Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

enable comparison between multiple medical and non-medical therapeutic approaches, it is crucial to use standardised universal definitions for the diagnosis and response to therapy of stricturing Crohn's disease, such as those introduced by the Stenosis Therapy and Anti-Fibrosis Research (STAR) consortium.[7,8] Novel imaging techniques to improve the characterisation of strictures as being predominantly inflammatory or fibrotic need to be developed for proper patient stratification.[9] Although this study dampens the enthusiasm for SEMS, alternative stent options—eg, biodegradable or custom-made stents—might prove useful, in particular for longer segment strictures. Effective non-surgical therapeutic options for long-segment strictures are still absent because EBD and stents are restricted by device length and endoscopic therapy. In general, treatment with EBD and stents becomes increasingly technically difficult with increased stricture length. Although no specific antifibrotic therapy is currently approved, the first randomised trial of an antifibrotic drug for stricturing Crohn's disease is underway (NCT05013385) with several other compounds under consideration striving to provide non-invasive means for the treatment of stricturing Crohn's disease. Finally, perhaps the strongest signal of this trial, is the need to compare any novel endoscopic stricture therapy with the current gold standard: EBD. Multiple other approaches, including needle-knife stricturotomy,[10] have been reported, but the evidence remains restricted to case series and observational studies. Putting those to the test in controlled head-to-head comparisons will prove or dispute their promise. On the basis of this well done investigation by Loras and colleagues,[6] the gold standard remains EBD.

FR is a consultant for Adnovate, Agomab, Allergan, AbbVie, Arena, Boehringer-Ingelheim, Celgene/ Bristol Myers Squibb, Clinical Data Interchange Standards Consortium, Cowen, Ferring, Galmed, Genentech, Gilead, Gossamer, Guidepoint, Helmsley, Index Pharma, Jannsen, Koutif, Mestag, Metacrine, Morphic, Organovo, Origo, Pfizer, Pliant, Prometheus Biosciences, Receptos, RedX, Roche, Samsung, Surmodics, Surrozen, Takeda, Techlab, Theravance, Thetis, UCB, Ysios, and 89Bio. IG declares no competing interests.

*Idan Goren, *Florian Rieder*
riederf@ccf.org

Department of Inflammation and Immunity, Lerner Research Institute (ID, FR), and Department of Gastroenterology, Hepatology and Nutrition, Digestive Diseases and Surgery Institute (FR), Cleveland Clinic Foundation, Cleveland, OH 44195, USA; Division of Gastroenterology, Rabin Medical Center, Petah Tikva, Israel, Affiliated with Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel (ID); Department of Gastroenterology, Hepatology and Nutrition, Digestive Diseases and Surgery Institute; Cleveland Clinic Foundation, Cleveland, USA (FR)

1 Rieder F, Fiocchi C, Rogler G. Mechanisms, management, and treatment of fibrosis in patients with inflammatory bowel diseases. *Gastroenterology* 2017; **152:** 340–50.
2 Bouhnik Y, Carbonnel F, Laharie D, et al. Efficacy of adalimumab in patients with Crohn's disease and symptomatic small bowel stricture: a multicentre, prospective, observational cohort (CREOLE) study. *Gut* 2018; **67:** 53–60.
3 Bettenworth D, Gustavsson A, Atreja A, et al. A pooled analysis of efficacy, safety, and long-term outcome of endoscopic balloon dilation therapy for patients with stricturing Crohn's Disease. *Inflamm Bowel Dis* 2017; **23:** 133–42.
4 Karstensen J, Christensen K, Brynskov J, Rønholt C, Vilmann P, Hendel J. Biodegradable stents for the treatment of bowel strictures in Crohn's disease: technical results and challenges. *Endosc Int Open* 2016; **4:** E296–300.
5 Loras C, Pérez-Roldan F, Gornals JB, et al. Endoscopic treatment with self-expanding metal stents for Croh thelancethaematology-D-21-00689 n's disease strictures. *Aliment Pharmacol Ther* 2012; **36:** 833–39.
6 Loras C, Andujar X, Gornals JB, et al. Self-expanding metal stents versus endoscopic balloon dilation for the treatment of strictures in Crohn's disease (ProtDilat study): an open-label, multicentre, randomised trial. *Lancet Gastroenterol Hepatol* 2022; published online Jan 20. https://doi.org/10.1016/S2468-1253(21)00386-1.
7 Rieder F, Bettenworth D, Ma C, et al. An expert consensus to standardise definitions, diagnosis and treatment targets for anti-fibrotic stricture therapies in Crohn's disease. *Aliment Pharmacol Ther* 2018; **48:** 347–57.
8 Gordon IO, Bettenworth D, Bokemeyer A, et al. International consensus to standardise histopathological scoring for small bowel strictures in Crohn's disease. *Gut* 2021; published online May 5. https://dx.doi.org/10.1136/gutjnl-2021-324374.
9 Bettenworth D, Bokemeyer A, Baker M, et al. Assessment of Crohn's disease-associated small bowel strictures and fibrosis on cross-sectional imaging: a systematic review. *Gut* 2019; **68:** 1115–26.
10 Lan N, Shen B. Endoscopic stricturotomy with needle knife in the treatment of strictures from inflammatory bowel disease. *Inflamm Bowel Dis* 2017; **23:** 503–13.

Is the attenuated humoral response to COVID-19 vaccination in anti-TNF users relevant?

Published **Online** February 3, 2022 https://doi.org/10.1016/S2468-1253(22)00040-1

See **Articles** page 342

The COVID-19 pandemic has led to considerable morbidity, mortality, and strain on health-care services across the world, causing more than 5 million deaths since it began. Systemic immunosuppression might increase the risk of COVID-19-associated complications, and, as a result, individuals with inherent or acquired immunosuppression have been prioritised for vaccination and for receiving booster doses. Approximately a third of individuals living with inflammatory bowel disease (IBD) use immunosuppressive biologic medications chronically, and 5–10% of people with IBD in any given year are exposed to corticosteroids. The CLARITY-IBD study[1] was the first to show that the immune response to a

single dose of COVID-19 vaccine was attenuated in patients treated with anti-tumour necrosis factor (TNF) medications. However, whether this reduced immune response among people on anti-TNF therapies persists in those who receive subsequent doses of COVID-19 vaccines is not well described, and the efficacy of COVID-19 vaccination in people on immunosuppressive therapies commonly used in IBD has not yet been assessed.

In *The Lancet Gastroenterology & Hepatology*, James L Alexander and colleagues[2] have addressed this important knowledge gap, showing a persistent reduction in anti-SARS-CoV-2 spike protein antibody titres among individuals with IBD being treated with infliximab (geometric mean ratio 0·12, 95% CI 0·08–0·17; p<0·0001) and tofacitinib (0·43, 0·23–0·81; p=0·0095) in the 53–92 days following the second dose of a COVID-19 vaccine. Importantly, ustekinumab, vedolizumab, and thiopurine monotherapy did not affect the immunogenicity of vaccination.

Antibody titres are recognised as an important indicator of vaccine effectiveness in the general population, with lower antibody titres after COVID-19 vaccination being associated with a higher risk of breakthrough infections.[3,4] Globally, the reduction of antibody titres with time has led to the widespread adoption of booster doses to maintain immunity and protection from COVID-19-related hospitalisation and death. Alexander and colleagues' findings suggest that a considerable proportion of patients with IBD could be functionally unvaccinated, despite being adherent to the recommended vaccination regimen at the time, and indicate that individuals with IBD on anti-TNF agents might require early booster vaccinations or serological confirmation of an antibody response to vaccination. In some countries, fourth doses are being offered to individuals being treated with immunosuppressive medications on the basis of concerns regarding suboptimal serological responses to COVID-19 vaccination.

Despite concerns surrounding the robustness of the immune response to vaccination among people being treated with anti-TNF therapies, these same patients do not seem to be at an increased risk of contracting COVID-19 compared with people with IBD not on biological therapy and the age-matched general population.[5–7] In fact, anti-TNF use might be a protective factor against severe COVID-19-related outcomes among individuals with autoimmune diseases,[8] which could be due to these therapies inhibiting the maladaptive systemic inflammatory response that often characterises severe COVID-19. This reduction in the risk of severe outcomes might also be related to the association between anti-TNF therapy and reduced IBD-related disease activity; higher levels of disease activity in IBD have been shown to increase the risk of adverse COVID-19-related outcomes.[9] Furthermore, individuals with IBD have been shown to have high levels of adherence to physical distancing and isolation recommendations, which might decrease their likelihood of being exposed to infection.[10]

Given the paucity of data showing the relationship between humoral antibody titres and SARS-CoV-2 infection risk in people on anti-TNF therapies, and the lack of evidence that anti-TNF increases the risk of severe COVID-19, it remains unclear as to whether people being treated with anti-TNF truly require accelerated booster dosing or monitoring for antibody responses. Recommending additional or earlier booster doses is not without a downside; because patients with IBD often have high baseline levels of health anxiety, the messaging that users of anti-TNF might be insufficiently protected by COVID-19 vaccination could have negative mental health consequences or result in increased social isolation.[11] There is also a concern that this heightened concern about the attenuated immunological response to vaccination might lead to hesitancy in initiating biologic therapy that is otherwise indicated among individuals with moderate-to-severe IBD.

Most frustratingly, even with the rapidity of the generation and publication of new findings, the contours of the pandemic change faster still. With the emergence of the omicron variant (B.1.1.529) and the transition towards endemicity, the relevance of this study's findings has waned. Clinicians are currently concerned with the timing of a fourth dose of COVID-19 vaccine in the immunosuppressed, and thus a study assessing antibody titres after two doses might have more reduced clinical applicability than it did when this project was conceived and conducted.

As the COVID-19 pandemic evolves, clinicians will need to continue to adjust their practice on the basis of emerging evidence regarding the effectiveness and impact of COVID-19 vaccines among patients with

IBD and the risk of severe COVID-19-related outcomes among people being treated with immunomodulating medications. At this time, encouraging booster doses among individuals on anti-TNF medications 3–4 months after the most recent vaccine dose is reasonable, especially for those with additional risk factors for serious COVID-19, such as advanced age and other markers of frailty. Patient education will be of utmost importance; first and subsequent vaccine doses need to be reinforced as the most crucial measure to prevent COVID-19 in patients with IBD as we enter the next stages of the pandemic.

TC declares no competing interests. LET has received grants and consulting fees from AbbVie Canada, Pfizer Canada, Takeda Canada, Janssen Canada, Roche Canada, Merck Canada, Sandoz Canada, and Janssen Canada; consulting fees from Celltron Canada; and payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing, or education events from Takeda Canada, Janssen Canada, and AbbVie Canada.

*Tarun Chhibba, *Laura E Targownik*
laura.targownik@sinaihealth.ca

Division of Gastroenterology and Hepatology, Department of Medicine, University of Toronto, Toronto, ON, Canada (TC, LET); Mount Sinai Hospital IBD Centre, Division of Gastroenterology, Mount Sinai Hospital, Toronto, ON M5G 1X5 , Canada (LET)

1 Kennedy NA, Goodhand JR, Bewshea C, et al. Anti-SARS-CoV-2 antibody responses are attenuated in patients with IBD treated with infliximab. *Gut* 2021; **70:** 865–75.

2 Alexander JL, Kennedy NA, Ibraheim H, et al. COVID-19 vaccine-induced antibody responses in immunosuppressed patients with inflammatory bowel disease (VIP): a multicentre, prospective, case-control study. *Lancet Gastroenterol Hepatol* 2020; published online Feb 3. https://doi.org/10.1016/S2468-1253(22)00005-X.

3 Khoury DS, Cromer D, Reynaldi A, et al. Neutralizing antibody levels are highly predictive of immune protection from symptomatic SARS-CoV-2 infection. *Nat Med* 2021; **27:** 1205–11.

4 Earle KA, Ambrosino DM, Fiore-Gartland A, et al. Evidence for antibody as a protective correlate for COVID-19 vaccines. *Vaccine* 2021; **39:** 4423–28.

5 Khan N, Patel D, Xie D, Pernes T, Lewis J, Yang Y-X. Are patients with inflammatory bowel disease at an increased risk of developing SARS-CoV-2 than patients without inflammatory bowel disease? Results from a nationwide veterans' affairs cohort study. *Am J Gastroenterol* 2021; **116**: 808–10.

6 Burke KE, Kochar B, Allegreti JR, et al. Immunosuppressive therapy and risk of COVID-19 infection in patients with inflammatory bowel diseases. *Inflamm Bowel Dis* 2021; **27:** 155–61.

7 Lev-Tzion R, Focht G, Lujan R, et al. COVID-19 vaccine is effective in inflammatory bowel disease patients and is not associated with disease exacerbation. *Clin Gastroenterol Hepatol* 2021; published online Dec 23. https://doi.org/10.1016/j.cgh.2021.12.026.

8 Akiyama S, Hamdeh S, Micic D, Sakuraba A. Prevalence and clinical outcomes of COVID-19 in patients with autoimmune diseases: a systematic review and meta-analysis. *Ann Rheum Dis* 2020; published online Oct 13. https://doi.org/10.1136/annrheumdis-2020-218946.

9 Bezzio C, Saibeni S, Variola A, et al. Outcomes of COVID-19 in 79 patients with IBD in Italy: an IG-IBD study. *Gut* 2020; **69:** 1213–17.

10 Feitosa MR, Parra RS, Parra de Camargo H, et al. COVID-19 quarantine measures are associated with negative social impacts and compromised follow-up care in patients with inflammatory bowel disease in Brazil. *Ann Gastroenterol* 2021; **34:** 39–45.

11 Graff LA, Walker JR, Clara I, et al. Stress coping, distress, and health perceptions in inflammatory bowel disease and community controls. *Am J Gastroenterol* 2009; **104:** 2959–69.

A call for advocacy and patient voice to eliminate hepatitis B virus infection

Hepatitis B virus (HBV) infection is estimated to affect around 300 million individuals worldwide, but has been neglected by health-care provision, education, research, and policy.[1,2] In light of the WHO goal to eliminate viral hepatitis as a public health threat by 2030, there is an urgent need for enhanced advocacy for HBV. Organisations representing and led by individuals with tuberculosis, HIV, and hepatitis C virus (HCV) infection have set a precedent for the provision of infrastructure, education, peer support, fundraising, and advocacy, often with support from large international donors. Parallel examples of advocacy for HBV are scarce, highlighted by a patient describing the HBV community as "the forgotten people" (appendix p 1). Enhanced interdisciplinary action, which can have far-reaching benefits, is urgently needed to promote and diversify representation of people with lived experience of HBV infection (figure). We convened an interdisciplinary group to gather evidence and set out a framework for action, which we present here, considering the challenges and barriers to engagement, and reflecting on the need for patient voices to drive progress.

See Online for appendix

Many communities most affected by HBV infection have been systematically underserved by existing health-care infrastructure. Neglect is faced by many countries where chronic hepatitis B infection is highly prevalent in the general population. In high-income nations, chronic hepatitis B primarily affects minority ethnic groups, who are often sidelined by clinical services, and might feel disengaged, marginalised, and lost in the system. Migrant populations face further challenges of discrimination, high mobility, unfamiliar health-care systems, and lack of trusted health-care providers.[3] Chronic hepatitis B is also more prevalent in other groups at risk of marginalisation and discrimination, including subgroups of the LGBTQ+