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Addressing mental health comorbidities can ease disease burden for patients with IBD.

Psychological difficulties persist among IBD patients

BY HEIDI SPLETE
MDedge News

Psychological issues in patients with inflammatory bowel disease should be addressed at both personal and systemic levels, according to a review of current literature.

In a review published in the Journal of Clinical Gastroenterology (2021 Jan;55[1]:30-5), researchers highlighted data on the burden of mental disorders in inflammatory bowel disease (IBD) patients and presented several strategies for addressing them.

"From a systems perspective, underrecognized and/or suboptimally treated mental health problems in patients with IBD are associated with increased disability, poorer adherence, and more admissions and surgeries, driving increased health care utilization and costs," Maia S. Kredentser, PhD, of the University of Manitoba, Winnipeg, and colleagues wrote, citing a 2018 study's findings (Gen Hosp Psychiatry. Mar-Apr 2018;51:71-8).

"There is ample evidence

See **IBD** · *page 20*

Ergonomic consultation spares endoscopists a pain in the neck

BY HEIDI SPLETE
MDedge News

Assessment of position and posture by a physical therapist can help reduce and prevent injury in endoscopists, based on data from a pilot study of eight individuals.

Musculoskeletal injuries among endoscopists are gaining more attention: One technical review (Gastrointest Endosc. 2009 Jul;70[1]:145-53) indicated that the "prevalence of musculoskeletal pain or injuries ranged from 29% to 89% of gastroenterologists." While data on avoiding musculoskeletal injury related to endoscopy are limited, recognition of the role of ergonomics is increasing, Stacy A. Markwell, a physical therapist in Chapel Hill, N.C., and colleagues, wrote in a study published in Gastrointestinal Endoscopy (2021 Feb 6. doi: 10.1016/j.gie.2021.01.045).

The researchers reviewed data from eight endoscopists who were aged 32-71 years; these endoscopists had a range of clinical experience and were performing 6-30 colonoscopies and 3-21

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INSIDE

AGA Clinical Practice Update

H. pylori eradication strategies outlined

BY AMY KARON
MDedge News

Antimicrobial resistance is the most common cause of treatment-refractory *Helicobacter pylori* infection, but before switching antibiotics, clinicians should screen for factors such as treatment nonadherence or inadequate suppression of gastric acid, according to a clinical practice update from the American Gastroenterological Association.

"Inadequate acid suppression is associated with *H. pylori* eradication failure. The use of high-dose and more potent PPIs [proton pump inhibitors],

See **Eradication** · *page 23*

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LETTER FROM THE EDITOR

History made, history revisited

The Biden administration has passed and signed the $1.9 trillion American Rescue Plan, which contains a plethora of moneys targeted to people, businesses, and health systems impacted by the pandemic. According to the Economist, the bill would bring the amount of COVID-related spending since December 2020 to $3 trillion (14% of prepandemic GDP) and to $6 trillion since the start of the pandemic ("Joe Biden's stimulus is a high-stakes gamble for America and the world." Economist. 2021 Mar 13). This type of stimulus (regarded as income, not savings, by most people) will generate unprecedented consumer spending. The risk, of course, is inflation, rising interest rates, and long-term debt.

Dr. Allen

During the Clinton presidency, welfare "as we know it" changed to include work requirements.

There is substantial funding for scientific research, vaccine distribution, public health entities, rural health care, and more. I estimate the Centers for Disease Control and Prevention will see $12 billion in incremental funding, $10 billion for public health projects including $3 billion for community health centers and federally qualified health centers, and over $3 billion for mental and behavioral health. The Department of Health & Human Services will see substantial funding for various projects. Teaching health centers will see $330 million additional funds (including a $10,000 per-resident increase and payments to establish new residency training programs).

The impact on low-income families and childhood poverty will be substantial and reverses the philosophical underpinning of recent welfare reforms. U.S. welfare dates back to the early 1900s and the philosophical foundation has evolved over time. According to the Constitutional Rights Foundation (www.crf-usa.org), it began after food riots broke out during the Great Depression. The Great Depression affected children and the elderly most severely, so the nation's willingness to implement federal welfare was high. Prior to the Depression, the only federal program providing money to low-income people was the "mothers pension" designed to support poor fatherless children, but it excluded divorced, deserted, and minority mothers. President Roosevelt was able to pass the Social Security Act (1935), which supported the elderly and began Federal welfare. During the Clinton presidency, welfare "as we know it" changed to include work requirements. With the passage of the current Biden legislation, those requirements are rolled back and funds are targeted broadly to low-income Americans and children.

John I. Allen, MD, MBA, AGAF
Editor in Chief

Top cases

Physicians with difficult patient scenarios regularly bring their questions to the AGA Community (https://community.gastro.org) to seek advice from colleagues about therapy and disease management options, best practices, and diagnoses. The following is a preview of a recent popular clinical discussion:

From John Fang, MD: Update on feeding tubes: Indications and troubleshooting complications.

GIs are uniquely positioned to manage individuals with feeding tubes as their training underscores principles in digestion, nutrition support, and enteral tube placement. Adequate management of individuals with feeding tubes and, importantly, complications arising from feeding tube use and placement requires both right education and experience. Therefore, gastroenterologists are well suited to both place and manage individuals with feeding tubes in the long term.

Questions

1. Are gastroenterologist best suited for placement and management of feeding tubes (vs. interventional radiology or surgery)?
2. Are gastroenterologists adequately trained to place and manage feeding tubes?
3. What are the most difficult complication(s) of feeding tubes to manage?

The conversation stems from the February In Focus article from The New Gastroenterologist, "Update on feeding tubes: Indications and troubleshooting complications."

See how AGA members responded and join the discussion: https://community.gastro.org/posts/23639.

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Racial differences seen in right vs. left colon

BY M. ALEXANDER OTTO, PA, MMS

The right colon appears to age faster in Black people than in White people, perhaps explaining the higher prevalence of right-side colon cancer among Black Americans, according to results from a biopsy study. The findings were published online in the Journal of the National Cancer Institute (2020 Dec 30. doi: 10.1093/jnci/djaa206). For the study, investigators analyzed colon biopsy specimens from 128 individuals who underwent routine colorectal screening.

The researchers compared DNA methylation levels in right and left colon biopsy samples from the same patient. They then assigned epigenetic ages to the tissue samples based on DNA methylation using the Hovarth clock; DNA methylation is influenced by age and environmental exposures, the researchers explained.

The epigenetic age of the right colon of the Black patients was 1.51 years ahead of their left colon; the right colon of the White patients was 1.93 years younger than their left colon. The right colon was epigenetically older than the left colon in 60.2% of Black patients; it was younger in more than 70% of White patients.

"Our results provide biological plausibility for the observed relative preponderance of right colon cancer and younger age of onset in African Americans as compared to European Americans," wrote the investigators, led by Matthew Devall, PhD, of the University of Virginia, Charlottesville.

If these findings are "corroborated in African Americans in future studies, these results could potentially explain racial differences in the site predilection of colorectal cancers," Amit Joshi, MBBS, PhD, and Andrew Chan, MD, of Harvard Medical School, Boston, wrote in an accompanying editorial.

A higher proportion of Black patients smoked (37.5% vs. 15%), and Black patients were younger (median age, 55.5 vs. 61.7 years). Body mass indexes were higher for Black patients (31.36 vs. 28.29 kg/m^2).

The work was supported the National Cancer Institute, the Case Comprehensive Cancer Center, and the University of Virginia Cancer Center. The authors and editorialists have disclosed no relevant financial relationships.

A version of this article first appeared on Medscape.com.

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AGA Resource

AGA applauds researchers who are working to raise our awareness of health disparities in digestive diseases. AGA is committed to addressing this important societal issue head on. Learn more about AGA's commitment through the AGA Equity Project. More AGA comments can be found in the online version.

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Liver stiffness measurements predict hepatic events in nonalcoholic fatty liver disease

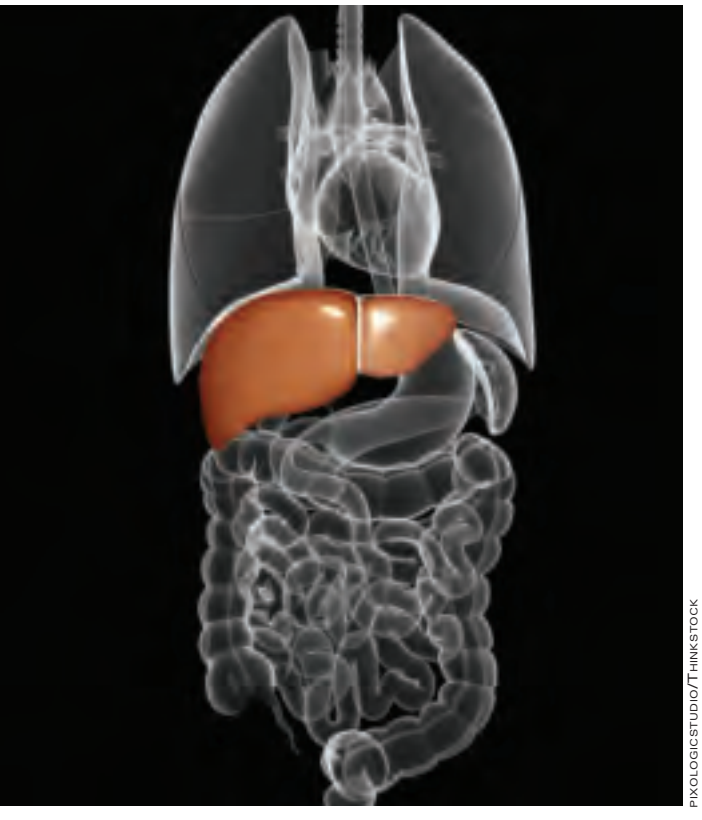
BY WILL PASS
MDedge News

Among patients with nonalcoholic fatty liver disease (NAFLD) and compensated advanced chronic liver disease, liver stiffness measurements (LSMs) are associated with risks of hepatic events, according to a retrospective analysis of more than 1,000 patients.

"[N]oninvasive markers that can predict liver disease severity and outcomes in patients with NAFLD and advanced fibrosis are a major unmet need," wrote lead author Salvatore Petta, MD, of the University of Palermo (Italy), and colleagues. Their report is in Clinical Gastroenterology and Hepatology (2020 Jul 2. doi: 10.1016/j.cgh.2020.06.045). "Data about the accuracy of LSM in the prediction of events in NAFLD, and especially in patients with NAFLD and F3-F4 fibrosis, are scarce."

To address this knowledge gap, the investigators retrospectively analyzed data from 1,039 consecutive patients with NAFLD who had baseline LSMs of more than 10 kPa and/or histologically diagnosed F3-F4 fibrosis. Patients were prospectively recruited at 10 centers in six countries, then followed for a median of 35 months, ranging from 19 to 63 months.

All patients had their liver stiffness measured with an M or XL probe at baseline. In addition, approximately half of the patients (n = 533) had a follow-up measurement using the same method, generating a subgroup with changes in liver stiffness. "Improved" liver stiffness was defined as a decrease in LSM greater than 20% from baseline, "impaired" liver stiffness was defined as an increase in LSM greater than 20% from baseline, and "stable" liver stiffness was defined as a change falling between 20% lower and 20% higher than baseline.



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At baseline, mean LSM was 17.6 kPa. Cox regression analysis revealed that baseline LSM was independently associated with HCC (hazard ratio, 1.03; 95% confidence interval, 1.00-1.04; *P* = .003), liver decompensation (HR, 1.03; 95% CI, 1.02-1.04; *P* < .001), and liver-related death (HR, 1.02; 95% CI, 1.00-1.03; *P* = .005), but not extrahepatic events.

According to the investigators, the association between LSM at baseline and risk of liver decompensation was maintained after adjustment for the severity of liver disease and for surrogate markers of portal hypertension, they noted. Furthermore, patients with a baseline LSM of at least 21 kPa – which indicates high risk of clinically significant portal hypertension (CSPH) – were at greater risk of liver decompensation than were those with an LSM less than 21 kPa (HR, 3.71; 95% CI, 1.89-6.78; *P* = .04).

In the subgroup with follow-up measurements, approximately half of the patients had an improved LSM (53.3%), while 27.2% had a stable LSM, and 19.5% had an impaired LSM, a pattern that was significantly associated with diabetes at baseline (*P* = .01).

"These data agree with the available literature identifying diabetes as a risk factor for liver disease progression and liver-related complications," the investigators wrote.

Cox regression showed that, among those with follow-up LSM, changes in LSM were independently associated with hepatocellular carcinoma (HR, 1.72; 95% CI, 1.01-3.02; *P* = .04), liver decompensation (HR, 1.56; 95% CI, 1.05-2.51; *P* = . 04), liver-related mortality (HR, 1.96; 95% CI, 1.10-3.38; *P* = .02), and mortality of any cause (HR, 1.73; 95% CI, 1.11-2.69; *P* = .01).

These risks could be further stratified by level of change in liver stiffness, with greater impairment predicting greater risk: The crude rate of liver decompensation was 14.4% among those with impaired LSM, compared with 6.2% among those with stable LSM and 3.8% among those with LSM improvement. That said, the categories of changes in LSM were not predictive of decompensation among patients with high risk of CSPH at baseline; however, they remained predictive among those with low risk of CSPH at baseline.

"[T]his study ... showed that an integrated assessment of baseline LSM or [changes in LSM] can help in stratifying the risk of development of liver-related complications and of both hepatic and overall mortality," the investigators concluded. "These data, if further validated, could help personalize prognosis and follow-up in NAFLD with [compensated advanced chronic liver disease]."

The investigators disclosed relationships with AbbVie, Novo Nordisk, Gilead, and others.

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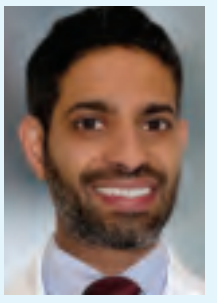
As the prevalence of nonalcoholic fatty liver disease (NAFLD) continues to rise, risk-stratifying those who will develop liver-related complications remains a major challenge. Although progression of liver fibrosis is a key risk factor for developing liver-related complications, the clinical application of noninvasive fibrosis markers for prognostication has been largely unexplored in NAFLD.



Dr. Cholankeril

This study by Dr. Petta and colleagues highlights the potential for liver stiffness measurements (LSMs) as a noninvasive method. Increased LSM that was suggestive of clinically significant portal hypertension (kPa > 21) had a nearly fourfold risk of hepatic decompensation. Furthermore, a longitudinal increase in LSM by greater than 20% was associated with a greater than 50% increased risk for hepatic decompensation, hepatocellular carcinoma, and death.

Transient elastography is a widely available and accurate tool for the noninvasive assessment of liver fibrosis for NAFLD in routine clinical practice. Routine serial measurements of LSM with transient elastography during clinic visits can provide clinicians with important information in the management of NAFLD, which can aid in treatment decisions, response to therapy, and monitoring of disease progression.

Further research is needed to validate these findings and to evaluate how longitudinal changes in LSM and other noninvasive fibrosis markers can prognosticate outcomes in NAFLD.

George Cholankeril, MD, MS, is an assistant professor in the section of gastroenterology & hepatology of the department of medicine and in the division of abdominal transplantation of the department of surgery at Baylor College of Medicine in Houston. He reported having no conflicts of interest.

"[N]oninvasive markers that can predict liver disease severity and outcomes in patients with NAFLD and advanced fibrosis are a major unmet need. Data about the accuracy of LSM in the prediction of events in NAFLD, and especially in patients with NAFLD and F3-F4 fibrosis, are scarce."

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Mitochondrial DNA variant increases gallstone risk

BY WILL PASS
MDedge News

A mitochondrial DNA variant may increase the risk of gallstone disease more than fourfold, according to investigators.

Mitochondrial DNA 827A>G disrupts mitochondrial function and leads to abnormal cholesterol transport, which increases gallstone development, reported Dayan Sun, of Fudan University, Shanghai, China, and colleagues.

The investigators noted that the findings add support to a genetic role in gallstone development, which could allow for identification of at-risk individuals and implementation of preventive measures.

"The etiology of gallstone disease is multifactorial; age, sex, pregnancy, diet (macronutrients, alcohol, and coffee), and other factors are involved," the investigators wrote in Cellular and Molecular Gastroenterology and Hepatology (2020 Dec 3. doi: 10.1016/j.jcmgh.2020.11.015). "Moreover, the significant familial predisposition and ethnic differences in prevalence of this disease indicate the potential influences of genetic factors."

In 2002, Nakeeb and colleagues reported that at least 30% of gallstone disease cases stemmed from genetic factors (Ann Surg. 2002 Jun;235[6]:842-9). And genetics may play an even greater role in certain populations, such as Native Americans, among whom more than 70% of women have gallstone disease, based on a study by Everhart and colleagues (Hepatology. 2002 Jun;35[6]:1507-12).

According to Ms. Sun and colleagues, a variety of genetic drivers of gallstone disease have been identified, such as ABCG8, identified as the most common genetic risk factor by at least one study (Nat Genet. 2007 Aug;39[8]:995-9), along with a list of other rare mutations, such as one affecting CFTR that leads to altered bile composition.

Based on previous research that linked mitochondrial DNA variants with metabolic defects and, more specifically, aberrations in lipid metabolism, as well as an observed "maternal bias in the maternal transmission of gallstone disease" that suggest mitochondrial influence, the investigators looked for patterns specifically in mitochondrial DNA variants among patients with gallstones.

The study enrolled 104 probands with confirmed gallstone disease and 300 unrelated controls. After collecting DNA samples from all participants, the investigators sequenced mitochondrial DNA HVS1 regions. A comparison of haplogroups showed that B4b'd'e'j was more common among patients with gallstone disease than among controls (odds ratio, 4.428; P = .00012), and further analysis pinpointed 827A>G, a variant in 12S ribosomal RNA.

"During the evolutionary history of modern humans, haplogroup B4 might have originated in East Asia approximately 40,000 years ago," the investigators wrote, noting that B2, a subhaplogroup of B4, "was a founder haplogroup and expanded in the Americas after the Last Glacial Maximum (approximately 20,000 years ago)."

According to the investigators, this may explain why Native Americans have a higher prevalence of gallstones than East Asians (14%-35% vs. 3%-12%) because they are more often carriers of B4 (14%-44% vs. 2%-8%).

The investigators sought to characterize the impact that the 827A>G variant has on mitochondrial function and found effects ranging from lower respiratory chain complex activity, diminished mitochondrial function, activated mitochondrial protein quality control and retrograde signaling pathways, abnormal lipid metabolism, and abnormal cholesterol transport processes.

For example, the researchers investigated respiratory chain complex activity by creating two sister branch haplogroup cell models, including six cybrids for 827A and six more for 827G, which is how they detected the lower activity. Another step the investigators took was corroborating this finding by detecting OXPHOS function in the 827A and 827G cybrids to determine mitochondrial function.

"In summary, our study demonstrates a potential link between mitochondrial DNA 827A>G and gallstone disease," the investigators wrote. "Our findings provide a significant biological basis for the clinical diagnosis and prevention of gallstone disease in the future."

The study was funded by the National Natural Science Foundation of China, the 111 Project, the Shanghai Municipal Science and Technology Major Project, the Scientific and Technology Committee of Shanghai Municipality, and the CAMS Innovation Fund for Medical Sciences. The investigators reported no conflicts of interest.

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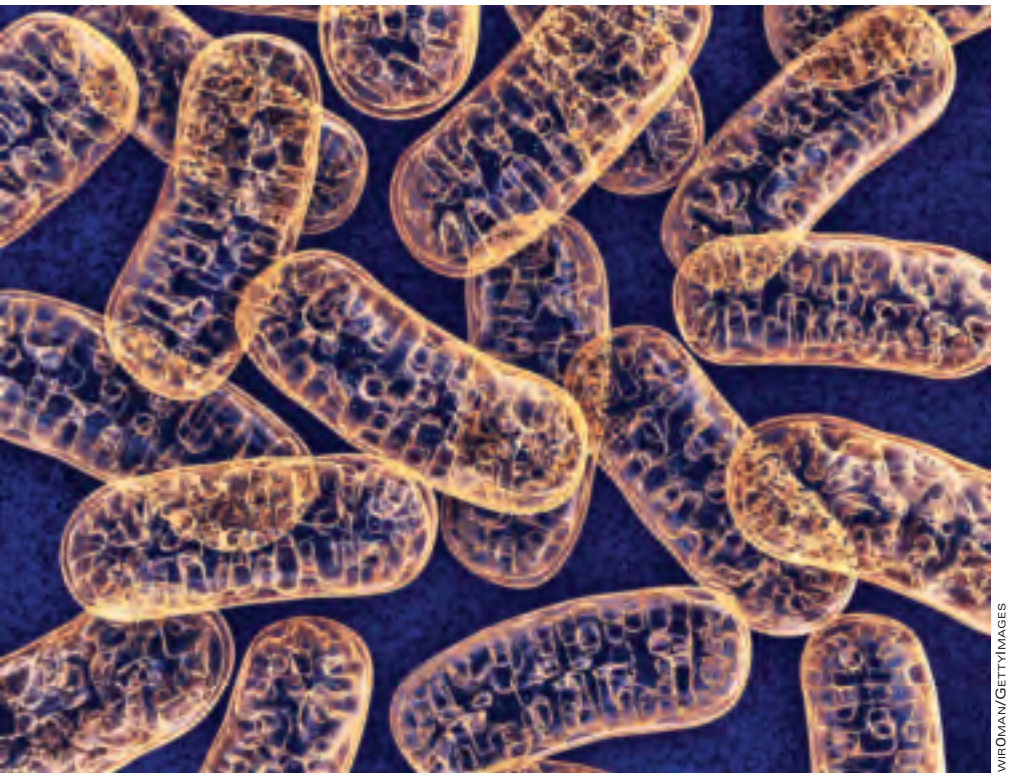

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Illustration of mitochondria is shown.

Cholesterol gallstone disease results from imbalances in cholesterol metabolism. Other than the well-known lifestyle risk factors, there is also a strong genetic predisposition to gallstone formation. This study by Sun and colleagues examined the possible association between mitochondrial DNA (mtDNA) variants and cholesterol gallstone development because of the importance of the mitochondria in cellular metabolism and the increased maternal transmission of gallstone disease.

Dr. Zhao

The investigators compared sequencing data obtained from 104 patients with gallstones versus 300 controls in the Chinese population and identified 827A>G in the mitochondrial 12S ribosomal RNA as the most likely disease conferring variant. In order to functionally validate this polymorphism, the investigators generated cybrid cell lines. They found that, compared with the 827A cybrids, the 827G cybrids exhibited diminished mitochondrial function and increased production of reactive oxygen species. Moreover, there was activation of mitochondrial-nuclear signaling pathways in the 827G cybrids that increased the expression of the lithogenic genes ABCG5/8, which mediate hepatobiliary cholesterol export, especially in gallstone-promoting conditions.

This study highlighted gallstone disease as a multifactorial condition that results from complex interaction between genetic and environmental factors. Interestingly, the allele frequency of the 827A>G mtDNA variant was noted to be higher in Native Americans, which may partially explain the high prevalence of gallstones in this population. Further studies are needed to identify additional genetic risk factors in ethnic groups that also have a significant burden of cholelithiasis.

Xiao Zhao, MD, is an assistant professor of medicine of division of digestive diseases in the department of medicine at Columbia University, New York. She reported having no conflicts of interest.

PPIs reduce inflammation in FD

BY WILL PASS
MDedge News

Proton pump inhibitors (PPIs) improve functional dyspepsia (FD) by reducing duodenal eosinophils and mast cells, according to a prospective study.

This suggests that the anti-inflammatory effects of PPIs are responsible for symptom improvement, and not barrier-protective or acid-suppressive effects, a finding that may guide future therapies and biomarkers, reported lead author Lucas Wauters, PhD, of University Hospitals Leuven (Belgium), and colleagues reported in Gastroenterology (2020 Dec 17. doi: 10.1053/j.gastro.2020.12.016).

"FD is a common and unexplained disorder with unknown pathophysiology, hampering a conclusive diagnosis and the development of effective drugs," the investigators wrote. Although PPIs are currently used as first-line FD therapy, ostensibly for acid suppression, "the exact mechanism of action of PPIs in FD is unknown," the investigators noted.

According to Dr. Wauters and colleagues, previous FD studies, such as a 2020 study published in Gut (2020 Mar;69[3]:591-600), have reported a variety of pathophysiological findings in the duodenum, including increased eosinophils and mast cells, as well as activation of duodenogastric reflexes, which suggests "a primary role for duodenal pathology in FD symptom generation." Several drivers of this pathology have been proposed. Some, such as aberrations in bile salts and acidity, point to local, luminal changes, whereas others, such as dysregulated hypothalamic-pituitary-adrenal axis responsiveness and psychosocial factors, implicate a broader set of drivers, the investigators wrote.

The present study explored this landscape through a prospective trial that enrolled 30 healthy volunteers and 47 patients with FD (2 patients with FD did not complete the study).

Patients with FD were subgrouped into "FD-starters" who had not taken PPIs and/or acid suppression for at least 3 months (n = 28) and "FD-stoppers" who had refractory symptoms after at least 1 month of daily PPI usage (n = 19). Among participants with FD, 25 had postprandial distress syndrome (PDS), 9 had epigastric pain syndrome (EPS), and 13 had subtype overlap.

For the trial, FD-starters and healthy volunteers took 4 weeks of pantoprazole 40 mg once daily, whereas FD-stoppers ceased PPI therapy for 8 weeks. Before and after these respective periods, certain study procedures were conducted, including duodenal biopsy collection, duodenal fluid aspiration, and questionnaires for symptoms and stress, as well as Ussing chambers for biopsies, immunohistochemistry, and bile salt measurements.


Dr. Wauters

FD-starters were significantly more symptomatic than healthy volunteers were at baseline. After starting PPIs, those with FD had symptom improvements, confirming "clinical efficacy of a standard course of PPIs in all FD subtypes," whereas healthy volunteers showed no significant change in symptoms.

Similarly, baseline duodenal eosinophil counts were higher in FD-starters than in healthy volunteers. On starting PPIs, however, eosinophil counts in these two groups moved in opposite directions: FD-starters' counts dropped from a mean of 331 to 183 eosinophils/mm^2, whereas healthy volunteers' counts rose from a mean of 115 to 229 eosinophils/mm^2 ($P < .0001$). Changes in mast cells and paracellular passage followed the same pattern, falling in FD-starters and rising in healthy volunteers. On the other hand, symptoms actually improved in the FD-stoppers after they went off PPIs, although they did not reach symptom levels of the healthy volunteers.

"Differential effects of PPIs in healthy volunteers point to the role of luminal changes in determining low-grade mucosal immune activation in the duodenum, which can also occur in FD after long-term use and provide arguments against continued use in refractory patients," the investigators wrote. They suggested that their findings could guide future approaches to FD management.

The study was supported by the clinical research fund of the University Hospitals Leuven. The investigators reported no conflicts of interest.

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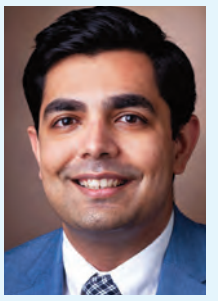
Functional dyspepsia (FD) is a commonly encountered diagnosis among primary care and gastroenterology clinics with estimated prevalence of 5%-11% worldwide. However, the pathophysiology of this entity is not well understood, and most of the patients who undergo upper endoscopy for dyspepsia tend to have normal findings.


Dr. Patel

The differential effects of PPIs on duodenal inflammation among the groups in this study are perplexing and the findings are limited by the short duration of follow-up testing and lack of a placebo group. Duodenal eosinophils, mast cells, and permeability were higher in treatment-naive FD, and a 4-week course of PPIs reduced this inflammation in FD but apparently increased it in healthy volunteers. Furthermore, when patients with PPI-refractory FD were studied, withdrawal of the PPI led to improvement in symptoms and trends toward less duodenal inflammation.

The discordant impact of PPIs among these groups on duodenal inflammation raises questions regarding the true effect from PPIs or changes driven by other systemic factors (brain-gut axis). This is hard to differentiate without a placebo group. Focus in future studies should be placed on how to clinically phenotype and predict PPI responders versus nonresponders along with use of longer durations to see if even PPI responders tend to lose response over time, regardless of changes in the duodenal inflammation and permeability.

Dhyanesh A. Patel, MD, is an assistant professor of medicine at the center for esophageal disorders, Vanderbilt University Medical Center, Nashville, Tenn. He has no conflicts.

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Digestive Diseases Self-Education Program

Quick Quiz

Q1. A 55-year-old woman presents with a 1-year history of large-volume foul-smelling stools that float in water associated with 40-pound weight loss. Laboratory evaluation reveals low vitamin A and D levels. An upper endoscopy with duodenal biopsies reveals complete villous blunting with decreased goblet and Paneth cells, absence of surface intraepithelial lymphocytes, and increased crypt apoptosis. She denies nonsteroidal anti-inflammatory drug use, celiac serologies were not elevated, and a glucose hydrogen breath test was negative. She also has coexisting rheumatoid arthritis and multiple sclerosis.

Which of the following tests can help establish the diagnosis?

A. Antinuclear antibodies
B. Anti–smooth muscle antibodies
C. Anti–gastric parietal cell antibodies
D. Antienterocyte antibodies
E. Antithyroglobulin antibodies

Q2. A 26-year-old White male presented with fever and sore throat for 5 days along with erythematous, nonpruritic rash involving the extremities and arthralgias. He subsequently developed right lower–quadrant pain, aggravated with meals, and associated with watery diarrhea. Labs show showed white blood cell count of 14,900/microL and a C-reactive protein level of 12.6 mg/dL. A magnetic resonance enterography showed 20 cm of thickened ileum. An upper endoscopy showed multiple erosions in the duodenum and antrum while a colonoscopy showed erythema and inflammation in the terminal ileum and cecum. Biopsies from both areas demonstrated evidence of leukocytoclastic vasculitis. Skin biopsy also showed leukocytoclastic vasculitis.

Which of the following agents would you recommend next?

A. Sulfasalazine
B. Prednisone
C. Azathioprine
D. Infliximab
E. Vedolizumab

Answers on page 23

2020 left many GIs unhappy in life outside work

BY RICHARD FRANKI

MDedge News

A year ago, 81% of gastroenterologists were happy outside of work. Not anymore.

In these COVID-19–pandemic times, that number is down to 54%, according to a survey of more than 12,000 physicians in 29 specialties that was conducted by Medscape.

"Whether on the front lines of treating COVID-19 patients, pivoting from in-person to virtual care, or even having to shutter their practices, physicians faced an onslaught of crises, while political tensions, social unrest, and environmental concerns probably affected their lives outside of medicine," Keith L. Martin and Mary Lyn Koval of Medscape wrote in the Gastroenterologist Lifestyle, Happiness & Burnout Report 2021.

Surprisingly, perhaps, the proportion of GIs who say that they're burned out or are both burned out and depressed now is only a little higher (40%) than in last year's survey (36%). It's also just under this year's burnout rate of 42% for all physicians, which has not changed since last year.

COVID-19 may have had some effect on burnout, though. Among the gastroenterologists with burnout, 15% said it began after the pandemic started, which was, again, less than physicians overall, who had a distribution of 79% before and 21% after. The GIs were slightly less likely to report that their burnout had a severe impact on their everyday lives than physicians overall – 44% versus 47% – but more likely to say that it was bad enough to consider leaving medicine – 15% versus 10%.

"The chief causes of burnout remain consistent from past years and are pushing physicians to the breaking point," the Medscape report noted, citing one physician who called it "death by 1,000 cuts." The biggest contributor to burnout over this past year was, for 60% of gastroenterologists, the excessive number of bureaucratic tasks, followed by spending too much time at work (44%) and increasing computerization (41%).

The two pandemic-related contributors included in the survey were near the bottom of the list for gastroenterologists: stress from social distancing/societal issues (15%) and stress related to treating COVID-19 patients (8%), based on data for the 12,339 physicians – of whom about 2% were GIs – polled from Aug. 30 to Nov. 5, 2020.

To deal with their burnout, many gastroenterologists are exercising – at least 51% of them, anyway. Other popular coping mechanisms include talking with family members and close friends (39%), playing or listening to music (38%), isolating themselves from others (36%), and sleeping (26%). For all physicians, the top choices were exercise (48%), talking with family members/friends (43%), and isolation (43%).

When the subject of professional help was raised, a large majority (84%) of GIs planned to forgo such care. That information was not available for physicians as a group, but 70% of internists agreed, as did 83% of nephrologists, 80% of cardiologists, 80% of oncologists, 89% of urologists, and 80% of general surgeons. A majority of gastroenterologists (58%) said that their symptoms weren't severe enough to warrant such help, but 38% said they were too busy, and 11% didn't want to risk disclosure.

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EDU21-004

Fighting back against payer coverage policies

BY SUSHOVAN GUHA, MD, PHD, AGAF, AND BENNIE UPCHURCH, MD, AGAF

The medical community may have paused during the COVID-19 pandemic, but commercial payers kept pushing forward with new coverage restrictions, expanding the number of services and procedures requiring prior authorization (PA) and restricting covered drugs. As 2020 closed and with 2021 barely underway, the American Gastroenterological Association has been holding discussions with major payers to stop implementation of policies restricting gastroenterologists' ability to prescribe the most appropriate drugs for their patients' clinical situations.

The Government Affairs Committee's Coverage and Reimbursement Subcommittee (CRS) works with commercial payers on issues affecting gastroenterologists and identifies outside experts on the policy subject when necessary. The subcommittee recently worked with UnitedHealthcare on a coverage policy change to make Inflictra (infliximab-dyyb) and Avsola (infliximab-axxq) its preferred products and move Remicade (infliximab) and Renflexis (infliximab-abda) to its nonpreferred list, as announced in UnitedHealthcare's Medical benefit specialty drug update bulletin. The CRS identified Sundeep Singh, MD, an inflammatory bowel disease (IBD) specialist from Stanford (Calif.) University, to engage in discussion with UnitedHealthcare on behalf of AGA and lead a multisociety effort with the North American Society for Pediatric Gastroenterology, Hepatology & Nutrition; the American Society for Gastrointestinal Endoscopy; and the American College of Gastroenterology.

After conversations with our physician experts, UnitedHealthcare agreed to notify its medical directors to allow pediatric patients 16 years and younger and currently on a nonpreferred product, such as Remicade, to remain on it if that is the recommendation of the treating physician. Adult patients meeting the following conditions may be allowed to remain on nonpreferred products, but will require the prescribing provider to request a review and a determination will be made on a case-by-case basis:

- Adult patients currently on induction of Remicade for less than 18 months will not be required to switch.
- Adult patients who are having a flare of active disease, who are, therefore, not stable, will not be required to switch.

AGA experts are a vital part of CRS's work with commercial payers. Dr. Singh and his fellow IBD experts who participated in discussion with UnitedHealthcare helped the payer understand why its original policy implementing nonmedical switching without exceptions was harmful to patients. Dr. Singh had this to say about his experience with the process:

"Thanks to the coordinated efforts between AGA, NASPGHAN, ACG, ASGE, and UnitedHealthcare, we were able to reconcile the policy and knowledge gaps to protect our patients with inflammatory bowel disease. While there are significant cost savings associated with biosimilar use, we wanted to temper the health plan's initial enthusiasm with the potential costs in patients whose clinical and economic outcomes are not certain yet. As we anticipate other health plans will implement similar policies, this effort may provide a road map for the future."

The CRS also works with pharmacy benefit management organizations. The AGA joined the ASGE and ACG to ask Express Scripts to not exclude coverage of brand colonoscopy preparations such as Suprep, Clenpiq, and Plenvu. The formulary currently plans to cover only generic products for colon cleansing beginning April 1, 2021, primarily 4-liter polyethylene glycol electrolyte solutions (PEG-ELS).

Clinical representatives and staff from AGA, ACG, and ASGE participated in a fruitful discussion with the leadership of Express Scripts and presented several key discussion points in favor of keeping coverage of brand colonoscopy bowel preparations in addition to PEG-ELS. The multisociety group presented views from practicing gastroenterologists as well as from academicians about the safety and benefits of low-volume preparations for a quality screening colonoscopic exam especially in certain patient populations. Limiting choices of bowel preparations will deter patients from undergoing screening colonoscopies, which have been proven to prevent colorectal cancers. After the multisociety group pointed out the need to individualize the choice of bowel preparation to ensure safety and tolerability, Express Scripts will hopefully agree with the significance of having options for our patients. It was clear that the importance of patient preference and clinical appropriateness for different bowel preparation options was heard by the Express Scripts representatives, so we await their decision with hope.

The AGA is working to address issues with commercial payers, but to be effective we need to hear your experiences. We know commercial payers continue to develop increasingly restrictive PA policies and coverage conditions. Reach out to the AGA via the AGA Community, Twitter, or via email to Leslie Narramore, the director of regulatory affairs at AGA, at lnarramore@gastro.org to let us know what's happening.

Dr. Guha is with the University of Texas Health Science Center in Houston. Dr. Upchurch is with Adena Health System in Chillicothe, Ohio. Both are AGA Coverage and Reimbursement Subcommittee members. The authors have no conflicts to declare.

Seven options to consider if your PA has been rejected or claim has been denied

1. **Ask for the credentials of the payer representative who initially denied the request.** Even when payer representatives are physicians, they are often not gastroenterologists. Ask to speak with a representative actively practicing gastroenterology.
2. **Ask to record your conversation with the payer representative for documentation purposes.**
3. **Ask to speak directly to the payer's medical director.**
4. **Bring the complaint to the payer's attention on social media.** Using social media to bring attention to a denial can sometimes elicit quick, personal outreach from the payer to address the issue.
5. **Let the AGA know what's happening.** Reach out to the AGA via the AGA Community, via Twitter, or by emailing Leslie Narramore, the director of regulatory affairs at AGA (lnarramore@gastro.org).
6. **File a complaint with the State Insurance Commissioner.** State Insurance Commissioners are responsible for regulating the insurance industry in their state and can investigate to ensure the laws in their state are being followed and providers and patients are being treated fairly. While insurance law and regulation are established at the state level, the insurance commissioners are members of the National Association of Insurance Commissioners, which allows them to coordinate insurance regulation among the states and territories. Find out your state's complaint process because many state insurance commissioners have an online complaint forms. Keep records of all interactions with the insurance company to document that you have attempted to resolve the matter with the payer first.
7. **File a complaint at the federal level for states without an external review process.** If your state doesn't have an external review process that meets the minimum consumer protection standards, the federal government's Department of Health & Human Services oversees an external review process for health insurance companies in your state. See www.healthcare.gov/appeal-insurance-company-decision/external-review/ for more information. In states where the federal government oversees the process, insurance companies may choose to participate in an HHS-administered process or contract with independent review organizations. If your plan doesn't participate in a state or HHS-Administered Federal External Review Process, your health plan must contract with an independent review organization.

Smart giving in 2021

Last year was anything but normal. The pandemic hit the economy hard and forced many people to keep a close eye on their finances. Many of us are still thinking twice about when to spend. If supporting the American Gastroenterological Association Research Foundation is important to you, consider these simple ways to give that don't spread your finances thin.

- **Grant from your donor advised fund (DAF).** This popular one-stop giving solution lets you care for multiple causes and organizations with minimal paperwork. And when you use your existing DAF to recommend a gift, it means you can invest in our future without impacting your budget today.
- **Distribution from your IRA.** When you are 70.5 years or older, you can make a tax-free gift directly from your IRA to the AGA Research Foundation. With the return of the required minimum distribution this year, now is a great time to use your IRA to make a difference at the AGA Research Foundation.
- **Gift in your will.** With as little as one sentence, you can create a brighter tomorrow at the AGA Research Foundation without parting with assets today. You can designate the AGA Research Foundation as the beneficiary of a specific asset or, as many of our donors do to ensure that their family is protected, as the recipient of a percentage of the total estate.
- **Beneficiary designation.** Adding the AGA Research Foundation as a beneficiary of your retirement plan or other assets is simple and can usually be completed entirely online in just a few minutes.

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Supporting the AGA Research Foundation doesn't have to mean giving up assets today. Learn more about including a gift to the AGA Research Foundation in your future plans by visiting https://gastro.planmylegacy.org.

ABGH joins the pursuit of equity

The Association of Black Gastroenterologists and Hepatologists focuses on promoting health equity in Black communities, advancing science, and developing the careers of Black gastroenterologists, hepatologists, and scientists.

AGA Institute President Bishr Omary, MD, AGAF, says that "AGA looks forward to partnering with ABGH on their mission – promoting health equity in Black communities, advancing science, and developing the careers of Black gastroenterologists, hepatologists, and scientists."

Through the AGA Equity Project, AGA has been committed to a multiyear effort spanning all aspects of our organization to achieve equity and eradicate disparities in digestive diseases.

Congratulations to the cofounders and board:
Sophie M. Balzora, MD, FACG, President
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Join AGA Advocacy Day – virtually!

With the 117th Congress getting started, there's never been a better time for us to visit Capitol Hill virtually and introduce ourselves to lawmakers who will be deciding the future of GI.

Join us for our virtual spring American Gastroenterology Association's Advocacy Day on Thursday, April 22, from 9 a.m. to 4 p.m. EDT, when we'll be meeting with congressional leaders to educate them about the reality of patient care in their communities. This is a unique opportunity for all AGA members – clinicians, researchers, allied health professionals, and administrators – to share their personal experiences and influence how health care policies will be discussed for years to come. Key issues we'll be sharing include the following:

- Reducing prior authorization burdens for clinicians and patients.
- Providing a transparent appeal process for patients subjected to step therapy.
- Increasing funding for the National Institutes of Health and VA Medical and Prosthetic Research Program.
- Including GI-specific diseases in the Department of Defense's Congressionally Directed Medical Research Programs.
- Offering supplemental funding to offset investigators' COVID-19–related research setbacks.

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Members with all levels of advocacy experience are encouraged to participate. AGA staff will coordinate your appointments, provide a legislative briefing, and offer the training you need to be an effective storyteller.

Get to know DDW® 2021 Virtual

The world's premier meeting for gastroenterology, hepatology, endoscopy, and gastrointestinal surgery professionals will be a fully virtual event, May 21-23, 2021. We invite you to take advantage of this unique opportunity to exchange knowledge with colleagues from all over the world and explore the latest advances in the field – all from the convenience of your home. Plus, your registration grants you access to everything offered at Digestive Disease Week® (DDW) this year (no additional ticketed sessions).

Learn more and register at ddw.org.

AGA celebrates women in GI

Since 2014, the AGA Women's Leadership Conference has brought together women from varying work settings to develop and leverage the skills of both early-career and accomplished women in GI and hepatology. The 2021 conference hosted 22 trailblazing faculty in GI, psychology, and professional leadership training to empower the women of GI to continue to excel, achieve their goals, and impact the field. Special thanks to all faculty, attendees, and especially the event working group Milena Suarez, MD; Jenny Sauk, MD, AGAF; Richa Shukla, MD; Lilani Perera, MD, AGAF; Ani Kardashian, MD; and Sonia Godambe, MD, as well as the cochairs Sharmila Anandasabapathy, MD, AGAF, and Monina Pascua, MD, PharmD, for a spectacular event.

Better posture could mean less pain

Ergonomics *from page 1*

upper endoscopies per week.

These endoscopists volunteered for an ergonomic intervention involving use of an individualized wellness plan. They completed the Nordic Musculoskeletal Questionnaire to evaluate musculoskeletal complaints during the past 12 months and the past 7 days. Three of the eight participants reported pain at work at initial assessment, which often worsened over the course of the day, and five mentioned fatigue while working. They specified 22 pain sites, mainly in the neck and back. In addition, participants were photographed to evaluate posture in a static position and self-selected "tired" positions.

"When frequent or consistent posturing resulted in suboptimal joint alignment, muscle length, loading at end range of muscle or joints, and/or prolonged static active positioning, participants were photographed to provide personalized feedback for wellness education," the researchers wrote.

The physical therapist used information from the evaluation and photographs to develop individual plans to improve the ergonomics of the endoscopic suite with adjustments to the location of the bed and positioning of chairs, standing surfaces, and monitors and keyboards. In addition to adjusting the endoscopic suite, the physical therapist developed individual wellness plans including exercises to relieve pain and improve posture, as well as pain education to help clinicians recognize and manage pain and fatigue.

By the end of the study, in a follow-up 6-12 months after the wellness intervention, 63% of pain sites (14 of 22) reported by participants were reduced in intensity or resolved, 32% were unchanged (7 of 22), and 4% increased (1 of 22).

"All endoscopists reported that the wellness plan was helpful, with procedure suite and posture recommendations being the most beneficial," the researchers reported. "Upon gaining insight with visualization of their posture and movement during endoscopy, participants' understanding and motivation to make corrections was intensified."

The study findings were limited by several factors including the small size, use of a single physical therapist, short follow-up, lack of controls, and use of a single site, the researchers noted. However, "our study provides a detailed, pragmatic, and reproducible framework for performing an individualized physical therapist–directed comprehensive assessment and personalized wellness plan in the workplace to help meet the challenges of ergonomics in endoscopy."

Value of ergonomics

"Endoscopy-related injury and disability is a known hazard of our profession," said Gyanprakash A. Ketwaroo, MD, MSc, of Baylor College of Medicine, Houston, in an interview. "Any studies to assess and, more importantly, offer ways to prevent such injury are immediately relevant. In this context,

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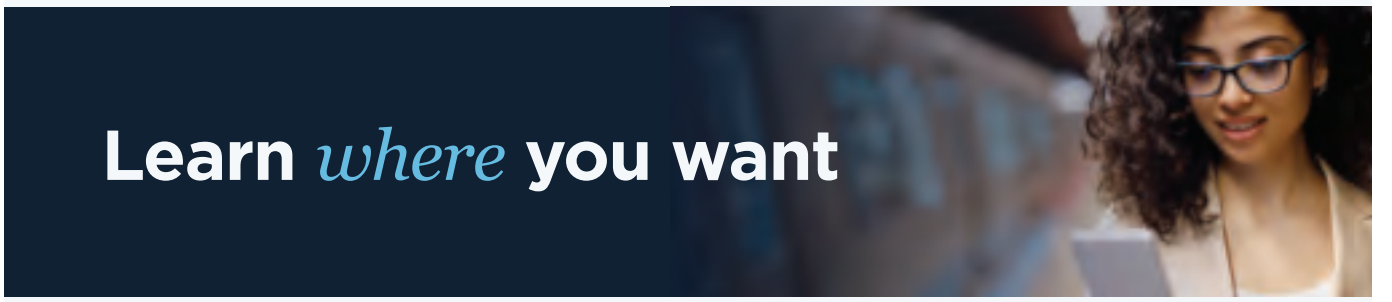

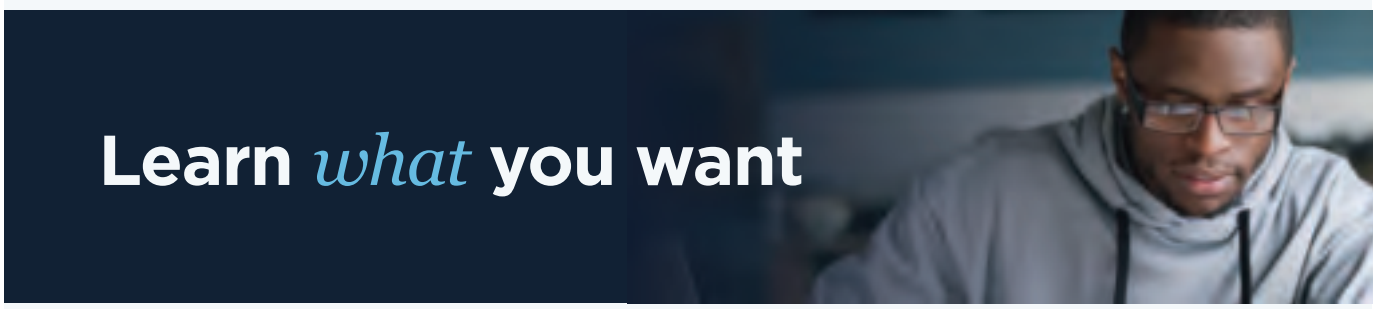

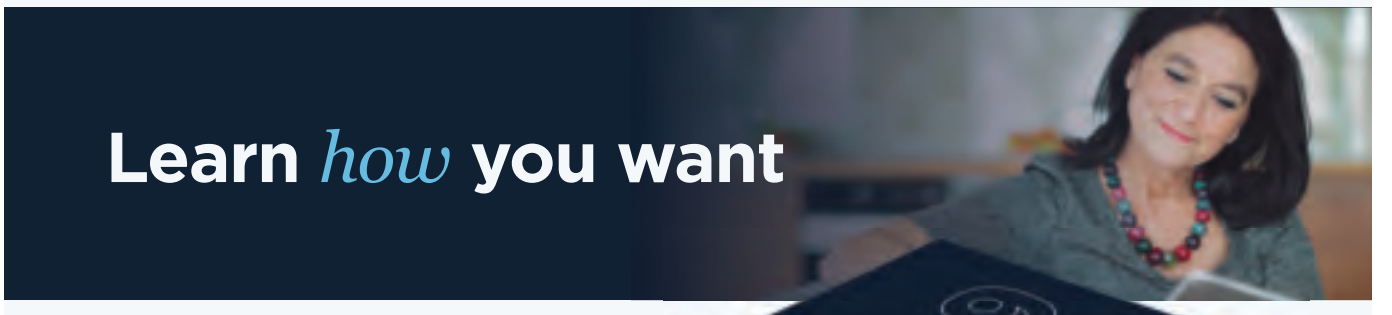

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EDU19-45

Care needs to include mental health

IBD *from page 1*

for a higher prevalence of mental disorders in IBD, in particular depression and anxiety, compared with the general population," the authors wrote.

They cited a recent population-based study in which the incident rate ratios were significantly higher for IBD patients, compared with matched controls for depression (IRR, 1.58), anxiety disorder (IRR, 1.39), bipolar disorder (IRR, 1.82), and schizophrenia (IRR, 1.64) (Inflamm Bowel Dis. 2019 Jan 10;25[2]:360-8).

Mental disorders associated with IBD also include issues of body image and sexuality. Although research on the impact of disease activity on sexual function is inconsistent, one study suggested that body image "may be an important target of treatment in women reporting poor quality of life and psychological distress," the researchers noted (Qual Life Res. 2017 Feb;26[2]:429-36). A French study from 2017 published in the Journal of Crohn's and Colitis showed that approximately half of men and women reported problems with erectile or sexual dysfunction (J Crohns Colitis. 2017 Oct 27;11[11]:1347-52).

Issues related to environmental stressors may contribute to IBD by promoting chronic inflammation, the researchers wrote. For example, data from longitudinal, population-based research suggest that adverse childhood experiences can promote proinflammatory states across inflammatory illnesses (Mol Psychiatry. 2016 May;21[5]:642-9). Research has also suggested that people with IBD have higher rates of these adverse childhood experiences than the general population (Inflamm Bowel Dis. 2019 Sep 18;25[10]:1700-10). However, data also show that many are able to cope and adapt: "Many patients with IBD are resilient, experience growth, and in fact, thrive," the researchers added. One longitudinal study suggested that patients with IBD who identified with "thriving" had "stronger coping efficacy (the perceived ability to meet illness demands), illness acceptance, and social support and lower depression" and that this was associated with life satisfaction 6 months later (Br J Health Psychol. 2017 Nov;22[4]:920-39).

Dr. Kim L. Isaacs says there is a large burden of mental health issues.

Fatigue also has been shown to be a factor for patients with IBD. The researchers cited one population-based study showing fatigue in 57%-72% of IBD patients with active disease (Inflamm Bowel Dis. 2011 Sep;17[9]:1882-9). IBD patients with quiescent disease also report fatigue. The psychological and behavioral factors driving fatigue could be related to mental disorders or other factors such as suboptimal sleep, stress, and use of caffeine and alcohol, they noted. Management strategies include improving sleep hygiene and evaluation of mental health concerns.

Treatment approaches

"Addressing psychological comorbidity in IBD requires individual and systemic approaches focused on both the prevention and treatment of mental health concerns," the researchers wrote. "Because of the pervasiveness of psychological comorbidities in IBD, and recent evidence that they may be part of the disease process itself, assessment of psychological functioning in IBD is considered an essential aspect of disease management."

Evidence-based psychological interventions include cognitive-behavioral therapy, which includes training in relaxation; treating with clinical hypnosis; and encouraging mindfulness through acceptance and commitment therapy, which focuses on developing psychological flexibility to cope with suffering. In addition, a small but evolving body of research shows some benefit to motivational interviewing (a strategy focused on behavior change) for IBD patients. Notably, one review of four studies showed benefits of motivational interviewing for improving medication adherence and advice seeking (J Clin Med Res. 2017 Aug;9[8]:659-66), the researchers reported.

"To facilitate this important research and optimize patient care, the integration of psychologists and other mental health providers into IBD care is considered best practice and provides exciting opportunities for improving patient care and outcomes," the researchers concluded.

Mental health needs

"There is a large burden of mental health issues in patients with inflammatory bowel disease, with depression and anxiety leading the way," Kim L. Isaacs, MD, PhD, AGAF, of the University of North Carolina at Chapel Hill, said in an interview.

"There are multiple reasons for this, including dealing with chronic pain, social concerns around using the bathroom, body-image issues due to surgery, and drug side effects. There is increasing evidence that the inflammatory process in IBD may be driving some of the changes in the brain which lead to further mental health dysfunction," she noted.

"Addressing depression, anxiety, [and] sleep disturbance in patients will not only improve quality of life from a mental health perspective but has been shown to improve control of disease," Dr. Isaacs emphasized.

"Small things like increased medication compliance have a large impact on disease management and decreased need for hospitalization," said Dr. Isaacs. "As gastroenterologists we need to expand our focus beyond the gut and address the emotional needs of our patients – identifying those patients who need increased mental health support."

Barriers to better care

The greatest barriers to treating mental health issues in IBD patients are time and knowledge, said Dr. Isaacs. "Many gastroenterologists have limited time in the office to do more than address the acute issues of the patients such as rectal bleeding and worsening diarrhea. It takes time and trust to explore what is going on in a patient's life. Is the patient anxious and depressed? How are they coping with their current disease manifestations? Simple screening tools may help with this, but then there need to be resources to support interventions."

Some IBD practices, especially academic ones, have a psychologist in the IBD center or one that's readily available for consultation. "This is an investment for the practice that may reduce significantly disease burden. The IBD specialty home model includes resources for management of psychiatric issues and nutritional concerns, as well as disease management," she added.

More research in several areas and increased resources for patients can help reduce the mental health burden of IBD. "Further work developing health care systems, such as the medical home, that allow for maximum disease management and decreased system costs will go far in implementation of models of care that address the needs of the entire patient with inflammatory bowel disease."

The review received no outside funding. The researchers had no financial conflicts to disclose. Dr. Isaacs disclosed consulting on the data safety monitoring board for Janssen.

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ergonomics for endoscopy is an increasing area of research."

Dr. Ketwaroo said that the study results were not surprising. "I agree with authors that there is a paucity of general ergonomic training and assessment. Specific individualized wellness plans are rare. Developing an individual plan based on observation by physical therapists, and taking into account baseline injury or predisposition to injury would be expected to be more high yield for preventing injury and improving performance."

"I believe the main take-home message from the study is that an individualized ergonomic plan based on assessment and feedback by physical therapists appears promising for optimizing endoscopic performance to minimize injury and reduce fatigue," Dr. Ketwaroo said. However, "long-term studies in much larger samples will be needed to document objective findings of reduced injury or fatigue."

The study received no outside funding. The researchers had no financial conflicts to disclose. Dr. Ketwaroo serves on the GI & Hepatology News editorial advisory board.

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AGA Clinical Practice Update

Palliative care management in cirrhosis

BY AMY KARON
MDedge News

Clinicians who manage patients with cirrhosis should incorporate palliative care "irrespective of transplant candidacy," according to a clinical practice update from the American Gastroenterological Association.

"[T]his care should be based on needs assessment instead of prognosis alone, delivered concurrently with curative or life-prolonging treatments, and tailored to the stage of disease," wrote Puneeta Tandon, MD, of University of Alberta in Edmonton and associates. Their report is in Clinical Gastroenterology and Hepatology (2020 Nov 18. doi: 10.1016/j.cgh.2020.11.027).

Even compensated cirrhosis incurs "a high burden of physical and psychological symptoms," which increases as cirrhosis progresses.

Cirrhosis has a median survival ranging from 2 years for decompensated disease to 12 years for compensated disease, according to one systemic review (J Hepatol. 2006 Jan;44[1]:217-31). Moreover, even compensated cirrhosis incurs "a high burden of physical and psychological symptoms," which increases as cirrhosis progresses, the update authors noted.

According to another review (JAMA. 2016 Nov 22;316[20]:2104-14), there is established evidence outside cirrhosis that palliative care – including comprehensive symptom management, advance care planning, and timely referrals to specialty palliative care and hospice support – has the potential to significantly improve quality of life, end-of-life care, health care costs, coordination among providers, and caregiver outcomes.

However, the update authors noted that there remain few guidelines or guidance statements regarding palliative care in cirrhosis. Hence, the clinical practice update reviews 10 best practices to help clinicians fill this gap.

Providers "from any specialty, within any healthcare setting" can help provide palliative care for patients with cirrhosis, the experts emphasized. This is, in part, because of the growing population with cirrhosis being met with a limited number of palliative care specialists; dealing with this reality can be helped by inviting other providers to learn about and engage in palliative care.

Another best practice statement addressed assessing symptoms "within physical, psychological, social, and spiritual domains related to [patients'] liver disease, its treatment, and prognosis." This approach is needed because of the complex effects that a life-threatening illness and its symptoms can have on many variables, including

Continued on following page

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EDU20-080

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loss of independence/identity, financial stress, and impact on personal relationships. A systematic review of symptom prevalence in end-stage liver disease revealed a complex milieu, including pain, muscle cramps, sexual dysfunction, insomnia, and anxiety (Palliat Med. 2019 Jan;33[1]:24-36).

High-quality communication is important in palliative care, including discussion of prognosis and goals of care. Providers specializing in gastroenterology/hepatology should reevaluate prognosis and clarify prognosis and goals of care with patients and caregivers during routine visits and sentinel events, such as new complications, a hospital or intensive care admission, and when transplant eligibility is determined. However, prognostication in cirrhosis can be challenging, the experts noted. The update authors also acknowledged that, while more research is needed to inform practice regarding communicating with patients with serious illness about palliative care and goals of care, there are courses and resources meant to help improve those skills, including those provided by Vital Talk (https://courses.vitaltalk.org/courses/), Respecting Choices (https://respectingchoices.dcopy.net/category/Online-Learning), and the Serious Illness Conversation Guide (http://www.instituteforhumancaring.org/documents/Providers/Serious-Illness-Guide-old.pdf).

Cirrhosis "has physical, mental, and financial consequences" for caregivers, especially when patients have decompensated disease. To support caregivers, clinicians can routinely evaluate their burdens and needs. Tools such as the Caregiver Strain Index (http://www.npcrc.org/files/news/caregiver_strain_index.pdf) are useful and can be administered by ancillary staff. Clinicians also can reach out to primary care and palliative care providers to identify local resources for caregiver support.

"Because lack of time is one of the major barriers to administering palliative care, healthcare providers should consider how they can optimize efficiencies in palliative care delivery," the experts wrote. Examples include identifying local billing codes, arranging for ancillary staff to screen patients on their palliative care needs, and setting up multidisciplinary teams that work together to deliver palliative care. If access to specialty palliative care is limited, providers can collaborate with local specialist teams to set "clear triggers and pathways for referral."

Finally, hospice referrals are often delayed for patients with cirrhosis. "Find out your local referral criteria for hospice and what would be required to refer a cirrhosis patient there," the experts advised. "Healthcare providers caring for patients with cirrhosis should provide timely referral to hospice for patients who have comfort-oriented goals and prognosis of 6 months or less."

The authors of the clinical practice update received no funding support. They reported having no relevant conflicts of interest.

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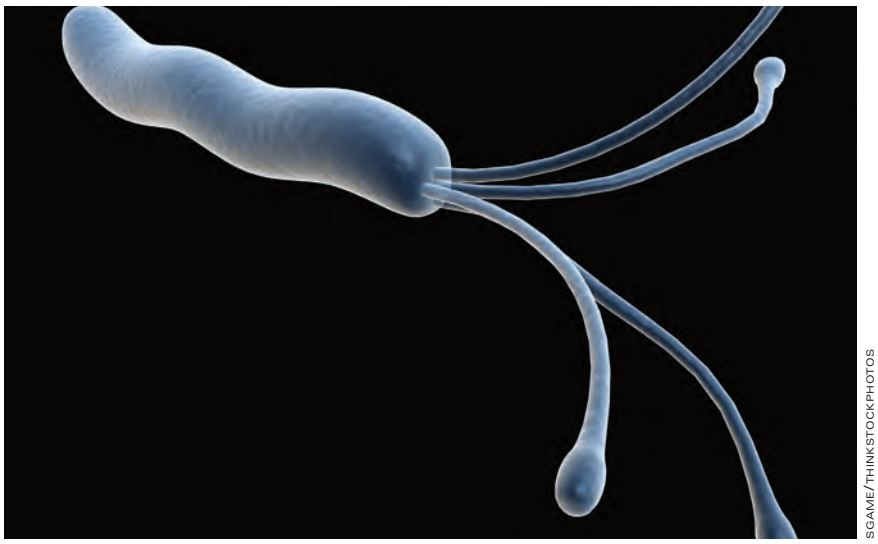
Nonadherence remains an issue

Eradication *from page 1*

PPIs not metabolized by CYP2C19, or potassium-competitive acid blockers, if available, should be considered in cases of refractory *H. pylori* infection," wrote Shailja C. Shah, MD, MPH, and coauthors Prasad G. Iyer, MD, MS, and Steven F. Moss, MD. Their report is in Gastroenterology (2021 Jan 28. doi: 10.1053/j.gastro.2020.11.059).

H. pylori infection is the most common cause of gastric cancer. Although eradication is widely recommended, it can be challenging because of strain diversity, rising antimicrobial resistance, a dearth of recent head-to-head clinical trials, and sparse epidemiologic and sensitivity data, the experts noted. For this reason, before selecting an eradication regimen, it is vital to thoroughly review a patient's history of antibiotics – for example, any prior macrolide or fluoroquinolone exposure should preclude the use of clarithromycin- or levofloxacin-based regimens "given the high likelihood of resistance," the experts wrote. They also advised that clinicians should avoid levofloxacin unless the *H. pylori* strain is known to be sensitive to it or if population rates of levofloxacin resistance are known to be less than 15%. However, amoxicillin, tetracycline, and rifabutin resistances are rare, and these agents "can be considered for subsequent therapies in refractory *H. pylori* infection."

A longer antimicrobial regimen (such as 14 vs. 7 days) is more likely to eradicate *H. pylori*. If first-line bismuth quadruple therapy (such as a PPI plus bismuth, metronidazole, and tetracycline) fails, then second-line options include another bismuth-containing quadruple-agent regimen, or triple therapy with rifabutin or levofloxacin plus high-dose dual-PPI therapy and amoxicillin. The authors also note that, when used, amoxicillin should be dosed at 2 g/day in three to four divided doses in order to avoid low trough levels, as this might be associated with *H. pylori* eradication failure. For metronidazole, regardless of in vitro resistance, eradication is more likely if patients receive 1.5-2 g/day, in divided doses, with concomitant bismuth.



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Dr. Shah

***H. pylori* infection is the most common cause of gastric cancer. Although eradication is widely recommended, it can be challenging because of strain diversity, rising antimicrobial resistance, a dearth of recent head-to-head clinical trials, and sparse epidemiologic and sensitivity data.**

Treatment nonadherence contributes to refractory *H. pylori* infection and may be caused by the treatment regimen's complexity, high pill burden, and side effects. To improve adherence, the experts advised counseling patients on the rationale for the treatment regimen, the dosing instructions, and the importance of completing the full course of therapy, and providing anticipatory guidance regarding common side effects. If a patient adheres to second-line treatment and it still fails, then susceptibility testing is advised before starting another regimen. Depending on the results, options may include levofloxacin-based quadruple therapy, another round of bismuth-based quadruple therapy, a PPI plus amoxicillin and rifabutin, or high-dose PPI therapy plus high-dose amoxicillin (2-3 g/day divided across three to four doses).

Other considerations include how to approach patients and caregivers, particularly the elderly and other vulnerable patients, with shared decision-making to help them weigh the potential benefits of continuing to try to eradicate *H. pylori* against the risk of possible adverse effects and the "inconvenience of repeated exposure to antibiotics and high-dose acid suppression," the experts wrote. They also advised tracking rates of eradication success and relevant demographic and clinical data, including patients' antibiotic history. Publicly sharing aggregated, deidentified results can help other local clinicians select eradication regimens. Finally, the use of probiotics and other adjunctive therapies "should be considered experimental" since these have no clear benefit for treating refractory *H. pylori* infection.

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DDSEP 9
Digestive Diseases Self-Education Program

Quick Quiz answers

Q1. Correct answer: D. Antienterocyte antibodies

Rationale

Autoimmune enteropathy (AIE) is characterized by a severe malabsorption and secretory diarrhea, and is differentiated from celiac disease on small-bowel biopsy by the decreased numbers or absence of surface intraepithelial lymphocytes, apoptotic bodies present in the intestinal crypts, and absent goblet and Paneth cells. Patients with AIE may also carry other autoimmune conditions such as rheumatoid arthritis and multiple sclerosis. A group at the Mayo Clinic has published a set of diagnostic criteria based on their case series of adult AIE that requires ruling out other causes of chronic diarrhea in adults, specific histology supportive of AIE, and presence of malabsorption and ruling out other causes of villous atrophy. The presence of antienterocyte or antigoblet cell antibodies are supportive of a diagnosis of AIE, but their absence does not exclude the diagnosis.

References

Akram S et al. Clin Gastroenterol Hepatol. 2007;5(11):1282-90.
Montalto M et al. Scan J Gastroenterol. 2009;44(9):1029-36.

Q2. Correct answer: B. Prednisone

Rationale

This is a case of Henoch-Schönlein purpura, which is a self-limited, systemic, nongranulomatous, autoimmune complex, small-vessel vasculitis with multiorgan involvement. It is characterized by a classic tetrad of nonthrombocytopenic palpable purpura, arthritis or arthralgias, gastrointestinal involvement, and renal involvement. GI involvement may mimic Crohn's disease, although the biopsies are usually diagnostic. Most cases are self-limiting, but oral steroids are indicated in patients with severe colicky abdominal pain; usually they're started as prednisone or methylprednisolone at 1-2 mg/kg per day for 1-2 weeks and then tapering to a stop in the next 1-2 weeks. Steroids may prevent major complications such as gastrointestinal bleeding or intussusception. Immunosuppressive drugs (cyclophosphamide, azathioprine, cyclosporine A, and mycophenolate mofetil) in combination with high-dose IV pulse steroids are recommended if there is no benefit from steroids alone.

Reference

Sohagia AB et al. Gastroenterol Res Pract. 2010. doi: 10.1155/2010/59764.

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