IBD Research Review™

Making Education Easy

Issue 53 - 2021

In this issue:

Abbreviations used in this issue:

CD = Crohn's disease; **ED** = emergency department; **HR** = hazard ratio; **IBD** = inflammatory bowel disease; **IPAA** = ileal pouch anal anastomosis; **JAK** = Janus kinase; **PSC** = primary sclerosing cholangitis; **TNF** = tumour necrosis factor; **UC** = ulcerative colitis.

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Welcome to issue 53 of IBD Research Review.

The first paper selected for this issue has assessed the impact that the consumption of ultra-processed foods has on the risk of developing IBD. The JAK inhibitor tofacitinib is the focus of several papers included in this issue, including an evaluation of its use as a rescue therapy for patients who have been hospitalised with UC flare, a report on its safety in a real-world cohort of patients with UC, and the impact of reducing the dosage for patients in stable UC remission on a maintenance dosage of 10mg twice daily. There are also papers on the impact that maternal and paternal IBD medication use has on birth outcomes.

Please keep sending your comments and feedback – we do appreciate it.

Kind Regards,

Associate Professor Britt Christensen
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Association of ultra-processed food intake with risk of inflammatory bowel disease: prospective cohort study

Authors: Narula N et al.

Summary: The relationship between ultra-processed food intake and IBD risk was prospectively evaluated in 116,087 adults (from 21 countries), 90 and 377 of whom developed incident CD and UC, respectively, during median follow-up of 9.7 years. A significant increased risk of incident IBD was seen for ultra-processed food intakes of ≥5 and 1–4 vs. <1 daily serving (respective adjusted HRs 1.82 [95% CI 1.22–2.72] and 1.67 [1.18–2.37]; p=0.006 for trend), with the increased risk seen across ultra-processed food subgroups and similar risks for CD and UC. Incident IBD risk was not affected by intake of white meat, red meat, dairy, starch, fruit, vegetables or legumes.

Comment: The incidence of IBD has increased in newly industrialised countries over the last several decades, and this increase has paralleled the adoption of a western diet. It has therefore been hypothesised that increased intakes of refined sugars and dietary fats, such as n-6 polyunsaturated fatty acids and decreased intake of fibre, are potential risk factors for the development of IBD. A systematic review has also previously found that high intakes of total fats, polyunsaturated fatty acids and omega-6 fatty acids are associated with an increased risk of IBD. The PURE study aimed to further analyse dietary risk factors and evaluate if consumption of processed foods was associated with increased IBD incidence. Data from a prospective observational cohort study on 136,384 adults aged 35–70 years with dietary information assessed using country-specific validated food frequency questionnaires originally for a cardiac risk study were analysed. Patients were followed for a median of 9.7 years and 467 participants developed incident IBD (90 with CD and 377 with UC). After adjustment for potential confounding factors, consuming ≥5 servings per day of ultra-processed food was found to almost double the risk of incident IBD. This was found to be true for consumption of soft drinks, refined sweetened foods, salty snacks and processed meat, and for both UC and CD. Interestingly, white meat, red meat, dairy, starch, and fruit, vegetables and legumes were not associated with incident IBD. In conclusion, higher processed food intake was associated with increased risk of developing IBD, and the risk is seen with all categories of processed foods. Further studies are required, but in high-risk patients, a low-processed Mediterranean style diet to reduce the risk of IBD onset could be advised.

Reference: BMJ 2021;374:n1554
Abstract

Superior treatment persistence with ustekinumab in Crohn's disease and vedolizumab in ulcerative colitis compared with anti-TNF biological agents

Authors: Ko Y et al.

Summary: Retrospective, population-based data from the Australian PBS (n=2499; 8219 person-years of follow-up) were used to evaluate the persistence of adalimumab, infliximab, vedolizumab and ustekinumab in CD and UC. Ustekinumab had greater persistence in patients with CD than anti-TNF agents (HR 1.79 [95% CI 1.32–2.38]); the 12-month persistence rates with ustekinumab, vedolizumab, infliximab and adalimumab were 80.0%, 73.5%, 68.1% and 64.2%, respectively (p=0.01). In patients with moderate-to-severe UC, vedolizumab had greater persistence than anti-TNF agents (HR 1.67 [95% CI 1.27–2.18]); the 12-month persistence rates for vedolizumab, infliximab and adalimumab were 73.4%, 61.1% and 45.5%, respectively (p<0.001). Cotherapy with immunomodulators did not increase persistence with non-anti-TNF agents, but thiopurines significantly increased persistence of anti-TNF agents in both CD and UC, whereas methotrexate significantly increased such persistence only in CD.

Comment: Medication persistence is an important efficacy endpoint, as it is tied to real-world treatment effectiveness, tolerability and prescriber and patient acceptability. There are multiple biologic classes available to treat both UC and CD. Differentiating effectiveness and determining treatment placement of each agent can be difficult. Currently there has been only one head-to-head trial of biologic therapies to date (comparing vedolizumab versus adalimumab in moderate-to-severe UC for up to 1 year). Therefore, further data to guide treatment decisions are required.

The PANIC study analysed the persistence of prescribing in an Australian cohort of UC and CD patients for adalimumab, infliximab, vedolizumab and ustekinumab. Ko et al. found that ustekinumab treatment was associated with persistence as first-, second- and third-line therapies in CD, and that vedolizumab was associated with treatment persistence as first-line therapy but not as second- or third-line therapy in UC. For fistulising CD, only adalimumab and infliximab were analysed and there was no significant difference in persistence. Cotherapy with any immunomodulator in CD and thiopurine cotherapy in moderate-to-severe UC and acute severe UC significantly increased persistence of anti-TNF therapy. Immunomodulator cotherapy did not improve persistence of ustekinumab or vedolizumab.

Overall, the PANIC study demonstrates superior persistence of ustekinumab and vedolizumab over anti-TNF agents in the treatment of CD and UC, respectively. Obviously, the data are limited as they are not head-to-head and do not include endoscopic or biochemical data. However, they do provide evidence that these newer non-TNF therapies have a role as first-line therapy in IBD and show promising real-world signs of improved persistence. The study also highlights the need for immunomodulator cotherapy when prescribing anti-TNF therapy, and confirms a drop in persistence with each subsequent therapy, substantiating the need to optimise and select correctly the first-line therapy.

Reference: Aliment Pharmacol Ther 2021;54:292–301
Abstract

Tofacitinib as salvage therapy for 55 patients hospitalised with refractory severe ulcerative colitis

Authors: Uzzan M et al., GETAID-TALC Study Group

Summary: This analysis of prospective and retrospective data from the GETAID cohort evaluated rescue tofacitinib in 55 patients hospitalised for UC flare, including 49 with prior infliximab failure and 19 with prior cyclosporin exposure. Over median follow-up of 6.5 months, the estimated 3- and 6-month colectomy-free survival rates were 78.9% and 73.6%, respectively, and the respective 6-week clinical response, clinical remission and steroid-free clinical remission rates were 60%, 45.5% and 37.5% with respective 14-week rates of 41.8%, 34.5% and 32.7%. Three patients discontinued tofacitinib due to adverse events, and two patients aged >60 years developed herpes zoster infections. There were no venous thrombotic or major adverse cardiovascular events or deaths.

Comment: Up to 25% of patients with UC have a severe flare that requires an admission to hospital. Many do not respond to steroids alone and require a second line of treatment, which usually consists of infliximab or cyclosporin. These treatments have similar efficacy and decrease the need for colectomy. However, there is a significant treatment gap and new therapeutic options are required. Tofacitinib is a rapidly acting, oral, small-molecule JAK inhibitor recently approved for moderate-to-severe UC. Its onset of action is within days, and recent case series demonstrated that high-intensity tofacitinib could lead to improvement in patients with acute severe UC who have previously failed anti-TNF therapy.

This current study was an observational, multicentre study from the GETAID registry in France. Fifty-five patients admitted for a UC flare (75% with Lichtiger score ≥10) were treated with standard-dose tofacitinib 10mg twice daily. The majority of patients had previously failed anti-TNF therapy. At week 14 following tofacitinib initiation, 42%, 35% and 33% of patients were in clinical response, clinical remission and steroid-free clinical remission, respectively. At the end of follow-up, 28 patients (50.9%) were still on tofacitinib. In this treatment-refractory cohort, 27% of patients underwent colectomy at median follow-up of 7 months. Adverse events were in line with clinical trials, with the most significant adverse events being two patients who experienced herpes zoster. Overall, colectomy rates in this treatment-resistant cohort were similar or just above those demonstrated in studies of cyclosporin and infliximab in steroid-refractory acute severe UC.

Overall, these results appear encouraging, and other studies have supported the positive results. However, it is important to note that one quarter of patients in this study did not meet clinical criteria for acute severe colitis. Furthermore, a recently published study in 40 patients with acute severe colitis who received tofacitinib either 10mg twice daily or three times daily and who were matched to controls found that when stratified according to treatment dosage, 10mg three times daily was protective for colectomy but 10mg twice daily was not. This is an important point, as this current study only utilised the standard dosage of 10mg twice daily. Therefore, further work is required to determine the optimal dosage, timing and positioning of tofacitinib in acute severe UC. Tofacitinib should therefore be reserved for carefully selected patients where more traditional therapies have been exhausted. Importantly, colectomy should not be delayed in older or severe patients.

Reference: Aliment Pharmacol Ther 2021;54:312–9
Abstract

Paternal exposure to immunosuppressive and/or biologic agents and birth outcomes in patients with immune-mediated inflammatory diseases

Authors: Meserve J et al.

Summary: In a retrospective cohort analysis of data from an administrative claims database, US researchers examined the effect of immunosuppressive and/or biologic agent exposure around conception in 7453 fathers with immune-mediated inflammatory diseases, including IBD. Compared with the prevalence of major congenital malformations in unexposed fathers (3.4%), there was no difference in risk after exposure to thiopurines (relative risk 1.12 [95% CI 0.66–1.76]), methotrexate (0.67 [0.21–1.55]), TNFα antagonists (1.14 [0.81–1.57]) or non-TNF-targeting biologic agents (1.75 [0.80–3.24]). There was also no association between paternal medication exposure and risk of preterm birth or low birthweight.

Comment: Treatment of IBD generally consists of immunosuppressive therapies. Many studies have addressed the safety of maternal exposure to these medications on birth outcomes; however, there are limited data on paternal exposure. This study aimed to address this knowledge gap by examining the effect of exposure around conception to immunosuppressive and/or biologic agents on neonatal outcomes in expectant fathers with immune-mediated inflammatory diseases. There were 7453 expectant fathers with immune-mediated inflammatory diseases examined (461 exposed to thiopurines, 171 to methotrexate, 1082 to TNFα antagonists and 132 to non-TNF-targeting biologics versus 5607 unexposed fathers in the periconception period), and there was no increase with any of the exposures on the risk of major congenital anomalies, risk of low birthweight or preterm birth in neonates.

This study adds to the data from prior studies that have demonstrated that paternal exposure to thiopurines, methotrexate and anti-TNF agents does not appear to adversely affect birth outcomes and confirms that the non-anti-TNF biologics ustekinumab and vedolizumab are also likely to be safe. These findings support continuing pharmacotherapy without interruption in fathers planning conception. Paternal counselling should focus on the importance of maintaining disease remission with reassurance about medication safety. Of note, data regarding the safety of tofacitinib in the preconception phase were not looked at in this study; practically, due to the risk of flare these medications are also continued in most male patients in the preconception and conception stage.

Reference: Gastroenterology 2021;161:107–15
Abstract

High-dose vitamin D does not prevent postoperative recurrence of Crohn's disease in a randomized placebo-controlled trial

Authors: de Bruyn JR et al., on behalf of the Dutch-Belgian The Effect of Vitamin D3 to Prevent Postoperative Relapse of Crohn's Disease: A Placebo-controlled Randomized Trial Study Group

Summary: Patients with CD who had undergone ileocolonic resection with ileocolonic anastomosis were randomised to oral vitamin D 25,000IU (n=72) or placebo (n=71) each week for 26 weeks; serum 25-hydroxy vitamin D level increased significantly in the vitamin D group but not in the placebo group. There was no significant difference between the vitamin D and placebo arms for the primary endpoint of endoscopic recurrence at 26 weeks (58% vs. 66% [p=0.37]) or for the cumulative clinical recurrence rate (18.1% vs. 18.3% [p=0.91]). Few adverse events were reported.

Comment: Many studies have confirmed that vitamin D has an anti-inflammatory effect and can modulate the innate immune response. Furthermore, in CD patients, low serum vitamin D levels have been associated with an increased risk of surgery compared with high vitamin D levels. Yet the role of vitamin D supplementation is unclear. In IBD, reports on the anti-inflammatory effects of vitamin D supplementation have been contradictory. To try and answer the question of whether vitamin D supplementation can modulate inflammation in IBD, 143 postoperative CD patients were randomised to 25,000IU of vitamin D weekly versus placebo. De Bruyn et al. found that although serum vitamin D levels doubled after 6 weeks and then remained stable in those supplemented with vitamin D and did not increase in those on placebo, there was no difference in the incidence of endoscopic or clinical recurrence at week 26 in either group. Endoscopic recurrence was defined by a Rutgeert's score i2b or higher, and the endoscopic studies were blinded and centrally read, adding to the study strength. Therefore, vitamin D should be prescribed when levels are low for bone health, but there is no convincing evidence of its benefit in modulating inflammation in patients with IBD.

Reference: Clin Gastroenterol Hepatol 2021;19:1573–82
Abstract

Safety of tofacitinib in a real-world cohort of patients with ulcerative colitis

Authors: Deepak P et al.

Summary: Adverse events associated with tofacitinib for UC were reported for 260 participants from the US Tofacitinib Real-world Outcomes in Patients with Ulcerative Colitis and Crohn's Disease Consortium study. Adverse events were reported for 15.7% of the participants, 36.6% of which were serious (respective incidence rates, 27.2 and 10.0 per 100 patient-years). Infections were recorded in 13 participants (5%), including herpes zoster in five. Two participants, both receiving tofacitinib 10mg twice daily, developed venous thromboembolism. Tofacitinib discontinuation was recorded in 12 participants (4.6%).

Comment: Tofacitinib has recently been approved for the PBS in Australia. This is an exciting development; however, with any new medication, knowledge surrounding adverse events is imperative. Adverse events including reactivation of herpes zoster and thromboembolism have been reported in clinical trials. As clinical trial data often differ significantly from the real-world, this study aimed to determine the rates of such complications in the real-world setting. It analysed the UC data from the Tofacitinib Real-world Outcomes in Patients with Ulcerative Colitis and Crohn's Disease Consortium study. Sixteen percent of the 260 patients examined experienced an adverse event. Specifically, five patients developed shingles and two developed a thromboembolism; both of these patients were on tofacitinib 10mg twice daily. There were no major cardiovascular events reported in the 64 patients who were aged 50 years and older, and no patient discontinued tofacitinib due to abnormal lipid profiles, although a handful were managed medically. These data suggest that real-world safety signals for tofacitinib are similar to those from clinical trials. Previous studies have confirmed a higher risk of adverse events in the 10mg twice a day group. This suggests that, although there are no new safety signals for tofacitinib, dose de-escalation to 5mg twice daily should occur as early and where clinically possible to maintain remission.

Reference: Clin Gastroenterol Hepatol 2021;19:1592–601
Abstract

Incidence, risk factors, and outcomes of pouchitis and pouch-related complications in patients with ulcerative colitis

Authors: Barnes EL et al.

Summary: These researchers reported on pouchitis during the first 2 years after proctocolectomy with IPAA (ileal pouch-anal anastomosis) for UC in 594 patients. The respective 2-year cumulative incidences of isolated acute and recurrent pouchitis were 29% and 19%. Compared with patients with isolated acute pouchitis, those with recurrent pouchitis had significantly more outpatient visits, ED visits and inpatient admissions. Significant predictors of pouchitis were prior PSC (primary sclerosing cholangitis; adjusted odds ratio 3.94 [95% CI 1.05–14.8]) and preoperative anti-TNFα exposure (1.63 [1.09–2.45]). Patients who developed pouchitis had a cumulative frequency of new immunosuppressive therapy of 40% and a cumulative incidence of pouch excision of 1.0%. The cumulative incidence of a new CD diagnosis post-IPAA for UC was 9.0%.

Comment: Acute antibiotic-responsive pouchitis is very common following IPAA surgery, with some studies estimating the incidence to be approximately 40% within 12 months and 80% overall. Pouchitis can significantly impair quality of life, particularly when it is recurrent or chronic. This study aimed to clarify rates of pouchitis more accurately in a larger population study. A claims database was examined to determine rates of prescriptions, ED presentations and inpatient hospitalisations in patients who had undergone IPAA surgery. To be included, patients had to be enrolled with the insurance company for 6 months prior to surgery and for 2 years postsurgery. There were 594 patients included, of whom 284 (48%) developed an episode of pouchitis; 173 (29%) of these were one isolated incidence and 111 (19%) developed recurrent pouchitis. Risk factors for pouchitis were similar to previous studies, and included having a codiagnosis of PSC and having exposure to anti-TNF therapy prior to surgery. Forty percent of patients who developed an episode of pouchitis went on to need immunosuppression but only 1% had pouch excision. Those that developed recurrent pouchitis had greater healthcare utilisation including ED visits and inpatient admissions. These findings confirm that pouchitis is a common complication following IPAA surgery, and that PSC and prior anti-TNF exposure are risk factors. Despite this, pouch excision rates were low. Future studies need to determine if risk factors can be mitigated or if pouchitis can be prevented, perhaps with proactive microbiome therapy including use of probiotics.

Reference: Clin Gastroenterol Hepatol 2021;19:1583–91
Abstract

A scoring system to determine patients' risk of colectomy within 1 year after hospital admission for acute severe ulcerative colitis

Authors: Le Baut G et al., for the Saint Antoine IBD Network

Summary: These authors analysed retrospective data for 270 patients admitted for acute severe UC, and treated with corticosteroids, cyclosporin or TNF antagonists, to develop a system to determine a patient's risk of colectomy within 1 year of hospitalisation. A derivation cohort (median follow-up 30 months) had a cumulative colectomy risk of 12.3%, with risk factors (on multivariate analysis) used in the model being prior TNF antagonist or thiopurine exposure (HR 3.86 [95% CI 1.82–8.18]), *Clostridioides difficile* infection (3.73 [1.11–12.55]), serum C-reactive protein level >30 mg/L (3.06 [1.11–8.43]) and serum albumin level <30 g/L (2.67 [1.20–5.92]). The respective 1-year cumulative risks of colectomy for derivation cohort patients with scores of 0, 1, 2, 3 and 4 were 0.0%, 9.4%, 10.6%, 51.2% and 100%; negative predictive values were 87–92%, and validation cohort findings were consistent.

Comment: Acute severe UC affects up to 25% of patients with UC. Management usually consists of step-up therapy, commencing with intravenous corticosteroids and escalating to infliximab or cyclosporin in those who do not respond. Despite this, colectomy is required in a substantial subgroup of patients. Predictors of response and colectomy are needed to determine which patients may warrant more aggressive, earlier treatment and closer postdischarge follow-up to decrease morbidity and mortality. The aim of this study was to develop a score and identify factors that could predict colectomy within the first year of acute severe UC. Although current scores exist, they were developed before the era of biologics and calculated on day 3 of admission. The study identified four factors on day 1 of admission associated with colectomy: previous treatment with anti-TNF therapies or thiopurines, *C. difficile* infection, increased serum level of C-reactive protein >30 mg/L and decreased albumin <30 g/L. There were 270 patients included, and colectomy was performed in 12% at 1 year and 33% at 5 years after index hospitalisation. Patients who had 0, 1, 2, 3 and 4 of the factors present on admission had cumulative colectomy rates of 0%, 9%, 11%, 51% and 100% at 1 year, respectively. The findings were accurately validated in a further cohort of 185 patients.

This study provides an attractive tool to quickly be able to prognosticate a patient's disease severity on admission with acute severe UC. Although not dissimilar to other tools, the advantage of this score is that it can be calculated on day 1 and is simple. Utilising this system, patients can be assessed on admission, and those with one or two risk factors, who would be considered low risk, can have a lower threshold for discharge and outpatient management. Those with three or four risk factors need to be managed aggressively. The study is limited by a lack of endoscopic or faecal calprotectin data. However, this easy-to-calculate score provides an accurate prediction model and can help inform the aggressiveness of the treatment on admission and follow-up.

Reference: Clin Gastroenterol Hepatol 2021;19:1602–10
Abstract

Outcomes of tofacitinib dose reduction in patients with ulcerative colitis in stable remission from the randomised RIVETING trial

Authors: Vermeire S et al.

Summary: The RIVETING trial's primary completion analysis was reported; RIVETING randomised 140 patients with UC in stable remission on tofacitinib 10mg twice daily to a dosage reduction to 5mg twice daily or continue on 10mg twice daily. The respective proportions of participants from the twice-daily 5mg and 10mg arms who maintained remission (according to modified Mayo score) at 6 months were 77.1% and 90.0% (adjusted difference, 12.9% [95% CI 0.5–25.0]), with smaller differences seen for participants with a baseline endoscopic subscore of 0 versus 1 (9.8% and 21.1%, respectively), and in those without versus with prior TNF inhibitor failure (9.5% and 17.4%, respectively). The two groups had similar incidences of adverse events and serious adverse events, and there were no deaths.

Comment: Tofacitinib is an oral small molecule JAK inhibitor that has recently been approved for moderate-to-severe UC in Australia. It has been approved at a dosage of 10mg twice a day for induction, and at a dosage of 5mg twice daily for maintenance where possible. This is secondary to the fact that deep vein thrombosis and infections have been found to occur more frequently at the higher dosage. Despite this, a dosage of 10mg twice daily in maintenance is allowed when required to keep inflammation under control, but should be limited to the shortest possible duration.

Although the lowest effective dosage should be used to maintain treatment response, this needs to be weighted against the risk of disease flare. To more accurately characterise this risk, this study looked at patients maintained on 10mg twice daily who were in remission long-term and analysed the safety and efficacy of de-escalating to 5mg twice daily. Patients were included if they had been on 10mg twice daily for ≥2 years and had been in stable remission for ≥6 months. Patients were randomised to continue on 10mg twice daily or de-escalate to 5mg twice daily, and were stratified by endoscopic subscore of 0 or 1. One hundred and forty patients were randomised and 77% of patients remained in remission on 5mg twice daily compared with 90% who were maintained on 10mg twice daily; although numerically different, the difference was not statistically significant. Notably, the difference between maintenance of remission was more pronounced in those who had failed anti-TNF treatment and in those with a baseline endoscopic subscore of 1 compared with 0 at time of de-escalation. Serious adverse events, including infections, were similar in the 5mg and 10mg twice daily groups, with safety consistent with known safety profiles from clinical trials.

Overall, this study suggests numerically that there is an increased risk of disease flare on de-escalation to 5mg twice daily in those in stable remission at 10mg twice daily. This is most significant in patients who have not achieved deep healing or have previously failed anti-TNF therapy. De-escalation in these patients should be considered carefully, but the majority of patients will maintain remission on a de-escalated dose. It is important to note that follow-up in this study was limited to only 6 months and longer-term data are needed to truly delineate the outcomes of de-escalation. In addition, future studies are needed to determine if clinical response is able to be recaptured following a flare on de-escalated dosing by escalating treatment back up to 10mg twice daily.

Reference: J Crohns Colitis 2021;15:1130–41
Abstract

Health outcomes of 1000 children born to mothers with inflammatory bowel disease in their first 5 years of life

Authors: Kanis SL et al., on behalf of the Initiative on Crohns and Colitis (ICC)

Summary: This retrospective study from The Netherlands reported health outcomes of 1000 children born to 381 mothers with CD, 25 with UC and 20 with IBD unclassified, and also assessed the impact of maternal IBD medication use on these outcomes. Intrauterine exposure to anti-TNFα therapy was documented for 196 of the children (60 with concomitant thiopurine exposure) and 240 had been exposed to thiopurine monotherapy; the 564 children not exposed to such treatments served as controls. No significant association was seen between *in utero* exposure to IBD treatment and adverse long-term health outcomes. There was an increased incidence of intrahepatic cholestasis of pregnancy in women receiving thiopurines, but birth and long-term health outcomes of their children were not impacted.

Comment: Patients with IBD need to maintain disease control during pregnancy to optimise mother and baby outcomes. This often requires maintenance of medical treatment. Although evidence suggests no harm to the infant in the first year of life, longer-term data are sparse. This multicentre, retrospective study assessed health outcomes in children born to mothers with IBD with follow-up of 5 years. Reassuringly, it was found that there was no association with maternal anti-TNF or thiopurine exposure with antibiotic-treated infections or severe infections in the child over the 5 years. There were also no associations with adverse reactions to vaccination, growth failure, autoimmune diseases or malignancies. Smoking during pregnancy did increase the risk of antibiotic-treated infections in offspring and breastfeeding for at least 1 month decreased the risk of antibiotic-treated infection in offspring. The use of systemic corticosteroids was associated with preterm birth but not infections in offspring. There was an association between thiopurine use during pregnancy and intrahepatic cholestasis of pregnancy without affecting birth outcomes or long-term health outcomes of children. This was thought to be perhaps due to changing metabolism of thiopurines during pregnancy, which has previously been demonstrated to lead to an increase in 6-methylmercaptopurine.

In conclusion, the findings of this study confirm that anti-TNF therapies and thiopurines can be used during pregnancy to maintain disease remission. This study also adds to the growing literature suggesting thiopurine monitoring of levels should occur during pregnancy, with dose adjustments made according to 6-methylmercaptopurine concentrations. Future studies need to look at the impact of other newer medications in the long-term development of children and analyse whether maternal inflammation itself is a risk factor for childhood development. This study is the largest long-term study to assess the implications of maternal IBD medication during pregnancy on multiple outcomes of children and is very reassuring.

Reference: Gut 2021;70:1266–74
Abstract

Independent commentary by Associate Professor Britt Christensen

Britt holds a senior medical staff appointment at the Royal Melbourne Hospital, where she is the Head of the Inflammatory Bowel Disease Unit and is a Clinical Associate Professor at the University of Melbourne. Britt studied Medicine at the University of Melbourne, graduating with honours in 2006 and has completed a Masters of Public Health at Monash University, for which she was awarded a Medal of Academic Excellence. After completing her gastroenterology training at St Vincent's and Alfred Hospital, she was awarded the Joseph B. Kirsner fellowship and spent over 2 years undertaking advanced training in IBD at the prestigious University of Chicago Medicine, one of the largest and most prominent IBD centres in the world. Whilst there, she undertook research toward a PhD looking at histological outcomes and novel therapies in IBD. She is currently supervising multiple PhD students, is the princible investigator on large international clinical trials and has presented her research at numerous national and international conferences and has been published widely. In addition, Britt is a co-founder of the Victorian Immune Diseases Bio Bank and is the author of several book chapters on IBD and is a reviewer for a number of the top journals in the field of gastroenterology.

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