The NEW GASTROENTEROLOGIST

A Quarterly Supplement to GI & Hepatology News | Summer 2017

Reflux Diagnostics

Modern Techniques and Future Directions 7

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,

Congratulations to the new gastroenterology fellows who have just begun their fellowships and also to those who have just finished and are starting their careers. It is certainly an exciting time of year for so many! To start off this issue, a letter from AGA President Sheila Crowe details the benefits and opportunities our organization offers GIs entering practice and academia.

In this issue's feature article, Amit Patel (Duke University) and Prakash Gyawali (Washington University in St. Louis) provide a fantastic overview of ambulatory reflux testing. They outline the basics of the different methods of reflux testing, discuss whether testing should be done on or off PPI therapy, and provide useful tips for patient management.

This issue also contains an informative perspective about pursuing a career in medical education by Suzanne Rose (University of Connecticut), an incredibly passionate educator who has dedicated her career to this endeavor. Additionally, Katherine Garman (Duke University) and Latha Alaparthi (Gastroenterology Center of Connecticut/Yale University) provide a recap of this year's AGA Women's Leadership conference, which brought together a large group of early-career and experienced women from many different career pathways within the field of gastroenterology.

As student loans are an issue for many, CommonBond, the AGA's official student loan partner, highlights an early-career gastroenterologist's experience with student loans, as well as important factors to consider in refinancing and paying off student loans. Finally, in the first of a two-part series on medical malpractice, an experienced group of attorneys from Eckert Seamans Cherin & Mellott, LLC (Philadelphia) provide a concise overview of the basics of malpractice as well as tips to help minimize your risk of being sued.

I hope that you enjoy this issue of *The New Gastroenterologist*. For those in the early-career group on the AGA Community (http://community.gastro.org/), these articles will be posted to the library to further enhance access. You can also find *The New Gastroenterologist* online and via the free app. If you have ideas for future issues or would be interested in contributing, please e-mail either me at bryson.katona@uphs.upenn.edu or Managing Editor Ryan Farrell at rfarrell@gastro.org.

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

The NEW GASTROENTEROLOGIST

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ON THE COVER

Dr. Amit Patel, left, and Dr. C. Prakash Gyawali
Photo by Robert Boston

IN THIS ISSUE

Dear Trainees and Young GIs,

As I begin my time as President of AGA, I am reflecting on other new beginnings in my career. Though time has passed, I vividly recall the excitement and uncertainty of beginning training and, subsequently, my career. It's a career that I've enjoyed immensely and I hope that you will as well.

Throughout my career, and especially in the early years, AGA provided invaluable support. For example, it provides a diverse array of professional and educational tools and offers us many opportunities to enhance our knowledge and expertise no matter the path we take, whether it be academia or clinical practice.

All our resources are available online at www.gastro.org and we have a suite of apps including guidelines, image challenges, DDSEP, and publications that you can download to your mobile device. You can learn more about those at www.gastro.org/mobile-offerings.

Another great resource is the AGA Community, where you can join a private online conversation with other early-career gastroenterologists. You can access a library of resources there and talk with gastroenterologists who are in the same career phase as you are. Join the conversation at community.gastro.org.

The New Gastroenterologist is the perfect place to start your professional journey and to stay on the cutting edge of the field. It provides a wealth of information you won't find in other publications. Its unique focus promises that you'll read content that meets your immediate needs as a trainee or early-career gastroenterologist.

On behalf of the AGA Governing Board, I wish you great success in this exciting field!

Sincerely,
Sheila E. Crowe, MD, AGAF
President, AGA Institute
Professor of Medicine and Director of Research,
University of California, San Diego

A Rare Endoscopic Clue to a Common Clinical Condition

Published previously in Gastroenterology (2017;152:492-3)

By Bradley Anderson, MD, and Seth Sweetser, MD

Dr. Anderson and Dr. Sweetser are in the Division of Gastroenterology and Hepatology, Mayo Clinic College of Medicine, Rochester, Minn.

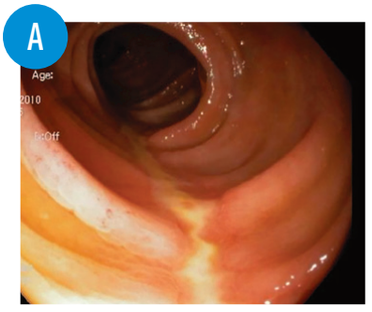
A 64-year-old woman presented to a local emergency department after noting large-volume passage of bright red blood from her colostomy site over several days. She denied any associated abdominal pain, recent changes in bowel pattern, nausea, vomiting, orthostatic symptoms, abdominal trauma, NSAID use, or recent manipulation of the ostomy concurrent with her symptoms. Her past medical history was significant for hypertension and remote stage 1B cervical cancer complicated by radiation-induced enteritis, proctitis, and terminal ileal stricture. Four years prior to her current presentation, surgical resection of the terminal ileum had been performed with a side-to-side ileoascending colostomy and creation of an end-sigmoid colostomy for management of persistent diarrhea and fecal incontinence.

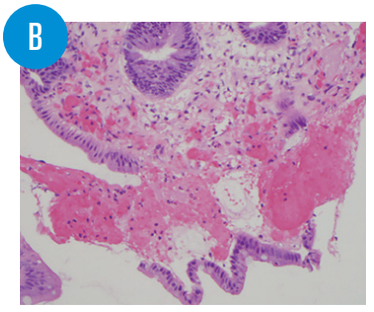
On examination, the patient was mildly hypotensive (BP 100/65 mm Hg) with bright red blood visible in the ostomy bag. Laboratory testing revealed normal hemoglobin (15 g/dL) and an upright abdominal x-ray showed changes consistent with her prior surgical history. Because of ongoing ostomy bleeding, the patient was transferred to a tertiary facility where repeat labs now showed mild anemia (hemoglobin 13 g/dL). A colonoscopy demonstrated unilateral linear ulceration of the distal transverse colon, measuring 5 cm long and 8 mm in diameter with a clean white base (Figure A). The remaining colonic mucosa was unremarkable except for scattered diverticula within the transverse colon. Biopsies obtained from the ulcer showed foci of cryptitis, focal fibrosis, and hemorrhage within the lamina propria (Figure B).

Which of the following is the most likely cause for the patient's symptoms?

A. Diverticular disease–associated colitis
B. Cytomegalovirus colitis
C. Colonic ischemia
D. Radiation colitis

See the Answer on page 23





News from the AGA

Ask Our Expert: Life in Medical Education

Suzanne Rose, MD, MSEd, offers her advice and insight into a career as a medical educator in this issue of *The New Gastroenterologist*. Read the article and then bring your burning questions and concerns to the AGA Community Early Career Group forum Aug. 21-25, when she'll be available for a members-only question-and-answer session.

During the eQ&A, Dr. Rose can elaborate on topics such as how her job has evolved over the years, finding a job in medical education, and more examples of available resources. You can also use this time to seek her advice for a current situation or career next steps. This is your time to use her background and expertise to help you and your colleagues advance your careers.

Visit the Early Career Group for more information, at http://community.gastro.org/EarlyCareerGroup. ■

Don't Let Your AGA Benefits Lapse

Current medical residents, students, and trainees should renew their AGA membership by Aug. 31 to ensure the continuation of career-enhancing benefits, like discounted rates on AGA journals, Digestive Disease Week® 2018 registration, and the GI board exam prep resource DDSEP®. Trainees and early-career members can take advantage of the AGA Mentor and Advisor Program and AGA Community Early Career Group, which provide the chance to seek advice from and network with peers and experts year-round.

For those who are completing fellowships in the summer of 2017, AGA offers free membership for the remainder of the year to support the transition to the early-career rate. If you have any questions, please contact AGA Member Relations at member@gastro.org or 301-941-2651 ■

Advice on Choosing Your GI Career Path

Mariam Naveed, MD, opened a discussion in the Early Career Group forum in AGA Community that invited GIs to share how or when they knew which career path was the best fit. Among those sharing their stories were Peter Liang, MD, MPH; Avinash Ketwaroo, MD; Maisa Abdalla, MD, MPH; Tara Altepeter, MD; Elliot Tapper, MD; and Brijen Shah, MD. Their expertise spans across the GI spectrum, including academia, research, drug development, and regulatory science.

For Dr. Liang, the key to succeeding on the research path is to be passionate about your topic(s), enjoy reading and writing, and be able to accept constructive criticism and rejection. Dr. Altepeter encourages all GIs early in their career to be open to exploring a variety of career options, as regulatory science was not a career path she was aware of at the beginning of training.

The conversation continued when trainee and early-career members brought their career-specific questions, including the possibility of achieving tenure without publishing.

View a summary of advice shared at http://community.gastro.org/calling. The discussions around finding your GI calling are in the AGA Community Early Career Group at http://community.gastro.org/EarlyCareerGroup. ■

2018 AGA Grants Cycle Now Open

The AGA Research Foundation is excited to announce the start of its 2018 Research Grants cycle. This year the foundation will be awarding over $2 million in funding to support researchers within gastroenterology and hepatology. Now is your chance to view upcoming opportunities and plan your applications. Visit www.gastro.org/research-funding for the full list of award opportunities and contact awards@gastro.org with any questions. Also, be sure to keep your eyes on the AGA Community for advice on how to write a winning grant application, straight from previous Research Scholar Award recipients. ■

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

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

Sept. 13-14; Oct. 11-12, 2017
2-Day, In-Depth Coding and Billing Seminar
Become a certified GI coder with 2-day, in-depth training course provided by McVey Associates, Inc.
Atlanta, GA (9/13-14); Las Vegas, NV (10/11-12)

Nov. 13, 2017
ABIM® Gastroenterology Certification Exam

Dec. 1, 2017
Digestive Disease Week® (DDW) 2018 Abstracts
Abstracts may be submitted for consideration to DDW® 2018 online beginning on Oct. 19, 2017. The submission site will close on Thursday, Dec. 1, 2017.

Jan. 18-20, 2018
Crohn's & Colitis Congress™
The Crohn's & Colitis Foundation and AGA are partnering on a new annual conference for health care professionals and researchers. This is 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.
Las Vegas, NV

June 2-5, 2018
DDW®
DDW® is the premier meeting for the GI professional.
Washington, DC

June 4-8, 2018
Exosomes/Microvesicles: Heterogeneity, Biogenesis, Function, and Therapeutic Developments (E2)
Deepen your understanding of the structural and functional complexity of extracellular vesicles, their biogenesis and function in health and disease.
Breckenridge, CO

Awards Application Deadlines

Research Scholar Award (RSA)
Deadline: Sept. 8, 2017

AGA-Takeda Pharmaceuticals Research Scholar Award in Inflammatory Bowel Disease
Deadline: Sept. 8, 2017

AGA-Rady Children's Institute for Genomic Medicine Research Scholar Award in Pediatric Genomics
Deadline: Sept. 8, 2017

AGA-Elsevier Pilot Research Award
Deadline: Jan. 12, 2018

AGA-Elsevier Gut Microbiome Pilot Research Award
Deadline: Jan. 12, 2018

AGA-Caroline Craig Augustyn & Damian Augustyn Award in Digestive Cancer
Deadline: Jan. 12, 2018

AGA-Pfizer Young Investigator Pilot Research Award in Inflammatory Bowel Disease
Deadline: Jan. 12, 2018

AGA-Rome Foundation Functional GI and Motility Disorders Pilot Research Award
Deadline: Jan. 12, 2018

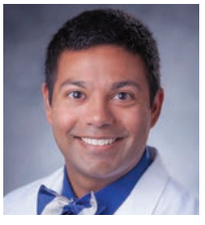
AGA-Allergan Foundation Pilot Research Award in Irritable Bowel Syndrome
Deadline: Jan. 12, 2018

AGA-GRG Fellow Abstract Award
Deadline: Feb. 2, 2018

AGA Student Abstract Award
Deadline: Feb. 2, 2018

Reflux Diagnostics: Modern Techniques and Future Directions

By Amit Patel, MD, and C. Prakash Gyawali, MD, MRCP



Dr. Patel is assistant professor of medicine, division of gastroenterology, Duke University School of Medicine and the Durham Veterans Affairs Medical Center, Durham, N.C. Dr. Gyawali is professor of medicine, division of gastroenterology, Washington University School of Medicine, St. Louis, Mo.

Introduction

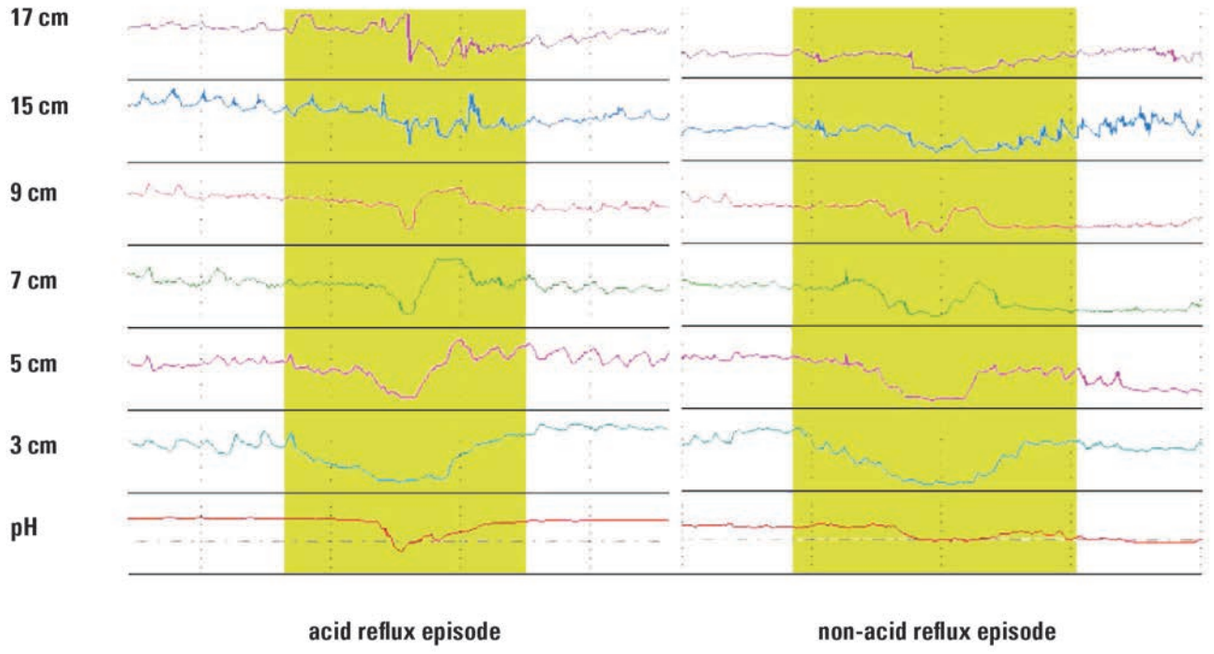
Chronic esophageal symptoms attributed to gastroesophageal reflux disease (GERD) are common presenting symptoms in gastroenterology, leading to high health care costs and adverse quality of life globally.[1,2] The clinical diagnosis of GERD hinges on the presence of "troublesome" compatible typical symptoms (heartburn, acid regurgitation) or evidence of mucosal injury on endoscopy (esophagitis, Barrett's esophagus, peptic stricture).[3] With the growing availability of proton pump inhibitors (PPIs), patients and clinicians often utilize an empiric therapeutic trial of PPI as an initial test, with symptom improvement in the absence of alarm symptoms indicating a high likelihood of GERD.[4] A meta-analysis of studies that used objective measures of GERD (in this case, 24-hour pH monitoring) showed that the "PPI test" has a sensitivity of 78%, but a specificity of only 54%, as a diagnostic approach to GERD symptoms.[5] Apart from noncardiac chest pain, the diagnostic yield is even lower for atypical and extra-esophageal symptoms such as cough or laryngeal symptoms.[6]

Therefore, when symptoms persist despite seemingly adequate PPI therapy, esophageal investigation may start with endoscopy but continues with ambulatory reflux and motility testing.[7] At endoscopy, exclusion of eosinophilic esophagitis with esophageal biopsies represents an important component of initial evaluation when symptoms are refractory to PPIs.[8] Further, the more atypical the presentation, the greater the need for esophageal testing prior to long-term PPI therapy. Esophageal function testing is also indicated when confirmation of GERD is needed prior to surgical or endoscopic reflux procedures.

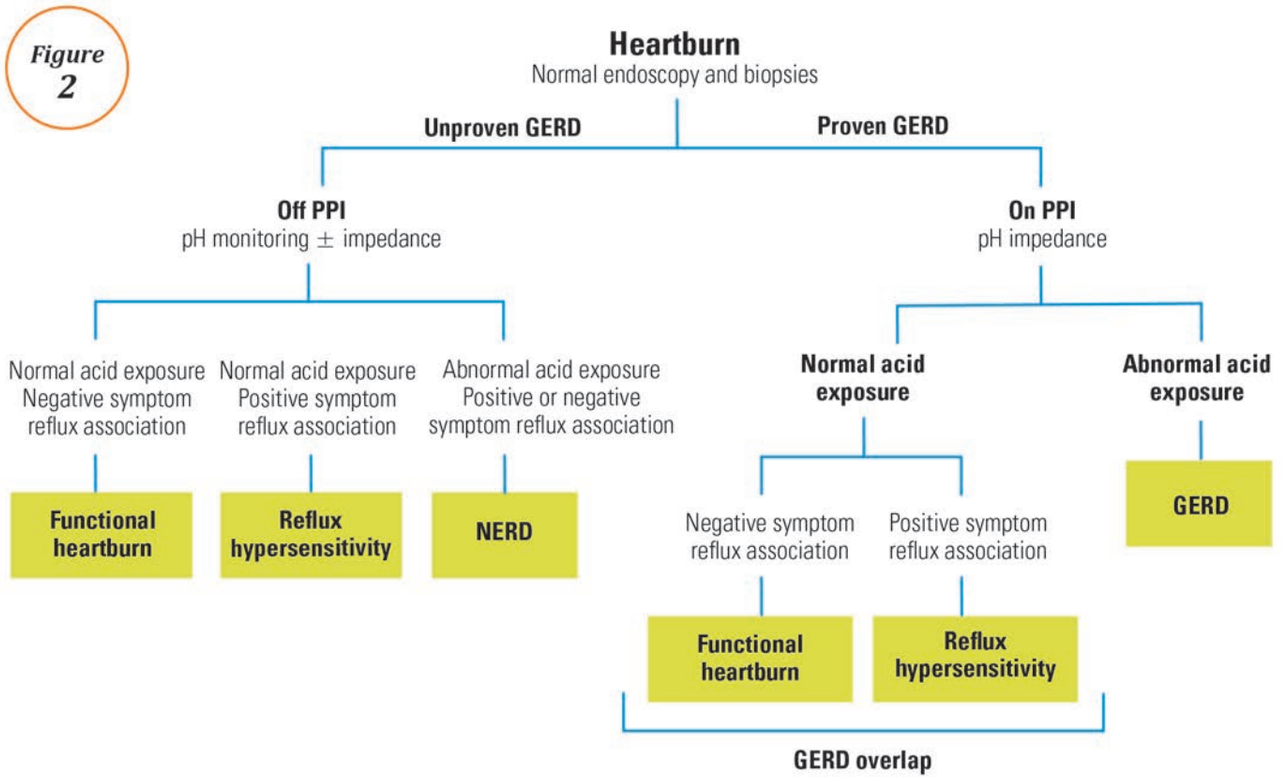
The "nuts and bolts" of reflux testing

Ambulatory reflux testing assesses esophageal reflux burden and symptom-reflux association (SRA). Individual reflux events are identified as either a drop in esophageal pH to less than 4 (acid reflux events), or a sharp decrease in esophageal impedance measurements in a retrograde fashion (impedance-detected reflux events), with subsequent recovery to the baseline in each instance. Ambulatory reflux testing affords insight into three areas: 1) measurement of esophageal acid exposure time (AET); the cumulative time duration when distal esophageal pH is less than 4 at the recording site, reported as a percentage of the recording period; 2) measurement of the number of reflux events both acidic (from pH monitoring) and weakly

Figure 1



Representative esophageal pH-impedance tracings of reflux episodes (examples of acid and non-acid reflux episodes).



Rome IV Algorithm for the Evaluation of Heartburn. This figure was published in Aziz A., Fass R., Gyawali C.P., Miwa H., Pandolfino J., Zerbib F. Esophageal Disorders. Gastroenterology 2016;150:1368-79. Copyright Elsevier/AGA.

acidic/alkaline (from impedance monitoring); and 3) quantitative evaluation of the association between reported symptom episodes and reflux events.

The three available modalities of ambulatory reflux monitoring consist of catheter-based pH, wireless pH, and combined catheter-based pH-impedance monitoring. Catheter-based pH monitoring, introduced in the 1970s, requires transnasal catheter placement and typically records for 24 hours before catheter removal. The catheter is positioned with the distal pH sensor 5 cm proximal to the upper margin of the manometrically identified lower esophageal sphincter (LES). New guidelines suggest AET less than 4% is reliably normal, while AET greater than 6% is pathologic; values in between are considered borderline and require alternate evidence for GERD, such as endoscopic findings.[7]

Wireless pH probes are placed 6 cm proximal to the squamocolumnar junction at endoscopy and communicate with a pager-sized receiver worn by the patient.[9] Patient comfort is not compromised, with less restriction of typical patient activities compared to catheter-based testing, facilitating longer recording periods of 48-96 hours, which can overcome day-to-day variations in esophageal reflux burden.[7] With catheter-based pH-impedance monitoring, multiple pairs of impedance sensors measure the resistance to flow of a tiny electrical current between sensors. Since resistance to flow (that is, impedance) is low in the presence of a bolus or refluxate in the esophageal lumen, the impedance tracing drops during reflux events in a retrograde fashion across the esophageal impedance sensor pairs, regardless of the acidity of the reflux (Figure 1).[10] Combined pH-impedance testing thus detects refluxate in the esophagus regardless of pH, improving the sensitivity of detection of reflux events over pH testing alone, thereby promoting greater yield of SRA. However, there remains wide inter-observer variation on the designation of impedance reflux events.[11]

The two most commonly utilized SRA metrics are the symptom index (SI) and symptom-association probability (SAP). Individual symptom episodes are designated as related to preceding reflux events if they occur within 2 minutes of the reflux events. The SI represents the simple ratio of the number of reflux-related symptoms to the total number of symptom episodes reported during the ambulatory reflux study, with values above 50% designated as positive.[12] For calculation of the SAP, the ambulatory reflux study is divided into 2-minute intervals. For each interval, the presence or absence of a reflux event and a symptom episode is assessed; the final counts are tabulated on a 2 x 2 table, and a Fisher exact test is applied to generate a "*P*" value. The SAP is positive if *P* is less than 0.05, corresponding to an SAP of

greater than 95%, or a less than 5% chance that the observed association between symptoms and reflux events occurred by chance.[13] The SAP can also be calculated post hoc with data typically extracted during a pH study, using statistical modeling; termed the Ghillebert Probability Estimate,[14] this corresponds well with the former method of SAP calculation.[15]

The SI and SAP can be calculated individually for acid-detected reflux events and for impedance-detected reflux events. Since reflux events are better detected with impedance, combined pH-impedance testing increases the yield of detecting positive SRA, especially when performed off PPI therapy.[16,17] Because these indices are heavily reliant on patient reporting of symptom episodes, SRA can be overinterpreted;[18] positive associations are more clinically useful than negative results in the evaluation of symptoms attributed to GERD.[19] Despite these concerns, the two most consistent predictors of symptomatic outcome with antireflux therapy on pH-impedance testing are abnormal AET and positive SAP with impedance-detected reflux events.[17]

Along with reflux testing, an esophageal high-resolution manometry (HRM) study is typically performed to establish the location of the LES for placement of reflux catheters. Beyond this primary indication, HRM serves the important role of excluding significant esophageal motor disorders in these patients, particularly achalasia spectrum disorders.[20] Despite a diametrically opposite pathophysiology compared to GERD, achalasia can present with retrosternal discomfort (often interpreted as heartburn) and esophageal regurgitation (potentially interpreted as acid regurgitation).[21] Therefore, achalasia spectrum disorders can be mistaken for GERD and managed with acid suppression, thereby contributing to the pool of symptomatic patients refractory to PPI therapy. HRM has high accuracy and specificity for the diagnosis of achalasia and other major esophageal motor disorders.[22] Other foregut disorders diagnosed using HRM (typically combined HRM and impedance, or HRiM) include rumination and supragastric belching. The exclusion of a major esophageal motor disorder is also a requirement for the diagnosis of a functional esophageal disorder, where esophageal reflux testing is normal.[23]

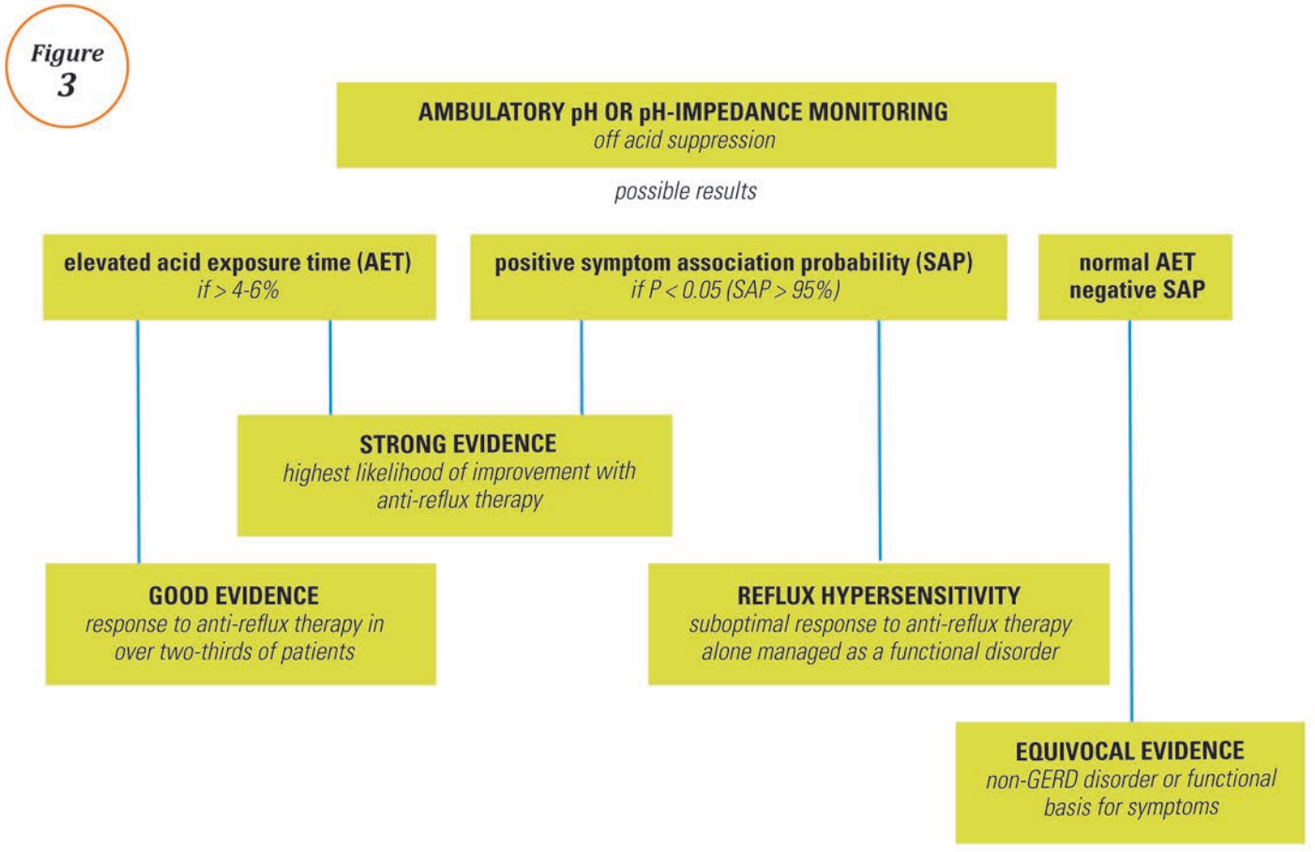
Testing on or off PPI?

For symptoms attributable to GERD that persist despite properly administered PPI therapy, the 2013 American College of Gastroenterology guidelines suggest upper endoscopy with esophageal biopsies for typical symptoms and appropriate referrals for atypical symptoms.[24] However, if these evaluations are unremarkable, reflux monitoring is recommended, with PPI status for testing guided by the pre-test probability of GERD: With a low pre-test probability of GERD, reflux testing is best performed off PPI with either pH or combined pH-impedance testing. In contrast, with a high pre-test probability of GERD, testing is best performed on PPI with combined pH-impedance testing. A similar concept is proposed in the Rome IV approach (Figure 2)[23] and on GERD consensus guidelines:[7] When heartburn or chest pain persists despite PPI therapy and endoscopy and esophageal biopsies are normal, evidence for GERD (past esophagitis, Barrett's esophagus, peptic stricture, or prior positive reflux testing) prompts pH-impedance monitoring on PPI therapy (i.e., proven GERD). Those without this evidence for proven GERD (i.e., unproven GERD) are best tested off PPI, and the test utilized can be either pH alone or combined pH-impedance.

GERD phenotypes and management

The presence or absence of the two core metrics on ambulatory reflux monitoring – abnormal AET and positive SRA – can stratify symptomatic GERD patients into phenotypes that predict symptomatic improvement with antireflux therapy and guide management of symptoms (Figure 3).[25,26] The presence of both abnormal AET and positive SRA suggests "strong" evidence for GERD, for which symptom improvement is likely with maximization of antireflux therapy, which can include BID PPI, baclofen (to decrease transient LES relaxations), alginates (such as Gaviscon), and consideration of endosopic or surgical antireflux procedures such as fundoplication or magnetic sphincter augmentation. Abnormal AET but negative SRA is regarded as "good" evidence for GERD, for which similar antireflux therapies can be advocated. Normal AET but positive SRA is designated as "reflux hypersensitivity,"[23] with increasing proportions of patients meeting this phenotype when tested with combined pH impedance

The presence or absence of the two core metrics on ambulatory reflux monitoring – abnormal AET and positive SRA – can stratify GERD patients into phenotypes that predict symptomatic improvement with antireflux therapy and guide management of symptoms.



Phenotyping of GERD based on distal esophageal acid exposure time and symptom association probability.

and off-PPI therapy.[27] Both normal AET and negative SRA suggest equivocal evidence for GERD and the likely presence of a functional esophageal disorder, such as functional heartburn.[23] For reflux hypersensitivity and especially functional esophageal disorders, antireflux therapy is unlikely to be as effective and management can include pharmacologic neuromodulation (such as tricyclic antidepressants administered at bedtime) as well as adjunctive nonpharmacologic approaches (such as stress reduction, relaxation, hypnosis, or cognitive-behavioral therapy).

The future of reflux diagnostics

Reflux testing, especially 24-hour catheter-based monitoring, offers cross-sectional assessment of reflux burden and does not take day-to-day variations in reflux exposure into account in a disease characterized by chronic symptoms and long-term management implications. This shortcoming has prompted interest in novel reflux diagnostics that may afford further insight into longitudinal reflux exposure. Baseline mucosal impedance, which can be gleaned from pH-impedance tracings during nocturnal resting periods[28] or by using prototype devices at endoscopy,[29] can segregate erosive and nonerosive GERD from controls and may serve as a surrogate marker for reflux-induced mucosal changes and esophageal mucosal integrity.[29-32] Postreflux swallow-induced peristaltic wave index, or the frequencies with which reflux events are followed by clearing esophageal peristaltic waves, represents another novel reflux metric extracted from pH-impedance tracings that may be a marker of refluxate clearance and resolution of esophageal mucosal acidification.[33] Finally, there has been revived interest in the value of dilated intercellular spaces on electron microscopy to assess esophageal mucosal integrity to provide evidence of longitudinal – rather than cross-sectional – reflux exposure.[34]

Conclusions

For esophageal symptoms potentially attributable to GERD that persist despite optimized PPI therapy, esophageal testing should be undertaken, starting with endoscopy and biopsies and proceeding to ambulatory reflux monitoring with HRM. The decisions between pH testing alone versus combined pH-impedance monitoring, and between testing on or off PPI therapy, can be guided either by the pre-test probability of GERD or whether GERD has been proven or unproven in prior evaluations (Figure 2). Elevated AET and positive SRA with impedance-de-

tected reflux events can predict the likelihood of successful management outcomes from antireflux therapy. These two core metrics can be utilized to phenotype GERD and guide management approaches for persisting symptoms (Figure 3). Novel impedance metrics (baseline mucosal impedance, post-reflux swallow-induced peristaltic wave index) and markers for esophageal mucosal damage continue to be studied as potential markers for evidence of longitudinal reflux exposure. ■

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DDSEP® eight QUESTIONS

Digestive Diseases Self-Education Program

// Answers on page 27

Q1: A 34-year-old woman presents with a 3-year history of watery, nonbloody diarrhea with associated weight loss, and recurrent bacterial bronchitis and pneumonias. Laboratory studies show iron-deficiency anemia, low 25-OH vitamin D, and a slightly elevated INR. Celiac serologies were negative, and small-bowel biopsies revealed near total villous atrophy, increased intraepithelial lymphocytes and crypt hyperplasia with absent plasma cells.

What is the most appropriate initial treatment strategy?
A. Gamma globulin
B. Prednisone
C. Infliximab
D. Gluten-free diet
E. Rifaximin

Q2: Testing for *Helicobacter pylori* infection is recommended for the following patients who have never previously been tested, EXCEPT:
A. 55-year-old asymptomatic man with one episode of upper GI bleeding due to an uncomplicated duodenal ulcer seen on EGD 6 years ago.
B. 60-year-old asymptomatic woman who is status post recent mucosal resection of early gastric adenocarcinoma.
C. 25-year-old healthy Hispanic woman who presents with mild, intermittent epigastric discomfort without other symptoms.
D. 45-year-old asymptomatic man of Irish decent whose son was recently diagnosed with *H. pylori* infection
E. 48-year-old woman with cirrhosis who was found to have a small, clean-based gastric ulcer incidentally during EGD for variceal screening.

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AGA's 2017 Women's Leadership Conference: Developing Skills in Advocacy and Personal Branding

By Katherine S. Garman, MD, and Latha Alaparthi, MD, AGAF, FACG

Dr. Garman is an assistant professor of medicine in the division of gastroenterology at Duke University, Durham, N.C. Dr. Alaparthi is managing partner of Gastroenterology Center of Connecticut and assistant clinical professor of medicine at Yale School of Medicine, Conn., and Frank Netter School of Medicine, Conn.

The 2017 AGA Women's Leadership Conference brought together 38 women from across the United States and Mexico for an inspiring and productive meeting. The group included 21 early-career and 17 experienced track women in GI. Among the attendees were 3 PhDs, 9 private practitioners, 1 pediatric gastroenterologist, and 25 academic gastroenterologists. We were particularly fortunate to benefit from the strong representation of AGA leadership, including Marcia Cruz-Correa, MD, PhD, AGAF (At-Large Councillor) and Deborah Proctor, MD, AGAF (Education and Training Councillor), as well as Ellen Zimmermann, MD, AGAF (Chair of the Women's Committee) and Sheila Crowe, MD, AGAF (President, AGA Institute Governing Board).

Susan Reynolds, MD, PhD (President and CEO of The Institute for Medical Leadership) led the meeting in her characteristically dynamic and open style. Dr. Reynolds presented content that highlighted key success factors for women physicians and scientists including the ability to build trust, encourage teamwork, and inspire vision.

The program included lively problem-solving sessions and a passionate discussion about negotiating skills. The latter topic was of particular interest given data indicating that pay inequity still exists. The group engaged in animated conversation about advocating for fair pay in academics and private practice.

The early-career track women gathered with Dr. Proctor to share stories of their own mentorship. From this discussion, it emerged that excellent mentorship is critical for successful career development. Women shared examples of how strong mentors can guide us to opportunities, offer important career advice, and provide encouragement. Mentors can provide specific feedback on clinical skills as well as managing relationships with challenging patients and colleagues. Research mentors help guide research projects, identify funding opportunities, and develop grants. Moreover, they can play pivotal roles in finding job opportunities and encouraging a greater work-life balance. Connecting with a mentor, or a group of mentors for different aspects of one's life and career, can be challenging: Creating space for mentorship through local gatherings with other gastroenterologists or researchers is a key part of success. Women were encouraged to reach out to others to deepen those supportive relationships after returning home.

In addition to strong mentorship,

Left to right: Sheila Crowe, University of California, San Diego, Latha Alaparthi, Gastroenterology Center of Conn.; Celena NuQuay, AGA; Ellen Zimmermann, University of Florida; Katherine S. Garman, Duke University Medical Center; Carol Brown, AGA; Marcia Cruz-Correa, UPR Comprehensive Cancer Center.

the early-career group discussed the importance of discerning one's own individual passions. Identifying professional and personal ambitions can allow us to focus our energy and activities. We were encouraged to write down one personal and one professional goal on an annual basis. These goals can offer clarity for a range of decisions such as when to accept new responsibilities and how to structure activities and manage time at work and at home.

The more experienced women GIs participated in a classroom style discussion led by Dr. Reynolds. The topic, "Keys to Association and Career Advancement: Reinvigorating Your Career," effectively conveyed the concept of leading through shared anecdotal experiences and related strategies. Dr. Reynolds also addressed skills for working with mentees of different generations including open communication and the importance of engagement.

The AGA leaders in attendance shared inspiring stories of their own paths to leadership. These paths were not linear and it was reassuring to discover common themes of finding and developing personal strengths, identifying passions, and building areas of expertise. We learned, how once identified, strengths and passions can be connected to areas of need within a home institution or an organization such as the AGA. Dr. Zimmermann offered moving commentary about her own journey as a clinician, scientist, and mother. She encouraged those in attendance with small children to take the time to be present at home, knowing that there will be opportunities to assume leadership roles in the future. Of course, for others, the time to assume leadership roles may be now, and the Women's Leadership Conference offered the chance to network and forge new connections within the AGA.

Left to right (first row sitting): Njideka Momah, University of Kentucky Medical Center; Baharak Moshiree, University of Miami; Lily Dara, University of Southern California Keck School of Medicine. Left to right (second row standing) Jeanetta Frye, University of Virginia Health System; Sara Horst, Vanderbilt University Medical Center; Suzette Rivera MacMurray, Digestive Disease Association.

Two important and timely topics were added to this year's leadership conference. First, the subject of advocacy was presented by Dr. Latha Alaparthi. In this presentation, Dr. Alaparthi explained to the group the meaning of advocacy in general, types of advocacy groups, political action committees, and ways in which we can become involved. Examples of laws affecting our patients, clinics, endoscopy centers, hospitals, medication coverage, payments, and funding for research were shared. Then, Dr. Proctor shared her personal experience at the 2016 AGA Advocacy Day.

Left to right: Jami Kinnucan, University of Chicago Medical Center; Joan Culpepper-Morgan; Harlem Hospital; Dilhana Badurdeen, Johns Hopkins University, Mariam Naveed, University of Iowa Hospital and Clinics.

One conference attendee noted that while she had participated in advocacy as a student, she hadn't understood that the AGA relies upon its members to meet with representatives at local, state, and national levels. We also learned how AGA's Governmental Affairs Office manages financial contributions to promote advocacy for high-quality care and utilizes NIH funding to promote research in digestive diseases.

The second new topic was addressed in a powerful session on personal branding by Dr. Cruz-Correa. Personal branding involves identifying and communicating who one is to the world in a memorable way. Dr. Cruz-Correa emphasized that creating a personal brand is essential for leadership and critically important for advancing one's career. Developing a personal brand should include crafting a statement of one to two sentences that considers both one's values and the target audience. The statement should be memorable and punchy with an emphasis on solutions. Branding expands beyond indicating an area of interest; a personal brand should demonstrate consistent delivery of high-quality work. An example of a personal brand could be "Physician, fitness fanatic, and fearless foodie empowering patients and colleagues to lead healthy fulfilling lives." An alternative might be: "Physician, teacher, empowering colleagues, advocating for patients, and evolving with the times." Creating a personal brand that highlights action and solutions emphasizes a theme of the meeting: Follow-through after accepting responsibilities is critically important.

Once created, a personal brand can be disseminated through professional social media accounts. Tweets can link to websites with additional content such as a summary of a recent presentation or highlights from a published manuscript. Participants were encouraged to closely monitor their professional profiles and, if needed, work with a firm to establish an online presence. These strategies can be useful for connecting with potential patients and collaborators.

In summary, the 2017 AGA Women's Leadership Conference provided an invigorating curriculum as well as many opportunities for establishing new networks of strong women in our field. Participants were charged with bringing some of the content back home, and we're already receiving reports about these local events. Be sure to look for future content from the AGA at http://www.gastro.org/about/people/committees/womens-committee.

Creating a personal brand is essential for leadership and critically important for advancing one's career. Developing a personal brand should include crafting a statement of one to two sentences that considers both one's values and the target audience. Branding expands beyond indicating an area of interest; a personal brand should demonstrate consistent delivery of high-quality work.

Acknowledgments: Dr. Garman and Dr. Alaparthi would like to offer heartfelt thanks to the AGA as well as to Celena NuQuay and Carol Brown for their support.

Legal Issues for the Gastroenterologist: Part I

By Peter J. Hoffman, Esquire, member and chair of the Professional Liability Group; Andrew J. Bond, Esquire (Associate); Andrew F. Albero, Esquire (Associate); Alexandra Rogin, Esquire (Associate); and Brittany C. Wakim, Esquire (Associate); Eckert, Seamans, Cherin & Mellott, LLC, Philadelphia.

An unfortunate fact for many physicians practicing in the United States is that they will contend with medical malpractice suits at some point in their careers. While data specific to gastroenterology malpractice claims are difficult to find,[1] the Physician Insurers Association of America has reported that out of the 28 specialty fields of medicine analyzed from 1985 to 2004, gastroenterology ranked 21st in the number of claims reported,[2] representing about 2% of the total overall number of claims.

A 2007-2008 survey of 5,825 physicians, not limited by subspecialty, showed that 42.2% of all physicians had a malpractice claim filed against them at some point in their career.[3] Of all physicians aged 55 and older, 60.5% of respondents had been sued at some point during their career.[3] Incidents of medical liability claims were much higher among men (47.5%) than among women (23.9%). [3] The average cost to defend these cases through trial is more than $100,000, but the average cost diminishes to $21,163 with cases that are dropped, dismissed, or withdrawn prior to trial.[3]

In 2017, *JAMA Internal Medicine* published additional statistical findings related to medical malpractice claims.[4] *JAMA* reported that the rate of claims paid on behalf of all physicians had declined by 55.7% between 1992 and 2014; from 20.1 per 1,000 physicians to 8.9 per 1,000 physicians.[4] The mean payment for the 280,368 claims reported in the National Practitioner Data Bank during this time frame was $329,565 (adjusted to 2014 dollars).[4]

JAMA also reported that, between 2004 and 2014, diagnostic error served as the most prevalent basis for allegations of medical negligence against all physicians.[4] These allegations comprised 31.8% of claims during this period.[4] With respect to gastroenterologists, prior data for 1985-2004 similarly suggests that diagnostic interview, evaluation, or consultation results in the most claims against this group of physicians.[4] The most common allegations specific to gastroenterologists involve malignant neoplasms of the colon and rectum, followed by abdominal and pelvic symptoms, regional enteritis, colitis, and malignant neoplasms of the stomach.[2] Errors in diagnosing stomach, colon, and rectal cancers resulted in the highest average indemnity payment.[2]

Professional liability

Patients can allege or establish malpractice liability against a doctor based on a number of things; we will discuss a few of the most common types of liability, offer suggestions as to how you might minimize your risk of being sued, and how best to cope when you are sued.

Negligence: One of the most common theories you may be sued under is negligence. To state a negligence claim against a physician, a plaintiff must show that the doctor owed the patient a duty recognized by law, that the physician breached that duty, that the alleged breach resulted in injury to the patient, and that the patient sustained legally recognized damages as a result. In a lawsuit brought on the basis of claimed medical negligence, a patient claims that a physician, in the course of rendering treatment, failed to meet the applicable standard of care.

Informed consent: Another theory is informed consent. A physician must obtain full, knowing, and voluntary informed consent from her patient for any nonemergency surgical procedure. A patient's lack of consent claim is premised on the allegation that the physician failed to reveal a significant risk, which caused harm to the plaintiff, and that, had the potential risk been disclosed, a reasonable person would not have consented to the treatment or procedure. Informed consent requires more from a physician than simply

having the patient sign a form. The physician performing the procedure for which consent is required must ensure that the patient is aware of the benefits of the proposed treatment, the material risks of the treatment, alternative options to the proposed treatment, and possible consequences of declining the treatment. This information must be communicated to a patient so that she clearly understands it.

Contractual liability of doctor to patient: Physicians and patients can enter into express written contracts regarding the care provided. These contracts can include various treatment plans, the likelihood of success, and even the physician's promise to cure. Traditionally, courts have respected a physician's freedom to contract as he or she chooses. However, once a contract is formed, a plaintiff may have a cause of action for breach of contract if the outcome of the treatment is not what was promised.

Minimizing risk

Opportunities exist to decrease the chances of being sued. One major area involves documentation, as the patient's records will serve as the basis of the litigation. Accordingly, physicians should ensure notations are legible so that lawyers, jurors, and others participating in the patient's care do not misunderstand the records. This has been made easier by the recent implementation of electronic health records. Records should also be comprehensive and kept contemporaneously with treatment to maintain accuracy and to avoid the appearance of impropriety. Subsequent entries must be clearly identified and dated. Never change records after a patient commences a suit against you. Remember that everything you write can come out during the investigation phase of the lawsuit.

Another opportunity to decrease your chances of being sued is to keep informed about recent developments in your field. Make a point to read pertinent literature, attend seminars, and do whatever is necessary to stay aware of, and to incorporate into your practice, current methods of treatment and diagnosis.

Physicians should also be cognizant of contractual liability. When discussing treatment, never guarantee results. Additionally, once a physician-patient relationship is established, you cannot withdraw from the relationship without providing adequate notice to the patient in time to obtain alternative care. Terminating the relationship without such is called abandonment, and can result in professional discipline and civil liability.

Finally, physicians should be aware of how relationships with the patient, institutions, and health care providers can affect liability. Communication is key to fostering a good doctor-patient relationship, and studies support that the quality of the doctor-patient relationship is a primary factor in determining whether a patient will sue her physician.[2] You should also understand how your relationship with your workplace affects your potential liability. For example, your workplace may be vicariously liable for negligence found on your part, and therefore, deemed ultimately responsible for any verdict or settlement amount. Conversely, you could be found vicariously liable for the actions of health care providers with whom you work. In the surgery context, the basis for this type of liability is that the surgeon is in a position of highest authority and has ultimate control over everything that occurs during the course of surgery. Therefore, you should understand the consequences of your relationships with the patients, facilities, and providers with which you work.[5]

Communication is key to fostering a good doctor-patient relationship, and studies support that the quality of the doctor-patient relationship is a primary factor in determining whether a patient will sue her physician.

Conclusion

Before a lawsuit, and as a regular part of your practice, it is important that you thoroughly and legibly document all aspects of care provided, stay current with medical advances, and take the time to create a relationship with your patients involving quality communication. It is impossible for us to provide you with enough information to adequately prepare you for the day on which you may be sued. We nevertheless hope that following the aforementioned suggestions will be of some help. ■

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Postfellowship Pathways: Blazing a Trail in Medical Education

By Suzanne Rose, MD, MSEd, AGAF

Dr. Rose is a professor of medicine and senior associate dean for education at the University of Connecticut School of Medicine.

What led you to pursue a career in medical education?
Believe it or not, I pursued my path in medical education even prior to attending medical school. I was a high school teacher with a master's in education, working during the summer of 1979 under the auspices of the Student Conservation Association at Grand Canyon National Park. Sitting on the edge of the canyon at sunset, I made the momentous decision to attend medical school, requiring attendance at a postbaccalaureate program at Columbia University. While considering medical schools, I knew that I wanted to combine my interest in education with medicine and I therefore chose to attend Case Western University School of Medicine. Since the mid-1950s, Case had been committed to innovative educational programs with a systems-based approach to the curriculum.

Throughout my career I focused on medical education, preparing my senior resident talk on "the resident as teacher" – not yet a hot topic. My path as a GI fellow, including a chief fellow year at the Cleveland Clinic, reconfirmed my interest in education leadership. During my first postfellowship position at the University of Pittsburgh, I was able to lead the GI second-year course, oversee GI electives for students and residents, and work on the GI fellowship curriculum. It was at that time that I began my involvement in AGA with committee work related to education and women's issues in GI. I also refocused my scholarly work in education, eventually editing a textbook in GI and hepatobiliary pathophysiology, and working on other projects.

What do you enjoy most about working in medical education?
There are so many aspects of medical education that make work fun and rewarding. Perhaps the most rewarding is the ability to make a difference that affects the learner as well as the patients and communities that they will serve. I also enjoy the diverse experiences and opportunities in education and the ability to work with others in creative endeavors.

What are your responsibilities in a typical week?
One of the great things about a focus in education is that there never is a typical week. In the 32 years since my graduation from medical school, I have had the great fortune to fill many different roles: course director, electives director, fellowship program director, associate dean for student affairs, associate dean for undergraduate medical education, and associate dean for continuing medical education. For the past 6 years, I have been the senior associate dean for education at the University of Connecticut School of Medicine, overseeing undergraduate medical education, graduate medical education, continuing medical education, and the graduate school.

Over time I have had less interaction with students and residents as my administrative responsibilities have grown, but I know it is critical to maintain a presence with

learners and I endeavor to do so in limited ways. Since our current priorities are in implementing a new curriculum and in planning for an accreditation visit, there are many days that are filled with meetings, planning, organizing, and writing. To me, the most precious responsibility is shaping a vision and bringing together a team to operationalize that vision in a collaborative and creative way, with learners, teachers, and administrators working together.

What are the different career options available for early-career GIs who are interested in medical education?

There are so many options in medical education for early-career gastroenterologists. For those working in private, group, or community practices, there are opportunities to precept students, residents, and fellows. For those working in an academic setting, opportunities abound. It is often a good idea to start within the division: Get involved in teaching fellows in a clinical setting or creating a new simulation experience or case workshop for fellows. There are opportunities to teach and supervise students. One of my first opportunities was in teaching in the physical diagnosis course. There are options to be involved in curriculum committees, admissions, CME, and to engage in educational initiatives at your institution.

The Association of American Medical Colleges has defined five areas of scholarship in education, and it is possible to get promoted to full professor – and even to attain academic tenure, as I have – if you fulfill the requirements for promotion at your institution. These areas include teaching, curriculum development, assessment, mentorship/advising, and leadership. There are also many ways to get involved in the AGA (http://www.gastro.org/trainees) and other organizations.[1,2]

Are there advanced training options available for those interested in medical education?

The AGA Academy of Educators (http://www.gastro.org/about/initiatives/aga-academy-of-educators)[3] is a wonderful resource for networking. It has a competitive process for educational project grants as well as faculty development sessions and networking events at DDW®. There are also national leadership academies in medicine that have a focus in medical education. The Harvard Macy Institute is one such opportunity. Many medical schools have their own academies to support educators and teachers. I have been privileged to be one of the co-leaders of the AGA Future Leaders Program (http://www.gastro.org/about/initiatives/aga-future-leaders-program) and those with a niche interest in education can benefit and pursue related projects.[4] One group was successful in publishing an educational article after completing the Future Leaders program.[5] There are also several master's programs for further education and training in educational theory. Some of these programs are available online or largely online, with limited requirements for onsite classes.

How do you go about finding a job in medical education?

First of all, you have to do your "day job." In order to be a credible medical clinician-educator you must have clinical experience in patient care. It is important for the first years of your career to make sure that you have at least 70% clinical roles that can be reduced over time to accommodate advancing educational responsibilities. Get involved in teaching fellows. If you are in a practice, reach out to your local medical school or hospital to see how you might participate in educational programs. If you are in an academic setting, meet with the deans in education to express your interest and look for opportunities to get involved in an area of interest. If you are in academia, you have to make your work "count twice": Being productive in a scholarly way not only important is as a role model for learners, but it is important for you as a faculty member to grow and advance in your professional career.

It is always wise to think about when to say "yes" and when to say "no." An important point is not to overextend yourself. Your reputation of completing tasks not only well, but on time, and thoroughly, is critical to your success. This includes making sure your learner evaluations are submitted on time, that you complete the administrative work in order to participate in CME programs, and that you honor your commitments by attending committee meetings.

What are the resources available to early-career GIs interested in medical education?

It is easy to find resources within your practice, your institution, or externally. The AGA has many resources available with a good start being the AGA Academy of Educators. Opportunities for creativity are numerous and with new advances in team-based learning, simulation, and interprofessional learning, there are new areas for involvement evolving all the time.[6,7]

Finally, pursuing a career in education is exciting, fun, and fulfilling. Having the opportunity to influence learners, which in turn will impact patient care, is an awesome privilege. ■

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How One GI Is Tackling His Student Debt — And the Lessons He's Learned Along the Way

By Radhika Duggal, MBA

Ms. Duggal is vice president of marketing for CommonBond.

The AGA recently partnered with CommonBond (studentloans.gastro.org) to help its members save thousands by refinancing their student loans. Kevin Tin, MD, who is an AGA member, has a student loan story that can certainly offer guidance and perspective to others. Kevin earned his BS in health sciences from Stony Brook University and his MD from American University of Antigua. He completed his residency at Maimonides Medical Center in Brooklyn, N.Y., where he is currently a gastroenterology fellow.

As with many other aspiring gastroenterologists, Kevin took out more than $200,000 in federal and private student loans to pay his way through medical school. He recently refinanced these loans and picked up some lessons along the way. Below, he offers some tips for getting free of debt; taking Kevin's advice to heart can help you worry less about your loans and focus instead on serving your patients.

Dr. Kevin Tin

In your residency, plan to use a portion of your salary for paying off your student loans, even if it is only a small amount each month.

How was your medical school experience?

My medical school experience was memorable for many reasons, particularly because I had an opportunity to study in Antigua. My time there allowed me to experience a different culture and, ultimately, a different perspective. I believe this taught me how to relate to each of my patients' individual situations and to see things from their eyes. But, the overall cost of medical school (i.e., tuition, cost of living, medical supplies, and study resources) caught me off guard. By the time I graduated, I had amassed more than $200,000 in student loans; this was not something that I felt prepared to deal with.

How would you describe your initial experience with student loans?

Frustrating and stressful. I struggled to understand the complex application processes, the best type of loan for my personal situation, and to find the lowest rates. In addition, I later learned that my loans' interest capitalized while I was still in school, which made the volume of my debt greater than what I initially borrowed. It would have been helpful to know that up front, as I could have made small, monthly payments earlier.

What strategies have you implemented to pay off your student loans?

I've learned a few crucial strategies that any physician could, and should, take advantage of to save money on their student loans. First, be sure to spend responsibly while in medical school. I focused on finding free study resources and medical supplies as well as sharing materials with friends and roommates whenever possible. As I mentioned earlier, make small payments when you can; as soon as I entered residency, I started making interest payments on my loans. I wanted to contribute as much as I could, as early as I could, to get out of debt. Second, after graduation, endeavor to live frugally. Although I knew my salary would ultimately increase, I saved as much money as I could and put money toward paying off my loans. Finally, try to refinance your student loans; I refinanced mine with CommonBond. It was an unexpectedly pleasant experience: The website was extremely easy to navigate and any time I needed help, a representative was available to answer my questions. CommonBond also gave me the best rates I could find.

What were the benefits of refinancing your student loans?

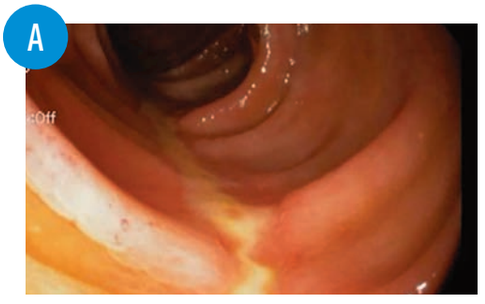
I initially had a 15-year student loan with a 5.75% APR. When I refinanced with CommonBond, I secured a 7-year, fixed-rate student loan with a 4.2% APR. I made this choice because I'll be saving $30,000-$40,000 over the life of my loan, and my monthly payment stays stable, regardless of how the market fluctuates. Refinancing my student loan has put me on the path to becoming debt free, which will allow me to focus more on my career.

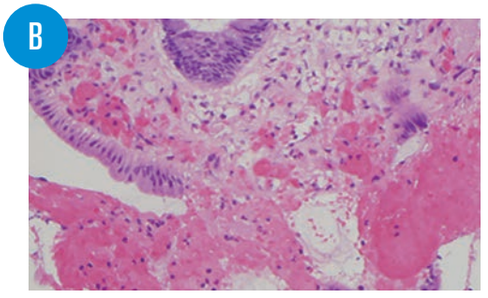
What is your advice to early-career GIs who have or need to take out loans?

Do your research and do it early. While in medical school, understand what options are available to you and learn to live within your means. In your residency, plan to use a portion of your salary for paying off your student loans, even if it is only a small amount each month. This will reduce the volume of interest that will capitalize, so your loan balance doesn't grow over time. When you start your full-time job, be financially responsible and limit your spending so you can devote additional funds to paying off your student loans.

If you would like to learn more about student loan refinancing with CommonBond, please visit studentloans.gastro.org. AGA members get a $200 cash bonus for refinancing! ■

The Answer // From page 4





The correct answer is C: colonic ischemia.

The endoscopic findings are notable for colon single-stripe sign (CSSS), which is a highly specific feature of colonic ischemia (Figure A). The diagnosis of colon ischemia is further supported by the histologic features of cryptitis, focal fibrosis, and hemorrhage within the lamina propria (Figure B). In this case, the patient's history of radiation exposure and hypotension were both likely predisposing factors for colonic hypoperfusion and subsequent colon ischemia. With conservative medical therapy, the patient experienced complete resolution of symptoms.

Diverticular disease–associated colitis (answer A) is less likely given the lack of interdiverticular mucosal involvement and linear ulceration pattern, which also contrasts with the deep, "punched-out" appearance typically associated with ulceration of cytomegalovirus colitis (answer B). The endoscopic findings associated with chronic radiation colitis (answer D) characteristically include evidence of mucosal scarring, friability, and scattered angioectasias. The CSSS was initially described as a manifestation of colonic ischemia by Zuckerman et al. who hypothesized the linear nature of this lesion likely reflected segmental vascular compromise.[1] Concordant with the presented case, of the 26 patients with CSSS included in the Zuckerman et al. study, all had a stripe measuring 5 cm in length while a minority (4 patients) had transverse colon involvement.[1] Also in parallel with this case, others have reported successful nonoperative management of patients with CSSS in the setting of ischemia.[1,2] Overall, the comparatively favorable outcome in patients with CSSS compared to those with circumferential colonic ischemia suggests this finding may reflect a more mild form of disease.[1] ■

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This article has an accompanying continuing medical education activity, also eligible for MOC credit (see gastrojournal.org for details). Learning Objective: Upon completion of this activity, successful learners will be able to recognize colon single-stripe sign as an endoscopic feature of colonic ischemia.

Snapshots from the AGA Journals

Aggressive HCC in Males Traced to Higher Serotonin

May 2017 Cellular & Molecular Gastroenterology and Hepatology (doi: org/10.1016/j.jcmgh.2017.01.002)

Key clinical point: The greater frequency and aggressiveness of hepatocellular carcinoma in men than in women might be attributable to greater synthesis and accumulation of serotonin in males.

Major finding: Serotonin levels were significantly elevated in 7 inflamed, 16 cirrhotic, and 30 cancerous livers, compared with 5 normal livers, among men but not among women.

Data source: Laboratory studies involving a zebrafish model of HCC and tissue samples from 60 human livers.

Disclosures: This study was supported by the National Medical Research Council and the Ministry of Education of Singapore. Dr. Yang and her associates reported no relevant financial disclosures.

Commentary

Mo Ebrahimkhani, MD, is an assistant professor in the school of biological and health systems engineering, Arizona State University, Tempe. He has no conflicts of interest.

Serotonin is a small molecule neurotransmitter with diverse functions such as modulation of mood, appetite, wound healing, gastrointestinal motility, and blood coagulation. It was shown that serotonin can promote liver regeneration in mice via a direct action on hepatocytes, the main building blocks of liver. However, other cell types such as liver stellate cells, the main liver fibrogenic cells, can also be influenced by serotonin. Serotonin action on liver stellate cells results in production of transforming growth factor–beta$_1$ (TGF-beta$_1$), a multifunctional cytokine. TGF-beta$_1$ can then inhibit regeneration of hepatocytes and promote fibrosis. In a new study, scientists have shown that the same pathway is active during hepatic carcinogenesis and promotes development of cancer in a zebrafish model. They also discovered that hepatocytes can produce serotonin and increase TGF-beta$_1$ synthesis in stellate cells. Interestingly, they uncovered a significant sexual dimorphism in both human and fish samples in components of this pathway (for example, more serotonin and TGF-beta$_1$ in males). This study unravels underlying mechanisms of sex differences in liver cancer. Importantly, it can provide a therapeutic opportunity to treat human liver cancer by modulation of serotonin signaling. This approach is attractive since potent and selective pharmacologic agents for serotonin signaling are already available for other purposes such as modulation of gut motility or neurological disorders. Future studies using human cells or samples will pave the path toward clinical translation of these findings. ■

Persistently Nondyplastic Barrett's Esophagus Does Not Protect Against Progression

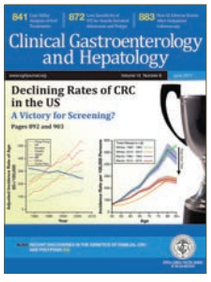
June 2017 Clinical Gastroenterology and Hepatology (doi: org/10.1016/j.cgh.2017.02.019)

Key clinical point: Patients with multiple consecutive biopsies showing nondysplastic Barrett's esophagus were statistically as likely to progress to esophageal adenocarcinoma or high-grade dysplasia as those with a single nondysplastic biopsy.

Major finding: Hazard ratios for progression ranged between 0.00 and 0.85, with no significant difference in estimated risk among groups stratified by number of consecutive nondysplastic biopsies (*P* = .68), after controlling for age, sex, and length of Barrett's esophagus.

Data source: A prospective multicenter registry of 480 patients with nondysplastic Barrett's esophagus and multiple surveillance biopsies.

Disclosures: The investigators did not report funding sources. They reported having no conflicts of interest.



Commentary

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Current practice guidelines recommend endoscopic surveillance in Barrett's esophagus (BE) patients to detect esophageal adenocarcinoma (EAC) at an early and potentially curable stage.

Endoscopic surveillance of BE has numerous limitations. Persistence of nondysplastic BE (NDBE) has previously been shown to be an indicator of lower risk of progression to high-grade dysplasia (HGD)/EAC. However, outcomes studies on this topic have reported conflicting results.

Krishnamoorthi and his colleagues bring the issue of persistent NDBE as a potential risk stratification variable to the forefront. Using the Mayo Clinic registry, the authors found no statistically significant decrease in the risk of progression in patients with persistent NDBE. Similar results were recently reported by Nguyen and colleagues using the national Veterans Health Administration datasets.

Where do we stand with regard to persistence of NDBE and its impact on surveillance intervals? Future large cohort studies are required that address all potential confounders and include a large number of patients with progression to HGD/EAC (a challenge given the rarity of this outcome). Based on the available data, surveillance intervals cannot be lengthened in patients with persistent NDBE. Future studies also need to focus on the development and validation of prediction models that incorporate clinical, endoscopic, and histologic factors in risk stratification. Until then, meticulous examination techniques, cognitive knowledge and training, use of standardized grading systems, and use of high-definition white light endoscopy are critical in improving effectiveness of surveillance programs in BE patients. ■

Improved Adenoma Detection Rate Found Protective Against Interval Cancers, Death

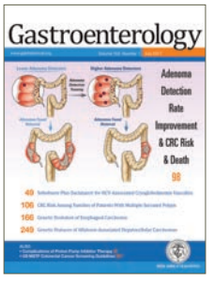
July 2017 Gastroenterology (doi: 10.1053/j.gastro.2017.04.006)

Key clinical point: An improved adenoma detection rate was associated with a significantly reduced risk of interval colorectal cancer and subsequent death.

Major finding: Adjusted hazard ratios were 0.6 for developing ICRC (95% CI, 0.5-0.9; P = .006) and 0.50 for dying of ICRC (95% CI, 0.3-0.95; P = .04).

Data source: A prospective registry study of 294 endoscopists and 146,860 individuals who underwent screening colonoscopy as part of a national screening program between 2004 and 2008.

Disclosures: Funders included the Foundation of Polish Science, the Innovative Economy Operational Programme, the Polish Foundation of Gastroenterology, the Polish Ministry of Health, and the Polish Ministry of Science and Higher Education. The investigators reported having no relevant conflicts of interest.



Commentary

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The U.S. Multi-Society Task Force on Colorectal Cancer proposed the adenoma detection rate (ADR) as a colonoscopy quality measure in 2002. The rationale for a new measure was emerging evidence of highly variable adenoma detection and cancer prevention among colonoscopists. Highly variable performance, consistently verified in subsequent studies, casts a pall of severe operator dependence over colonoscopy. In landmark studies from Kaminski et al. and Corley et al. in 2010 and 2014, respectively, it was shown that doctors with higher ADRs provide patients with much greater protection against interval colorectal cancer (CRC).

A huge body of work investigated whether colonoscopists can improve ADRs. After initial setbacks, methods of ADR improvement have been convincingly demonstrated.

Now Kaminski and colleagues from Poland have delivered a second landmark study, demonstrating for the first time that improving ADR prevents CRCs. We now have strong evidence that ADR predicts the level of cancer prevention, that ADR improvement is achievable, and that improving ADR further prevents CRCs and CRC deaths. Thanks to this study, ADR has come full circle. Measurement of and improvement in detection is now a fully validated concept that is essential to modern colonoscopy. In 2017, ADR measurement is mandatory for all practicing colonoscopists who are serious about CRC prevention. The tools to improve ADR that are widely accepted include ADR measurement and reporting, split or same-day preparations, lesion recognition and optimal technique, high-definition imaging, double examination (particularly for the right colon), patient rotation during withdrawal, chromoendoscopy, mucosal exposure devices (caps, cuffs, balloons, etc.), and water exchange. Tools for ADR improvement that are emerging or under study are brighter forms of electronic chromoendoscopy, and videorecording. ■

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Q1: Answer: B

Objective: Recognize the features of CVID associated noninfectious gastrointestinal manifestations

Explanation: This patient has gastrointestinal manifestations of common variable immune deficiency (CVID), which can present similarly to celiac disease or inflammatory bowel disease. Histologically, intestinal biopsies will reveal villous atrophy, crypt hyperplasia, and intraepithelial lymphocytosis similar to celiac disease. However, while plasma cells are increased in celiac disease, they are absent in common variable immune deficiency.

The initial treatment strategy for CVID typically includes oral corticosteroids, either prednisone or budesonide, with other immunosuppressants such as the thiopurines or antitumor necrosis factor agents reserved for steroid-dependent or refractory disease.

Gluten-free diet is ineffective for the treatment of CVID-associated enteropathy. Intravenous immunoglobulin therapy reduces the frequency of infections associated with CVID, but does not affect the noninfectious GI symptoms. While bacterial overgrowth can occur in CVID, it is typically the consequence of the luminal changes, not the cause.

Reference

1. Agarwal S., Mayer L. Gastrointestinal manifestations in primary immune disorders. Inflamm Bowel Dis. 2010;16:703-11.

Q2: Answer: D

Current recommendation suggests *H. pylori* testing for patients with active or a documented history of peptic ulcer disease, gastric MALT lymphoma, or gastric carcinoma. The *H. pylori* test-and-treat strategy is also recommended for patients less than 55 years of age who presents with dyspepsia symptoms without "alarm features."

There is currently no recommendation for asymptomatic family members of patients diagnosed with *H. pylori* infection to be tested, unless there are known factors that may increase the patient's risk for gastric malignancy (e.g., family history of gastric carcinoma, and ethnic background from areas with high prevalence of *H. pylori* and gastric cancer such as East Asia, Latin America, and Eastern Europe).

References

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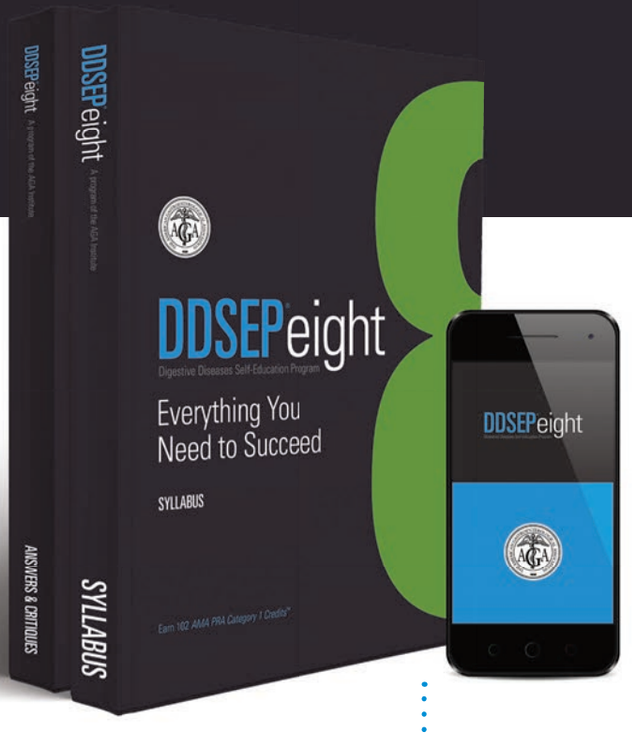

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