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GI & HEPATOLOGY NEWS

THE OFFICIAL NEWSPAPER OF THE AGA INSTITUTE

CLEVELAND CLINIC

Dr. Miguel Regueiro described his experience with IBD medical homes at AGA Partners in Value 2018.

Treating IBD in medical home reduces costs

BY TARA HAELLE
MDedge News

REPORTING FROM AGA PARTNERS IN VALUE 2018

DALLAS – In the midst of the ever-increasing costs of patient care for chronic disease, one model for care of a specific, complex condition is the medical home, according to a presentation at the American Gastroenterological Association's Partners in Value meeting.

The medical home concept came out of pediatrics and primary care, where patients' health care needs could vary greatly over several years but benefited from coordinated care, Miguel Regueiro, MD, AGAF, professor of medicine and chair of the department of gastroenterology, hepatology, and nutrition at the Cleveland Clinic, told attendees at the meeting.

The medical home is ideal for a disease such as inflammatory bowel disease because it brings together the different care providers essential for such a complex condition and allows for the kind of coordinated, holistic care that's uncommon in America's typically fragmented health care system.

The two key components of a specialist medical home are a population of patients whose principal care requires a specialist and a health plan partnership around a chronic disease.

See **Medical home** · *page 26*

Guideline: Early CRC screening warranted for family history

With nonhereditary colorectal cancer

BY AMY KARON
MDedge News

New consensus guidelines strongly recommend screening colonoscopy for individuals who have at least one first-degree relative with nonhereditary colorectal cancer or advanced adenoma.

Published in the November issue of Gastroenterology, the guideline cites moderate-quality evidence for this recommendation and reserves fecal immunochemical testing for individuals who refuse colonoscopy, are at increased risk for complications, or face barriers accessing the procedure.

Most colorectal cancer screening guidelines have focused on average-risk individuals or those at highest risk because of heritable germline mutations. However, hereditary syndromes comprise only about 5% of colorectal cancers, noted Desmond Leddin, MB, MSc, FRCPC, FRCPI, of the University of Limerick (Ireland) and David A. Lieberman, MD, AGAF, FACG, of Oregon Health and Science University, Portland, with their associates from the Canadian Association of Gastroenterology Banff Consensus.

To develop the guideline, they searched the literature for studies of family history and colorectal can-

See **Family history** · *page 34*

Obesity, weight gain linked to CRC risk in younger women

BY ANDREW D. BOWSER
MDedge News

Obesity and weight gain are linked to increased risk of colorectal cancer in younger women, according to an analysis of a large, prospective U.S. cohort study.

Young women who were obese had a nearly twofold increase in risk of early-onset colorectal cancer, compared with women of normal weight, authors of the study reported in JAMA Oncology.

The findings suggest body weight could be used to "personalize and complement" early cancer screening strategies among

See **Weight gain** · *page 24*

INSIDE

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LETTER FROM THE EDITOR: Please stay involved as leaders


DR. ALLEN

By the time you receive this issue, we will know election results. The effects on medical care, medical coverage, Medicare, and Medicaid will be profound. American medicine is integrally linked to Congress and the Supreme Court because on July 30, 1965, Lyndon Johnson signed Title 18 of the Social Security Act and created Medicare – a move that took medical care out of personal law and into public law.

In November, CMS will publish its "final rule" about documentation and reimbursement changes, site of service reimbursement, and several other impactful policy changes. We have an extended article from the AGA Partners in Value conference about these potential changes.

This month we highlight the medical home concept for IBD – an idea that is gaining traction. More intense colon cancer screening may be needed for families with nonhereditary colon cancer. An interesting article from JAMA suggests that obesity may play a role in colon cancer rates in young women.

Antibiotic resistance in *H. pylori* infections is reaching alarming levels and this information may alter our practice. We feature an "In Focus" section on endosopic treatment for obese patients. We also continue highlighting some popular and interesting discussion chains emanating from the AGA Community.

Please stay involved as leaders in health care economics, delivery, and politics. We need thoughtful discussions and we need to bring patient stories to our politicians. It often seems that our advocacy does little to alter the national debate but who better to speak for the people that entrust us with their care?

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

DDSEPeight
Digestive Diseases Self-Education Program

Quick Quiz

Q1. A 52-year-old man is referred because of diarrhea, with up to six loose bowel movements per day for the past 7 months. His stool has been nonbloody. He denies rashes or eye problems, but he has had significant arthralgias. He has lost 15 pounds and also reports having newly developed headaches over this time. A colonoscopy performed 1 year ago for routine screening was unremarkable. Celiac serologies checked last month were negative. Stool cultures, ova and parasite evaluation, and *Clostridium difficile* toxin assay were all negative.

An upper endoscopy reveals grossly unremarkable mucosa throughout, and duodenal biopsies are performed. Besides routine evaluation, what additional testing should be requested for the pathologist to perform on the duodenal specimens?

A. Congo red staining
B. Sudan staining
C. Birefringence
D. Periodic acid-Schiff staining
E. Immunohistochemistry

Q2. An 18-year-old female college student has a 6-month history of vomiting, with associated 15-pound weight loss during this time period. Her medical history is significant for a gastroenteritis about 1 year ago and surgery for pyloric stenosis as an infant. She has no psychiatric history. Current medication includes an oral contraceptive. She describes the vomiting episodes as effortless regurgitation of food within 30 minutes of a meal. She also reswallows the food if she is in public. The vomiting occurs with almost every meal, either solid or liquid. An upper endoscopy, 4-hour gastric emptying test by scintigraphy and basic blood work are performed. Upper endoscopy is normal with no retained food. She cannot complete the gastric emptying test due to vomiting the radiolabeled test meal. Her blood work demonstrates a normal fasting blood glucose and complete blood count.

What is the most likely etiology of her symptoms?

A. Recurrent small-bowel obstruction
B. Adaptation to the belch reflex
C. Idiopathic gastroparesis
D. Bulimia

The answers are on page 9.

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FROM THE AGA JOURNALS

Crohn's disease tied to anal canal high-risk HPV

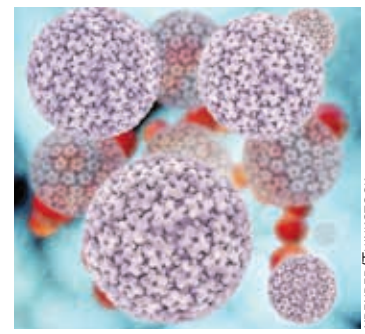
BY AMY KARON
MDedge News

Crohn's disease was significantly associated with anal canal high-risk human papillomavirus (HPV) infection in a prospective, single-center study of patients undergoing colonoscopy for various indications.

High-risk HPV and HPV strain 16 were detected in 30% of patients with Crohn's disease and 18% of patients without Crohn's disease (P = .005), said Lucine Vuitton, MD, of University Hospital of Besançon (France) and her associates. "Increasing our knowledge of HPV infection of anal tissues could help physicians identify populations at risk and promote prophylaxis with vaccination and adequate screening," the investigators wrote in the November issue of Clinical Gastroenterology and Hepatology.

Most anal cancers are squamous cell carcinomas, for which infection with high-risk HPV (especially high-risk HPV16) is a driving risk factor. Case studies and literature reviews have linked Crohn's disease to increased rates of anal canal cancers, but population-based data were lacking, the researchers wrote. Therefore, they prospectively analyzed anal tissue samples from 467 consecutive patients undergoing colonoscopy at a tertiary care center in France. Median age was 54 years (interquartile range, 18-86 years), and 52% of patients were women. No patient had detectable macroscopic neoplastic lesions at the anal margin at baseline.

The researchers used the QIAamp DNA Blood minikit (Qiagen) for DNA extraction and the INNO-LiPA HPV Genotyping Extra kit (Fujirebio Diagnostics) for HPV DNA detection and genotyping. These methods identified HPV DNA in anal tissue samples from 34% of the patients and high-risk HPV DNA in 18% of patients. The most prevalent genotype was HPV16 (detected in 7% of samples), followed by HPV51, HPV52, and HPV39.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A total of 112 patients were receiving at least one immunosuppressive treatment for inflammatory bowel disease or another condition. Seventy patients had Crohn's disease, and 29 patients had ulcerative colitis. The prevalence of anal canal high-risk HPV and HPV16 infection in patients with ulcerative colitis was similar to that seen in those without inflammatory bowel disease. However, patients with Crohn's disease were more likely to have anal canal high-risk HPV infection (30%) and HPV16 infection (14%), compared with patients without Crohn's disease (18% and 7%, respectively). Additionally, among 22 patients with Crohn's disease and perianal involvement, 11 had HPV DNA in the anal canal versus 30% of other patients with inflammatory bowel disease.

Women were more likely to have anal canal high-risk HPV (23%) infection than were men (13%; P = .004). In a multivariable analysis of self-reported data and medical data, significant risk factors for high-risk HPV infection included female sex, a history of sexually transmitted infections, having more than 10 sexual partners over the life course, having at least 1 sexual partner during the past year, current smoking, and immunosuppressive therapy. The multivariable analysis also linked Crohn's disease with anal canal high-risk HPV16 infection (odds ratio, 3.8), but the association did not reach statistical significance (95% confidence interval, 0.9-16.9).

Most patients with Crohn's disease were on immunosuppressive therapy, "which markedly affected statistical power," the researchers commented. Nonetheless, their findings support HPV vaccination for patients with Crohn's disease, as well as efforts to target high-risk patients who could benefit from anal cancer screening, they said.

The work was funded by the APICHU research grant from Besançon University Hospital and by the Région de Franche-Comté. Dr. Vuitton disclosed ties to AbbVie, Ferring, Hospira, Janssen, MSD, and Takeda. Three coinvestigators disclosed relationships with AbbVie, Hospira, Mayoli, MSD, and Roche.

ginews@gastro.org

SOURCE: Vuitton L et al. Clin Gastroenterol Hepatol. 2018 Nov. doi: 10.1016/j.cgh.2018.03.008.

Correction:
In the story "Commentary: Composite risk, not age, is key for timing first colorectal cancer screening" (Oct. 2018, page 10), Thomas F. Imperiale, MD, should have been identified as the first author.

H. pylori antibiotic resistance reaches 'alarming levels'

BY AMY KARON
MDedge News

Over the past decade, *Helicobacter pylori* strains have reached "alarming levels" of antimicrobial resistance worldwide, investigators reported in the November issue of Gastroenterology.

In a large meta-analysis spanning 2007-2017, *H. pylori* isolates showed a 15% or higher pooled prevalence of primary and secondary resistance to clarithromycin, metronidazole, and levofloxacin in almost all World Health Organization (WHO) regions. "Local surveillance networks are required to select appropriate eradication regimens for each region," concluded Alessia Savoldi, MD, of the University of Tübingen (Germany) and her associates.

Typically, the threshold of antimicrobial resistance for choosing empiric regimens is 15%, Dr. Savoldi and her associates noted. Their systematic review and meta-analysis included 178 studies comprising 66,142 isolates from 65 countries. They defined *H. pylori* infection as a positive histology, serology, stool antigen, urea breath test, or rapid urease test. They excluded studies of fewer than 50 isolates, studies that reported resistance only as a percentage with no denominator, studies that failed to specify time frames or clustered data over more than 3 years, and data reported in guidelines, conference presentations, or letters without formal publication.

The prevalence of primary clarithromycin resistance exceeded 15% in the WHO European Region (18%; 95% confidence interval, 16%-20%), the Eastern Mediterranean Region (33%), and the Western Pacific Region (34%) and reached 10% in the Americas and the South East Asia region. Furthermore, primary resistance to metronidazole exceeded 15% in all WHO regions, ranging from 56% in the Eastern Mediterranean Region to 23% in the Americas. Resistance to levofloxacin was at least 15% in all WHO regions except the European region (11%).

'Local surveillance networks are required to select appropriate eradication regimens for each region.'

In most regions, *H. pylori* also accrued substantially more antimicrobial resistance over time, the investigators said. Clarithromycin resistance rose from 13% during 2006 through 2008 to 21% during 2012 through 2016 (P less than .001). Levofloxacin resistance in the Western Pacific region increased from 12% to 31% during the same two time periods (P less than .001). Several other WHO regions showed less significant trends toward increasing resistance. Multidrug resistance also rose. Resistance to both clarithromycin and metronidazole increased markedly in all WHO areas with available data, reaching 14% in the Eastern Mediterranean and Western Pacific regions and 23% in the European region.

Secondary analyses linked resistance with dramatic increases in the odds of treatment failure. For example, clarithromycin resistance conferred a sevenfold increase in the odds of treatment failure for

Continued on following page

FROM THE AGA JOURNALS

MELD-sodium score tied to better transplant outcomes

BY AMY KARON
MDedge News

Factoring hyponatremic status into liver graft allocations led to significant reductions in wait-list mortality, researchers reported in the November issue of Gastroenterology.

Hyponatremic patients with low MELD scores benefited significantly from allocation based on the end-stage liver disease–sodium (MELD-Na) score, while its survival benefit was less evident among patients with higher scores, said Shunji Nagai, MD, PhD, of Henry Ford Hospital, Detroit, and his associates. "Therefore, liver allocation rules such as Share 15 and Share 35 need to be revised to fulfill the Final Rule under the MELD-Na based allocation," they wrote.

The Share 35 rule offers liver grafts locally and regionally to wait-listed patients with MELD-Na scores of at least 35. Under the Share 15 rule, livers are offered regionally or nationally before considering local candidates with MELD scores under 15. The traditional MELD scoring system excluded hyponatremia, which has since been found to independently predict death from cirrhosis. Therefore, in January 2016, a modified MELD-Na score was implemented for patients with traditional MELD scores of at least 12. The MELD-Na score assigns patients between 1 and 11 additional points, and patients with low MELD scores and severe hyponatremia receive the most points. To assess the impact of this change, Dr. Nagai and his associates compared wait-list and posttransplantation outcomes during the pre– and post–MELD-Na eras and the survival benefit of liver transplantation during the MELD-Na period. The study included all adults wait-listed for livers from June 2013, when Share 35 was implemented, through September 2017.

Mortality within 90 days on the wait list fell significantly during the MELD-Na era (hazard ratio, 0.74; *P* less than .001). Transplantation conferred a "definitive" survival benefit when MELD-Na scores were 21-23 (HR versus wait list, 0.34; *P* less than .001). During the traditional MELD period, the equivalent cutoff was 15-17 (HR, 0.36; *P* less than .001). "As such, the current rules for liver allocation may be suboptimal under the MELD-Na–based allocation and the criteria for Share 15 may need to be revisited," the researchers wrote. They recommended raising the cutoff to 21.

The study also confirmed mild hyponatremia (130-134 mmol/L), moderate hyponatremia (125-129 mmol/L), and severe hyponatremia (less than 125 mmol/L) as independent predictors of wait-list mortality during the traditional MELD era. Hazard ratios were 1.4, 1.8, and 1.7, respectively (all *P* less than .001). The implementation of MELD-Na significantly weakened these associations, with HRs of 1.1 (*P* = .3), 1.3 (*P* = .02), and 1.4 (*P* = .04), respectively.

The probability of transplantation also rose significantly during the MELD-Na era (HR, 1.2; *P* less than .001), possibly because of the opioid epidemic, the researchers said. Although greater availability of liver grafts might have improved wait-list outcomes, all score categories would have shown a positive impact if this was the only reason, they added. Instead, MELD-Na most benefited patients with lower scores.

Finally, posttransplantation outcomes worsened during the MELD-Na era, perhaps because of transplant population aging. However, the survival benefit of transplant shifted to higher score ranges during the MELD-Na era even after the researchers controlled for this effect. "According to this analysis," they wrote, "the survival benefit of liver transplant was definitive in patients with score category of 21-23, which could further validate our proposal to revise Share 15 rule to 'Share 21.'"

The investigators reported having no external funding sources or conflicts of interest.

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SOURCE: Nagai S et al. Gastroenterology. 2018 Jul 26. doi: 10.1053/j.gastro.2018.07.025.

Continued from previous page

regimens containing clarithromycin (odds ratio, 7.0; 95% CI, 5.2 - 9.3; *P* less than .001). Corresponding ORs were 8.2 for levofloxacin resistance, 2.5 for metronidazole resistance, and 9.4 for dual clarithromycin-metronidazole resistance.

The investigators acknowledged several limitations. Of publications in this meta-analysis, 85% represented single-center studies with limited sample sizes, they wrote. Studies often excluded demographic and endoscopic details. Furthermore, only three studies provided prevalence data for the WHO Africa Region, and these provided overall estimates only without stratifying by resistance type.

The German Center for Infection Research, Clinical Research Unit, and the WHO Priority List Pathogens project helped fund the work. One coinvestigator disclosed ties to RedHill Biopharma, BioGaia, and Takeda related to novel *H. pylori* therapies.

ginews@gastro.org

SOURCE: Savoldi A et al. Gastroenterology. 2018 Nov. doi: 10.1053/j.gastro.2018.07.007.

The first-line treatment of individuals with *Helicobacter pylori* infection using clarithromycin-based triple therapies or, if penicillin allergic, bismuth-based quadruple therapies is generally effective. However, reports of declining therapeutic efficacy have led published guidelines to recommend confirmation of *H. pylori* eradication after completing a course of antibiotics. It is believed that increasing antibiotic use in agriculture and medicine around the globe have contributed to the increasing *H. pylori* antibiotic resistance and declining efficacy of standard *H. pylori* regimens.

Savoldi et al. performed a systematic review and meta-analysis to assess the distribution of *H. pylori* resistance to commonly used antibiotics and to measure the association between antibiotic resistance and treatment failure over the past 10 years. They found alarming trends of increasing antibiotic resistance globally that correlated with rising rates of treatment failure. The authors recommend establishing local antibiotic resistance surveillance networks to guide clinical decisions in selecting effective antibiotic regimens.

Indeed, most *H. pylori* guidelines recommend antibiotic sensitivity testing after failing two courses of treatment; however, performing such testing successfully may require sending fresh gastric biopsy samples to an in-house *H. pylori* culture lab within 1 hour, which is generally not available to most clinicians. Clearly, the gap in knowledge of local antibiotic resistance could be addressed by having a readily accessible culture facility and the testing should be reimbursed by health insurance.

Single-center experiences with antibiotic sensitivity–guided salvage therapy in the United States, however, registered a lower efficacy rate of approximately 50%, which indicates that other host factors (such as gastric acidity pH less than 5.5 or body mass index greater than 30 kg/m^2) may affect the minimum inhibitory concentration (MIC) of the antibiotics against *H. pylori*.


DR. KAO

In order to better study the effects of these host factors relative to the effect of antibiotic resistance on therapeutic efficacy, it is critical that we practice precision medicine by determining the antibiotic sensitivity of the *H. pylori* strain prior to initiating the antibiotic treatment. It may be possible to achieve more than 90% therapeutic efficacy given known antibiotic sensitivities of the bacteria and optimized host factors to lower the MIC. In addition, with the increasing awareness of the importance of gut microbiota in health and disease, clinicians should strive to narrow the antibiotic coverage that will be possible if antibiotic sensitivity is known (for example, use high-dose amoxicillin and proton pump inhibitor dual therapy).

John Y. Kao, MD, AGAF, is the current chair of the Esophageal, Gastric and Duodenal Disorders section of American Gastroenterological Association Institute, a physician investigator in the University of Michigan Center for Gastrointestinal Research, and an associate professor in the department of medicine in the division of gastroenterology & hepatology and an associate program director of the GI Fellowship Program at Michigan Medicine at the University of Michigan, Ann Arbor. He has no conflicts.

FROM THE AGA JOURNALS

Proximal adenoma location does not predict high-grade dysplasia

BY AMY KARON
MDedge News

Proximal adenoma location did not predict high-grade dysplasia in a large registry study.

In fact, the odds of high-grade dysplasia were about 25% lower for proximal versus distal adenomas (odds ratio, 0.75), reported Thomas Rösch, MD, of University Hospital Hamburg-Eppendorf, Hamburg, Germany, and his associates. A third of adenomas in the study lacked location data, but in sensitivity analyses, the odds of high-grade dysplasia fell to 0.72 when these lesions were assumed to be proximal and rose to 0.96 when assumed to be distal.

Interval colorectal cancers probably are more likely to be proximal than distal because of a "combination of endoscopy-related factors and biology," not because of histologic differences, the researchers wrote in the report, published in Clinical Gastroenterology and Hepatology.

Interval cancers are more common in the right colon, as several studies have noted. However, it is unclear whether this phenomenon represents a higher miss rate, a lower rate of successful polypectomy, or an increased risk of malignant histology in the proximal colon, the researchers wrote. Accordingly, they analyzed data on 594,614 index adenomas detected during more than 2.5 million screening colonoscopies performed between 2007 and 2012 and entered into the German National Screening Colonoscopy Registry.

A total of 3.5% of index adenomas showed high-grade dysplasia, which correlated most strongly with larger size, said the researchers. The odds of high-grade dysplasia were 10-fold higher when index adenomas were at least 1 cm than when they were smaller. High-grade dysplasia also was significantly more frequent when patients were older than 64 years, were male, and had pedunculated versus flat lesions. Given the large size of the dataset, all these associations were statistically significant.

Sessile lesions were slightly more likely to be high-grade than flat lesions, the investigators noted. Many proximal interval cancers arise from sessile serrated polyps, which may be subtle and difficult to detect or to resect completely. At the same time, colonoscopy also might be more likely to miss flat, serrated lesions when they are located proximally, and these lesions can become more aggressive over time. Thus, "[e]ndoscopist factors, such as missed lesions or incompletely removed lesions, may account for the predominance of proximal interval colorectal cancers."

Like other registry studies, this study lacked uniform histopathologic definitions or central histopathology review. The dataset also covered only the largest or most histologically remarkable adenoma for each patient. However, the findings did not change substantially after the researchers controlled for patients with missing location data, which presumably included patients with multiple polyps in both proximal and distal locations.

The researchers did not disclose external funding sources. They reported having no conflicts of interest.

ginews@gastro.org

SOURCE: Rösch T et al. Clin Gastroenterol Hepatol. 2018 Jun 11. doi: 10.1016/j.cgh.2018.05.043.

Colorectal cancers detected in a short interval after a complete and clearing colonoscopy are referred to as postcolonoscopy colon cancers or interval cancers, and are approximately three times more likely to occur in the proximal colon compared with the distal colon. Reasons for this difference are not known and possible explanations include alternative and accelerated tumor biology and rapid cancer progression, such as through the CpG island methylation phenotype pathway, missed cancers or precursor lesions in the proximal colon, or incomplete polyp resection.

DR. SHAUKAT

In the current study, the authors address whether the biology of polyps removed in the proximal colon is different; i.e., are these adenomas more likely to exhibit high-grade dysplasia compared to adenomas in the distal colon in approximately 2.5 million screening colonoscopies performed between 2007 and 2012, obtained from a screening colonoscopy registry in Germany?

The authors did not find a difference in frequency of high-grade dysplasia between proximal and distal polyps. As expected, adenoma size, male sex, and older age were associated with finding of high-grade dysplasia, but contrary to current literature, the authors found that distal location and pedunculated (versus sessile) form were associated with high-grade dysplasia. A major limitation of the study is that sessile serrated polyps were not included, and the authors did not have information on villous histology. The study reinforces the hypothesis that missed and incompletely resected adenomas play a bigger role in missed proximal cancers, and that the goal of high-quality colonoscopy should be to detect and completely resect adenomas with equal vigilance in both the proximal and distal colon.

Aasma Shaukat, MD, MPH, AGAF, is professor of medicine in the division of gastroenterology and hepatology at the University of Minnesota, Minneapolis, and the GI Section Chief at the Minneapolis VA Medical Center. She has no conflicts of interest.

FROM THE AGA JOURNALS

Antibiotics trigger proteolytic activity that leads to chronic colitis

BY WILL PASS
MDedge News

Antibiotics are associated with increased large intestinal proteolytic activity and gut barrier disruption, raising the risk of chronic colitis in susceptible individuals, a recent study found.

Although the association between antibiotics and chronic colitis has been previously described, this is the first study to demonstrate the causative role of high proteolytic activity, reported Hongsup Yoon, PhD, chair of nutrition and immunology at Technische Universität München in Freising-Weihenstephan, Germany, and colleagues.

"In the context of IBD, several clinical studies have already revealed that early and frequent antibiotic therapies, especially metronidazole or fluoroquinolone treatments, are associated with increased risk for Crohn's disease," the authors wrote in Cellular and Molecular Gastroenterology and Hepatology.

Previous studies showed that antibiotic therapy often causes high luminal proteolytic activity in the large intestine, likely because of the elimination of antiproteolytic bacteria that normally control pancreatic protease levels. Other studies have shown that exposing murine colonic mucosa to fecal supernatants with high proteolytic activity increases gut barrier permeability, which triggers chronic inflammation via translocation of luminal antigens.

"In view of these data," the authors wrote, "we hypothesized that the antibiotic-increased proteolytic activity in the large intestine is a relevant risk factor for the development of colitis in susceptible organisms."

The first component of the study used transwell experiments to evaluate the impact of high proteolytic activity on gut barrier integrity. High proteolytic activity was induced by several antibiotics, including fluoroquinolones with or without an imidazole (ciprofloxacin and levofloxacin plus or minus metronidazole), a beta-lactam (amoxicillin + clavulanate), cephalosporins with or without a macrolide (azithromycin and ceftriaxone plus or minus azithromycin), and a rifamycin (rifaximin).

"All tested antibiotic classes mediated a major proteolytic activity increase in some patients but not in others," the authors wrote, "demonstrating individual-specific vulnerability of the intestinal microbiota toward antibiotic therapies, which is likely caused by the high interindividual variability of human microbial ecosystems."

One-quarter of patients had a 400% or greater increase in large intestinal proteolytic activity following antibiotic therapy, and several had an increase greater than 900%. Analysis indicated that proteolytic activity was caused by pancreatic proteases such as chymotrypsin and trypsin.

Subsequent cell-line testing showed that stool supernatants with high proteolytic activity damaged the epithelial barrier, but samples with low proteolytic activity did not. Of note, the negative impact of high proteolytic activity on epithelial cells could be mitigated by incubating stool supernatants with a serine protease inhibitor.

In analogous experiments, mice were given a combination of vancomycin and metronidazole (V/M). In contrast with the various proteolytic activity levels observed in humans, all mice had high proteolytic activity levels following treatment, suggesting that V/M eliminated almost all antiproteolytic bacteria.

The loss of antiproteolytic bacteria was clarified by cecal microbiota transplantation tests. Transplants from untreated mice were capable of normalizing proteolytic activity levels in germ-free mice (which have high proteolytic activity levels), but transplants from V/M-treated mice were ineffective, suggesting a near-total loss of antiproteolytic bacteria. The identity of these antiproteolytic bacteria remains a mystery.

'All tested antibiotic classes mediated a major proteolytic activity increase in some patients but not in others, demonstrating individual-specific vulnerability of the intestinal microbiota toward antibiotic therapies, which is likely caused by the high interindividual variability of human microbial ecosystems.'

The next part of the study involved wild-type and interleukin (IL)-10−/− mice, the latter of which serves as a model of human colitis. Both types of mice were given V/M with or without an oral serine protease inhibitor, a potential therapy intended to limit proteolytic activity and associated intestinal barrier damage.

Although both wild-type and IL-10−/− mice had increased intestinal permeability after V/M treatment, only IL-10−/− mice showed lasting inflammation. Of note, coadministration of an oral serine protease inhibitor with V/M protected against colitis in IL-10−/− mice.

The protective benefit of an oral serine protease inhibitor in IL-10−/− mice prompts the development of antiproteolytic strategies in humans. These would target "large intestinal proteolytic activity [e.g., oral administration of encapsulated serine protease inhibitors, commensal antiproteolytic bacteria, or genetically modified bacteria expressing protease inhibitors] to protect the large intestinal mucosa from adverse effects of antibiotic-induced or diarrhea-induced high proteolytic activity," the authors wrote.

The study was funded by the Deutscher Akademischer Austauschdienst. There were no conflicts.

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SOURCE: Yoon H et al. Cell Mol Gastroenterol Hepatol. 2018 May 29. doi: 10.1016/j.jcmgh.2018.05.008.

DDSEP eight
Digestive Diseases Self-Education Program

Quick Quiz Answers

Q1. Correct Answer: D

Rationale
This patient's symptoms are most concerning for Whipple's disease in light of the diarrhea, weight loss, arthralgias, and CNS symptoms. This diagnosis requires identification of periodic acid-Schiff staining macrophages in the duodenal lamina propria. Further PCR analysis can also be used to identify RNA of the causative pathogen, *Tropheryma whipplei*. Congo Red staining is indicated if amyloidosis is suspected. Sudan staining is used to test stool for fat. Birefringence is used to detect crystals, most typically in synovial fluid. Immunohistochemistry has many applications and is commonly employed to evaluate for *H. pylori*.

Reference
1. Moos V., Schneider T. Changing paradigms in Whipple's disease and infection with *Tropheryma whipplei*. Eur J Clin Microbiol Infect Dis. 2011;30(10):1151-8.

Q2. Correct Answer: B

Rationale
The patient clinically has rumination syndrome or an adaptation to the belch reflex, with effortless regurgitation, with voluntary re-swallowing of the regurgitated material. Recurrent small bowel obstruction is less likely as the pattern of regurgitation is with almost every meal, within minutes and does not follow the typical pattern of a bowel obstruction. Idiopathic gastroparesis is less likely as the pattern of regurgitation is not consistent with gastroparesis, in addition she is not diabetic.

She has no psychiatric history and there are no findings suggestive of bulimia.

Reference
1. Marrero F.J., Shay S.S. Regurgitation and rumination. In: Richter, J.E. Castell, D.O., eds. The Esophagus, 5th ed. West Sussex, England: Wiley-Blackwell; 2012.

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AGA's investment in the future of GI

Each year, we provide more than $2 million in research funding.

What will the practice of gastroenterology look like in 20 years? It is our hope that physicians have an abundance of new tools and treatments to care for their patients suffering from digestive disorders.

How will we get there? New treatments and devices are the result of years of research.

To help make this dream a reality, AGA – through the AGA Research Foundation – has made a commitment to support investigators in GI and hepatology with its Research Awards Program. In the past year, the foundation provided over $2 million in research funding to 41 highly qualified investigators. These diverse researchers range from young investigators to more seasoned leaders in GI, all embarking on novel research projects that will advance our understanding of digestive conditions and pave the way for future discoveries in the field.

The AGA Research Foundation sincerely thanks all of its donors – without your gifts, this work wouldn't be possible.

Please join us to help spark the scientific breakthroughs of today so clinicians will have the tools to improve care tomorrow. **Donate your tax-deductible gift today at www.gastro.org/donateonline.**

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Top AGA Community patient cases

Physicians with difficult patient scenarios regularly bring their questions to the AGA Community to seek advice from colleagues about therapy and disease management options, best practices, and diagnoses.

In case you missed it, here are the most popular clinical discussions shared in the forum recently:

1. Addressing early-onset CRC
With the recommendation by the American Cancer Society to start colorectal cancer screening at 45, Dr. Samir Gupta and Dr. Peter Liang led a hearty discussion on the intended and unintended consequences of widespread implementation of these recommendations.

2. Surveillance colonoscopies in IBD patients
The question "are GIs doing too many surveillance colonoscopies in IBD patients" evolved into a call for more clinical guidance on the topic. IBD experts, AGA President Dr. David Lieberman, and the AGA Guidelines and Clinical Practice Update Committees tackle next steps and recommendations.

3. Patient case: severe colitis in asymptomatic patient
When a 51-year-old patient was seen for a colonoscopy screening, subsequent biopsies revealed severe active chronic colitis with lymphoplasmacytic infiltrate, crypts, and crypt abscesses and no granulomas. Would you treat as ulcerative colitis or wait?

4. Patient case: IBD patient with steroid dependency
A 35-year-old female who was seen for refractory diarrhea and cramps tested positive for perinuclear antineutrophil antibodies cytoplasmic (pANCA). Her symptoms resolved after she received prednisone for an unrelated issue. The physician asks: is a low dose of prednisone "safer" than Remicade (infliximab)?

More clinical cases and discussions are at https://community.gastro.org/discussions.

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A guide to talking with patients about probiotics

Two recent studies published in Cell, "Personalized Gut Mucosal Colonization Resistance to Empiric Probiotics Is Associated with Unique Host and Microbiome Features" and "Post-Antibiotic Gut Mucosal Microbiome Reconstitution Is Impaired by Probiotics and Improved by Autologous FMT," have received significant media coverage and are causing questions and concern among physicians and patients who use probiotic supplements.

The AGA Center for Gut Microbiome Research and Education provides three reminders for talking to your patient about probiotics:

1. Probiotics are generally thought to be safe for healthy individuals, but we don't know the long-term consequences. For individuals who have a chronic disease, are immunocompromised, or otherwise vulnerable (such as the elderly), patients should seek guidance from physicians on whether probiotics may be appropriate for them. In general, probiotics should not be used indiscriminately; potential risk and benefit should be considered as for all human interventions.

2. This research does not conclude that probiotics are unsafe or useless for everyone. However, the results suggest that individuals may respond very differently to the same probiotic product depending on their diet, genetics, microbiome, and other aspects of their health. Experts are trying to better understand which bacteria are best for whom, under which conditions as we transition from an era of empiric medicine to precision medicine.

3. Probiotics currently on the market are foods or dietary supplements. To date, no probiotic products have been approved by the Food and Drug Administration to treat, mitigate, cure, or prevent specific diseases.

AGA has recently developed educational materials for patients on probiotics, which can be accessed at www.gastro.org/probiotics in English and Spanish. Share this resource with your patients by printing it out, emailing it, or uploading it to your patient portal.

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AGA advocates on Capitol Hill

Thank you to members who met with their congressperson and who participated in Virtual Advocacy Day.

Advocates met with House and Senate offices to push for passage of the Removing Barriers to Colorectal Cancer Screening Act, legislation that waives the coinsurance for screening colonoscopies that become therapeutic and has broad, bipartisan and bicameral support. They made the argument that paying for prevention services saves the government money in the long term by preventing treatment costs on cancer treatment.

H.R. 2077, the Restoring Patient's Voice Act, addresses step therapy protocols that threaten the physician-patient relationship and delay timely treatment to care. Support for the legislation is growing and our advocates were able to relay experiences they have encountered with their patients' care being delayed and also the administrative burden this policy places on practices.

Katherine Clark, D-Mass., a member of the House Labor-HHS Appropriations Subcommittee, met with our advocates and let them know that the House-Senate conferees agreed to the $2 billion increase in NIH funding in the final bill. Rep. Clark is a strong supporter of NIH and called it the "pillar of our economy." AGA members encouraged their legislators to support the final Labor-HHS package that includes this $2 billion increase, which amounts to a 5.5% increase. The Senate recently approved the final agreement on Labor-HHS for fiscal year 2019 and we call on the House to follow suit.

AGA appreciates all those advocates who took time out of their busy schedules to advocate on behalf of their colleagues and patients. We also appreciate those who took time to participate in Virtual Advocacy Day. Remember, if we don't advocate for GI, no one will.

To learn more about how you can get involved, visit www.gastro.org/advocacy.

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For information about UPMC Complex Care Connect™, visit **careconnect.upmc.com**.

In Focus
Brought To You By The New Gastroenterologist

Endoscopic management of obesity

BY PICHAMOL JIRAPINYO, MD, MPH, ABOM AND CHRISTOPHER C. THOMPSON, MD, MSC, FASGE, AGAF, FACG

Dr. Jirapinyo is an advanced and bariatric endoscopy fellow, Brigham and Women's Hospital, Harvard Medical School, Boston; **Dr. Thompson** is director of therapeutic endoscopy, Brigham and Women's Hospital, and associate professor of medicine, Harvard Medical School. Dr. Jirapinyo has served as a consultant for GI Dynamics and holds royalties for Endosim. Dr. Thompson has contracted research for Aspire Bariatrics, USGI Medical, Spatz, and Apollo Endosurgery; has served as a consultant for Boston Scientific, Covidien, USGI Medical, Olympus, and Fractyl; holds stocks and royalties for GI Windows and Endosim, and has served as an expert reviewer for GI Dynamics.

Obesity is a rising pandemic. As of 2016, 93.3 million U.S. adults had obesity, representing 39.8% of our adult population.[1] It is estimated that approximately $147 billion is spent annually on caring for patients with obesity. Traditionally, the management of obesity includes lifestyle therapy (diet and exercise), pharmacotherapy (six Food and Drug Administration–approved medications for obesity), and bariatric surgery (sleeve gastrectomy [SG] and Roux-en-Y gastric bypass [RYGB]). Nevertheless, intensive lifestyle intervention and pharmacotherapy are associated with approximately 3.1%-6.6% total weight loss (TWL),[2-7] and bariatric surgery is associated with 20%-33.3% TWL.[8] However, less than 2% of patients who are eligible for bariatric surgery elect to undergo surgery, leaving a large proportion of patients with obesity untreated or undertreated.[9]

Endoscopic bariatric and metabolic therapies (EBMTs) encompass an emerging field for the treatment of obesity. In general, EBMTs are associated with greater weight loss than are lifestyle intervention and pharmacotherapy, but with a less- invasive risk profile than bariatric surgery. EBMTs may be divided into two general categories – gastric and small bowel interventions (Figure 1 and Table 1, page 19). Gastric EBMTs are effective at treating obesity, while small bowel EBMTs are effective at treating metabolic diseases with a variable weight loss profile depending on the device.[10,11]

Of note, a variety of study designs (including retrospective series, prospective series, and randomized trials with and without shams) have been employed, which can affect outcomes. Therefore, weight loss comparisons among studies are challenging and should be considered in this context.

GASTRIC INTERVENTIONS

Currently, there are three types of EBMTs that are FDA approved and used for the treatment of obesity. These include intragastric balloons (IGBs), plications and suturing, and aspiration therapy (AT). Other technologies that are under investigation also will be briefly covered.

Intragastric balloons

An intragastric balloon is a space-occupying device that is placed in the stomach. The mechanism of action of IGBs involves delaying gastric emptying, which leads to increased satiety.[12] There are several types of IGBs available worldwide differing in techniques of placement and removal (endoscopic versus fluoroscopic versus swallowable), materials used to fill the balloon (fluid-filled versus air-filled), and the number of balloons placed (single versus duo versus three-balloon). At the time of this writing, three IGBs are approved by the FDA (Orbera, ReShape, and Obalon), all for patients with body mass indexes of 30-40 kg/m^2, and two others are in the process of obtaining FDA approval (Spatz and Elipse).

Orbera gastric balloon (Apollo Endosurgery, Austin, Tex.) is a single fluid-filled IGB that is endoscopically placed and removed at 6 months. The balloon is filled with 400-700 cc of saline with or without methylene blue (to identify leakage or rupture). Recently, Orbera365, which allows the balloon to stay for 12 months instead of 6 months, has become available in Europe; however, it is yet to be approved in the United States. The U.S. pivotal trial (Orbera trial) including 255 subjects (125 Orbera arm versus 130 non-sham control arm) demonstrated 10.2% TWL in the Orbera group compared with 3.3% TWL in the control group at 6 months based on intention-to-treat (ITT) analysis. This difference persisted at 12 months (6 months after explantation) with 7.6% TWL for the Orbera group versus 3.1% TWL for the control group.[13,14]

ReShape integrated dual balloon system (ReShape Lifesciences, San Clemente, Calif.) consists of two connected fluid-filled balloons that are endoscopically placed and removed at 6 months. Each balloon is filled with 375-450 cc of saline mixed with methylene blue. The U.S. pivotal trial (REDUCE trial) including 326 subjects (187 ReShape arm versus 139 sham arm) demonstrated 6.8% TWL in the ReShape group compared with 3.3% TWL in the sham group at 6 months based on ITT analysis.[15,16]

Obalon balloon system (Obalon Therapeutics, Carlsbad, Calif.) is a swallowable, gas-filled balloon system that requires endoscopy only for removal. During placement, a capsule is swallowed under fluoroscopic guidance. The balloon is then inflated with 250 cc of nitrogen mix gas prior to tube detachment. Up to three balloons may be swallowed sequentially at 1-month intervals. At 6 months from the first balloon placement, all balloons are removed endoscopically. The U.S. pivotal trial (SMART trial) including 366 subjects (185 Obalon arm versus 181 sham capsule arm) demonstrated 6.6% TWL in the Obalon group compared with 3.4% TWL in the sham group at 6 months based on ITT analysis.[17,18]

Two other balloons that are currently under investigation in the United States are the Spatz3 adjustable balloon system (Spatz Medical, Great Neck, N.Y.) and Elipse balloon (Allurion Technologies, Wellesley, Mass.). The Spatz3 is a fluid-filled balloon that is placed and removed endoscopically. It consists of a single balloon and a connecting tube that allows volume adjustment for control of symptoms and possible augmentation of weight loss. The U.S. pivotal trial was recently completed and the data are being reviewed by the FDA. The Elipse is a swallowable fluid-filled balloon that does not require endoscopy for placement or removal. At 4 months, the bal-

Continued on page 23

Gastroenterologists are becoming increasing involved in the management of obesity. While prior therapy for obesity was mainly based on lifestyle changes, medication, or surgery, the new and exciting field of endoscopic bariatric and metabolic therapies has recently garnered incredible attention and momentum.

In this quarter's In Focus article, brought to you by *The New Gastroenterologist*, Pichamol Jirapinyo and Christopher Thompson (Brigham and Women's Hospital) provide an outstanding overview of the gastric and small bowel endoscopic interventions that are either already approved for use in obesity or currently being studied. This field is moving incredibly fast, and knowledge and understanding of these endoscopic therapies for obesity will undoubtedly be important for our field.

Bryson W. Katona, MD, PhD
Editor in Chief, The New Gastroenterologist

Figure 1

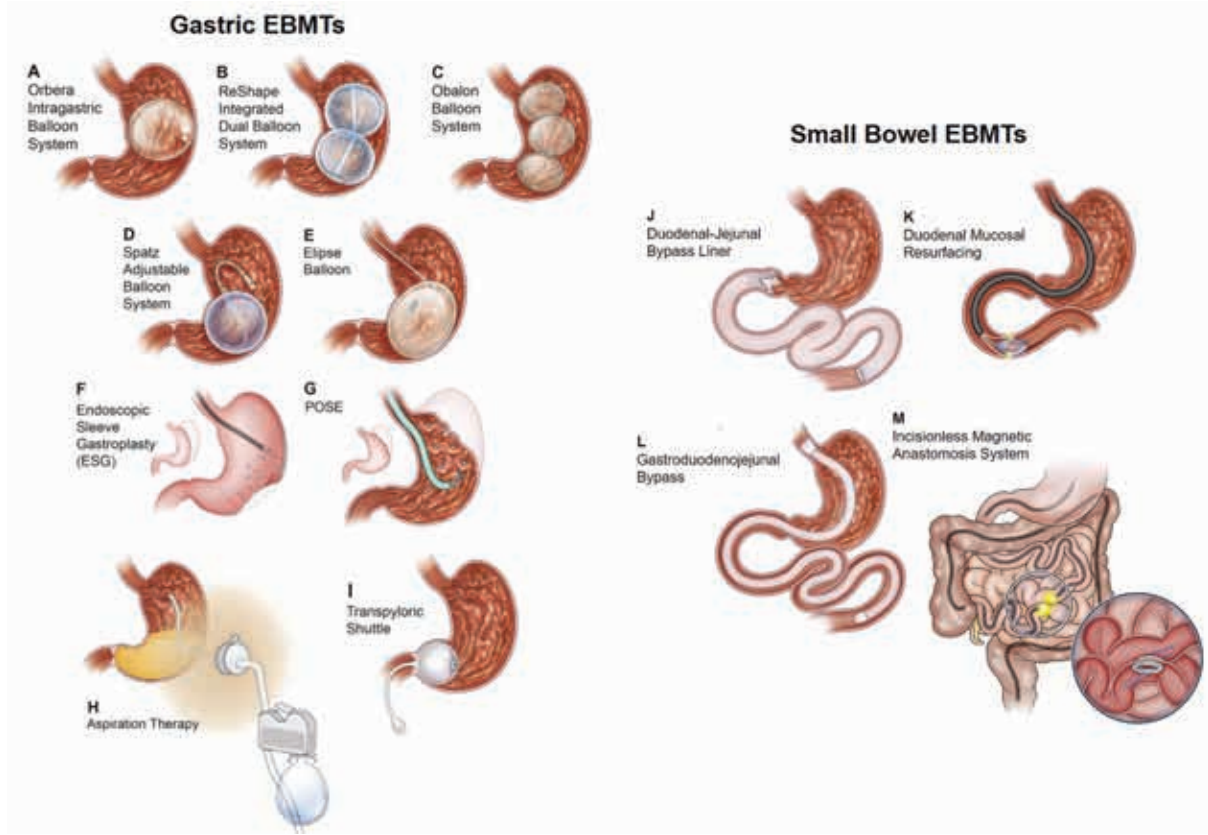

Figure 1. Endoscopic bariatric and metabolic therapies (EBMTs): A) Orbera intragastric balloon system, B) ReShape integrated dual balloon system, C) Obalon balloon system, D) Spatz adjustable balloon system, E) Elipse balloon, F) endoscopic sutured/sleeve gastroplasty (ESG), G) primary obesity surgery endoluminal (POSE), H) aspiration therapy, I) transpyloric shuttle, J) duodenal-jejunal bypass liner, K) duodenal mucosal resurfacing, L) gastroduodenojejunal bypass, M) incisionless magnetic anastomosis system. This figure was adapted from an article published in Clinical Gastroenterology and Hepatology 2017;15(5):619-30. Copyright Elsevier and AGA Institute (2017).

Table 1. Primary endoscopic bariatric and metabolic therapies

Endoscopic bariatric and metabolic therapies (EBMTs)	Manufacturer	Description	FDA approval
Gastric interventions			
Orbera gastric balloon	Apollo Endosurgery, Austin, TX	• Single fluid-filled balloon • Endoscopic placement and removal • Filled with 400-700 cc of saline	• BMI 30-40 kg/m^2 • Age 22 or older
ReShape integrated dual balloon system	ReShape Lifesciences, San Clemente, CA	• Two connected fluid-filled balloons • Endoscopic placement and removal • Each balloon filled with 375-450 cc of saline with methylene blue	• BMI 30-40 kg/m^2 with one obesity-related comorbidity • Age 22-60
Obalon balloon system	Obalon Therapeutics, Carlsbad, CA	• Gas-filled balloon • Swallowable with fluoroscopic guidance for placement and endoscopic removal • Three balloons administered over 9- to 12-week period • Each balloon filled with 250 cc of a nitrogen mix gas	• BMI 30-40 kg/m^2 • Age 22 or older
Spatz3 adjustable balloon system	Spatz Medical, Great Neck, NY	• Single fluid-filled balloon with a connecting tube for volume adjustment • Endoscopic placement and removal • Filled with 400-550 cc of saline with methylene blue • Volume may be adjusted down to 300 cc or up to 800 cc	• Under FDA review
Elipse balloon	Allurion Technologies, Wellesley, MA	• Single fluid-filled balloon • Swallowable with fluoroscopic guidance for placement and self-emptying mechanism at 4 months for removal • Filled with 550 cc of saline	• In U.S. clinical trial • Not currently FDA approved
Primary obesity surgery endoluminal (POSE)	USGI Medical, San Clemente, CA	• One of the applications of the Incisionless Operating Platform (IOP) • Endoscopic plications of the gastric fundus and/or body	• Device approved for the general indication of tissue apposition
Endoscopic sleeve gastroplasty (ESG)	Apollo Endosurgery, Austin, TX	• One of the applications of the Overstitch Endoscopic Suturing System • Endoscopic suturing along the greater curvature of the stomach to create a sleeve-like structure	• Device approved for the general indication of tissue apposition
Aspiration therapy	Aspire Bariatrics, King of Prussia, PA	• 26-French gastrostomy tube with 15-cm internal fenestrated drainage catheter • Endoscopic placement and removal • Patients aspirate 25% to 30% of ingested calories at 30 minutes after meals	• BMI 35-55 kg/m^2 • Age 22 or older
Transpyloric shuttle	BAROnova Inc., Goleta, CA	• A spherical bulb tethered to a smaller cylindrical bulb • Endoscopic placement and removal • Located across the pylorus creating intermittent obstruction	• Under FDA review
Small-bowel interventions			
Duodenal-jejunal bypass liner	GI Dynamics, Boston	• A 60-cm fluoropolymer liner anchored at the duodenal bulb and ending at the jejunum • Endoscopic placement and removal	• In U.S. clinical trial • Not currently FDA approved
Duodenal mucosal resurfacing	Fractyl, Lexington, MA	• Endoscopic thermal ablation of the duodenal mucosa using a balloon filled with heated water	• In U.S. clinical trial • Not currently FDA approved
Gastroduodenal-jejunal bypass	ValenTx Inc., Hopkins, MN	• A 120-cm sleeve anchored at the gastroesophageal junction and ending at the jejunum	• Not currently FDA approved
Incisionless magnetic anastomosis system	GI Windows, West Bridgewater, MA	• Self-assembling magnets that form a compression anastomosis between the jejunum and ileum	• Not currently FDA approved

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loon releases fluid allowing it to empty and pass naturally. The U.S. pivotal trial (ENLIGHTEN trial) is currently underway.

A meta-analysis of randomized controlled trials revealed improvement in most metabolic parameters (diastolic blood pressure, fasting glucose, hemoglobin A_{1c}, and waist circumference) following IGB compared with controls.[19] Nausea and vomiting are seen in approximately 30% and should be addressed appropriately. Pooled serious adverse event (SAE) rate was 1.5%, which included migration, perforation, and death. Since 2016, 14 deaths have been reported according to the FDA MAUDE database. Corporate response was that over 295,000 balloons had been distributed worldwide with a mortality rate of less than 0.01%.[20]

Plication and suturing

Currently, there are two endoscopic devices that are approved for the general indication of tissue apposition. These include the Incisionless Operating Platform (IOP) (USGI Medical, San Clemente, Calif.) and the Overstitch endoscopic suturing system (Apollo Endosurgery, Austin, Tex.). These devices are used to remodel the stomach to create a sleeve-like structure to induce weight loss.

The IOP system consists of a transport, which is a 54-Fr flexible endoscope. It consists of four working channels that accommodate a G-Prox (for tissue approximation), a G-Lix (for tissue grasping), and an ultrathin endoscope (for visualization). In April 2008, Horgan performed the first-in-human primary obesity surgery endoluminal (POSE) procedure in Argentina. The procedure involves the use of the IOP system to place plications primarily in the fundus to modify gastric accommodation.[21] The U.S. pivotal trial (ESSENTIAL trial) including 332 subjects (221 POSE arm versus 111 sham arm) demonstrated 5.0% TWL in the POSE group compared with 1.4% in the sham group at 12 months based on ITT analysis.[22] A European multicenter randomized controlled trial (MILEPOST trial) including 44 subjects (34 POSE arm versus 10 non-sham control arm) demonstrated 13.0% TWL in the POSE group compared with 5.3% TWL in the control group at 12 months.[23] A recent meta-analysis including five studies with 586 subjects showed pooled weight loss of 13.2% at 12-15 months following POSE with a pooled serious adverse event rate of 3.2%.[24] These included extraluminal bleeding, minor bleeding at the suture site, hepatic abscess, chest pain, nausea, vomiting, and abdominal pain. A distal POSE procedure with a new plication pattern focusing on the gastric body to augment the effect on gastric emptying has also been described.[25]

Figure 2

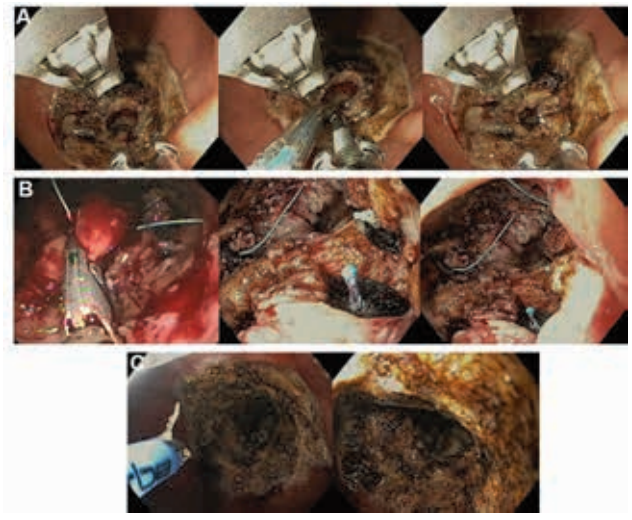

Figure 2. Endoscopic treatments of weight regain following Roux-en-Y gastric bypass: A) transoral outlet reduction (TORe), B) restorative obesity surgery endoluminal (ROSE), C) argon plasma coagulation (APC).

The Overstitch is an endoscopic suturing device that is mounted on a double-channel endoscope. At the tip of the scope, there is a curved suture arm and an anchor exchange that allow the needle to pass back and forth to perform full-thickness bites. The tissue helix may also be placed through the second channel to grasp tissue.

In April 2012, Thompson performed the first-in-human endoscopic sutured/sleeve gastroplasty (ESG) procedure in India, which was published together with cases performed in Panama and the Dominican Republic.[26-28] This procedure involves the use of the Overstitch device to place several sets of running sutures along the greater curvature of the stomach to create a sleeve-like structure. It is thought to delay gastric emptying and therefore increase satiety.[29] The largest multicenter retrospective study including 248 patients demonstrated 18.6% TWL at 2 years with 2% SAE rate including perigastric fluid collections, extraluminal hemorrhage, pulmonary embolism, pneumoperitoneum, and pneumothorax.[30]

Aspiration therapy

Aspiration therapy (AT; Aspire Bariatrics, King of Prussia, Pa.) allows patients to remove 25%-30% of ingested calories at approximately 30 minutes after meals. AT consists of an A-tube, which is a 26-Fr gastrostomy tube with a 15-cm fenestrated drainage catheter placed endoscopically via a standard pull technique. At 1-2 weeks after A-tube placement, the tube is cut down to the skin and connected to the port prior to aspiration. AT is approved for patients with a BMI of 35-55 kg/m^2.[31] The U.S. pivotal trial (PATHWAY trial) including 207 subjects (137 AT arm versus 70 non-sham control arm) demonstrated 12.1% TWL in the AT group compared to 3.5% in the control group at 12 months based on ITT analysis. The SAE rate was 3.6% including severe abdominal pain, peritonitis, prepyloric ulcer, and A-tube replacement due to skin-port malfunction.[32]

Transpyloric shuttle

The transpyloric shuttle (TPS; BAROnova, Goleta, Calif.) consists of a spherical bulb that is attached to a smaller cylindrical bulb by a flexible tether. It is placed and removed endoscopically at 6 months. TPS resides across the pylorus creating intermittent obstruction that may result in delayed gastric emptying. A pilot study including 20 patients demonstrated 14.5% TWL at 6 months.[33] The U.S. pivotal trial (ENDObesity II trial) was recently completed and the data are being reviewed by the FDA.

Revision for weight regain following bariatric surgery

Weight regain is common following RYGB[34,35] and can be associated with dilation of the gastrojejunal anastomosis (GJA).[36] Several procedures have been developed to treat this condition by focusing on reduction of GJA size and are available in the United States (Figure 2). These procedures have level I evidence supporting their use and

Continued from previous page

include transoral outlet reduction (TORe) and restorative obesity surgery endoluminal (ROSE).[37] TORe involves the use of the Overstitch to place sutures at the GJA. At 1 year, patients had 8.4% TWL with improvement in comorbidities.[38] Weight loss remained significant up to 3-5 years.[39,40] The modern ROSE procedure utilizes the IOP system to place plications at the GJA and distal gastric pouch following argon plasma coagulation (APC). A small series showed 12.4% TWL at 6 months.[41] APC is also currently being investigated as a standalone therapy for weight regain in this population.

SMALL BOWEL INTERVENTIONS

There are several small bowel interventions, with different mechanisms of action, available internationally. Many of these are under investigation in the United States; however, none are currently FDA approved.

Duodenal-jejunal bypass liner

Duodenal-jejunal bypass liner (DJBL; GI Dynamics, Boston, Mass.) is a 60-cm fluoropolymer liner that is endoscopically placed and removed at 12 months. It is anchored at the duodenal bulb and ends at the jejunum. By excluding direct contact between chyme and the proximal small bowel, DJBL is thought to work via foregut mechanism where there is less inhibition of the incretin effect (greater increase in insulin secretion following oral glucose administration compared to intravenous glucose administration due to gut-derived factors that enhance insulin secretion) leading to improved insulin resistance. In addition, the enteral transit of chyme and bile is altered suggesting the possible role of the hindgut mechanism. The previous U.S. pivotal trial (ENDO trial) met efficacy endpoints. However, the study was stopped early by the company because of a hepatic abscess rate of 3.5%, all of which were treated conservatively.[42] A new U.S. pivotal study is currently planned. A meta-analysis of 17 published studies, all of which were from outside the United States, demonstrated a significant decrease in hemoglobin A_{1c} of 1.3% and 18.9% TWL at 1 year following implantation in patients with obesity with concomitant diabetes.[43]

Duodenal mucosal resurfacing

Duodenal mucosal resurfacing (Fractyl, Lexington, Mass.) involves saline lifting of the duodenal mucosa circumferentially prior to thermal ablation using an inflated balloon filled with heated water. It is hypothesized that this may reset the diseased duodenal enteroendocrine cells leading to restoration of the incretin effect. A pilot study including 39 patients with poorly controlled diabetes demonstrated a decrease in hemoglobin A_{1c} of 1.2%. The SAE rate was 7.7% including duodenal stenosis, all of which were treated with balloon dilation.[44] The U.S. pivotal trial is currently planned.

Gastroduodenal-jejunal bypass

Gastroduodenal-jejunal bypass (ValenTx., Hopkins, Minn.) is a 120-cm sleeve that is anchored at the gastroesophageal junction to create the anatomic changes of RYGB. It is placed and removed endoscopically with laparoscopic assistance. A pilot study including 12 patients demonstrated 35.9% excess weight loss at 12 months. Two out of 12 patients had early device removal due to intolerance and they were not included in the weight loss analysis.[45]

Incisionless magnetic anastomosis system

The incisionless magnetic anastomosis system (GI Windows, West Bridgewater, Mass.) consists of self-assembling magnets that are deployed under fluoroscopic guidance through the working channel of colonoscopes to form magnetic octagons in the jejunum and ileum. After a week, a compression anastomosis is formed and the coupled magnets pass spontaneously. A pilot study including 10 patients showed 14.6% TWL and a decrease in hemoglobin A_{1c} of 1.9% (for patients with diabetes) at 1 year.[46] A randomized study outside the United States is currently underway.

SUMMARY

Endoscopic bariatric and metabolic therapies are emerging as first-line treatments for obesity in many populations. They can serve as a gap therapy for patients who do not qualify for surgery, but also may have a specific role in the treatment of metabolic comorbidities. This field will continue to develop and improve with the introduction of personalized medicine leading to better patient selection, and newer combination therapies. It is time for gastroenterologists to become more involved in the management of this challenging condition.

See references at mdedge.com/gihepnews

Findings reinforce risks of obesity

Weight gain *from page 1*

adults younger than 50 years, said investigator Po-Hong Liu, MD, of Washington University, St. Louis, and coauthors.

"Given that most of these younger cases are diagnosed symptomatically with more advanced tumors and with a significant influence on years of life lost, our findings reinforce the benefits of maintaining a healthy weight throughout life," Dr. Liu and coinvestigators said in their report.

Their analysis was based on the ongoing Nurses Health Study II, which began in 1989 and enrolled a total of 116,430 women between the ages of 25 and 42 years in 14 U.S. states. Women completed questionnaires on demographics, medical and health information, and lifestyle factors every 2 years after enrollment.

Dr. Liu and colleagues were able to document 114 cases of colorectal cancer over a median of 13.9 years of follow-up in 85,256 women who had no cancer or inflammatory bowel disease when they were enrolled in the study. The median age at diagnosis for these cancers was 45 years.

'Given that most of these younger cases are diagnosed ... with more advanced tumors and with a significant influence on years of life lost, our findings reinforce the benefits of maintaining a healthy weight throughout life.'

Obesity was independently associated with increased risk of these early-onset colorectal cancers, the investigators found in multivariable analysis.

Women with a body mass index of 30 kg/m^2 or higher had a relative risk of 1.93 (95% confidence interval, 1.15-3.25) versus women with normal BMIs in the 18.5 to 22.9-kg/m^2 range, according to results of the analysis, they reported.

There was an apparent linear trend between increasing weight and increasing colorectal cancer risk, they added in their report.

They also found links between BMI in early adulthood and risk of early-onset colorectal cancer, including a relative risk of 1.63 for women who reported a BMI of 23 kg/m^2 or higher at 18 years of age, versus women with a BMI of 18.5-20.9 kg/m^2 at that age.

Similarly, increase in weight since early adulthood was associated with increased cancer risk, they reported.

While the link between excess weight and colorectal cancer incidence and mortality is well established in previous studies, this study is one of few reports looking at the association in younger individuals, according to Dr. Liu and colleagues.

This is thought to be the first prospective study looking at the link between obesity and risk of colorectal cancer diagnosed before the age of 50, they added.

The study was funded by grants from the National Institutes of Health. Dr. Liu had no conflict of interest disclosures related to the study. One coauthor reported consulting fees from Bayer Pharma AG, Janssen, and Pfizer.

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SOURCE: Liu P-H et al. JAMA Oncol. 2018 Oct 11. doi: 10.1001/jamaoncol.2018.4280.

AGA Resource
Visit the AGA GI Patient Center for education to share with your patients about obesity, colorectal cancer and other GI disorders at patient.gastro.org.

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GI & HEPATOLOGY NEWS

THE OFFICIAL NEWSPAPER OF THE AGA INSTITUTE

Team-based care is challenging

Medical home *from page 1*

The major attributes of a medical home, he explained, are accessibility; comprehensive, coordinated care; compassionate, culturally sensitive, patient- and family-centered care; and team-based delivery.

After initially building an IBD medical home in Pittsburgh, Dr. Regueiro brought the concept to Cleveland Clinic and shared with attendees how he did it and the challenges and benefits it involved.

He advises starting with a small team and expanding as demands or needs dictate. He began with a GI specialist, a psychiatrist, a dietitian, a social worker, a nurse, and three in-house schedulers. The patient ratio was 500 patients per nurse and 1,000 patients per gastroenterologist, psychiatrist, and dietitian.

Key clinical point
Total ED visits dropped by 47% from the year before the medical home total care model was implemented to the year after; hospitalizations similarly declined by a third 36%.

Dr. Regueiro explained the patient flow through the medical home, starting with a preclinic referral and patient questionnaire. The actual visit moves from intake and triage to the actual exam to a comprehensive care plan involving all relevant providers, plus any necessary referrals to any outside services, such as surgery or pain management. The work continues, however, after the patient leaves the clinic, with follow-up calls and telemedicine follow-up, including psychosocial telemedicine.

The decision to include in-house schedulers is among the most important, though it may admittedly be one of the more difficult for those trying to build a medical home from the ground up.

"I think that central scheduling is the worst thing that's ever happened to medicine," Dr. Regueiro told attendees. It's too depersonalized to serve patients well, he said. His center's embedded schedulers begin the clinical experience from a patient's first phone call. They ask patients their top-three problems and the top-three things they want from their visit.

"If we don't ask our patients what they want, the focus becomes physician centered instead of patient centered," Dr. Regueiro said, sharing anecdotes of patients who came in with problems, expectations, and requests that differed, sometimes dramatically, from what he anticipated. Many of these needs were psychosocial, and the medical home model is ideally suited to address them in tandem with physical medical care.

"I firmly believe that the secret sauce of all our medical homes is the psychosocial care of patients by understanding the interactions between biological and environmental factors in the mind-body illness interface," he said.

The center also uses provider team huddles before meeting a patient at intake and then afterward for follow-up. Part of team communication involves identifying patients as "red," "yellow," or "green" based on the magnitude of their needs and care utilization.

"There are a lot of green-zone pa-

tients: They see you once a year and really don't need the intensive care" his clinic can provide, he said. "We did as much as we could to keep the patient at home, in their community, at school, more than anything else," Dr. Regueiro said. "It's not just about their quality of life and disease but about the impact on their work-life balance."

One way the clinic addressed those needs was by involving patient stakeholders to find out early on – as they were setting up the center – what the patient experience was and what needed to improve. As they learned about logistical issues that frustrated the patient experience, such as lost medical records, central scheduling, or inadequate parking, they could work to identify solutions – thereby also addressing patients' psychosocial needs.

But Dr. Regueiro was upfront about the substantial investment and challenges involved in setting up an IBD medical home. He would not have been able to meet his relative value–unit targets in this model, so those were cut in half. When an audience member asked how the clinic successfully worked with a variety of commercial insurers given the billing challenges, Dr. Regueiro said he didn't have a good answer, though several large insurers have approached him with interest in the model.

"I do think the insurers are interested because of the cost [savings] part of this."

Those cost savings showed up in the long-term outcomes. At the Pittsburgh center, total emergency department visits dropped by nearly half (47%) from the year before the medical home total care model was implemented to the year after, from 508 total ED visits among the patient population to 264 visits. Hospitalizations similarly declined by a third (36%), from 208 to 134.

Part of the reason for that decline, as Dr. Regueiro showed in a case study example, was halting the repetitive testing and interventions in the ED that did not actually address – or even find out – the patient's needs, particularly when those needs were psychosocial. And many psychosocial needs could even be met outside the clinic: 35% of all behavioral visits were telemedicine.

Still, payment models remain a challenge for creating medical homes. Other challenges include preventing team burnout, which can also deter interest in this model in the first place, and the longitudinal coordination of care with the medical neighborhood.

Despite his caveats, Dr. Regueiro's presentation made a strong impression on attendees.

Mark Tsuchiyose, MD, a gastroenterologist with inSite Digestive Health Care in Daly City, Calif., found the presentation "fantastic" and said using medical homes for chronic GI care is "unquestionably the right thing to do." But the problem, again, is reimbursement and a payer model that works with a medical home, he said. Dr. Regueiro needed to reduce his relative value–unit targets and was able to get funding for the care team, including in-house schedulers, Dr. Tsuchiyose noted, and that's simply not feasible for most providers in most areas right now.

Sanjay Sandhir, MD, of Dayton (Ohio) Gastroenterology, said he appreciated the discussion of patient engagement apps in the medical home and helping patients with anxiety, depression, stress, and other psychosocial needs. While acknowledging the payer hurdles to such a model, he expressed optimism.

"If we go to the payers, and the payers are willing to understand and can get their head around and accept [this model], and we can give good data, it's possible," Dr. Sandhir said.

John Garrett, MD, a gastroenterologist with Mission Health and Asheville (N.C.) Gastroenterology, said he found the talk – and the clinic itself – "truly amazing."

"It truly requires a multidisciplinary approach to identify the problems your IBD patients have and manage them most effectively," he said. But the model is also "incredibly labor intensive," he added.

"I think few of us could mobilize a team as large, effective, and well funded as his, but I think we can all take pieces of that and do it on a much more economical level, and still get good results," he said, "I think most important would be to identify whether significant psychosocial issues are present and be ready to treat those."

Dr. Regueiro has consulted for Abbvie, Allergan, Amgen, Celgene, Janssen, Pfizer, Takeda, and UCB, and has received research grants from Abbvie, Janssen, and Takeda. Dr. Tsuchiyose, Dr. Sandhir, and Dr. Garrett had no disclosures.

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Gastroenterology has released a special collection of IBD articles, which gathers the best IBD research published over the past 2 years. View it at https://www.gastrojournal.org/content/inflammatory_bowel_disease.

Black patients present sicker, get more transplants

BY JEFF CRAVEN
MDedge News

PHILADELPHIA – Black patients are more likely to be put on a transplant list because of acute liver failure, be listed as status 1, and receive a liver transplant, compared with white patients, according to a recent presentation at the annual meeting of the American College of Gastroenterology.

Lauren D. Nephew, MD, MSCE, of Indiana University in Indianapolis, and her colleagues performed a retrospective cohort study of black and white patients with a minimum age of 18 years in the United Network of Organ Sharing database who were wait-listed for a liver transplantation during 2002-2016. They examined patient clinical characteristics, acute liver failure (ALF) etiologies, wait-list status, and posttransplant survival outcomes through Kaplan Meier analysis.

"We really wanted to explore this topic in patients with acute liver failure, some of the sickest patients that we see," Dr. Nephew said in her presentation. "We wanted to really

Continued on following page

JEFF CRAVEN/MDEDGE NEWS

Dr. Lauren D. Nephew and colleagues analyzed the UNOS database, 2002-2016.

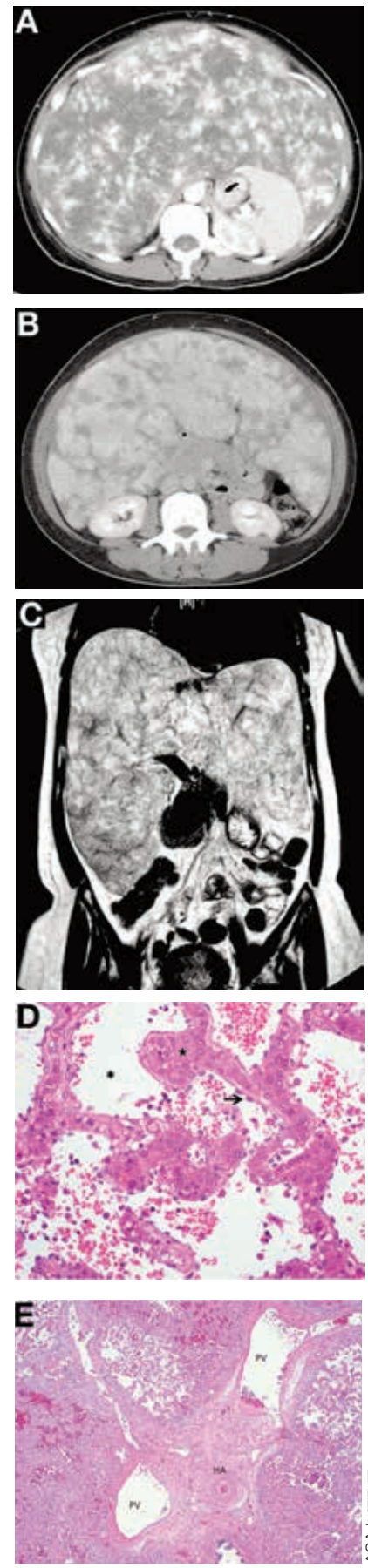
CLINICAL CHALLENGES AND IMAGES

What is your diagnosis?

By Anand Kumar, MD, William W. Bivin, Jr., MD, and Katherine Sun, MD, PhD. Published previously in Gastroenterology (2016;151[6]:1081-2).

A 50-year-old Guyanese woman was found to have abnormal liver tests on routine testing with total bilirubin, 1.8 mg/dL (normal, 0.2–1.2); alkaline phosphatase, 189 U/L (normal, 47–154); aspartate transaminase, 57 U/L (normal, 11–42); and alanine transaminase, 33 U/L (normal, 0–20). Besides chronic fatigue, she was asymptomatic. Contrast-enhanced computed tomography of the abdomen revealed marked hepatomegaly and innumerable progressively enhancing lesions throughout the liver (Figure A, arterial phase; Figure B, delayed phase). On T2-weighted magnetic resonance imaging, the nodules displayed hyperintense signals (Figure C). A liver biopsy demonstrated a honeycomb meshwork of dilated, telangiectatic sinusoidal channels formed by cords of hepatocytes and fibrovascular tissue and lined by a distinctive nonproliferating endothelium (Figure D, stain: hematoxylin and eosin; original magnification: ×400; asterisk, vascular channels; arrow, endothelium; star, cords of hepatocytes); and dilated portal vein branches expanding the portal tracts and extending into periportal areas (Figure E, stain: hematoxylin and eosin; original magnification: ×40; PV, portal vein; HA, hepatic artery; BD, bile duct). She denied history of skin lesions, bone pain, or similar disease in family members. Magnetic resonance imaging of the brain and computed tomography of the chest and bone scan showed no evidence of vascular lesions. Her blood alpha-fetoprotein level was normal.

See the diagnosis on page 34.



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determine whether or not there were differences in clinical characteristics and etiologies of acute liver failure in patients by race who are listed for liver transplantation."

"Then, we wanted to compare wait-list outcomes," she added, such as "differences by race in liver transplantation or wait-list removal because of death or becoming too sick for transplant."

There were 11,289 patients in the white ALF group and 2,112 patients in the black ALF group; 2,876 (25.5%) of patients in the white ALF and 790 (37.4%) in the black ALF group were listed as status 1, which indicated an expected survival of 7 days or less. There were similar clinical characteristics for the white and black ALF status 1 patients regarding age (34.2 vs. 36.3 years), Model for End-Stage Liver Disease (MELD) score (34 vs. 36; *P* less than .001), international normalized ratio (INR) test (mean 4.5 vs. mean 5.0; *P* = .001), creatinine levels (2.1 vs. 1.9 mg/dL; *P* less than .001), and percentage of patients who were hepatic encephalopathy grade 3 or 4 (60.0% vs. 63.2%; *P* = .10). However, Dr. Nephew noted significantly higher bilirubin levels in the black ALF status 1 cohort (17.9 mg/dL), compared with the white ALF status 1 cohort (11.3 mg/dL; *P* less than .001).

'White patients were significantly more likely to be removed from the wait-list because of improvement, compared with black patients.'

The causes for ALF in each group included drug-induced liver failure (white status 1 cohort, 34.1%; black status 1 cohort, 20.6%), autoimmune hepatitis (2.7% vs. 9.4%), Wilson's disease (0.58% vs. 0.13%), unknown etiology (34.5% vs. 42.5%), and other etiology (22.9% vs. 17%). Black patients were more likely to be listed to status 1 and transplanted at 62% (490 patients), compared with white patients at 53% (1,524 patients). There were 713 white patients (24.8%) removed from the transplant list, compared with 114 (13.8%) of black patients.

"If you are transplanted and you don't die, then you are likely removed from the list for other reasons, and the most common reason is that you improved and became well, and so white patients were significantly more likely to be removed from the wait-list because of improvement, compared with black patients," Dr. Nephew said.

In a competing risk analysis, the researchers found the hazard ratio for white patients who were status 1 and removed from the wait-list because of death or becoming too sick was 1.04 (95% confidence interval, 0.89-1.21) and those white patients who were listed as status 1 and then transplanted was 1.2 (95% CI, 1.08-1.30). In a multivariate analysis, the hazard ratio for white patients who were listed as status 1 and transplanted, which contained bilirubin at transplant, was 1.08 (95% CI, 0.98-1.19). Kaplan Meier 1-year survival post transplant was 82.8% in white patients and 79.6% in black patients (*P* = .09).

Dr. Nephew reported no conflicts.

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SOURCE: Nephew LD et al. ACG 2018, Presentation 59.

Hereditary cancers account for only 5%

Family history *from page 1*

cer risk apart from hereditary Lynch syndrome, familial adenomatous polyposis, attenuated familial adenomatous polyposis, MUTYH-associated polyposis, Peutz-Jeghers syndrome, juvenile polyposis syndrome, Cowden syndrome, serrated (hyperplastic) polyposis syndrome, hereditary pancreatic cancer, and hereditary gastric cancer.

The ensuant guideline cites two new systematic reviews and meta-analyses of 16 prospective studies, as well as 1 twin study, 4 retrospective cohort studies, 1 new systematic review of retrospective studies, and 3 prior systematic reviews and meta-analyses. The authors note that this is the first guideline to use the GRADE (Grading of Recommendation Assessment, Development, and Evaluation) approach to make screening recommendations for individuals who have a family history of nonhereditary colorectal cancer or advanced adenoma.

For those with one first-degree relative with colorectal cancer, the guideline recommends screening colonoscopy or fecal immunochemical testing beginning at age 40-50 years, or 10 years before the age of diagnosis of the first-degree relative, whichever is earlier. The authors recommend spacing subsequent screening colonoscopies by 5-10 years and spacing fecal immunochemical testing by 1-2 years. They offer the same recommendation for individuals with one or more first-degree relatives with confirmed advanced adenoma.

For individuals whose family history includes at least two first-degree relatives with colorectal cancer, the guideline recommends an initial screening colonoscopy at age 40, or 10 years earlier than the age of earliest-diagnosed first-degree relative, whichever is earlier. Screenings should occur every 5 years.

For persons with at least one second-degree relative with colorectal cancer, the guideline authors strongly recommend screening starting at age 50 with tests and intervals based on guidelines for average-risk individuals. Their recommendation is the same for individuals with at least one first-degree relative with nonadvanced adenoma or a polyp of unknown histology.

Given the low-quality evidence supporting most of these recommendations, the guideline calls for well-designed observational studies to better quantify the risk of colorectal cancer among individuals with a family history of nonheritable disease. Studies should especially focus on the optimal age of first screening and appropriate screening intervals, the guideline authors wrote. Also, they call for randomized controlled trials to assess whether colonoscopy, fecal immunochemical testing, or fecal occult blood screening might significantly reduce long-term risk for colorectal cancer and improve survival in this population.

Merck provided unrestricted funding for the work. Dr. Leddin reported having no conflicts of interest. Dr. Lieberman and several coauthors disclosed financial relationships with companies other than Merck. One coauthor disclosed advisory and consulting relationships with Merck.

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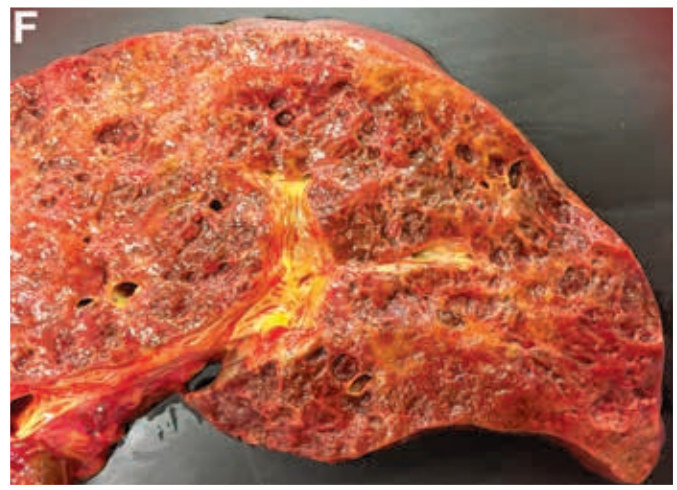
SOURCE: Leddin D et al. Gastroenterology. 2018 Aug 16. doi: 10.1053/j.gastro.2018.08.017.

CLINICAL CHALLENGES AND IMAGES

The diagnosis

Answer to "What is your diagnosis?" on page 32: Diffuse hepatic vascular malformation

Over the next 6 months she developed progressive liver failure (Model for End-Stage Liver Disease score, 34), and required several hospitalizations for worsening abdominal pain and debility. Despite the high risk of complications, she agreed to pursue a liver transplant. During the course of surgery, there was significant hemorrhage from tearing of the portal vein (PV) anastomosis and surrounding areas; despite all resuscitative efforts, she went into cardiac arrest and died. The sections of explanted liver revealed soft, spongy parenchyma with blood-filled cyst-like cavities measuring 1-6 mm in diameter (Figure F). The entire liver was affected by vascular malformations (VMs), and there was no evidence of malignancy. On elastin stain, the elastic lamina of the vascular wall appeared thin and disrupted; D2-40 and GLUT1 antibody stains were negative. The hilar PV wall thickness was variable with areas of intramural loose connective tissue separating smooth muscle bundles. This made the PV very friable, which, along with coagulopathy, was the likely cause of uncontrollable intraoperative bleeding. These findings indicate that the vascular spaces were derived from malformation of PV branches.



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VMs are rare liver lesions that can be idiopathic or associated with cirrhosis, traumatic injuries, and syndromes such as hereditary hemorrhagic telangiectasia. Although not always apparent, VMs are present at birth and grow proportionally with the patient's age.[1] They are usually solitary or multifocal, but rare cases of diffuse hepatic involvement have been reported.[2] To our knowledge, this is the first reported case of diffuse hepatic VM in an adult with no evidence of extrahepatic involvement. Diffuse hepatic VM may be confused with diffuse hepatic hemangiomatosis, another rare condition in adults characterized by replacement of the hepatic parenchyma with hemangiomatous lesions, but differs in that it is a vascular tumor and not VM. While vascular tumors, such as hemangioma, are characterized by abnormal endothelial proliferation, VMs develop from abnormal vascular morphogenesis, and are named after the vascular element they closely resemble, namely, capillary, venous, or arterial malformations. Although these are two distinct entities, the terms hemangioma and VM have been used indiscriminately and interchangeably in the literature to describe vascular anomalies.[1] Most hepatic VMs are asymptomatic, but depending on the extent of involvement, patients may develop high-output heart failure, portal hypertension, and biliary disease.[3] Despite extensive liver involvement, our patient did not manifest shunt physiology. The radiographic findings were nonspecific but indicative of diffuse vascular lesions in the liver. Histologic characteristics include dilated, irregular vascular channels, lined by a flat endothelium, separated by liver parenchyma and fibrovascular tissue.[2] Histochemical stains for collagen, elastin, and smooth muscle are often used to further characterize VMs.

Therapeutic options in focal VMs include sclerotherapy, embolization, and surgical resection. In severe cases with progressive hepatic failure, liver transplantation may be the only feasible option. A case of successful living donor liver transplant in a 14-year-old with VMs involving liver and colon has been described in literature.[3] Unfortunately, our patient did not survive the surgery. More reports using accurate terminology to describe hepatic vascular anomalies are needed for further understanding of this rare yet fatal disease.

References

1. George A., Mani V., Noufal A. Update on the classification of hemangioma. J Oral Maxillofac Pathol. 2014;18:S117-20.

2. Sato K., Amanuma M., Fukusato T., et al. Diffuse hepatic vascular malformations with right aortic arch. J Hepatol. 2005;43:1094-5.

3. Hatanaka M., Nakazawa A., Nakano N., et al. Successful living donor liver transplantation for giant extensive venous malformation. Pediatr Transplant. 2014;18:E152-6.

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Task force advises behavioral intervention for obese adults

BY HEIDI SPLETE
MDedge News

The U.S. Preventive Services Task Force advises clinicians to refer or offer intensive behavioral weight loss interventions to obese adults, according to an updated recommendation statement published in JAMA.

Obesity affects more than one-third of U.S. adults, according to federal statistics. It carries increased risk for comorbidities including heart disease, diabetes, and various cancers, as well as increased risk of death among adults younger than 65 years, noted lead author Susan J. Curry, PhD, of the University of Iowa, Iowa City, and members of the Task Force.

The B recommendation applies to obese adults; obesity was defined as a body mass index of 30 kg/m^2 or higher. The evidence review focused on interventions for weight loss and weight maintenance that could be provided in primary care or referred from primary care, such as nutrition counseling, exercise strategies, and goal setting.

Key clinical point
The researchers found behavioral interventions were associated with greater weight loss and less risk of developing diabetes, compared with control interventions.

The Task Force found adequate evidence that behavior-based weight-loss interventions improved weight, reduced incidence of type 2 diabetes, and helped maintain weight loss after interventions ended.

The Task Force found little to no evidence of harm associated with any of the behavioral weight loss interventions, which included group sessions, personal sessions, print-based interventions, and technology-based interventions (such as text messages). Although interventions that combined drug therapy with behavioral intervention resulted in greater weight loss over 12-18 months, compared with behavioral interventions alone, the attrition rates were high and data on weight loss maintenance after discontinuation of the drugs were limited, the Task Force noted.

"As a result, the USPSTF encourages clinicians to promote behavioral interventions as the primary focus of effective interventions for weight loss in adults," they wrote.

The Task Force acknowledged the need for future research in subgroups and to explore whether factors such as genetics and untreated conditions are barriers to behavior-based weight loss interventions.

In the evidence review published in JAMA, Erin S. LeBlanc, MD, of Kaiser Permanente in Portland, Ore., and her colleagues reviewed data from 122 randomized, controlled trials including more than 62,000 persons and 2 observational studies including more than 209,000 persons.

The researchers found behavioral

Continued on page 37

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PERSPECTIVE

Behavioral therapies alone may not be enough


DR. STREETT

In the USPSTF Recommendation Statement on Behavioral Weight Loss Interventions to Prevent Obesity-Related Morbidity and Mortality in Adults, the Task Force updates their 2012 statement and recommends that patients with obesity be referred for intensive, multicomponent behavioral weight loss interventions and weight loss maintenance. Reiterating the importance of intensive behavioral and lifestyle support is to be commended and should be the cornerstone of treatment for people with overweight disorders.

As thoughtfully discussed in accompanying editorials by Haire-Joshu, Hill-Briggs, and Yanovski, moving from recommendation to reality will require access to high-quality programs for patients of all socioeconomic and ethnic backgrounds, less restrictive reimbursement for services, and broader involvement of the public health and food industry sectors.

However, the task force recommendations were limited in scope: They pertained to people with obesity defined as a BMI greater than 30 kg/m^2, to those without diagnosed obesity-associated disorders, and to patients seen in a primary care setting. This lessens the impact of the report for a disease which continues to be epidemic in the United States. Leaving out the overweight pre-obese in whom efforts toward prevention are essential, as well as people with obesity who have coexisting comorbidities restricts the recommendations to one slice of the large obesity pie. As more high-quality data pertaining to a broader range of people impacted by overweight disorders become available, more expansive guidelines for treatment will be important.

Furthermore, while behavioral weight loss interventions are meaningful, they fall short for many in bringing about sustained efficacy. The primary care setting should include referral for appropriate patients to be evaluated for combined multidisciplinary behavioral and surgical, endoscopic, or pharmacologic therapies that can improve clinical outcomes for those refractory to behavioral weight loss interventions alone. Finally, tackling the obesity epidemic requires that health care providers across a broad range of specialties become involved in a coordinated effort to help our patients. As digestive disease specialists treating a myriad of obesity-related diseases from fatty liver to colorectal cancer, we too need to help address the underlying disease by providing obesity therapy within our practices or making referrals for its multidisciplinary treatment.

Sarah Streett, MD, AGAF, clinical associate professor of medicine, division of gastroenterology and hepatology, Stanford (Calif.) University School of Medicine. She has no relevant disclosures.

Continued from page 35

interventions were associated with greater weight loss and less risk of developing diabetes, compared with control interventions.

Intensive behavioral interventions included counseling patients about healthy eating, encouraging physical activity, setting weight and health goals, and assisting with weight monitoring. The interventions ranged from text messaging to in-person sessions for individuals or groups. The average absolute weight loss in the trials included in the review ranged from –0.5 kg to –9.3 kg (–1.1 lb to –20.5 lb) for intervention patients and from +1.4 kg to –5.6 kg (+3.1 lb to –12.3 lb) in controls.

AGA Resource
At the American Gastroenterological Association, we created the Practice guide on Obesity and Weight management, Education and Resources (POWER) white paper to provide you with a comprehensive, multidisciplinary process to guide and personalize innovative obesity care for safe and effective weight management. You can review the paper and other obesity resources to help with your practice at www.gastro.org/obesity.

Limitations of the review included a lack of data on population subgroups and a lack of long-term data on weight and health outcomes, the researchers noted. However, the results support the value of behavior-based therapy for obesity treatment.

The final recommendation is consistent with the 2018 draft recommendation and updates the 2012 final recommendation on obesity management.

The researchers and Task Force members had no relevant financial conflicts to disclose.

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SOURCE: U.S. Preventive Services Task Force. JAMA. 2018;320(11):1163-71. doi:


VLADIMIRFLOYD/THINKSTOCK

Changes in GI payment models most likely through CMS

BY TARA HAELLE
MDedge News

REPORTING FROM AGA PARTNERS IN VALUE 2018

DALLAS – With the approaching midterm elections and relative silence on health care policy from Congress this year, new health care legislation is unlikely in the immediate foreseeable future. But that does not mean the door to federal changes in health care policy is completely closed, according to Robert S. Saunders, PhD, of the Duke–Margolis Center for Health Policy, Durham, N.C.

It's simply more likely to come from the new leadership at the Department of Health & Human Services including Secretary Alex Azar, Center for Medicare & Medicaid Services Administrator Seema Verma, and Center for Medicare & Medicaid Innovation Director Adam Boehler. In his keynote address for the American Gastroenterological Association's Partners in Value meeting, Dr. Saunders gave attendees an overview of the current landscape in Washington and what they might expect in the coming months.

"Assuming congressional gridlock continues, HHS is a primary outlet for policy," Dr. Saunders said, also noting CMMI's pledge to make value-based payment a priority.

Broadly speaking, six goals compose the current administration's future vision within CMS, Dr. Saunders said. CMS has been encouraging payment reform innovation and benefit flexibility in Medicare Advantage and promoting private sector leadership with payment reform.

CMS is also collecting information on how it might reform the Stark Law to streamline value-based payment (VBP) arrangements or establish a mechanism for direct provider contracting.

Three other goals include using CMMI to increase alternative payment model availability to specialists, expanding patients' access to their own health data, and adding more outcomes measures but reducing the total number of measures.

CMS is also collecting information on how it might reform the Stark Law to streamline value-based payment (VBP) arrangements or establish a mechanism for direct provider contracting.

Dr. Saunders highlighted two health policy developments already announced. First, CMS will continue to offer bundled payment options through the Bundled Payments for Care Improvement Advanced initiative, Dr. Saunders said. That program presents opportunities related to treatment of GI hemorrhage, GI obstruction, and most liver disorders (excepting cancer, cirrhosis, and alcoholic hepatitis).

Then, CMS is proposing several changes to existing programs, though it remains to be seen how those will develop. One of those is the proposed modification of the Accountable Care Organization program to shorten the period ACOs can spend in upside risk, thereby pushing for more downside risk taking. Instead of having 6 years in upside risk getting 50% of savings, the proposed Pathways to Success would reduce that period to 2 years of upside risk, after which the ACOs would be responsible for shared losses in adddition to potentially receiving savings.

Another proposed change is to make payments site neutral so that Medicare clinical visits are charged the same regardless of whether they occur at a doctor's office or in a hospital outpatient setting. Currently, hospital outpatient visits are reimbursed at a higher amount than are those in private physicians' offices.

Finally, a new proposed rule would collapse payments for evaluation and management services into two tiers, which would apply only to office and outpatient E/M codes.

But it's not clear yet how hard CMS will push for implementation of these changes. For example, the proposed rule on E/M policy is the most significant push so far to reduce documentation from this administration, Dr. Saunders said, but medical groups, particularly specialists, oppose the rule because they argue it incentivizes short, repeat visits.

The three probable scenarios are that CMS moves forward with the new rule, that CMS scales back and retains the existing system, or that the "medical community pushes for an alternative to E/M with a framework that rewards doctors for their time," Dr. Saunders said. The final rule, likely to come down by November, will also offer some insight into how forcefully CMS will

Continued on following page

With site-neutral payments, the devil is in the details

BY GREGORY TWACHTMAN
MDedge News

Physician groups are pushing back against a proposal to implement site-neutral payments, despite the fact that they generally support the concept of it.

In the proposed update to the Hospital Outpatient Prospective Payment System (OPPS) for 2019, the Centers for Medicare & Medicaid Services introduced a physician fee schedule–equivalent payment for clinic visit services when provided at an off-campus, provider-based department that is paid under the OPPS.

The American Medical Association said in a letter to the CMS that, while it "generally supports site-neutral payments, we do not believe that it is possible to sustain a high-quality health care system if site neutrality is defined as shrinking all payments to the lowest amount paid in any setting." The AMA said that the current proposed rule is "complex, confusing, and is not truly site neutral because the policies do not apply equally to all hospital outpatient clinics," adding that a contributor to the differential between private practice and hospital outpatient departments (HOPD) stems from physicians being underpaid in the physician fee schedule.

In a letter signed by the American College of Gastroenterology, the American Gastroenterological Association, and the American Society for Gastrointestinal Endoscopy, they wrote that, "while ambulatory surgical centers (ASCs) are a more efficient and lower-cost alternative to the HOPD for a number of gastroenterology procedures, it does not mean, however, that reimbursement rates for services provided in both the ASC and the HOPD should be the same. Our societies support payment rates appropriate for each site of service and using appropriate policy and payment levers that result in patients receiving care in the most cost-efficient site of service."

'Our [GI] societies support payment rates appropriate for each site of service and using appropriate policy and payment levers that result in patients receiving care in the most cost-efficient site of service.'

The American Academy of Family Physicians stated in a letter to Seema Verma, current administrator of the CMS, that, while it supports the idea of site-neutral payments, "we note that the payment methodology for 2019 will not assure equal payments for the same service, regardless of site of service." The AAFP noted that the goal of curbing hospital acquisition of independent physician practices may not come to fruition and that "hospitals may still be incentivized to buy physician practices based on the mix of services they provide and bill them as PBDs [provider-based departments] at Medicare rates higher than would have been paid had the practice not been bought by the hospital."

The American College of Cardiology offered support for site-neutral payments and, while it did not come out against the CMS's proposal, it did offer a series of recommendations to consider, including determining that payments reflect "the resources required to provide patient care in each setting" and that "payment differences across sites should be related to documented differences in the resources needed to ensure patient access and high-quality care."

The American Academy of Dermatology Association voiced its support for the proposal to the agency.

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promote its agenda, according to Dr. Saunders.

Hearing these points "helps confirm that we are all headed toward this value-based world, and so we should start to ready our practices in the way that we internally compensate physicians and the way we engage with patients toward that value-based world," Michael Weinstein, MD, president of the Digestive Health Physicians Association, said in an interview following the keynote.

But Dr. Weinstein expressed skepticism about CMS's power to alter regulations sufficiently to really move forward into value-based care more broadly. He pointed out the various obstacles in the private sector that simply require legislative fixes, such as Stark Law modernization; increased transparency on price, outcomes, and quality measures; and interoperability between systems.

"You have to keep knocking CMS to make the changes, but if CMS makes changes, it only makes changes for Medicare," Dr. Weinstein said. Many states have laws requiring commercial carriers to follow the same federal rules that are set up for Medicare, but those are not universal and remain limited in scope.

Dr. Saunders also discussed the Physician-Focused Payment Model Technical Advisory Committee (PTAC), created by the Medicare Access and CHIP Reauthorization Act of 2015 (MACRA) to review new options for alternative payment models.

Since beginning to accept submissions in December 2016, PTAC has reviewed two GI models in 2017: Project Sonar and a comprehensive colonoscopy APM. Project Sonar focuses on creation of an IBD/Crohn's medical home. Despite reservations about proprietary technology and about the evidence on Project Sonar, PTAC has recommended the program for further testing. The comprehensive colonoscopy APM, however, was withdrawn after preliminary reviews because the PTAC was concerned the proposal "was too reliant on site-of-service shift and wanted more information on how it would lead to better integrated care," Dr. Saunders explained.

Though PTAC's existence led to hope early on that it might stimulate the creation of APMs and help them spread, the reality has been much shakier.

"CMS has not implemented any of the models PTAC has approved for use, and CMS has also not yet created a formal pathway for limited testing," Dr. Saunders said. That has left members uncertain about the future.

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