promising. From the results shown it could aid in earlier diagnosis that should then provide better patient outcomes with earlier specialist care and medical intervention. Having a tool like this in primary care would help to identify at-risk patients and also help to reduce that patient group that is referred but where IBD pathology is less likely to be found. Once at-risk patients are referred into specialist services the clinical data obtained from the prediction tool could also be used to triage referrals enabling patients with a more severe phenotype to be seen sooner. As the health system in the UK is similar to our own here in New Zealand with a primary care service referring into secondary and specialised care, I could see this risk prediction tool been well utilised in our health setting and look forward to seeing further research and development of this tool.

Reference: J Crohns Colitis. 2025;19(4):jjaf044
Abstract

Contraception, fertility and inflammatory bowel disease (IBD): A survey of the perspectives of patients, gastroenterologists and women's healthcare providers

Authors: Le Cosquer G et al.

Summary: This French survey examined knowledge discrepancies among 100 IBD patients (63% CD), 50 gastroenterologists, and 72 women's healthcare providers about fertility and contraception in IBD patients. Almost half (47%) of the women had never discussed fertility or contraception with a gastroenterologist; only 22% had done so on request. Most respondents (80% of women, 54% of gastroenterologists) were unsure if IBD affects contraception efficacy, and 50% of women's healthcare providers believed oral contraceptives were less effective in IBD patients. The impact of IBD medication on pregnancy (51%), risk of passing on IBD (47%) and flare-ups during pregnancy (39%) were identified as key concerns influencing patient's fertility decisions.

Comment (CH): This survey highlights that we are potentially still not good at discussing issues such as contraception and fertility with our IBD patients. This small study was conducted in France in 2023 via a survey of the three groups as listed above; however, I find it interesting that IBD nurses were not included in this survey, as here in New Zealand the IBD nurse is often the healthcare professional that has a little more time with the patient and a big part of the role is to educate the patient and family around IBD and how IBD impacts aspects of their life. However, this study does highlight the need for us as healthcare professional involved in the care of IBD patients to have open honest conversations with our patients regularly to improve the exchange of knowledge in these topics and not to assume that this information has been provided by other health professionals.

Reference: BMJ Open Gastroenterol. 2025;12(1):e001669
Abstract

INDEPENDENT COMMENTARY BY
Christine Ho

Christine is a nurse practitioner in gastroenterology at Dunedin Hospital, Te Whatu Ora–Southern. Her role includes the diagnosis and management of patients with IBD and she is a nurse endoscopist within the department. Christine completed her Master of Nursing at the University of Auckland in 2020 and a Postgraduate Certificate in Health Science in preparation for the scope of practice change to a nurse practitioner in 2022. Christine has a varied nursing background including experience in surgical nursing, stomal therapy, bowel cancer screening in the UK, endoscopy nursing and developed the role of the IBD Clinical Nurse Specialist and IBD service at Te Whatu Ora-Southern.

SCIENCE BLOG

Macrophage polarisation: Targeted regulation in IBD treatment

Dr Srikantaiah Manjunatha BSc, MBBS, MD(Med), FRCP(Lond), FRACP Consultant Gastroenterologist (Retired)

Macrophages develop from haematopoietic stem cells in the bone marrow, and differentiate into monocytes and mature into macrophages in the tissues. They play a crucial role as a part of the innate immune system and are involved in detecting, engulfing and destroying pathogens and apoptotic cells. Macrophage polarisation refers to the process of differentiation by which they adopt different functions in response to signals from their micro-environment. This process is essential for their diverse roles in the body, including host defence, tissue repair and immune regulation.

Undifferentiated macrophages are termed M0 and can polarise into M1 and M2 subtypes. M1 macrophages are induced by pro-inflammatory signals such as interferon or lipopolysaccharide. They produce pro-inflammatory cytokines, reactive oxygen species and nitric oxide which are crucial for initiating inflammatory responses. M2 macrophages are diametrically opposite and are induced by anti-inflammatory signals such as IL-4 and IL-13. M2 macrophages produce anti-inflammatory cytokines and growth factors resulting in resolution of inflammation, tissue repair and immune regulation.

Role in IBD – M1 macrophages are associated with onset and exacerbation of IBD by the production of pro-inflammatory cytokines like TNF-α, IL-1β and IL-6. Excessive activation and infiltration of M1 macrophages can perpetuate inflammation and tissue damage. M2 macrophages produce anti-inflammatory cytokines such as IL-10 and TGFβ which help in restoring homeostasis and tissue repair. An imbalance with predominant M1 over M2 subtype can hinder resolution of infection and facilitate chronicity of IBD. Various signalling pathways are influenced by macrophage polarisation in IBD. The NF-kβ pathway promotes M1 phenotype. The JAK/STAT pathway plays a role in both M1 and M2 phenotypes. MAPK is another pathway associated with inflammation. There are various other pathways involved in IBD pathogenesis. Inhibition of these pathways reduces the M1 population and facilitates M2 numbers.

Modulating macrophage polarisation is a promising therapeutic strategy for IBD. Targeting the imbalanced axis of macrophage polarisation has been promising in experimental models of colitis. In experiments involving mice, injecting bone marrow-derived M2 macrophages reduced the severity of colitis. Conversely, mice deficient in M2 macrophages were found to be more susceptible to experimental colitis. A link between the down regulation of M1 macrophage polarisation and mucosal healing in IBD patients treated with infliximab has been demonstrated. It may be possible to reduce inflammation and promote tissue repair by shifting the balance from M1 to M2 macrophages.

Natural remedies in IBD and macrophage polarisation – Natural remedies are currently a promising alternative to traditional medicine for the treatment of IBD. Natural compounds derived from plants (phytochemicals) have shown the potential to promote M2 macrophage differentiation and inhibit M1 macrophages. A class of active polyphenols known as flavonoids, found in plants, are the focus of multiple studies for treatment of IBD. They are cheap, safe, and eco-friendly with great patient acceptance. The following are some of the phytochemicals of interest in the treatment of IBD, from a long list, as evidenced in mice with experimental colitis.

- Ginsenoside Rg1 – active component of *Panax Ginseng*, promotes M2 differentiation
- Baicalin - product of *Scutellaria baicalensis*, alters M1/M2 ratio
- Toosendanin – bark or fruits of Chinese herbal medicine
- Artemisinin – extracted from *Artemisia annua*, already well known as an antiviral, antiparasitic, tumour suppressive and anti-inflammatory agent
- Tiliroside – derived from linden, rosehip and strawberry
- Platycodin D – derived from *Platicodon grandiflorum*, promotes M2 macrophages
- Sulforaphane – found in cruciferous vegetables like broccoli, cabbage
- Rosemarinic acid – found in rosemary, lemon balm and mint
- Genistein – present in soy-based products
- Berberine – an alkaloid from the root of *Coptis chinensis.*

The importance of macrophage polarisation in IBD, further research into highly effective phytochemicals, or even combinations of these natural remedies with current treatments, are exciting prospects for future strategies of IBD treatment.

Further reading:

Zhang K et al. Macrophage polarization in inflammatory bowel disease. *Cell Commun Signal 2023;21:367*
Saurabh NK et al. A future avenue of treatment of ulcerative colitis targeting macrophage polarization: A phytochemical application. Crohns Colitis 360 2024;6(4):otae070