IBD Special Issue

The NEW GASTROENTEROLOGIST

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Health Maintenance

Letter
FROM THE EDITOR

Dr. Bryson W. Katona is an instructor of medicine in the division of gastroenterology at the University of Pennsylvania.

Dear Colleagues,

Inflammatory bowel disease (IBD) is becoming an increasingly important part of GI practice, and it is certainly an exciting time to be involved in the field. While new IBD therapeutics often get most of the attention, there are many other issues surrounding IBD care that are important for all of us. This special IBD-themed issue of *The New Gastroenterologist* provides expert opinions addressing some of these important issues that are critical to both the care of IBD patients and the development of an effective IBD practice.

First, as health maintenance should always be part of routine IBD care, Karen Chachu (Duke University) provides an overview of the pertinent health maintenance issues to consider when caring for IBD patients. Another hot topic in the field is drug-level monitoring, which has become an increasingly important tool when deciding whether to adjust or change IBD therapies. Konstantinos Papamichail and Adam S. Cheifetz (Beth Israel Deaconess Medical Center) provide an overview of the basics of drug-level monitoring for both anti-TNFs as well as thiopurines, which contains useful algorithms that will help guide the process of making these treatment decisions.

In this issue of *The New Gastroenterologist*, we also have several articles that will be very helpful to those who either have or are developing a practice with a significant IBD focus. First, Douglas Wolf (Atlanta Gastroenterology Associates) discusses the steps necessary to build a successful IBD practice, and, additionally, Nitin Gupta (University of Mississippi Medical Center) provides some useful tips to help physicians start collaborations with industry.

As MACRA looms over us all, it is only a matter of time before we will all have to firmly understand its intricacies. The implementation of MACRA and MIPS will undoubtedly affect quality measures in IBD, and, to help all of us understand the complexities of this issue, Ryan A. McConnell and Fernando Velayos (University of California, San Francisco) provide an overview of quality measures in IBD. Finally, although treatment, monitoring, and quality are all important in the care of IBD patients, so also are the relationships that we develop with our IBD patients. To give us input on this topic from a patient perspective, a group of IBD patients from the Crohn's and Colitis Foundation of America address what we as physicians can do to enhance our doctor-patient relationships.

If you want to read *The New Gastroenterologist* "on the go," please download our free app, or read our electronic version on www.mdedge.com/gihepnews or www.gastro.org. Additionally, if you have other topics you would be interested in reading about, or if you are interested in contributing to future issues, please e-mail me at bryson.katona@uphs.upenn.edu or *The New Gastroenterologist's* managing editor Ryan A. Farrell at rfarrell@gastro.org.

Sincerely,
Bryson W. Katona, MD, PhD
Editor in Chief

The NEW GASTROENTEROLOGIST

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Bryson W. Katona, MD, PhD

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ON THE COVER

Dr. Karen Chachu of Duke University, Durham, N.C., and a patient.

Photo by Shawn Rocco

IN THIS ISSUE

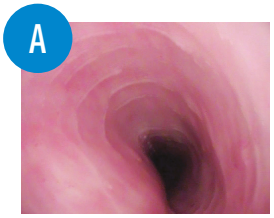
An 87-Year-Old Woman With Recurrent Dysphagia

Published previously in Gastroenterology (2016;151:1085-6)

By Roald F. Havre, MD, PhD, Trine Hallager, and Evangelos Kalaitzakis, MD

Dr. Havre and Dr. Kalaitzakis are in the Endoscopy Unit of Copenhagen University Hospital/Herlev, University of Copenhagen. Ms. Hallager is in the department of pathology, Copenhagen University Hospital/Herlev. The authors disclose no conflicts.

An 87-year-old woman was referred for dysphagia that had been present for several years. Three years prior to this presentation she had undergone an esophagogastroduodenoscopy (EGD) on the same indication showing a proximal and a distal esophageal benign-appearing stricture but no signs of esophagitis. Both were dilated and biopsied. Histopathology showed infiltration with lymphocytes and neutrophilic granulocytes, and superficially fungal hyphae and spores. No predominance of eosinophilic granulocytes was noted. A proton-pump inhibitor was prescribed, and she was scheduled for a control gastroscopy, but was lost to follow-up. She was otherwise healthy without any allergies.



Upon re-presentation, she was under treatment with pantoprazole 40 mg OD. Upon EGD a spiral-shaped proximal esophageal stricture with normal-appearing mucosa only passable with a nasal endoscope was observed. The rest of the esophagus was seen with mucosal concentric rings (Figure A). The esophageal mucosa was otherwise endoscopically normal throughout. Biopsies were taken from the distal and proximal esophagus. Balloon dilation of the proximal stricture was performed (CRE, Boston Scientific) to 13.5 mm. Subsequently, a standard gastroscope could be passed to the duodenum revealing normal-appearing gastric and duodenal mucosa.

What is the diagnosis?

A. Eosinophilic esophagitis
B. Reflux-associated esophagitis with stenosis
C. Lymphocytic esophagitis
D. Achalasia

See the Answer on page 31

News from the AGA

Introducing a New, Private Community Just for AGA's Trainee and Early Career Members

Networking is an important part of your career, between connecting with mentors, gaining valuable referrals and tackling that next rung on the career ladder. AGA created the Early Career Group in the AGA Community to help you connect and network through the forum and directory, but also to provide education tools you're not going to find anywhere else.

In case you haven't yet taken a tour, the group creates an open dialogue for trainees and early career members up to seven years out of training. Each month will host a new theme and corresponding presentation, webinars, journal articles or tip sheets, as well as other member-only online events, such as forums with leading experts in the field.

Also, the group's event calendar will help you stay on top of important deadlines, conferences and possibly even local meet-ups.

Visit http://Community.Gastro.org/EarlyCareerGroup/ today to take advantage of this collaboration space created just for you. ■

Announcing New Crohn's & Colitis Congress

AGA and the Crohn's & Colitis Foundation are partnering to co-sponsor a new annual conference for health care professionals and researchers. By joining the nation's leading IBD patient organization with the premier GI professional organization, this will be the must-attend IBD conference, bringing state-of-the-art comprehensive care together with the latest research to advance prevention, treatment and cures for IBD patients.

Save the date – Jan. 18-20, 2018, in Las Vegas. Get ready to expand your knowledge, network with other leaders, and be inspired! Stay tuned for our website launch and more details coming this spring. ■

New AGA Guidelines

AGA recently released new clinical guidelines that provide evidence-based recommendations to help guide your clinical practice decisions based on rigorous systematic reviews of the medical literature.

AGA Institute Guideline on the Management of Crohn's Disease After Surgical Resection: AGA developed this guideline, technical review and Clinical Decision Support Tool to outline strategies to reduce disease recurrence in Crohn's disease patients who have achieved remission following bowel resection. Prevention of endoscopic recurrence, a strong surrogate measure of surgical recurrence, was evaluated for the development of the guideline.

The guidelines are intended to reduce practice variation and promote high-value care. The current evidence supports the early prophylactic use of thiopurines and/or anti-TNF therapy in patients who are at higher risk for clinical recurrence. However, some patients at lower risk may opt for close endoscopic monitoring instead. Although all patients should undergo ileocolonoscopy at six to 12 months after surgical resection, surveillance for endoscopic recurrence is most important for patients not on any pharmacological prophylaxis. In general, those with endoscopic recurrence should undergo treatment with anti-TNF and/or thiopurine therapy.

This guideline is available in the January issue of *Gastroenterology*.

AGA Institute Guidelines for the Diagnosis and Management of Acute Liver Failure: AGA developed this guideline and technical review to provide recommendations about controversial diagnostic and treatment strategies and predictive models for outcome of acute liver failure (ALF), which have arisen since acute liver failure is difficult to study in randomized clinical trials.

Recommendations include a strong recommendation for the use of N-acetyl cysteine (NAC) in patients with ALF related to acetaminophen, but there remains a lack of data to allow recommendations for testing for Wilson's disease and varicella zoster virus in patients with ALF. Although there are low-quality data, because there are therapies that may be beneficial in patients with ALF, recommendations to test for herpes simplex virus and autoimmune hepatitis are supported, as is hepatitis E virus testing in pregnant women with ALF.

This guideline is available in the February issue of *Gastroenterology*. ■

18 GIs to Watch: The Newest Class of AGA Future Leaders

AGA has announced the second class of its Future Leaders Program, which was created in 2015 to identify early career gastroenterologists who have the potential to make a significant impact on the specialty. The 18 gastroenterologists selected to participate in the 2017-2018 program stood out for their current achievements, commitment to advancing the field, and potential for future success.

"AGA relies heavily on the engagement and expertise of volunteer leaders to develop programs that continue to advance our specialty and support our members through changes to the health-care delivery landscape," said Suzanne Rose, MD, MSEd, AGAF, co-program chair for the AGA Future Leaders Program. "The newest class of AGA Future Leaders shows exceptional promise and dedication to the field, and we look forward to working with these rising stars to cultivate the future leaders of AGA and the field of gastroenterology."

The AGA Future Leaders Program provides a pathway within AGA for selected participants who seek opportunities to support the gastroenterology profession, advance their careers, connect with potential mentors and develop the leadership skills necessary to serve the organization. During this year-long program, participants will receive leadership training and work closely with AGA mentors on projects linked to AGA's Strategic Plan.

AGA is pleased to announce the second class of the Future Leaders program:

- Arthur Beyder, MD, PhD, Assistant Professor, Mayo Clinic – Rochester
- Brigid S. Boland, MD, Assistant Adjunct Professor of Medicine, University of California, San Diego
- Lea Ann Chen, MD, Assistant Professor of Medicine, New York University School of Medicine, NY
- Bruno P. Chumpitazi, MD, MPH, Director, Neurogastroenterology and Motility Program, Texas Children's Hospital/Baylor College of Medicine, Houston, TX
- Matthew A. Ciorba, MD, Assistant Professor of Medicine, Washington University in St. Louis, MO
- Katherine S. Garman, MD, Assistant Professor of Medicine, Duke University Medical Center, Durham, NC
- Christina Y. Ha, MD, Assistant Professor of Medicine, University of Los Angeles, David Geffen School of Medicine, CA
- Bryson W. Katona, MD, MS, PhD, Instructor, University of Pennsylvania, Philadelphia
- Peter S. Liang, MD, MPH, Instructor, NYU/Manhattan VA, New York, NY
- Folasade P. May, MD, PhD, MPhil, Assistant Professor of Medicine, David Geffen School of Medicine at the University of California, Los Angeles; Department of Veterans Affairs, Los Angeles, CA
- Marty M. Meyer, MD, Gastroenterologist, The Ohio State University, Columbus, OH
- Susan N. Ramdhaney, MD, AGAF, Gastroenterologist, President Comprehensive Digestive Care, Manhasset, NY
- Jonathan A. Rosenberg, MD, Gastroenterologist, Illinois Gastroenterology Group, Highland Park
- N. Jewel Samadder, MD, Assistant Professor of Medicine, Huntsman Cancer Institute, Salt Lake City, UT
- Siddharth Singh, MD, Assistant Professor of Medicine, University of California, San Diego
- Maria I. Vazquez-Roque, MD, MSc, Gastroenterologist, Mayo Clinic, Jacksonville, FL
- Sachin B. Wani, MD, Associate Professor of Medicine, University of Colorado, Aurora
- Jennifer Weiss, MD, MS, Assistant Professor, University of Wisconsin School of Medicine and Public Health, Madison

Learn more about the AGA Future Leaders program on the AGA website: www.gastro.org. ■

Sessions at DDW® 2017 Designed for Trainees and Early Career GIs

AGA has developed special sessions at Digestive Disease Week® (DDW) 2017 to meet the unique needs of physicians who are new to the field. Participants will learn about all aspects of starting a career in clinical practice or research, have the opportunity to network with mentors and peers, and review board material.

If you're attending DDW, we hope to see you at the following sessions. With the exception of the 2017 AGA Postgraduate Course, all of the sessions are free, but you must register for DDW to attend.

- AGA Postgraduate Course: The Full Scope of GI Advances – Saturday, May 6, and Sunday, May 7 (learn more at http://pgcourse.gastro.org)
- Advancing Clinical Practice: GI Fellow-Directed Quality Improvement Projects – Sunday, May 7
- Board Review Course – Monday, May 8
- Career and Professional-Related Issues – Monday, May 8

For more information, visit www.ddw.org. ■

AGA Outlook

For more information about upcoming events and award deadlines, please visit http://www.gastro.org/education and http://www.gastro.org/research-funding.

Upcoming Events

May 11-12, 2017
HIV and Hepatitis Management
This advanced CME activity will provide participants with state-of-the-art information and practical guidance from internationally recognized experts on progress in managing HIV, hepatitis B, and hepatitis C.
New York, NY

Sept. 9-10, 2017
James W. Freston Conference: Extracellular Vesicles — Biology, Translation, and Clinical Application in GI Disorders
Examine the latest research on vesicle biogenesis and secretion and its relevance to GI diseases and clinical applications.
Saint Paul, MN

June 21-22; Aug. 16-17; Sept. 13-14; Oct. 11-12, 2017
Two-Day, In-Depth Coding and Billing Seminar
Become a certified GI coder with 2-day, in-depth training course provided by McVey Associates, Inc.
Nashville, TN (6/21-6/22); Baltimore, MD (8/16-8/17); Atlanta, GA (9/13-9/14); Las Vegas, NV (10/11-10/12)

Oct. 4, 2017
Gastroenterology Quarterly Update: October 2017
Audio conference timed with quarterly release of the Correct Coding Initiative edits.

Digestive Disease Week® (DDW) 2017 – May 6-9, Chicago, IL

• May 6-9
AGA Trainee and Early Career GI Sessions
Join your colleagues at special sessions to meet the unique needs of physicians who are new to the field. Participants will learn about all aspects of starting a career in clinical practice or research, have the opportunity to network with mentors and peers, and review board material. For questions related to the program, please contact Sandra Megally Amos, AGA Director of Education (samos@gastro.org).

• May 6, 8:15 a.m.–5:30 p.m; May 7, 8:30 a.m.–12.35 p.m.
AGA Postgraduate Course: The Full Scope of GI Advances
Step beyond basic learning and get the full scope of GI advances during this multi-topic course. In just 1.5-days, world-renowned leaders will test your knowledge in real time and provide your pathway for optimal care that will guide your clinical decisions all year long. To learn more and register, visit http://pgcourse.gastro.org/.

• May 7: 2-3 p.m.
AGA Early Career Networking Hour
Meet AGA volunteers and learn more about the organization while enjoying snacks. This will take place in the DDW Trainee and Young GI Lounge (South Hall A).

• May 7: 4:00–5:30 p.m.
Advancing Clinical Practice: GI Fellow-Directed Quality Improvement Projects
This trainee-focused session will showcase selected abstracts from GI fellows based on quality improvement, with a concluding state-of-the art lecture. Attendees will be provided with information that defines practical approaches to quality improvement from start to finish. Free coffee and tea will be available on a first-come, first-served basis.

• May 8, 12:30–1:30 p.m.
Career and Professional-Related Issues
Review strategies that trainees can use in third or advanced fellowship years to have a successful academic career as a clinician investigator or basic researcher; help trainees and early stage-gastroenterologists understand the private practice options, challenges and opportunities; and develop skills for work-life balance in order to have a sustainable and successful career path. Boxed lunches are available on a first-come, first-served basis.

• May 8, 1:30–5:30 p.m.
Board Review Course
This session, designed around content from DDSEP® 8, serves as a primer for third-year fellows preparing for the board exam as well as a review course for others wanting to test their knowledge. Session attendees will receive a $50 coupon to use at the AGA Store at DDW to purchase DDSEP 8. Successful completion of this CME activity enables the participant to earn up to four Maintenance of Certification points in the American Board of Internal Medicine's (ABIM) MOC program.

The 'Nuts and Bolts' of Drug Concentration Monitoring in IBD

By Konstantinos Papamichail, MD, PhD, and Adam S. Cheifetz, MD

Dr. Papamichail is a research fellow and Dr. Cheifetz is the director of the Center for Inflammatory Bowel Diseases, division of gastroenterology, Beth-Israel Deaconess Medical Center, Harvard Medical School, Boston.
Dr. Papamichail received a fellowship grant from the Hellenic Group for the study of IBD. Dr. Cheifetz received consultancy fees from AbbVie, Janssen, UCB, Takeda, Prometheus, and Pfizer.

Introduction

Anti–tumor necrosis factor (anti-TNF) therapy is the cornerstone of inflammatory bowel disease (IBD) treatment.[1] Nevertheless, up to 30% of patients show no clinical benefit, considered to be primary nonresponders, while another 50% lose response over time and need to escalate or discontinue anti-TNF therapy because of either pharmacokinetic (PK) or pharmacodynamic issues.[2] Therapeutic drug monitoring (TDM), defined as the assessment of drug concentration and anti-drug antibodies (ADA), is emerging as a new therapeutic strategy to better explain, manage, and hopefully prevent these undesired clinical outcomes.[3] Moreover, numerous studies have shown that higher serum anti-TNF drug concentrations both during maintenance and induction therapy are associated with favorable objective therapeutic outcomes, suggestive of a "treat-to-trough" in addition to a "treat-to-target" therapeutic approach.[4-6] This concept of TDM is not new in IBD. TDM has also been used for optimizing thiopurines.[7] This brief review will discuss a practical approach to the use of TDM in IBD with a focus on its use with anti-TNF therapies.

Reactive TDM of anti-TNF therapy

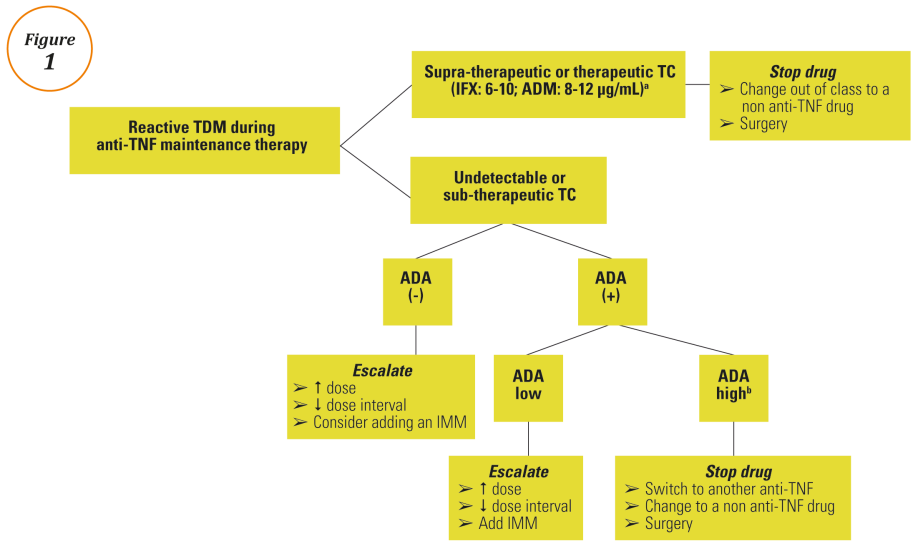
Reactive TDM more rationally guides therapeutic decisions for dealing with loss of response to anti-TNF therapy in IBD and is actually more cost effective.[8,9] Patients with subtherapeutic or undetectable drug concentrations without ADA derive more benefit from dose escalation (increasing the dose or decreasing the interval) compared with those switched to another anti-TNF agent. On the other hand, patients with therapeutic or suprathrapeutic drug concentrations have better outcomes when changing to a medication with a different mechanism of action (as their disease is probably no longer TNF driven).[3]

A recent study showed that trough concentration of adalimumab greater than 4.5 mcg/mL or infliximab greater than 3.8 mcg/mL at time of loss of response identifies patients who benefit more from alternative therapies rather than dose escalation or switching to another anti-TNF agent.[10] In clinical practice, in order to fully optimize the original anti-TNF, we will typically dose-optimize patients to drug concentrations of infliximab and adalimumab to greater than 10 mcg/mL before giving up and changing medications. Moreover, patients with high ADA titer have better outcomes when switched to another anti-TNF rather than undergoing further dose escalation.[3] Vande Casteele et al. showed that antibodies to infliximab (ATI) greater than 9.1 U/mL at time of loss of response resulted in a likelihood ratio of 3.6 for an unsuccessful intervention, defined as the need to initiate corticosteroids, immunomodulators (IMM), or other medications or infliximab discontinuation within two infusions after the intervention (shortening of infusion intervals, dose increase to 10 mg/kg, or a combination of both).[11] A proposed treatment algorithm for using reactive TDM for anti-TNF therapy is shown in Figure 1.

Proactive TDM of anti-TNF therapy

Proactive TDM with drug titration to a target concentration applied in patients with clinical response or remission also appears to improve the efficacy and cost-effectiveness of anti-TNF therapy.[13,14] An observational study from our center was the first to demonstrate a significantly greater durability on infliximab in IBD patients in clinical remission who underwent proactive TDM and dose optimization to a therapeutic trough concentration of 5-10 mcg/mL when compared to patients receiving standard-of-care and empiric dose escalation and/or reactive TDM.[13] Furthermore, this study showed that, among patients who achieved an infliximab concentration of at least 5 mcg/mL, there was no difference in infliximab duration between patients on monotherapy and those on combination therapy with an IMM, suggesting that IMM withdrawal can be considered in patients in clinical remission with adequate drug concentration on combination therapy.[13]

Optimized monotherapy and proactive dose optimization (greater than 5 mcg/mL) with infliximab should also be considered from the outset in patients who do not want to be on a concomitant IMM. Though there are no specific data published to date, we treat adalimumab similarly with dose optimization to concentration above 5-10 mcg/mL. Subsequently, the landmark TAXIT trial showed that patients who undergo proactive TDM to the therapeutic drug window of 3-7 mcg/mL need less rescue therapy and more often have detectable infliximab concentrations compared to the clinically based dosing group.[14] Moreover, this trial showed that, during the initial optimization phase, dose escalation in patients with Crohn's disease (with a suboptimal infliximab concentration) significantly increased the number of patients in clinical remission with a concomitant decrease in C-reactive protein levels.[13] A proposed treatment algorithm for using proactive TDM for anti-TNF therapy is shown in Figure 2.

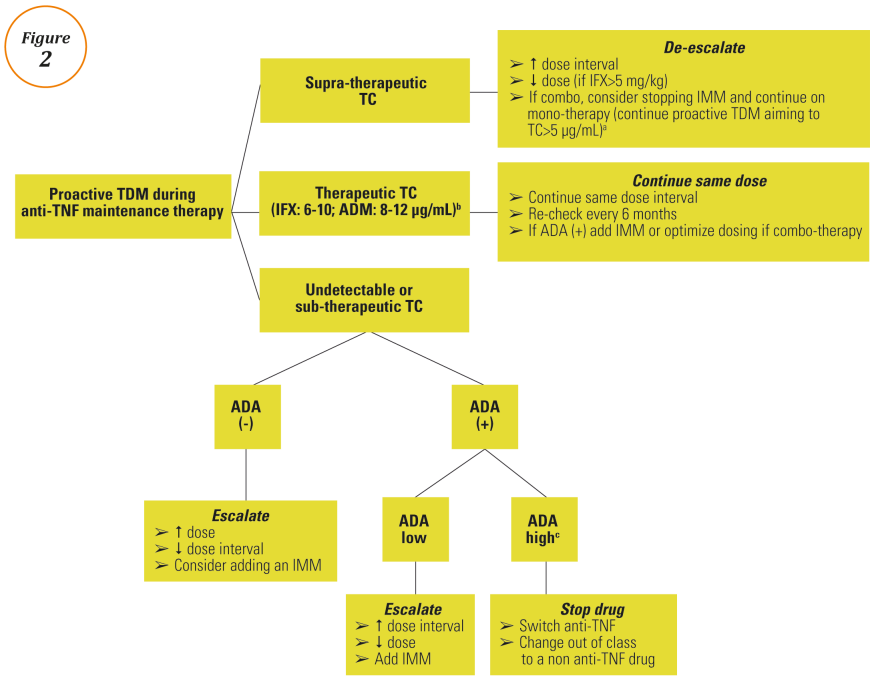


Proposed algorithm for reactive therapeutic drug monitoring of anti-TNF therapy in inflammatory bowel disease. [a]For achieving mucosal healing[6]; [b]For high-titer antibodies to infliximab greater than 8 mcg/mL-eq regarding enzyme–linked immunosorbent assay[12] and greater than 9.1 U/mL regarding HMSA.[9]

Preliminary data also show that higher drug concentrations early after the induction phase (at week 14 for infliximab, week 4 for adalimumab and week 8 for certolizumab pegol) are associated with short- and long-term favorable therapeutic outcomes.[4,5,15-22] These suggest the utility of an early optimization of anti-TNF therapy even during induction therapy in IBD. Although clinically relevant drug thresholds may vary based on the therapeutic outcome of interest, we typically aim for concentrations above 7 mcg/mL at week 4 for adalimumab and week 14 for infliximab. These patients with active inflammation clear drug more quickly (predisposing them to subtherapeutic drug concentrations), and therefore likely derive the most benefit from proactive TDM. Additionally, preliminary data show that proactive TDM may also be useful in other clinical scenarios including better guiding therapeutic decisions toward de-escalation or even discontinuation of anti-TNF in patients achieving clinical remission, or following re-introduction of anti-TNF therapy after a drug holiday.[23,24]

TDM of thiopurines

Measurement of thiopurine metabolites in IBD is typically used in a reactive setting, when lack/loss of response or a drug-related adverse event (leukopenia or abnormal transaminase) occurs.[7] However, TDM can be also utilized more proactively to confirm drug adherence and closely monitor patients, especially those with intermediate thiopurine methyltransferase (TPMT) activity or on allopurinol combination therapy.[7] Less commonly, proactive dose optimization to a threshold of 6-thioguanine nucleotide (6-TGN) levels greater than 230-250 pmol/8 x 10^8 red blood cells is performed.[25] Nevertheless, the utility of proactive TDM for optimizing thiopurine therapy in IBD clinical practice has not yet been proven, as a clearly defined



Proposed algorithm for proactive therapeutic drug monitoring of anti-TNF therapy in inflammatory bowel disease. [a]For achieving mucosal healing[6]; [b]based on references 12 and 14; [c]For high-titer antibodies to infliximab greater than 8 mcg/mL-eq regarding ELISA[12] and greater than 9.1 U/mL regarding HMSA.[9]

and clinically validated therapeutic window for thiopurine metabolites remains still largely unknown.[26,27] Recent data show that a 6-TGN level greater than 125 pmol/8 x 10^8 red blood cells is associated with higher infliximab concentration and less anti-drug antibody formation, suggesting patients on combination therapy may not need "therapeutic" 6-TGN levels to be effective.[28]

Anti-TNF TDM assays

Several methods are now available for evaluating concentrations of anti-TNF agents and ADA including the enzyme-linked immunosorbent assay (ELISA), radioimmunoassay (RIA), homogeneous mobility shift assay (HMSA), and the electro-chemiluminescence immunoassay, but none of them can be considered the gold standard.[3] The selection of assay is typically based on cost, local availability, and physician's preference. Recent data suggest that drug concentrations are generally comparable among the assays currently used, although the detection and quantification of ADA remains challenging, depending largely on the analytical properties of the assay used.[3,29] The HMSA, for example, is a drug-tolerant assay (can detect ADA in the presence of drug), while first-generation ELISAs are drug-sensitive assays and when drug is on board ADA cannot be detected (or reported).[3] Moreover, there is also lack of data for a clinically relevant low or high ADA titer with each assay. Consequently, standardization and clinical validation of ADA assays for comparison of results across studies are certainly needed.[30] It is critically important to understand the assay utilized, as mistakes can be made when antibodies are read out in units that make them appear to be high titer and clinically significant when, in fact, they are not.

Conclusions

A growing body of evidence demonstrates the clinical utility of TDM of anti-TNF therapy in IBD clinical practice and a move toward personalized medicine, as it is now clear that "one dose does not fit all patients." Nevertheless, before a TDM-based approach can be widely implemented and emerge as the new standard of care for anti-TNF therapy in IBD, several barriers regarding cost issues (insurance coverage and out-of-pocket expenses), time lag from serum sampling to test results (typically 5-10 days), proper interpretation and application of the results, type of assay used, and the optimal timing of serum collection should be overcome. Initiatives are already underway, including the development of accurate, easily accessible, and affordable rapid assays that will allow anti-TNF concentration measurement at the point-of-care site and software decision-support tools or "dashboards" that will incorporate a predictive pharmacokinetic model based on patient and disease characteristics.[31,32]

Additionally, more data from well-designed prospective studies and randomized controlled trials regarding both induction and maintenance treatment and for all available biologics (originators and biosimilars) are urgently needed. A panel consisting of members of the Building Research in Inflammatory Bowel Disease Globally research alliance (www.BRIDGeIBD.com), and recognized leaders in the field of TDM in IBD has recently published recommendations that help clinicians on the appropriate timing and best way to interpret and respond to TDM results depending on the specific clinical scenario.[33]

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DDSEP® eight QUESTIONS

Digestive Diseases Self-Education Program

// Answers on page 30

Q1: A 55-year-old obese white man with long-standing gastroesophageal reflux disease on proton-pump inhibitor therapy presents for an upper endoscopy. On exam, he is noted to have multiple tongues of salmon-colored mucosa extending 6 cm proximally from the gastroesophageal junction. Four quadrant biopsies are obtained every 2 cm and show intestinal metaplasia. In this area, a 6-mm raised nodule is also seen endoscopically, and biopsies show high-grade dysplasia confirmed by expert pathology review.

What is the best next step in management?
A. Endoscopic mucosal resection
B. Radiofrequency ablation
C. Photodynamic therapy
D. Esophagectomy
E. Anti-reflux surgery

Q2: A 33-year-old man is seen in consult regarding concerns about a strong family history of pancreatic cancer. He reports that his father and older brother both developed pancreatic cancer in their fifth decade. He is interested in early detection of pancreatic cancer and seeks an opinion on surveillance recommendations for high-risk individuals.

In which of the following patients is surveillance NOT generally recommended?
A. History of pancreatic cancer in two first-degree relatives (FDR)
B. Peutz-Jegher's syndrome
C. Familial atypical multiple melanoma syndrome (FAMM)
D. Cronkhite-Canada syndrome
E. BRCA2 mutation with affected FDR

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Health Maintenance and Preventive Care in Patients With Inflammatory Bowel Disease

By Karen Chachu, MD, PhD

Dr. Chachu is an assistant professor and gastroenterologist at Duke University, Durham, N.C.

Inflammatory bowel disease (IBD) consists of two chronic inflammatory diseases, Crohn's disease (CD) and ulcerative colitis (UC), as well as a small category of patients (~10%) who have atypical features called IBD-unclassified (IBD-U) or indeterminate colitis. The prevalence of IBD ranges from 0.3% to 0.5% overall in North America and Europe.[1] In North America, the incidences of CD and UC are estimated to be 3.1-14.6 per 100,000 person-years and 2.2-14.3 cases per 100,000 person-years, respectively; similar rates are seen in Europe.[2] However, incidences up to 19.2 and 20.2 per 100,000 for UC and CD, respectively, have been reported in Canada.[3,4] The incidences of both UC and CD are increasing over time in Western countries and in rapidly industrializing countries throughout Asia and South America.[5-8]

With the increased incidence and advances in the treatment of IBD, many more patients are being treated with corticosteroids, immunomodulators, and biologics. Over time, there has also evolved an understanding of the importance of health maintenance in IBD patients, especially since patients with IBD receive fewer recommended preventive health services than general medical patients even though the use of immunosuppression is an argument for more attention to these issues.[9]

Gastroenterologists may see patients more frequently than their primary care provider (PCP) or PCPs may be unaware of the specific needs of IBD patients. Therefore, it is important that gastroenterologists are knowledgeable about the health maintenance recommendations that can be made to patients and to communicate these to PCPs. Recent society guidelines endorse the importance of this aspect of our practice.[10] The discussion below highlights health maintenance issues that should be fundamental aspects of our IBD practices; however, it does not address colon cancer screening and surveillance since these are beyond the scope of this article.

Influenza vaccine and pneumococcal vaccine

Influenza A and B outbreaks are commonly seen during the fall and early spring and risk factors for pneumonia and hospitalization include older age, chronic medical conditions, and immunosuppression. The Centers for Disease Control and Prevention now recommend annual influenza vaccination for all individuals older than 6 months. For patients on immunosuppression, the vaccine administered should be the inactivated vaccine, as live attenuated vaccines should not be administered to these patients.

Patients with IBD also are at an increased risk of bacterial pneumonia, the most common etiology of which is pneumococcal pneumonia.[11] The Advisory Committee on Immunization Practices (ACIP) recommends that patients on immunosuppression receive a one-time dose of the pneumococcal conjugate vaccine PCV13, followed by a dose of the pneumococcal polysaccharide vaccine PPSV23 1 year later (8 weeks at the earliest). A second dose of PPSV23 should be given 5 years later and a third dose after 65 years of age.

In IBD patients, the influenza and pneumococcal vaccines are both well tolerated without an increased rate of adverse effects over the general population and without an increased risk of IBD flares after vaccination.[12] A common question for patients on biologic therapy is whether the vaccine should be timed at a specific point in the dose cycle. For infliximab, and likely other biologics, the timing does not change the vaccine immunogenicity and patients should be given these vaccines regardless of where they are in the cycle of administration of their biologic.[13] In addition, there is significant response to influenza and pneumococcal vaccines in patients on combination therapy with immunomodulators and anti–tumor necrosis factor (TNF) and concerns about a lack of response to vaccines should not discourage vaccination since benefits are still acquired by patients even if immunogenicity is somewhat decreased.[14,15]

Other vaccinations

In addition to the influenza and pneumococcal vaccines, adult and pediatric patients with IBD should follow the ACIP recommendations for tetanus, diphtheria, pertussis (Tdap), Td boosters, hepatitis A, hepatitis B, human papilloma virus (HPV), and meningo-

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coccal vaccinations.[16,17]

Live vaccines including measles mumps rubella (MMR), varicella, and zoster vaccines are, in general, contraindicated in immunosuppressed patients on corticosteroids, azathioprine/6-mercaptopurine, methotrexate, anti-TNFs, and anti-integrin biologics. An inactive varicella-zoster vaccine will likely be available in the near future and may obviate the need for the live vaccine, which is an important development given the increased risk of zoster in patients with IBD on immunosuppression.[18]

Osteoporosis screening

Both men and women with IBD have an elevated risk of osteoporosis and osteopenia as well as elevated fracture risk.[19] This is related to frequent chronic corticosteroid use, chronic inflammation (high disease activity), women with low body mass index, smoking, older age (women older than 65, men older than 70), terminal ileal disease or resection in patients with CD, and proctocolectomy and ileal pouch-anal anastomosis in patients with UC.

The recommendations are to obtain baseline bone density evaluation only in patients with risk factors, including young patients since osteopenia can be present at a young age. If osteopenia is noted, then calcium (1,000-1,200 mg daily) and vitamin D (1,000-4,000 IU daily) supplementation can be associated with improvement in osteopenia.[20] If osteoporosis is noted, patients should be referred to rheumatology or endocrinology for evaluation for bisphosphonate therapy, which is also associated with improved outcomes.[21] Bone density testing should be repeated every 2 years in patients with osteoporosis on treatment and less frequently when there is improvement.[22] Given the association of bone metabolism disorders with smoking, this is one more reason to encourage our patients to quit.

Skin cancer screening

Multiple studies have demonstrated that immunosuppression, especially with methotrexate and azathioprine/6-mercaptopurine is a risk factor for the development of initial and recurrent nonmelanoma skin cancer (NMSC) in IBD patients, the data for biologics are less definitive.[23-25] In addition, biologics are associated with increased risk of melanoma in IBD.[26]

The elevated risk of skin cancer begins in the first year of treatment with thiopurines and may continue after discontinuation. On the basis of these data, screening for melanoma and NMSC is recommended in IBD patients on immunosuppression. Especially for patients on thiopurines, it is reasonable for the initial dermatologist visit to occur in the first year of treatment and thereafter with at least annual visits for a full-body skin examination. In addition, it is reasonable to recommend regular sunscreen use and protective clothing such as hats.

Cervical cancer screening

A recent meta-analysis shows that women with IBD on immunosuppression have an increased risk of cervical high-grade dysplasia and cervical cancer.[27] HPV is the major risk factor for cervical cancer and is necessary for its development. The current American College of Gynecology guidelines for women on immunosuppression are to start cervical cancer screening at 21 and annual screening thereafter with Pap and HPV testing.[28]

Smoking

Smoking has well-known associations with poor outcomes in the

general population such as increased risk of lung and pancreatic cancers, as well as high risk of cardiovascular disease. In addition, smoking has risks specific to IBD. In CD, smoking is associated with increased disease activity, increased risk of postoperative recurrence, and increased severity of disease.[29] Smoking cessation is associated with improved long-term disease outcomes and less risk.[30] Making it a point to regularly discuss smoking cessation and partnering with PCPs to offer evidence-based quitting aids may be one of our most significant and beneficial interventions.

long chronic disease. It is therefore incumbent on us to be attentive to issues related to IBD patients' preventive care and collaborate with PCPs to coordinate care for our patients since many of these interventions have both short-term and long-term benefits. ■

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A recent systematic review of several studies suggested that antidepressant use in IBD patients benefits their mental health and may improve their clinical course as well.

Depression and anxiety

Several studies have shown high levels of depression and anxiety in IBD patients and higher levels of depression are associated with increased symptoms, clinical recurrence, poor quality of life, and decreased social support.[31-33] A recent systematic review of several studies suggested that antidepressant use in IBD patients benefits their mental health and may improve their clinical course as well.[34] As such, screening for depression and anxiety regularly and either offering treatment or referral to psychiatrists and psychologists for further management is recommended.[10]

Conclusion

Patients with IBD frequently develop long-term relationships with their gastroenterologists due to their life-

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Building and Maintaining a Successful Inflammatory Bowel Disease Practice

By Doug Wolf, MD

Dr. Wolf is director of IBD research, Atlanta Gastroenterology Associates.

Anyone can build a successful inflammatory bowel disease (IBD) practice. To do so requires commitment and focus in IBD including both Crohn's disease and ulcerative colitis. It also requires a fundamental knowledge of medicine as well as a desire to excel and learn all that one can in these areas. Given the high number of stakeholders, good interpersonal skills are vital. Establishing an IBD practice provides an opportunity to make a big difference in peoples' lives, and the age range of impact is about the broadest in all of medical practice. The more resources you have, the greater the potential impact of your care. Table 1 lists resources that are useful to provide optimal IBD patient care.

In the United States, the Crohn's and Colitis Foundation of America (CCFA) provides unparalleled resources for patients and families in addition to important tools for gastroenterologists, other medical specialists, and IBD caregivers. CCFA has a wealth of information, including electronic and personalized resources, to help educate and inform our patients. This is one of the most valuable services that our patients can receive. Physician membership in CCFA is essential and involvement at some level is helpful. As with any gastroenterologist, membership in local and state societies is important, as well as being an active member of the relevant national societies, such as AGA. These organizations help one maintain and display a patient- and practice-oriented approach, which forms the basis for quality of care.

You, the gastroenterologist, are the most important resource for the patient. Medical school, residency, fellowship, and postgraduate training serves as the foundation for your wealth of knowledge. Maximizing your training is of value, and this can be done by being part of an academic program, keeping abreast of current literature, and attending meetings and postgraduate courses. AGA offers a variety of publications (www.gastro.org/journals-and-publications) and continued training opportunities (www.gastro.org/education).

Visits with IBD patients can be complicated and lengthy. As an IBD expert, you will likely have new patients arrive with either incomplete or inaccessible records, which may necessitate a longer conversation to establish pertinent details. Some things can await a telephone or office follow-up but many cannot. When shared decision making and other factors enter the discussion, initial – as well as follow-up – visits can easily lengthen. One's electronic medical record schedule may need to be modified to accommodate these longer visits. I leave 30 minutes for new patients but will accommodate those who require 45 minutes to an hour. While a stable non-IBD follow-up visit can be completed in 15 minutes, this is rarely successful for an IBD patient, particularly when involving biologics, dose adjustments, new medications starts, etc. If there are quality measures that have been captured electronically (e.g., AGA Registry, https://agaibd.medconcert.com/), additional time should be allotted.

One further point regarding sched-

Table 1

Optimal IBD Practice Resources
Sound training and experience in GI/IBD
CCFA chapter and http://www.crohnscolitisfoundation.org/ access
Membership in local, state, national GI societies
Committed nurse or medical assistant
Flexible office schedule for patient care or add-ons
Support for diagnostic test and medication denials
Endoscopy unit
Pathology department interaction
Radiology department interaction
Infusion department interaction
Dietician
Utilization of Patient Assistance Programs
Pharma access, if approved by institution
Specialty access with prompt consultation
Clinical research option

uling is that one must be willing and able to see patients urgently, rather than sending them to the emergency room. ERs are appropriate for true emergencies, but are not an ideal place for care when an IBD patient has a flare and requires prompt follow-up. I try to avoid ER visits for my patients unless they are vomiting, have severe abdominal pain, have significant bleeding, or have clear signs of toxicity. In an ER, abdominal pain equals a CT scan; one should consider seeing these patients in the office and triaging accordingly.

With the increasing requirements of managed care and restrictive medical plans, there has been a similar rise in the frequency of diagnostic test as well as procedure and medication denials. Re-approval and recertification of biologics and other medications have become common, which can add a great deal to your workload and that of your staff. Integration of endoscopy, pathology, and imaging (e.g., ultrasound, CT/CTE) improves response time and dialogue, and can have a positive impact on care. Office infusion allows for a better integration of this service into your practice. There is typically better communication with the infusion nurses, expedited care, and fewer cancellations, infections, and other issues. This all helps avoid infusion procedure delays. Providing infliximab, vedolizumab, ustekinumab, and lyophilized certolizumab pegol as well as intravenous iron administration can expand services and enhance quality.

Having a medical assistant, nurse, and others in your practice to assist with patient services and care is a must. There will be many phone calls, emails, and other interactions regarding appointments, consults, routine lab testing, radiology testing, standard medications, biologics, and other treatments that necessitate an effective team approach. For this role, either a nurse or an experienced medical assistant would be well suited. Additional support staff and services can also aid our IBD patients. A dietician knowledgeable in IBD and practical dietary options can, in many instances, prove invaluable. Understanding and utilizing pharma-sponsored "Patient Assistance Programs" provides drug access for the 10%-20% (or more) of patients who do not have insurance or biologic coverage. Having specialty access and collegiality with colorectal surgeons, general surgeons, OB/GYNs, dermatologists, hematologists, oncologists, and others is important to expedite consults and provide collaborative care. Finally, offering clinical research options improves access for patients with limited and no coverage and also helps provide needed options for all IBD patients.

This brief overview has given you some insight into how to provide a higher level of evaluation and care for our IBD patients. These approaches have allowed me to build and maintain a successful IBD practice, and I hope that the integration of some or all of these strategies help you to build and sustain a successful IBD practice. ■

One must be willing and able to see patients urgently, rather than sending them to the emergency room. ERs are appropriate for true emergencies, but are not an ideal place for care when an IBD patient has a flare and requires prompt follow-up. I try to avoid ER visits for my patients unless they are vomiting, have severe abdominal pain, have significant bleeding, or have clear signs of toxicity. In an ER, abdominal pain equals a CT scan; one should consider seeing these patients in the office and triaging accordingly.

A Practical Guide for Developing a Relationship With the Pharmaceutical, Biotech, and Device Industries

By Nitin Gupta, MD

Dr. Gupta is an assistant professor of medicine, director of inflammatory bowel disease, and program director for the gastroenterology fellowship at University of Mississippi Medical Center in Jackson. He has worked in basic science, as well as translational and clinical research, and continues projects in these areas. He has experience working with industry via roles of being a primary investigator in several clinical trials and consulting relationships.

The primary goal of the biotechnology and pharmaceutical industry is to develop medications and medical devices for the treatment of patients, while earning financial gain for investors. An important component of achieving this goal is the role physicians play in the drug and medical device development process. In particular, a physician's role is to combine their clinical expertise with their knowledge of industry products to better diagnose and treat the ailments of their patients. Thus, medicine and industry have a dependent relationship. In recent times this relationship has been fraught with turmoil as the public, scientific community, and federal government have discovered real and perceived conflicts of interest.

For example, there has been public outrage in the past with reports of doctors receiving gifts, money, and lavish trips in return for prescribing medications or using certain medical devices. Because of this, Congress passed the Sunshine Act, deeming it necessary to report all physician and industry engagements that have any perceived financial value. The passage of this act was in addition to local policies set forth by academic institutions, hospitals, and private practices.

Despite the increased scrutiny physicians face when interacting with industry, it is as important as ever for doctors to keep an open mind and consider opportunities to work with biotech and pharmaceutical companies. Such involvement will enable physicians to offer newer treatments and diagnostic tools to help their patients. With this in mind, I will discuss ways to develop such a role that can have a positive impact.

How do I get started?

After a check with your institution, hospital or private practice administrator, the first step is to reach out to a local representative ("rep") of a pharmaceutical or biotech company in which you are interested. You can accomplish this via the website of the company or by visiting the booth at major gastrointestinal conferences such as Digestive Disease Week (DDW®).

Pharma and device reps are quite knowledgeable about the latest clinical studies regarding their products, disease states, and various competing products in the market. In addition to being a source of

valuable medical knowledge and disease-specific practice guidelines, they also can connect you with their medical science liaison (MSL). MSLs often have a background in pharmacy and/or research. Thus, they can provide insights into mechanisms of disease treatments and go beyond discussion of the product label, which pharmaceutical reps adhere to. They also know what therapies or diagnostic tools are in the phases of development and could be available for a clinical trial.

MSLs are also the gatekeepers for Investigator-Initiated Studies (IISs). An IIS is a research project that is industry funded and is solely designed and executed by the clinician. The application process is rigorous but awards may be easier to obtain for non–research-based clinicians who want to develop a disease-specific project that needs funding. Their grant application process can be brief, ideas may not require prior data, and turnaround time to funding may be shorter. IISs often lead to exploratory findings that may facilitate publications or lay groundwork for large-scale grants or even clinical trials. In some instances, you may be granted access to internal data and prescribing patterns, which can answer interesting clinical and research questions.

How do I get started with clinical trials?

Being a primary investigator on a clinical trial is a big responsibility. You are responsible to the trial sponsor in addition to your patients. For young clinicians who lack experience with clinical trials, the first thing to do is to find a clinician in your department or another department, who has expertise in performing an industry-sponsored study. These individuals can be invaluable for you in terms of guiding you through the study feasibility process, study start-up, and possibly being the lead or co-investigator with you. Partnering with someone with expertise in industry-sponsored clinical trials will help you gain the trust of the industry sponsor, which may be a requirement for some.

There are many additional requirements that need to be fulfilled aside from just having an appropriate and adequate patient population to pull from. You will need to have a coordinator for the study who will help you with patient care, data entry, and study-specific issues. Clinical trials require a significant amount of documentation and reporting that has to be performed within a timely manner. There is no degree prerequisite for the coordinator, but it can simplify things for the clinician if they have an RN or LPN degree. Having such a degree will facilitate dual roles of patient care, lab draws, drug administration, medical charting, and other patient care matters.

In addition, you will need to have approval from either your local or central institutional review board (IRB). Also, you will have to review budget and study-specific requirements for equipment and infrastructure with your department manager. You will need to demonstrate adequate ancillary support to process, store, and ship biological specimens. In some instances, you will need a dedicated pharmacist to mix or dispense study drugs.

The process is lengthy and involved, but rewarding in terms of being involved in the drug development process. You will have opportunities to attend meetings at which you can network with other clinicians and provide the sponsor feedback on how the study is going.

How do I develop a consulting role with industry?

It is important to check with your institution, hospital, or practice if there are any limitations to becoming a consultant for a pharmaceutical or device company. If it is allowed and will not interfere with your clinical duties, it is important to note that this role takes time to develop. It often comes about after years of experience doing research, clinical, and/or basic science, with publications to support expertise. Working on an IIS is a good way to work hand-in-hand with expert industry researchers and facilitate the consulting relationship. Being a primary investigator of clinical trials with successful enrollment of patients and meeting attendance will provide you with insight into the drug development process.

What if none of this works out for me?

Do not give up! Persistence, experience, and hard work are the keys to developing relationships with industry. Remember, industry has a vast network of clinicians and researchers they already work with. The overall pool of companies and experts is limited and can be difficult to break into. But it can be done. Some rely on their research experience, clinical training, and mentors to develop the necessary contacts. Others can develop the contacts via IIS applications. Industry lacks access to the physician-patient experience; this can be your greatest asset and key to your success if leveraged properly. You can consider applying for mentorship with experts in your field via AGA-sponsored events held annually at DDW® to get additional guidance.

Final thoughts

It is important to remember that all industry relationships require time to develop. They also come at an opportunity cost of time away from your clinical practice and your family, friends, and hobbies. However, these relationships also offer a way to increase your insight into new and old treatment and diagnostic paradigms. It is also a way to remain excited about your field and prevent the feeling that your day-to-day clinical practice is becoming routine. ■

The Vanishing Tide: As MACRA Moves In, IBD Quality Measures Move Out

By Ryan A. McConnell, MD, and Fernando Velayos, MD, MPH

Dr. McConnell is a fellow in gastroenterology and advanced inflammatory bowel disease, division of gastroenterology, University of California, San Francisco. Dr. Velayos is professor of medicine, co–medical director, Center for Crohn's and Colitis, University of California, San Francisco.

Your next patient is a 67-year-old Medicare beneficiary with corticosteroid-dependent ulcerative colitis. Despite 4 months of maximally dosed mesalamine, his colitis flares with prednisone taper below 20 mg daily. Hepatitis B serologies and tuberculin skin test were negative 10 months ago. Which of the following do you recommend?

A. Steroid-sparing therapy initiation

B. Repeat latent tuberculosis screening in anticipation of anti–tumor necrosis factor (TNF) therapy

C. Bone loss assessment

D. Pneumococcal vaccination

E. Tobacco use screening

All of the above may be appropriate for optimal clinical care, but only two (C and E) will impact your bottom line when using the new GI Measures Set to report quality measures through the Merit-Based Incentive Payment System (MIPS). For the 75.1% of physicians who have not heard of – or don't know much about – MIPS,[1] the gastroenterology world will come to know it as the dominant of two Quality Payment Program (QPP) tracks introduced as part of the Medicare Access and CHIP Reauthorization Act of 2015 (MACRA). Starting in 2017, the QPP handles quality measure reporting and reimbursement adjustments based on the quality and cost of care provided to Medicare beneficiaries. MIPS replaces the Physician Quality Reporting System (PQRS), Value-Based Payment Modifier, and electronic health record Meaningful Use programs that previously executed these tasks.

Quality measure reporting is a costly undertaking, with medical practices spending an average of 15.1 hours per physician per week ($40,069 per physician annually) dealing with external quality measures.[2] How did this expensive alphabet soup of quality measure reporting arise and how does it impact inflammatory bowel disease (IBD) care?

Why are IBD quality measures needed?

There is substantial variation in care provided to IBD patients. Examples include geographic variation in rates of prolonged corticosteroid[3] and biologic therapy use (Figure 1),[4] hospitalization, and colectomy.[5] IBD experts and community gastroenterologists manage IBD differently.[6,7] This variation reflects more than mere "art of medicine" stylistic differences. Patient, provider, and system-level factors contribute to practice variation, including the heterogeneity of IBD phenotypes, lack of knowledge about best practices, insufficient evidence on which to base treatment decisions, and variable access to care. Variation likely indicates resource underuse, overuse, and misuse and may be a marker of poor quality care.[8,9] Closing the gap between current and ideal IBD care – by reducing unnecessary variation – may reduce suboptimal outcomes, pre-

ventable complications, care costs, and waste. Financially incentivized quality metrics have been proposed as a performance improvement and standardization strategy.

What makes a good quality measure?

Quality must be defined and measured before it can be improved. This is easier said than done, especially for IBD where a gold standard in "ideal care" is ill defined and continually evolving as new research emerges. Nonetheless, hundreds of health care quality measures have been proposed. Desirable quality measure attributes should satisfy three broad categories: importance, scientific soundness, and feasibility.[10] Quality measures should address relevant and important aspects of health that are highly prevalent and for which evidence indicates a need for improvement. There should be strong evidence supporting the beneficial impact of adhering to a given measure.

From a practicality standpoint, measures should relate to actions that are under the control of the providers whose performance is being measured. Measures should also be parsimonious with a goal of minimizing the number of measures needed to adequately represent performance in a given area.[11] More simply stated, a good quality measure reflects consensus about a minimally acceptable level of care that applies broadly to all patients.

Quality measures are commonly classified as process measures or outcome measures. Process measures ("doing the right thing") are steps taken by providers in the care of an individual patient. These often derive from evidence-based best practices. Outcome measures ("having the desired result") identify what happens to patients as a result of care received.[8] Outcome

Table 1

Evolution of inflammatory bowel disease process measures, 2011-2017

IBD Process Measure*	2011 AGA	2013 CCFA	2016 AGA	2016 PQRS IBD Measures group	2017 MIPS GI Measure set
Documented assessment of IBD type, anatomic location, disease activity, and presence of extraintestinal manifestations[I]	x		x		
Steroid sparing therapy prescribed for patients on long-term steroids[I]	x	x	x	x	
Documented bone loss assessment for patients at risk for steroid-related injury[I]	x		x	x	x
Influenza vaccine administered or previously received[C]	x		x	x	
Pneumococcal vaccine administered or previously received[C]	x		x	x	
Latent tuberculosis testing performed and results interpreted within 6 months prior to first course of anti-TNF therapy[I]	x	x	x	x	
Hepatitis B virus status assessed and results interpreted within 1 year prior to first course of anti-TNF therapy[I]	x	x	x	x	x
Tobacco use screening and cessation counseling intervention[C]	x	x^	x	x	x
Testing for C. difficile in patients with diarrhea[I]	x#	x			
Prophylaxis for venous thromboembolism[I#]	x				
Sigmoidoscopy with biopsy and surgical consultation in patients with severe UC unresponsive to 3 days of IV steroids[#]		x			
TPMT testing prior to initiating thiopurine therapy		x			
Proctocolectomy or repeat surveillance within 6 months offered to UC patients with confirmed low-grade dysplasia in flat mucosa		x			
Surveillance colonoscopy every 1-3 years in patients with extensive UC or Crohn's colitis of 8-10 years' duration		x			
Vaccination education for patients on immunosuppressive agents		x			

** AGA and CCFA quality measure language varies despite similar intent. Refer to the primary documents for exact language.;*
I IBD-specific measure;
C cross-cutting measure;
^ Applicable only to patients with Crohn's disease;
 # inpatient measure;
AGA – American Gastroenterological Association;
CCFA – Crohn's & Colitis Foundation of American;
IBD – inflammatory bowel disease;
TNF – tumor necrosis factor;
UC – ulcerative colitis;
TPMT – thiopurine methyltransferase;

measures may be more meaningful, but there are limitations in using them to study quality of IBD care. For example, factors beyond physician control affect patient outcomes and long delays may exist between care decisions and subsequent outcomes (e.g., surgery, malnutrition).[8]

What IBD quality measures already exist?

Expert panels from the AGA and the Crohn's & Colitis Foundation of America (CCFA) produced IBD quality measure sets comprising mostly process measures (Table 1). The original 10 AGA measures released in 2011 address aspects of disease assessment, treatment, complication prevention, and health care maintenance.[12] They include seven IBD-specific measures, three cross-cutting measures – defined by Centers for Medicare & Medicaid Services (CMS) as being broadly applicable across multiple clinical settings – and two inpatient measures. A major goal of the AGA measures was to facilitate quality reporting to the former PQRS program.

The 2013 CCFA "Top 10" highly rated process measures were selected from over 500 candidate measures.[13] Five of these measures closely match the AGA measures; two unique items address dysplasia surveillance. Real-world studies demonstrate variable adherence to these quality measures across multiple care settings (individual measure compliance ranging from 17% to 90%),[14] supporting the need for improvement. Interventions can improve adherence by up to 20%,[15] which provides face validity that these measures capture aspects of care that can be improved. The CCFA also developed an aspirational list of 10 highly rated outcome measures (Table 2), the selection of which included patient input.[13] The CCFA measures are not eligible for use in CMS quality reporting programs but are incorporated into the IBD Qorus national quality improvement initiative.[16]

Table 2

Crohn's & Colitis Foundation of America "Top 10" inflammatory bowel disease outcome measures

Proportion of patients with steroid-free clinical remission for >12-month period
Proportion of patients taking prednisone (excluding those diagnosed within the last 112 days)
Number of days per month/year lost from school/work attributable to IBD
Number of days per year in the hospital attributable to IBD
Number of emergency room visits per year for IBD
Proportion of patients with malnutrition
Proportion of patients with anemia
Proportion of patients with normal disease-targeted health-related quality of life
Proportion of patients currently taking narcotic analgesics
Proportion of patients with nighttime bowel movements or leakage
Proportion of patients with incontinence in the last month

What are some quality measure limitations?

Quality measure development has an evidence base but designing an optimal measure and demonstrating impact can be challenging. Few IBD process measures are validated and thus there is often logic but not data linking process measure adherence to improved outcomes. The denominator (number of eligible patients) and potential impact of broad adherence vary for each quality measure. For example, only a small fraction of IBD patients are infected with hepatitis B and fewer than 10% will experience viral reactivation during anti-TNF therapy.[17,18] Even with optimal adherence to the hepatitis B measure, few reactivations will be prevented. The wording of some measures lacks precision, allowing physicians to potentially claim credit without improving care. For example, ordering a bone density scan satisfies the bone loss assessment measure, even if osteoporosis goes unrecognized and untreated. Finally, some measures relate to actions that may not be under the control of the gastroenterologist whose performance is being measured (e.g., administering vaccinations).

IBD quality measures under MIPS

Table 1 depicts the evolution of IBD process measures from 2011 to 2017. Rather than building upon initial experience to revise and refine IBD quality measures, the measures have instead been progressively culled with the changing pay-for-performance landscape. In 2016, AGA eliminated the two inpatient measures.[19] Seven of the remaining eight measures formed the IBD Measures Group which was reportable under PQRS. In 2017, MIPS brought a seismic shift in quality measure focus. The PQRS IBD Measures Group was abolished – as were all Measures Groups – and replaced by a 16-item GI Measures Set. Although AGA advocated for all of the IBD measures to be included, the new GI Measures Set deemphasized the IBD-specific measures in favor of expanded cross-cutting measures (e.g., screening for abnormal body mass index, documenting current medications, sending specialist report to referring provider).[20] This reflected a previously observed trend that gastroenterologists more often reported on cross-cutting measures than specialist-specific measures.[21] However, there was no evidence-based justification for dropping certain IBD-specific measures (especially the steroid-sparing therapy

measure) in favor of retaining the two chosen IBD-specific measures – bone loss assessment and hepatitis B screening – which apply to only a subset of IBD patients and have limited potential to impact clinical outcomes. Although it is not mandatory to report using the GI Measures Set, we suspect that many gastroenterologists will use this set to guide their initial reporting.

During the 2017 MACRA transition year, physicians need report only one quality measure to avoid a penalty. Even after the "pick your pace" MACRA program testing period concludes in 2018, MACRA-eligible clinicians will need to report their performance only on six quality measures. This low bar and shifting focus away from IBD-specific measures is disconcerting for IBD quality enthusiasts. Although MIPS applies only to the 26% of Medicare-eligible IBD patients who are at least 65 years old,[22] private payers are likely to adopt similar reimbursement programs.

There are formidable regulatory obstacles to improving the IBD quality measures included in MIPS. CMS requires that new quality measures proposed for inclusion in MIPS be fully specified and tested for validity and reliability by the individual measure developers (such as AGA). This is a costly and time-intensive process that has complicated efforts to successfully advocate for inclusion of GI-specific quality measures in MIPS, as there is no existing infrastructure for quality measure testing.

A word about Alternative Payment Models (APMs)

APMs represent the non-MIPS pathway for participating in the QPP. APMs focus on chronic disease care coordination and qualify for lump-sum incentive payments by adhering to stringent standards and financial risk-sharing requirements. A detailed overview of APMs is beyond the scope of this discussion, as the vast majority of MACRA-eligible gastroenterologists will participate in MIPS and there are currently no GI-specific APMs. However, this is an evolving area and Project Sonar has been submitted to the Physician-Focused Payment Model Technical Advisory Committee for consideration as an APM for Crohn's disease.[23]

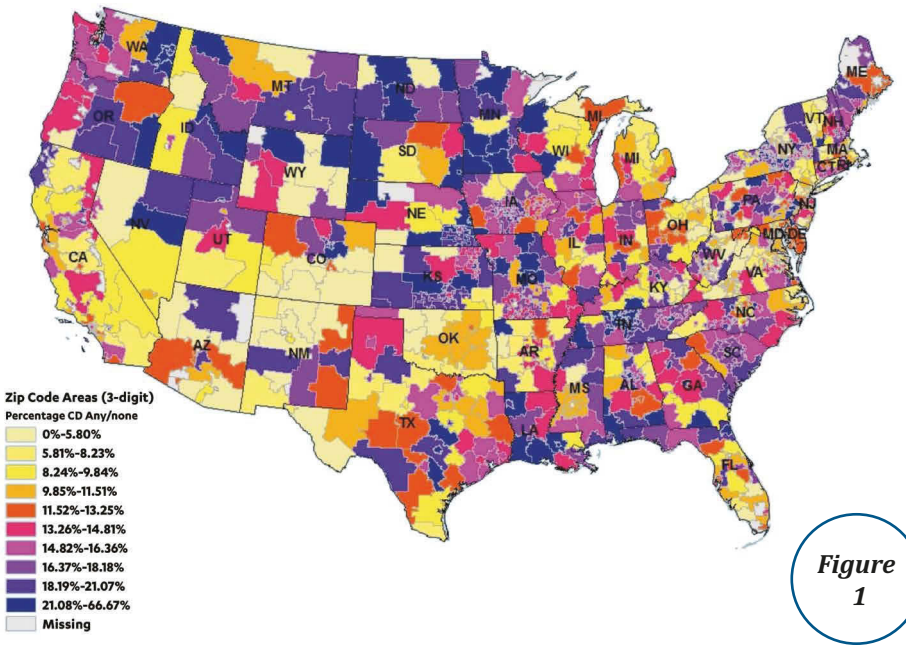

Figure 1

This image was published in David G, Gunnarsson CL, Lofland J, et al. Geographic variation in care of patients with inflammatory bowel disease suggests unequal quality of care in the United States. Gastroenterology. 2013;144:S-647, Copyright Elsevier/AGA.

Conclusion

Quality measurement and reporting are at a crossroads. Ideally, performance improvement should be an internally driven process that addresses specific local priorities and needs. Most medical practices (73%) believe that current externally driven quality measures do not represent care quality and only 28% use their quality scores to focus their internal quality improvement activities.[2] The burden and cost of external quality reporting demand better alignment with local priorities as resources are currently being diverted away from internally driven efforts that might have the greatest potential to improve patient outcomes.[24] The dawn of the MACRA era presents an opportunity to shape the future of the IBD quality movement. Through validating and prioritizing existing measures and developing novel, precisely stated, and high-value metrics, there remains vast (and measurable) potential to enhance patient outcomes. ■

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PATIENT PERSPECTIVES

What Makes an Excellent Gastroenterologist? IBD Patient Perspectives

The Patient Governance Committee for Crohn's & Colitis Foundation of America (CCFA) Partners: Brian Price, Susan M. Johnson, Jessica Burris, David Walter, Jennifer E. Dorand, and Nicholas Uzl

We are a group of six adult inflammatory bowel disease (IBD) patients who serve as the Patient Governance Committee for CCFA Partners – a patient-powered research network that assists IBD patients, researchers, and health care providers to partner in finding the answers to questions about patient care and improving the health and lives of patients living with these conditions. To find out more about us, please visit our website at https://ccfa.med.unc.edu/ or send an email to info@ccfapartners.org.

The foundation of good quality of care is the patient/physician relationship, and as patients we understand that foundation must be based on mutual respect, trust, and communication. There are a few themes that emerge when thinking about these salient qualities:

Open communication between patient and physician

Perhaps the single most important quality of a physician is a willingness to listen. IBD patients often don't feel like they are being heard. Starting with a conversation about the patient's goals

in terms of managing the disease as well as their goals in life will help the physician understand the patient's unique situation and concerns. This is really a twofold proposition: what are the patient's short-term goals and long-term goals? What is the most effective treatment plan to help them? How do the physician and the patient define treatment success?

Sometimes the most effective treatment strategy isn't the one that will improve overall quality of life. For example, adding immunomodulators to a biologic therapy may potentially increase the effectiveness or prolong treatment success; yet the adverse effects of immunomodulators on quality of life could outweigh any therapeutic benefits. Doctors should educate patients on the pros and cons of appropriate treatments, and should serve as a guide toward those plans that will have the most positive impact on overall well-being, as opposed to adopting a narrow focus on treating symptoms. We use the term "guide" with a very specific intent: If a patient comes to an appointment asking about a potential therapy, the doctor should take the time to discuss the topic with an open mind and help critically assess any potential benefits or hazards. The ability to guide treatments without dictating options or being closed minded requires a certain finesse.

At times, physicians and patients might disagree on treatment goals and patients will want their decisions respected, even if they differ from the physician's preference. Patients want the ability to be unreservedly open with their doctors and for their doctors to listen without being defensive. Having a chronic, incurable illness is a lifelong journey, and they need someone who will respect their autonomy as well as help them weather the ups and downs of a life with IBD.

Another key consideration in building trust with patients is honesty. Being clear about the prognosis of the disease, the side effects of particular therapies, and how quickly to expect symptom relief and/or remission are all critical in empowering patients to be active participants in their disease management. Beyond the technical aspects of caring for a patient, the physician should also be honest about their capacity to care for the patient's disease complexity and be able to devote the necessary time to developing a treatment strategy. This can especially be an issue in smaller towns, where some gastroenterologists who practice in a more generalist setting may be uncomfortable with therapy management that is outside the typical treatment algorithms. In those settings, it is highly appreciated when practitioners recommend second opinions or provide referrals.

Coordinating care and transitions

Ensuring coordinated care when making a transition – whether it is because of a geographic relocation, from pediatric care to adult, or a change in insurance – remains critical. While effective communication with patients is always important, it is especially so during a transition. It is valuable when physicians can work in a coordinated effort to manage care as a team. Patients are not always able to travel to a specialist or get an appointment every time treatments need reconsideration. The ability to access coordinated, specialized care in the local setting is very important. In recent years, the ability to seek medical advice via email check-ins (without the delay of office appointments) has become a tremendous value as diseases can sometimes flare out of control quickly and unpredictably.

When a patient needs to transfer to a new physician, it's important to help them find the right fit for their particular circumstances. Ask what is most important to patients. Is it the distance between their residence and their provider? Is it ability to manage complex disease? Is the physician in-network? All of these are import-

Perhaps the single most important quality of a physician is a willingness to listen. IBD patients often don't feel like they are being heard. Starting with a conversation about the patient's goals in terms of managing the disease as well as their goals in life will help the physician understand the patient's unique situation and concerns.

ant factors in helping the patient find the right care.

These considerations are not limited to times of transition. Despite advancements in electronic medical record systems, there continues to be poor documentation and communication between providers. Often, when patients initiate care with a new physician, that physician has not reviewed the medical history in depth and relies on the patient's explanation. This kind of communication carries with it a risk of important findings from another doctor falling through the cracks.

Holistic approach to treatment

Treating an IBD patient means treating the patient as a whole, not only their symptoms. IBD can lead to many challenges for patients and that is why treatment plans must consider not only physical, but also emotional and mental health, needs. One underserved area is pain management. While the dangers of opiates have been well documented, it seems the pendulum has swung too far in the opposite direction: Some doctors are ignoring the topic of pain management altogether or establishing policies against prescribing any narcotic pain medications. This trend is troubling. Pain management is not an issue that goes away by ignoring it and remains a very important part of overall care needs. Doctors should be encouraged to take the time to learn about the many different approaches to pain management, including nonnarcotic and nonmedication therapies.

There are so many concerns that patients have beyond IBD symptom management, but a compassionate approach and asking the right questions can immeasurably improve outcomes. Engaging with patients on the topic of navigating the 21st century American medical system – and the time, energy, and expense inherent to being a patient in that system – can help foster an appreciation for the myriad challenges patients face.

Conclusion

The mark of a high-functioning patient/physician relationship is that the patient feels empowered to be engaged with the management of their disease. An empowered patient is one who feels comfortable asking about new therapeutic options, explores new approaches to managing their disease without fear of being judged, and sticks with a treatment plan. By treating patients as partners in the fight against IBD, you can help patients accomplish their goals through a relationship based on mutual trust.

As a final note, we want to express our deepest thanks to gastroenterologists for the work that they do. Learning to manage IBD has been very challenging and the support and guidance of our doctors over the years has been so important. Thank you for choosing a career in helping people. ■

Since my diagnosis 15 years ago, the gastroenterologists who have cared for me were all effective clinicians who improved my quality of life. However, the best physicians asked me directly what aspects of my life I found most important.

My answer to this "life priority" question has changed over time. As a teenager, I wanted to fit in with my peer group as much as I could. In my early 20s, I wanted to take part in physical activity and reduce my pain as much as possible. Today, I prioritize being mentally sharp and reliable for those who depend on me professionally and maintaining empathy for those who depend on me emotionally.

I can imagine that my priorities are more easily relatable to an adult physician now than when I was in my teens, but the best gastroenterologists have empathetically listened and respected my wishes, within reason, throughout my entire experience of illness.

To me, what makes an excellent gastroenterologist is the ability to understand a patient's greatest priorities, the activities or feelings or connections that make that person feel most whole, and, whenever possible, to direct treatment strategy according to these priorities.

– Jessica Burris

As young physicians, you may feel the need to know the answers to all our questions or a thorny diagnostic problem we present. The truth is we don't expect you to know all the answers in the moment. It's OK to say you don't know, but stay curious in finding a solution.

Also, at times there is a third presence in the room with you and your patient: the electronic medical record. It can be easy to become distracted and not make eye contact with us, which can seem as if you aren't paying attention. Remember to always be fully present with your patient. Your patient will truly appreciate it.

– David Walter

Snapshots from the AGA Journals

Unique, multiomic profile found in children with autism and functional GI disorders

March Cellular and Molecular Gastroenterology and Hepatology (doi: 10.1016/j.jcmgh.2016.11.008)

Key clinical point: The mucosal microbiome of children with comorbid autism spectrum disorder and functional gastrointestinal disorders significantly differed from that of neurotypical children with and without FGIDs, and these differences correlated with altered levels of inflammatory cytokines, tryptophan, and serotonin.

Major finding: Children with ASD-FGID had significant increases in *Clostridium lituseburense* (P = .002), *Lachnoclostridium bolteae* (P = .02), *Lachnoclostridium hathewayi* (P = .03), *Clostridium aldenense* (P = .04), and *Oscillospira plautii* (P = .04), and significant decreases in *Dorea formicigenerans* (P = .006), *Blautia luti* (P = .020), and *Sutterella species* (P = .025). The ASD-FGID phenotype was characterized by significantly lower gut levels of tryptophan, with higher levels of the serotonin metabolite 5-HIAA, and with several proinflammatory cytokines. Several bacterial species correlated with tryptophan, serotonin, or proinflammatory cytokines.

Data source: A single-center cross-sectional study of 14 children with ASD-FGID and 21 neurotypical children, of whom 15 had FGIDs.

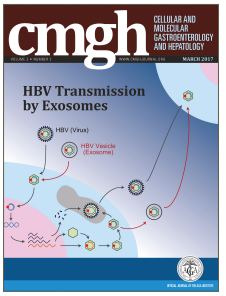
Disclosures: The U.S. Department of Health & Human Services funded the work. The investigators had no relevant disclosures.

Commentary

Jonathan Braun, MD, PhD, is professor and chair of pathology and laboratory medicine, UCLA David Geffen School of Medicine, UCLA Health System, Los Angeles. He has no conflicts of interest.

Autism spectrum disorder is a serious and increasingly prevalent developmental behavior disorder often accompanied and aggravated by a range of gastrointestinal and cognitive dysfunctions. Its etiology probably involves maternal diet and inflammatory events that alter central nervous system neurodevelopment critical to the cognition of social interaction. Candidate causal products of these events include the cytokines interleukin-6 and IL-17A, and certain bioactive amines, notably serotonin. Functional gastrointestinal disorders share these same molecules as biomarkers and disease modifiers, probably elicited in part by the intestinal microbiome. Hence, the comorbidity in ASD suggests these two disease processes are etiologically related.

The study by Luna and colleagues tightens the case for a microbial hub and serotonin and cytokine spokes in the gastrointestinal dysfunction of ASD: elevated mucosal tissue levels of select microbial taxa, mainly members of the genus Clostridium, and mucosal production of cytokines and serotonin-pathway bioamines associated with these and other select microbial species. Important and challenging questions loom ahead. What are the direct mucosal cell types and functions targeted of this network for the microbiota, and via what microbial products? Might they elicit epithelial or mucosal hematopoietic cell cytokine production that in turn causes mucosal bioamine secretion? And, what associated microbiota and products are just secondarily altered and not causally involved? The exciting study of Luna and colleagues raises confidence for this path ahead, and its promise for clarifying ASD pathogenesis and uncovering targetable elements for intervention. ■



Sofosbuvir with velpatasvir beat other HCV GT3 regimens

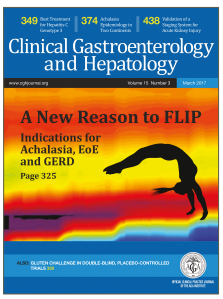
March Clinical Gastroenterology and Hepatology (doi: 10.1016/j.cgh.2016.10.03)

Key clinical point: Regimens containing sofosbuvir and velpatasvir were more effective than were other direct-acting antiviral combinations for treating genotype 3 hepatitis C virus infection, regardless of cirrhosis status.

Major finding: For patients without cirrhosis, sofosbuvir and velpatasvir with ribavirin for 12 weeks yielded the highest estimated likelihood of sustained viral response (99%). For patients with cirrhosis, the most effective regimen was sofosbuvir with velpatasvir for 24 weeks (estimated SVR, 96%).

Data source: A systematic review and meta-analysis of 27 studies: 16 randomized controlled trials, 6 single-arm studies, and 5 observational cohort studies.

Disclosures: Dr. Berden and four coinvestigators had no relevant financial disclosures. Senior author Joost Drenth, MD, PhD, disclosed serving on advisory boards and receiving research grants from several pharmaceutical companies.



Commentary

Norman L. Sussman, MD, is associate professor of surgery, Baylor College of Medicine, Houston; director, Project ECHO. He has received speaking and consulting fees for AbbVie, BMS, Gilead, and Merck.

The rapid development of direct-acting antiviral agents (DAAs) to treat hepatitis C has yielded many surprises and left some gaps in our knowledge. One of the surprises was that genotype 3, previously considered "easier to treat," proved quite resistant to the first generation of DAAs. One of the gaps in knowledge was a lack of randomized and head-to-head trials for current medications. One could argue that randomized trials have limited utility in a disease with essentially no spontaneous cures, and that head-to-head trials are pointless in a rapidly evolving field where regimens may be obsolete by the time the study is completed. On the bright side, a hard endpoint like sustained virologic response (SVR) makes comparison between trials possible. The paper by Bergen et al. offers some guidance in closing the knowledge gap. Their meta-analysis using Bayesian Markov Chain Monte Carlo methods examined the effectiveness of currently available antiviral agents in 27 studies that focused entirely on genotype 3.

All studies used antiviral agents that are currently available in the United States, and effectiveness was tested in both noncirrhotic and cirrhotic patients.

The results were uniformly excellent – 94%-99% SVR, substantially higher than reported in clinical trials. The analysis also showed that sofosbuvir plus velpatasvir was superior to sofosbuvir plus daclatasvir or sofosbuvir plus interferon plus ribavirin. This result conforms to in vitro data that show good inhibitory activity of velpatasvir against the NS5A replication complex inhibitor in genotype 3 replicons. The study also showed that the addition of ribavirin improved SVR in all groups, all durations of treatment, and with all drug combinations – not bad for a weak antiviral agent with an unknown mode of action.

The evolution of antiviral therapy has been amazing. After decades of incremental gains, we entered an era of dizzying progress. Genotype 3 went from great news to bad news, and genotype 1 went from a scourge to a piece of cake. ■

Infectious enteritis quadrupled short-term risk of IBS

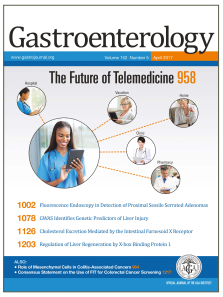
April Gastroenterology (doi: 10.1053/j.gastro.2016.12.039)

Key clinical point: Infectious enteritis more than quadrupled the risk of IBS in the subsequent year.

Major finding: A total of 10.1% of patients with infectious enteritis developed IBS in the next 12 months, a 4.2-fold increase in risk, compared with that of controls.

Data source: A systematic review and meta-analysis of 45 studies.

Disclosures: The National Institutes of Health and the American Gastroenterological Association funded the work. The investigators reported having no conflicts of interest.



Commentary

Robin Spiller, MD, is professor of gastroenterology, NIHR Nottingham Digestive Diseases Biomedical Research Unit, Nottingham Digestive Diseases Centre, University of Nottingham, England. He has no relevant conflicts of interest.

The phenomenon of IBS developing after a bout of gastroenteritis (postinfectious [PI]–irritable bowel syndrome) was first reported in 1950 and subsequently elaborated by studies from Oxford (Q J Med. 1962;123:307-22), Sheffield (Gut. 1999;44:400-6), and Nottingham (BMJ 1997;314:779-82; Gut. 2000;47:804-11). It has proven to be a fertile area for research, which is the basis for this excellent meta-analysis.

The authors identified 45 studies, 29 in the last decade including a total of 21,421 participants with exposure to gastroenteritis. The pooled prevalence for PI-IBS was 11.5% (95% confidence interval, 8.2%-15.8%) but with considerable heterogeneity, which the authors attempted to explain by a number of subgroup analyses. The authors report that protozoal infection seems to have a higher rate of PI-IBS than bacterial or viral infection, though some caution is warranted, since these figures rely on reports from just one outbreak of giardiasis in Bergen, Norway (Scand J Gastroenterol. 2012;47:956-61). However, if true, this might suggest that a different immune response could be responsible, a feature which others have suggested might predispose particular individuals to PI-IBS (Gut. 2016;65[8]1279-88).

Other notable findings were the higher incidence of PI-IBS in studies with low response rates, suggesting important bias is such studies. Thirty of the studies included controls to allow relative risk (RR) estimation. Pediatric series showed similar RRs to adults at 4.1 versus 3.8, respectively. Age strongly influences immune response and older age was protective in several studies (Clin Gastroenterol Hepatol. 2007;5:465-9; J Travel Med. 2014;21:153-8; BMJ. 1997;314:779-82) but other studies found no effect. This may relate to an inadequate age range since the differences were most marked in those older than 60 years (BMJ. 1997;314:779-82).

The meta-analysis confirms the consistent increased risk in female patients (odds ratio, 1.69), anxiety (OR, 1.97), and somatization (greatest RR, 4.05), all common risks for the development of IBS but not specific to PI-IBS. Initial disease severity indicators, including bloody stool and more than 7 days of initial illness, which might indicate the severity of underlying damage to the gut, were shown to be significant risk factors. Animal studies of acute infection, particularly parasitic infestation, indicate that significant changes can be seen in both nerve and muscle, but routine histology in PI-IBS patients is normal. Infection produces a striking increase in gut permeability (Gut.

2000;47:804-11), a feature of IBS whose molecular basis has been demonstrated by a series of elegant studies (Gut. 2017 Jan 12 [Epub ahead of print]; Gut. 2015;64:1379-88) demonstrating altered tight junctions and immune activation in IBS with diarrhea. The authors found treatment with antibiotics increased the risk of PI-IBS but whether this is attributable to confounding by indication is unclear.

This meta-analysis indicates that PI-IBS also potentially is the most common cause of IBS, given that both the Centers for Disease Control and Prevention in the United States and community surveys in the United Kingdom (BMJ. 1999;318:1046-50) indicate that gastroenteritis affects around one in five of the population each year. If the incidence of PI-IBS is around 10%, modeling suggests PI-IBS could account for the majority of new cases (J Neurogastroenterol Motil. 2012;18:200-4). ■

DDSEP® eight ANSWERS

Digestive Diseases Self-Education Program

// From page 10

Q1: Answer: A

Rationale: This is a case of high-grade dysplasia within a visible lesion in the setting of Barrett's esophagus. Guidelines recommend that any visible irregularities in Barrett's esophagus should be removed using endoscopic mucosal resection (EMR) for tumor staging. There is high-quality evidence to support this recommendation. High-grade dysplasia without a visible lesion can be treated with radiofrequency ablation (RFA). RFA reduces progression to esophageal cancer from a randomized sham-controlled trial. At this time, there is insufficient evidence for cryotherapy to achieve reversion in any stage of Barrett's esophagus. It should also be noted that this patient has several risk factors for Barrett's and esophageal cancer including white race, obesity, and long-standing gastroesophageal reflux disease.

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Q2: Answer: D

Objective: Recognize conditions associated with a high-risk of pancreatic cancer incidence.

Critique: Familial pancreatic cancer (two or more first-degree relatives with pancreatic cancer), Peutz-Jegher's, FAMM syndrome, BRCA2, and Lynch syndrome with affected first-degree relatives are generally considered candidates for surveillance based on consensus expert opinion.

Patients with Cronkhite-Canada syndrome have gastrointestinal polyposis and are at higher risk for gastrointestinal luminal cancers rather than pancreatic cancer. MRI or endoscopic ultrasound are considered to be the preferred tests for surveillance in the population at risk for this syndrome.

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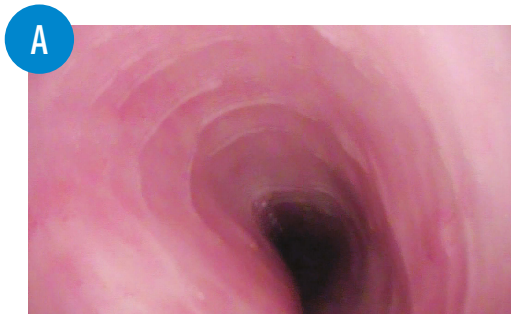
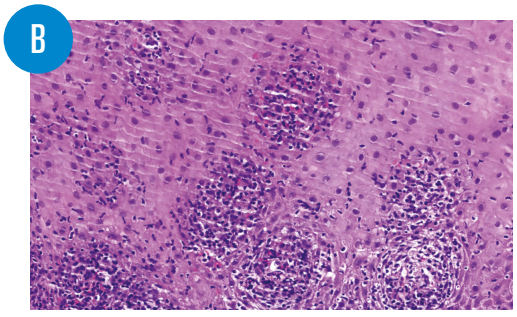
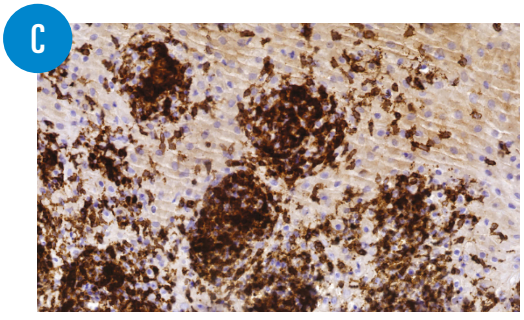
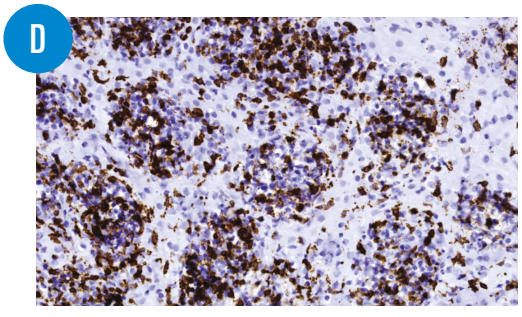
The Answer // From page 3









The correct answer is C: Lymphocytic esophagitis (LyE).

Histopathology showed well-differentiated squamous epithelium with dense intraepithelial lymphocytic infiltration of the peripapillary fields without neutrophilic or eosinophilic granulocytes. Focally there were areas with peripapillary intercellular edema/spongiosis (Figure B). There were CD3+/CD4+/CD8+ lymphocytes, without clear predominance of CD4+ or CD8+ lymphocytes (Figures C and D). Upon re-evaluation of the esophageal biopsies from the index endoscopy, neutrophilic granulocytes were reclassified as lymphocytes with shape alterations. Histopathology was diagnostic of LyE on both occasions.

The histologic findings of LyE were described in 2006[1] as abundant intraepithelial lymphocytes in the peripapillary fields of esophageal squamous mucosa with only rare neutrophils and/or eosinophils present. There are reports on associations with reflux, hypothyroidism, Crohn's disease, allergies, and asthma,[1,2] but published reports are not unanimous.[2,3] The etiology of LyE remains unknown. There is a wide age distribution and no clear gender predominance. The course of LyE is considered to be chronic but benign.[2] Endoscopic findings suggestive of eosinophilic esophagitis, such as rings, are observed in 33.6% of LyE patients.[3] Presenting symptoms are most often dysphagia or related to reflux. Treatment is symptomatic with proton-pump inhibitor or balloon dilatation of strictures.

The patient's dysphagia had improved 3 months following balloon dilation. She declined further follow-up. ■

References

1. Rubio, C.A., Sjodahl, K., Lagergren, J. Lymphocytic esophagitis: A histologic subset of chronic esophagitis. Am J Clin Pathol. 2006;125:432-7.

2. Cohen, S., Saxena, A., Waljee, A.K., et al. Lymphocytic esophagitis: A diagnosis of increasing frequency. J Clin Gastroenterol. 2012;46:828-32.

3. Haque, S., Genta, R.M. Lymphocytic oesophagitis: Clinicopathological aspects of an emerging condition. Gut. 2012;61:1108-14.

This article has an accompanying continuing medical education activity, also eligible for MOC credit (see Gastroenterology website for details). Learning Objective: Upon completion of this teaching case and questions, the learners will be able to identify one typical clinical and endoscopic presentation of the entity lymphocytic esophagitis, distinguish its histological pattern from other esophageal disorders, and recognize a variety of other clinical presentations of this condition.

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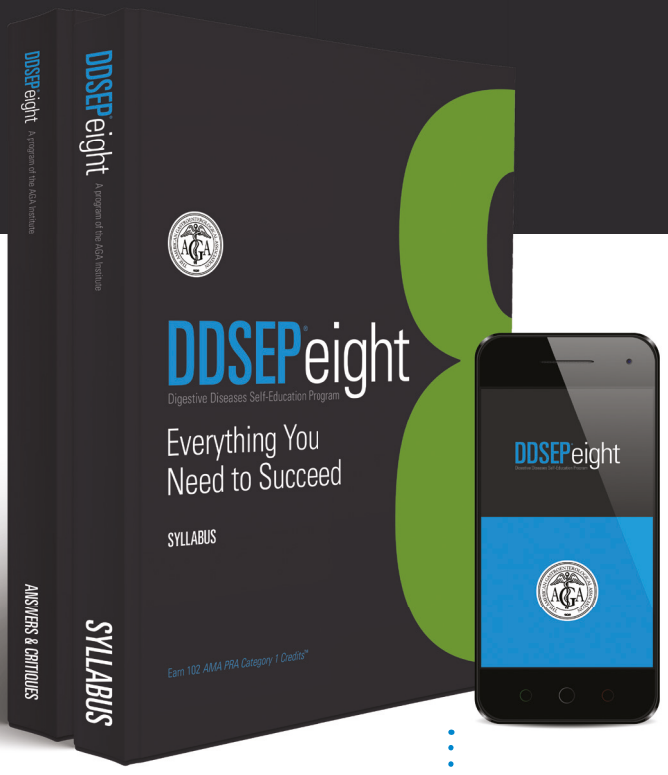

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