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GI & HEPATOLOGY NEWS

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BRUCE JANCIN/MDEDGE NEWS

Dr. Norah Terrault of the University of California at San Francisco believes that acute HCV infection is well worth treating in special populations.

Treatment of HCV in special populations

BY BRUCE JANCIN
MDedge News

MAUI, HAWAII – Treatment of acute rather than chronic hepatitis C infection is well worth considering in selected circumstances, Norah Terrault, MD, asserted at the Gastroenterology Updates, IBD, Liver Disease meeting.

This is not at present guideline-recommended therapy. Current American Association for the Study of Liver Disease/Infectious Diseases Society of America guidance states that, while there are emerging data to support treatment of acute hepatitis C, the evidence isn't yet sufficiently robust to support a particular regimen or duration. The guidelines currently recommend waiting 6 months to see if the acute infection resolves spontaneously, as happens in a minority of cases, or becomes chronic, at which point it becomes guideline-directed treatment time. But Dr. Terrault believes persuasive evidence to back treatment of acute hepatitis C (HCV) infection is forthcoming, and she noted that the guidelines leave the door ajar by stating, "There are instances wherein a clinician may decide that the benefits of early treatment outweigh waiting for possible spontaneous clearance."

See **HCV** · *page 18*

How anesthesia in GI endoscopy contributes to malpractice claims

BY ALICIA GALLEGOS
MDedge News

In a study of anesthesia medical malpractice cases involving gastrointestinal endoscopies, endoscopic retrograde cholangiopancreatography (ERCP) was the procedure that most often resulted in payouts to plaintiffs.

Lead author Alexander B. Stone, MD, of Brigham and Women's Hospital, Boston, and his colleagues examined 58 malpractice cases involving anesthesia providers between January 2007 and December 2016 from the Controlled Risk Insurance Company (CRICO) Comparative Benchmarking System, a database representing about 30% of annual malpractice cases in the United States.

Of these cases, 48% were associated with esophagogastroduodenoscopy, 19% involved ERCP, 14% resulted from colonoscopies, 14% stemmed from combined esophagogastroduodenoscopy and colonoscopy, and 5% involved endoscopic ultrasound. Investigators found that 91% of ERCP cases resulted in a payment to plaintiffs, compared with 37.5% of colonoscopy cases, 25% of combined esophagogastroduodenoscopy/

See **Malpractice** · *page 24*

Sucralose sparks appetite in obese, not lean, individuals

BY KARI OAKES
MDedge News

CHICAGO – Consumption of a sucralose-laden beverage stimulated appetite centers of the brain in individuals with obesity but not in lean participants of a recent study, even though hunger and satiety hormone levels didn't change. Those with obesity also consumed more calories after ingesting the artificial sweetener, though lean participants did not.

The study compared acute effects of consuming a set amount of glucose,

See **Sucralose** · *page 28*

INSIDE

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LETTER FROM THE EDITOR: A moment of grace


DR. ALLEN

She was my 3:45 p.m. return visit. She had been a new patient with dyspepsia and I had found *Helicobacter pylori* gastritis on endoscopy. She had marketplace-based coverage (silver, high-deductible plan), which was why she had to travel from her community to our university for care. That she did not look like me (older white male) was an understatement. She was so enthusiastic as she thanked me for helping her.

Then she described how she, her husband (both hourly-wage, working adults) and their two young kids had gathered around the dinner table to discuss how they could reduce their food allowance for 2 months to have money for mom's *H. pylori* medication. She said her entire family was grateful for the help to get her well. It was a moment of grace. She is why I keep fighting to make our health system great again.

Our cover articles this month discuss HCV treatment in patients with special risk factors or co-conditions. Fascinating information will emerge from studies like the article about artificial sweeteners. Scientists studied hunger-related enzyme levels and brain blood flow with functional MRI's in obese and lean individuals after ingesting placebo and sucralose-containing solutions. Results might influence our weight loss advice to patients. Worried about malpractice? See our third front page article.

Additional articles discuss a reversal agent for one of the direct-acting oral anticoagulants and a hemospray for GI bleeding. Clinically impactful articles from the AGA journals are highlighted.

Finally, I would like to thank all of you who filled out the readership survey last fall. We are proud that you identified *GI & Hepatology News* as the best overall source for news information in gastroenterology.

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

DDSEP eight Digestive Diseases Self-Education Program — Quick quiz

Q1. A 62-year-old man underwent deceased-donor liver transplant 36 hours ago for decompensated chronic hepatitis C cirrhosis. He did well initially post transplant with a steady decline in his transaminases and improvement in hepatic synthetic function. But he has had a rapidly progressive decline in his clinical status over the past 12 hours. On physical exam, his mental status is notable for new confusion. His temperature is 38.9º C. Laboratory data reveal the following: AST 10,300 U/L, ALT 14,550 U/L, total bilirubin 9.6 mg/dL, alkaline phosphatase 693 IU/L, INR 3.6, creatinine 4.6 mg/dL with oliguria.

What is the next most important diagnostic test for this patient?

A. CMV PCR
B. Liver biopsy
C. Hepatic ultrasound with Doppler
D. ERCP
E. MRCP

Q2. A 55-year-old obese man with long-standing type 2 diabetes mellitus complains of nausea and early satiety for over a year. His medical history is significant for retinopathy, neuropathy, and nephropathy. His diabetes is treated with subcutaneous insulin and an oral hypoglycemic agent, but his recent glycosylated hemoglobin was 11.2%. Since the onset of symptoms, he has lost approximately 30 pounds. Recent upper endoscopy was normal.

What is the next best step?
A. Dietitian consult
B. Endocrinology evaluation
C. Gastric scintigraphy
D. Trial of metoclopramide

The answers are on page 26.

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References: 1. IMS Health, NPA Weekly, May 2017. **2.** Rex DK, DiPalma JA, Rodriguez R, McGowan J, Cleveland M. A randomized clinical study comparing reduced-volume oral sulfate solution with standard 4-liter sulfate-free electrolyte lavage solution as preparation for colonoscopy. *Gastrointest Endosc.* 2010;72(2):328-336. **3.** SUPREP Bowel Prep Kit [package insert]. Braintree, MA: Braintree Laboratories, Inc; 2012. **4.** Rex DK, Schoenfeld PS, Cohen J, et al. Quality indicators for colonoscopy. *Gastrointest Endosc.* 2015;81(1):31-53.

HH13276BT-U May 2017

First reversal agent for apixaban, rivaroxaban approved

BY CATHERINE HACKETT
MDedge News

Andexanet alfa, the first agent shown to reverse the anticoagulant effects of rivaroxaban and apixaban, has been approved by the FDA, according to a May 3 statement from Portola Pharmaceuticals.

It is approved for use in patients treated with these factor Xa inhibitors when reversal of anticoagulation is needed because of life-threatening or uncontrolled bleeding, according to the company.

Andexanet alfa (Andexxa, Portola) received both U.S. Orphan Drug and FDA Breakthrough Therapy designations and was approved under the Food and Drug Administration's Accelerated Approval pathway.

"Today's approval represents a significant step forward in patient care and one that the medical community has been eagerly anticipating," said Stuart J. Connolly, MD, professor of medicine and an electrophysiologist at McMaster University in Hamilton, Ont., who is chair of the ANNEXA-4 executive committee. "Andexxa's rapid reversal of the anticoagulating effects of rivaroxaban and apixaban will help clinicians treat life-threatening bleeds, where every minute counts," he added in the statement.

Mitchel L. Zoler/MDedge News

Dr. Stuart J. Connolly said that andexanet will help treat life-threatening bleeds.

The approval was supported by two phase 3 trials in the ANNEXA series, which showed acceptable change from baseline in anti-Factor Xa activity in healthy volunteers. But the strongest data came from interim results from ANNEXA-4, a single-arm cohort study with 227 patients who were receiving a factor Xa inhibitor and were experiencing an acute major bleeding event.

Clinicians administered andexanet alfa as a bolus followed by a 2-hour continuous infusion, with hemostatic efficacy assessed 12 hours after the start of treatment. The results showed that factor Xa inhibition fell by a median 90% for rivaroxaban and 93% for apixaban.

Andexanet alfa is a factor Xa "decoy" molecule that acts by latching onto the inhibitor molecules and thereby preventing them from interacting with actual factor Xa, but andexanet also has a short half-life and hence the effect quickly reduces once treatment stops, Dr. Connelly reported at the American College of Cardiology annual meeting in March when presenting ANNEXA-4.

He noted at the time the results

Continued on following page

FDA approves marketing of device for GI bleeding

BY LORI LAUBACH
MDedge News

The Food and Drug Administration announced that it has permitted marketing of Hemospray, a new device used to help control certain types of bleeding in the gastrointestinal tract.

Hemospray is an aerosolized spray device that delivers a mineral blend to the bleeding site in the GI tract, is applied during endoscopic procedures, and can cover large ulcers or tumors.

The FDA evaluated data from clinical studies consisting of 228 patients with upper and lower GI bleeding, supplemented with evidence from medical literature, including an additional 522 patients. The studies found that Hemospray stopped GI bleeding in 95% of patients within 5 minutes of device usage. Results also found that bleeding recurred, usually within 72 hours, and up to 30 days following device usage, in 20% of patients. Bowel perforation was observed as a serious side effect in approximately 1% of patients.

"The device provides an additional, nonsurgical option for treating upper and lower GI bleeding in certain patients, and may help reduce the risk of death from a GI bleed for many patients," said Binita Ashar, MD, director, division of surgical devices, in the FDA's Center for Devices and Radiological Health in a press release.

Hemospray is not intended for patients who have a gastrointestinal fistula or are at high risk for GI perforation. The device is not intended for use in patients with variceal bleeding. The FDA permitted the marketing of the Hemospray device to Wilson-Cook Medical.

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Continued from previous page

placed andexanet in the same ballpark for efficacy and safety as idarucizumab (Praxbind) approved in 2015 for reversing the anticoagulant dabigatran (Pradaxa)

The prescribing information for andexanet states that treated patients should be monitored for signs and symptoms of arterial and venous thromboembolic events, ischemic events, and cardiac arrest. Further, anticoagulant therapy should be resumed as soon as medically appropriate following andexanet treatment to reduce thromboembolic risk.

The most common adverse reactions, occurring in at least 5% of patients, were urinary tract infections and pneumonia.

Portola intends to bring Andexxa to limited markets in early June; a broader commercial launch is anticipated in early 2019.

The FDA is requiring a postmarketing clinical trial that randomizes patients to either andexanet or usual care. The study is scheduled to begin in 2019 and report outcomes in 2023.

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FROM THE AGA JOURNALS

Scoring system quantified chances of HCV tx benefit

BY AMY KARON
MDedge News

A new scoring system predicted which patients with decompensated cirrhosis caused by hepatitis C virus (HCV) infection were most likely to experience meaningful benefits from direct-acting antiviral (DAA) therapy.

Dubbed BEA3, their scoring system assigns one point each for body mass index under 25 kg/m^2, absence of encephalopathy, absence of ascites, ALT more than 1.5 times the upper limit of normal, and albumin above 3.5 g/dL. Patients who scored 4 or 5 were more than 50 times more likely to improve to Child-Pugh Turcotte (CPT) class A (compensated) cirrhosis with DAA therapy than were patients who scored 0 (hazard ratio, 52.3; 95% confidence interval, 15.2-179.7; *P* less than .001), wrote Omar El-Sherif, MB, BCh, of St. James's Hospital, Dublin, together with his associates in the June issue of Gastroenterology.

Eradicating HCV does not necessarily improve the odds of transplant-free survival in the setting of decompensated cirrhosis, the researchers noted. Patients can end up in "MELD [Model for End-Stage Liver Disease] purgatory," meaning they are still decompensated despite achieving sustained virologic response and improved MELD scores. Such patients can face longer waits for liver transplantation than if they had foregone DAA therapy. "There is an urgent need for data to refine our understanding of the reversibility of hepatic decompensation with viral eradication, and, ultimately, define the "point of no return," the degree of liver dysfunction at which HCV therapy does not yield any meaningful clinical benefit, the researchers wrote.

Their study included 622 patients from the SOLAR-1, SOLAR-2, ASTRAL-4, and GS-US-334-0125 trials, which evaluated interferon-free sofosbuvir-based DAA therapy in patients with chronic hepatitis C virus infection and advanced liver disease. Patients received 12 or 24 weeks of therapy with ledipasvir, sofosbuvir, and ribavirin or velpatasvir, sofosbuvir, and/or ribavirin, or 48 weeks of treatment with sofosbuvir and ribavirin.

A total of 32% of patients with CPT class B cirrhosis improved to class A, as did 12% of patients with class C cirrhosis. Each factor in the scoring system independently affected the chances of reaching CPT class A cirrhosis, even after accounting for SVR.

Notably, patients with intermediate BEA3 scores of 1, 2, or 3 were significantly more likely to reach CPT class A cirrhosis than were patients with scores of 0, with hazard ratios ranging from 4.2 (for a score of 1) to 21.2 (for a score of 3). Most patients had scores of 0 (106 individuals), 1 (219 individuals), or 2 (180 individuals), and only 23 patients scored a 4 or a 5.

Patients with decompensated cirrhosis are now able to receive antiviral therapy without risk of worsening symptoms of decompensation. More clinics are able to offer DAA therapy to patients with hepatitis C, without the need for expertise in managing the side effects of interferon-based therapy.

The study by El-Sherif et al. summarizes well the benefits and potential pitfalls of treatment of hepatitis C in patients with decompensated cirrhosis. Their scoring system is largely intuitive and mirrors the traditional Child-Turcotte-Pugh score in that patients with low serum albumin, hepatic encephalopathy, and ascites are at risk of failing to improve clinically. Patients can have their hepatitis C successfully treated but can be trapped in "MELD purgatory," a state of significant symptoms of liver disease, without the objective priority points necessary to be candidates for liver transplantation.

As experience is gained in the use of DAA medications for HCV, it is incumbent on physicians to gather knowledge that will further refine their understanding of which patients with signs of liver decompensation might benefit. It is also clear that patients with decompensated cirrhosis should be managed by clinicians who have experience in liver transplantation, to ensure that patients are counseled regarding not just the benefits, but potential risks of DAA therapy for hepatitis C.

Roman E. Perri, MD, is assistant professor of medicine, division of gastroenterology and hepatology, Medical Director for Liver Transplantion, Vanderbilt University, Nashville, Tenn. He has no conflicts of interest.

CPT score reflects prothrombin time, serum albumin and bilirubin, and the presence or severity of ascites. The investigators called the new scoring system "a tool that can enhance shared decision making at the point of care, quantifying the potential benefits of DAA therapy for patients with decompensated cirrhosis in the pretransplant setting."

Dr. El-Sherif disclosed ties to Gilead Sciences, Bristol-Myers Squibb, and the Health Research Board of Ireland. Four coinvestigators disclosed employment with Gilead, and several other coinvestigators disclosed ties to Gilead, BMS, AbbVie, and other companies.

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SOURCE: El-Sherif O et al. Gastroenterology. 2018 Mar 10. doi: 10.1053/j.gastro.2018.03.022.

Meta-analysis supports endoscopic surveillance of Barrett's

BY AMY KARON
MDedge News

Endoscopic surveillance of patients with Barrett's esophagus led to significantly earlier detection of esophageal cancer in a systematic review and numerous meta-analyses.

Endoscopic surveillance also was associated with modest improvements in all-cause and cancer-specific mortality, said Don C. Codipilly, MD, of the Mayo Clinic in Rochester, Minn., with his associates. The Barrett's esophagus community "eagerly" await results from the multicenter, randomized BOSS trial (Barrett's Oesophagus Surveillance versus endoscopy at need Study), the reviewers wrote in the June issue of Gastroenterology.

Guidelines recommend endoscopic surveillance of patients with Barrett's esophagus, but it is unclear whether this practice improves survival. Hence, the reviewers searched databases such as Ovid MEDLINE, Embase, PubMed, and Scopus for studies published since 1996 that evaluated outcomes of endoscopic surveillance in Barrett's esophagus. Eligible studies included a case-control study of a large hospital database in northern California, 6 retrospective cohort studies of endoscopic Barrett's esophagus surveillance, and 11 prospective and retrospective studies comparing patients with esophageal adenocarcinoma (EAC) with and without a history of Barrett's esophagus.

The case-control study found no link between endoscopic surveillance and improved survival in Barrett's esophagus, said the reviewers. However, the retrospective cohort studies linked regular Barrett's esophagus endoscopic surveillance with a 40% lower risk of death from EAC, compared with incomplete or no endoscopic surveillance, which was statistically significant (risk ratio, 0.60; 95% confidence interval, 0.50-0.71). Individual results of these studies also were consistent with the results of their meta-analysis. A separate meta-analysis of the remaining studies also linked endoscopic surveillance with a significantly lower risk of EAC-related mortality (RR, 0.73; 95% CI, 0.57-0.94), but these studies had substantial heterogeneity, the investigators said.

Meta-analyses also supported endoscopic surveillance for earlier detection of EAC. Unadjusted data from four studies indicated that surveillance helped detect EAC while it was still early stage (stage 0 or 1) rather than later stage (RR, 2.1; 95% CI, 1.1-4.1). Similarly, patients who had already been diagnosed with Barrett's esophagus were significantly more likely to present with early-stage EAC (RR, 5.5; 95% CI, 3.7-8.2). In contrast, enrollment in a Barrett's esophagus surveillance program did not appear to affect the likelihood of esophagectomy.

Continued on page 8

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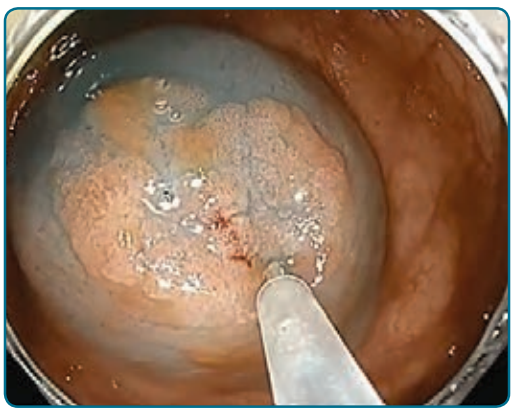

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References: 1. Data on File, Aries Pharmaceuticals, Inc. **2.** Eleview® Instructions for Use, Aries Pharmaceuticals, Inc. April 2017. **3.** Rex DK, Wallace M, Hassan C. A randomized, double-blind trial of a new injectable solution (SIC 8000) for endoscopic resection of large sessile polyps of the colon: an interim report. Abstract presented at: Digestive Disease Week®; May 6-9, 2017; Chicago, IL.

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FROM THE AGA JOURNALS

Colonic diverticulosis not tied to mucosal inflammation

BY AMY KARON
MDedge News

Colonic diverticulosis was not associated with mucosal inflammation or gastrointestinal symptoms in a single-center, prospective study of adults undergoing their first screening colonoscopy.

After adjustment for age, sex, and body mass index, there were no significant links between diverticulosis and tumor necrosis factor, CD4+ cells, CD8+ cells, CD57+ cells, irritable bowel syndrome (IBS), or chronic abdominal pain, reported Anne F. Peery, MD, with her associates at the University of North Carolina at Chapel Hill. "Our findings strongly question the rationale for treating symptomatic uncomplicated diverticular disease with mesalamine," they wrote in the June issue of Clinical Gastroenterology and Hepatology.


DR. PEERY

Colonic diverticula affect more than half of individuals in the United States over the age of 60 years, according to the results of past studies. "Although colonic diverticulosis can be complicated by the overt inflammation of acute diverticulitis, there is some thought that colonic diverticulosis is associated with low-grade mucosal inflammation," the researchers said. "Moreover, this low-grade diverticular inflammation is believed to contribute to chronic gastrointestinal symptoms." However, no rigorous prospective study had tested these assertions.

Accordingly, the researchers evaluated prospective data from 619 outpatients aged 30 years and older who underwent screening colonoscopies for the first time during 2013-2015. These patients had consented to participate in a study of risk factors for colonic diverticulosis. Most were white (76%) or black (21%), and most were aged 50-59 years.

A total of 255 individuals had diverticula while 364 controls did not. Patients with diverticula tended to be older and were more often male (47% vs. 41% of controls) and overweight or obese (72% vs. 62%). After adjustment for age, sex, and body mass index, there was no evidence linking diverticulosis with tumor necrosis factor alpha expression (odds ratio, 0.9; 95% confidence interval, 0.6-1.2), CD4+ cells (OR, 1.2; 95% CI, 0.9-1.6), CD8+ cells (OR, 1.0; 95% CI, 0.7-1.3), or CD57+ cells (OR, 0.8; 95% CI, 0.6-1.1).

Among 42 patients who met Rome III criteria for IBS, 11 had diverticulosis. Diverticulosis in IBS was not associated with changes in expression of the mucosal inflammatory markers interleukin-6, interleukin-10, tumor necrosis factor, CD4, CD8, or mast cell tryptase, said the researchers. A total of 63 patients had chronic abdominal pain, of whom 22 also had diverticulosis. There were no significant differences in mucosal inflammatory markers between symptomatic patients with diverticula and those without. Adjusted analysis found no association between number of diverticula and chronic abdominal pain (OR, 0.7; 95% CI, 0.4-1.2) or IBS (OR, 0.5; 95% CI, 0.3-1.1).

"Multianalyte profiling could be used to assess an array of cytokines, and markers for macrophages (CD68), global T cells (CD3), and B cells (CD19). Whether there is utility in further studies given our negative results is debatable."

The National Institutes of Health provided funding. The investigators reported having no conflicts of interest.

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SOURCE: Peery AF et al. Clin Gastroenterol Hepatol. 2017 Jun 8. doi: 10.1016/j.cgh.2017.05.051.

Continued from page 6

Additional meta-analyses suggested that endoscopic surveillance of Barrett's esophagus might confer a "potentially small" overall survival benefit, the reviewers said. A meta-analysis of adjusted data from three studies linked surveillance with a 25% reduction in risk of all-cause mortality, compared with no surveillance (hazard ratio, 0.75; 95% CI, 0.58-0.94). Having a prior Barrett's esophagus diagnosis also was associated with a 52% decrease in all-cause mortality, compared with having symptomatic cancer (RR, 0.48; 95% CI, 0.37-0.63) in a meta-analysis of unadjusted data from 12 studies. Five studies with adjusted data linked a prior Barrett's esophagus diagnosis with a 41% lower risk of all-cause mortality (HR, 0.59; 95% CI, 0.45-0.76).

The National Institutes of Health and a Public Health Service Award supported the study. Dr. Codipilly reported having no conflicts of interest. Five coinvestigators disclosed ties to Exact Sciences, C2 Therapeutics, and other companies.

ginews@gastro.org

SOURCE: Codipilly DC et al. Gastroenterology. 2018 Feb 17. doi: 10.1053/j.gastro.2018.02.022.

Study eyes liver transplantation after Region 5 UNOS downstaging

BY AMY KARON
MDedge News

Liver transplantation led to "excellent outcomes" when performed after downstaging hepatocellular carcinoma (HCC) using the UNOS (United Network for Organ Sharing) Region 5 protocol, investigators reported.

Downstaging succeeded for 58% of patients, and an estimated 87% of transplantation recipients were alive and recurrence free at 5 years, said Neil Mehta, MD, of the University of California, San Francisco, and his associates. The findings support expanding priority access to liver transplantation to include patients whose HCC has been downstaged, they said. "In the meantime, UNOS has recently approved the Region 5 downstaging protocol for receiving automatic HCC-MELD exception listing," they wrote. The report was published in the June issue of Clinical Gastroenterology and Hepatology.

This is the first multicenter study of HCC downstaging according to a uniform protocol, the researchers noted. In multivariable analyses, downstaging was significantly more likely to fail in the setting of moderate to severe (Child Pugh B or C) hepatic impairment (hazard ratio, 3.3; 95% confidence interval, 3.0-3.6; *P* less than .001) or baseline alpha-fetoprotein (AFP) level above 1,000 ng/mL (HR, 1.6; 95% CI, 1.4-1.9; *P* less than .001).

The incidence of HCC in the United States is expected to keep rising for at least another decade because of epidemic levels of fatty liver disease and chronic hepatitis C, the investigators noted. Downstaging HCC with locoregional therapy is a common bridge to transplantation, and successful treatment tends to reflect favorable tumor biology, which bodes well for transplantation. However, no multicenter study had evaluated these associations. Therefore, the investigators retrospectively studied 187 patients with HCC from three centers in California who underwent downstaging according to the UNOS Region 5 protocol between 2002 and 2012.

A total of 156 patients (83%) were successfully downstaged to within Milan criteria after a median of 2.7 months (interquartile range, 1.4-4.9 months), said the researchers. Among patients who were successfully downstaged but did not undergo transplantation, 37 patients had tumor progression or died from liver-related causes after a median of 6 months, while 10 patients remained on the transplant list. Among the 109 patients who underwent transplantation after a median of 13 months (IR, 6-19 months), median follow-up time was 4.3 years and estimated 5-year survival was 80%, and estimated recurrence-free survival was 87%.

Fully 68% of successfully downstaged patients required only one locoregional treatment, the researchers said. The Region 5 protocol considers patients eligible for downstaging if they have a single HCC lesion measuring up to 8 cm or multiple lesions whose combined diameters do not exceed 8 cm, and no evidence of extrahepatic disease or vascular invasion on multiphase computed tomography or magnetic resonance imaging.

The protocol considers downstaging successful if it results in one

Continued on following page

FROM THE AGA JOURNALS

Stromal cell lactoferrin may mediate protective effects in CD

BY CHHAVI JAIN
MDedge News

Inflammatory bowel disease (IBD) and Crohn's disease (CD), in particular, are characterized by an unusual ectopic extension of mesenteric adipose tissue. This intra-abdominal fat, which wraps around the intestine during the onset of CD, is associated with inflammation and ulceration of the small or large intestine. The role of this fat in the development of CD, and whether it is protective or harmful, however, is not clear.

The current study demonstrates that adipose-derived stromal cells (ADSCs), the precursor cell population of adipose tissue, promote colonocyte proliferation and exhibit a differential gene expression profile in a disease-dependent manner. CD patient–derived ADSCs attenuated the severity of experimental colitis by releasing extracellular mediators, which exhibits a protective role for mesenteric adipose tissue during intestinal inflammation, according to Jill M. Hoffman, MD, and her colleagues at the University of California, Los Angeles. Increased expression and release of lactoferrin by ADSCs – an iron-binding glycoprotein and antimicrobial peptide usually found in large quantities in breast milk – was shown to be a likely mediator that could regulate inflammatory responses during CD. These results were published in Cellular and Molecular Gastroenterology and Hepatology.

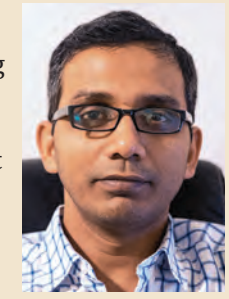
Intestinal inflammation is primarily mediated by cytokine production, and targeted anticytokine therapy is the current standard for IBD treatment. The cytokine profile from CD patient–derived mesenteric ADSCs and fat tissue was significantly different from that of these patients' disease-free counterparts. The authors hypothesized that mesenteric ADSCs release adipokines in response to disease-associated signals; this release of adipokines results from differential gene expression of mesenteric ADSCs in CD vs. control patients. As a test of this hypothesis, conditioned media from CD patient–derived ADSCs were used to study gene expression in colonic intestinal epithelial cells in vitro and in mice with experimental colitis in vivo.

With use of the Human LncRNA Expression Microarray V4.0, expression of 20,730 protein-coding mRNA targets was analysed, and 992 mRNA transcripts were found to be differentially (less than or equal to twofold change) expressed in CD patient–derived ADSCs, compared with control patient–derived ADSCs. Subsequent pathway analysis suggested activation of cellular growth and proliferation pathways with caspase 8 and p42/44 as top predicted networks that are differentially regulated in CD patient–derived ADSCs with respect to those of control patients.

The investigators treated intestinal epithelial cells – specifically, NCM460 – with conditioned 233 media from the same CD or control patient–de-

Continued on following page

Inflammatory bowel disease (IBD), including Crohn's disease, is a chronic inflammatory condition of the gastrointestinal tract that is often associated with changes in adipose tissue. However, the pathophysiological significance of fat wrapping in Crohn's disease remains largely elusive. A correlation of IBD with obesity has been established by a number of studies, which report 15%-40% of adults with IBD are obese. Obesity is found to have a negative effect on disease activity and progression to surgery in patients with Crohn's disease. In contrast, adipose-derived stromal or stem cells exhibit regenerative and anti-inflammatory function.


DR. BISWAS

A recent study published in Cellular and Molecular Gastroenterology and Hepatology by Jill M. Hoffman and her colleagues highlighted the immune-modulatory function of adipose-derived stromal cells (ADSCs) in Crohn's disease patients. They observed that patient-derived ADSCs promote colonocyte proliferation and exhibit distinct gene expression patterns, compared with healthy controls. The authors successfully identified ADSC-derived lactoferrin, an iron-binding glycoprotein and an antimicrobial peptide, as a potential immunoregulatory molecule.

They concluded that the disease-dependent alterations in mesenteric adipose tissue–derived ADSCs might have a protective role in the pathophysiology of Crohn's disease. The study elegantly highlighted the therapeutic potential of lactoferrin in IBD and provided new insight into the biology of ADSC.

Amlan Biswas, PhD, is an instructor in pediatrics at Harvard Medical School, Boston, and is affiliated with Boston Children's Hospital in the division of gastroenterology and nutrition. He has no conflicts of interest.

Continued from previous page

lesion measuring up to 5 cm or no more than three lesions of up to 3 cm each. Thus, patients who start out with four or five lesions must have complete necrosis of at least one to two tumors. Successfully downstaged patients must remain free of acute hepatic decompensation for at least 3 consecutive months before undergoing transplantation, according to the protocol.

"Slight refinements in the inclusion criteria for downstaging seem warranted [given] that all Child's B/C patients with pretreatment AFP greater than 1,000 ng/mL suffered poor outcomes when downstaging was attempted," the investigators noted. They reported that the 1-year risk of failed downstaging was 70% among patients with both Child's B/C cirrhosis and AFP level at or above 1,000 ng/mL, 32% among patients with one risk factor, and 14% among patients with no risk factors (*P* less than .001).

The National Institutes of Health provided partial funding. The investigators reported having no conflicts of interest.

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SOURCE: Mehta N et al. Clin Gastroenterol Hepatol. 2017 Nov 23. doi: 10.1016/j.cgh.2017.11.037.

Liver transplantation of selected patients with HCC is an accepted indication and associated with excellent outcomes. Until recently, criteria for liver transplantation were based on the Milan criteria that took only size and number of tumors under consideration. In this multicenter study, patients who were outside of Milan criteria were successfully downstaged to within Milan criteria with locoregional therapy and subsequently transplanted with excellent outcomes. Salient features included the following. 1) Six months waiting after the first treatment and 3 months after downstaging was required to ensure that the tumor stage remained within Milan criteria. 2) Any specific type of locoregional therapy was allowed. 3) Downstaging was possible in a majority of patients after a single treatment. 4) Patients with alpha-fetoprotein greater than 1,000 ng/mL (approximately 10%) as well as presence of substantial decompensated liver disease (approximately 40%) did not have favorable outcomes. 4) On multivariable analysis, tumor biology was a stronger predictor of poor outcomes than was stage of liver disease.


DR. ASRANI

The study is important because it supports incorporating tumor biology and concomitant liver disease status (Child A versus Child B/C) in addition to size and number of tumors (Milan criteria) for identifying a further slice of patients with HCC who may benefit from transplant. Indeed, downstaging protocols are now part of the Organ Procurement and Transplantation Network MELD exception pathway for liver transplantation of HCC patients in the United States, as long as locoregional therapy results in successful downstaging and AFP (if elevated) decreases to below 500 ng/mL.

Sumeet K. Asrani, MD, MSc, is associate professor in medicine and hepatologist at Baylor University Medical Center, and medical director of the Center for Advanced Liver Disease, Dallas. He has no conflicts of interest.

FROM THE AGA JOURNALS

Continued from previous page

rived ADSCs; subsequent microarray profiling using the GeneChip Human Gene ST Array showed increased expression of interleukin-17A, CCL23, and VEGFA. Ingenuity Pathway Analysis of mRNA expression indicated convergence in injury and inflammation pathways with the SERPINE1 gene, which suggests it's the central regulator of the differential gene expression network.

In vivo, mice with active dextran sulfate sodium (DSS) colitis that were treated with daily injections of conditioned media from CD patients showed attenuation of colitis as compared with mice treated with vehicle or conditioned media from control patients. Furthermore, the mRNA expression of proinflammatory cytokines was reduced with increased proliferative response (as measured by Ki67 expression) in intestinal epithelial cells in the dextran sulfate sodium–treated mice receiving media from CD patients, compared with that in mice receiving media from control patients or vehicle-treated mice.

Cell proliferation was studied in real time (over 120 hours) using the xCELLigence platform. The authors suggested that mesenteric adipose tissue–derived mediators may regulate proliferative responses in intestinal epithelial cells during intestinal inflammation, as observed by enhanced cell-doubling time in conditioned media from CD patient–derived ADSCs.

Levels of lactoferrin mRNA (validated by real-time polymerase chain reaction; 92.70 ± 18.41 versus 28.98 ± 5.681; *P* less than .05) and protein (validated by ELISA; 142.2 ± 5.653 versus 120.1 ± 3.664; *P* less than .01) were increased in human mesenteric ADSCs and conditioned media from CD patients, respectively, compared with that from controls.

"Compared with mice receiving vehicle injections, mice receiving daily injections of lactoferrin had improved clinical scores (5.625 ± 0.565 versus 11.125 ± 0.743; n = 8) and colon length at day 7 (6.575 ± 0.1688 versus 5.613 ± 0.1445; n = 8). In addition, we found epithelial cell proliferation was increased in the colons of lactoferrin-treated mice with colitis, compared with vehicle-treated controls ($3.548e^7$ ± $1.547e^6$ versus $1.184e^7$ ± $2.915e^6$; *P* less than .01)," said the authors.

Collectively, the presented data were suggestive of a protective role of mesenteric adipose tissue–derived mediators, such as lactoferrin, in the pathophysiology of CD.

The study was supported by the Broad Medical Research Program (IBD-0390), an NIDDK Q51856 Ruth L. Kirschstein National Research Service Award Postdoctoral Fellowship 1857 (F32 DK102322), the Neuroendocrine Assay and Models of Gastrointestinal Function and Disease Cores (P50 DK 64539), an AGA-1858 Broad Student Research Fellowship, the Blinder Center for Crohn's 1859 Disease Research, the Eli and Edythe Broad Chair, and NIH/NIDDK grant DK047343.

The authors disclosed no conflicts of interest.

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SOURCE: Hoffman JM et al. Cell Molec Gastro Hepatol. doi: 10.1016/j.jcmgh.2018.02.001.

Uninsured rate on the rise again

BY RICHARD FRANKI
MDedge News

The uninsured rate among Americans aged 19-64 years, which was 12.7% in early 2016, has climbed to 15.5%, according to a survey by the Commonwealth Fund.

Medicaid expansion has had a significant effect on that increase. The uninsured rate among working-age adults living in states that did not expand their Medicaid programs has gone from 16.1% in 2016 to 21.9% in 2018, while the rate in states that did expand Medicaid rose from 10.4% to 11.4% over that same time, Commonwealth Fund researchers said in reporting the results of their latest (Feb. 6, 2018, to March 30, 2018) Affordable Care Act Tracking Survey.

The uninsured rate among working-age adults living in states that did not expand their Medicaid programs has gone from 16.1% in 2016 to 21.9% in 2018, while the rate in states that did expand Medicaid rose from 10.4% to 11.4% over that same time.

The situation was somewhat similar when looking at income: For adults living in households with earnings less than 250% of the federal poverty level (about $30,000 for an individual and $61,000 for a family of four), the uninsured rate rose from 20.9% in 2016 to 25.7% in 2018. Those with incomes above 250% of the poverty line have seen the uninsured rate increase from 4.4% in 2016 to 6.2% in 2017 and then decrease to 5.8% in 2018, they said.

A similar increase/decrease since 2016 was experienced by respondents who identified as Democrats: The rate for the group went from 9.9% in 2016 to 10.4% in 2017 and then dropped to 9.1% in 2018.

Those identifying as Republicans started with a lower rate of 7.9% in 2016 but have since seen it rise to 9.9% in 2017 and 13.9% in 2018, results from the survey of 2,403 adults showed.

"In the absence of bipartisan support for federal action [on the ACA], legislative activity has shifted to the states. Eight states have received, or are currently applying for, federal approval to establish reinsurance programs in their states," the investigators wrote, but "leaving policy innovation to states will ultimately lead to a patchwork quilt of coverage and access to health care across the country, a dynamic that will fuel inequity in overall health, productivity, and well-being."

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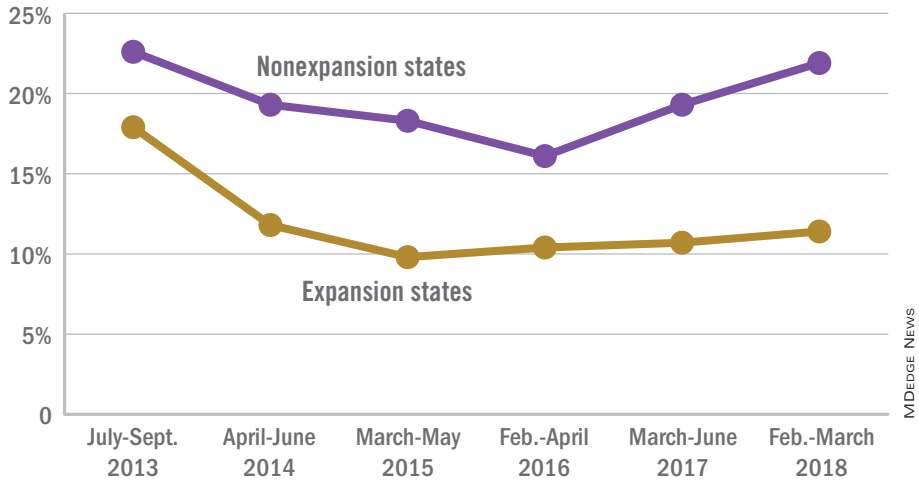
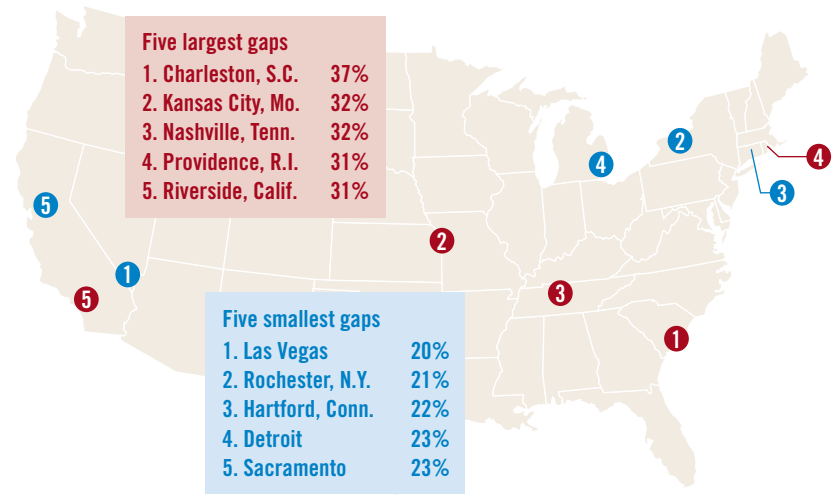
Tracking survey: Uninsured rate by Medicaid-expansion status



Note: Most recent Affordable Care Act Tracking survey involved 2,403 adults aged 19-64 years.
Source: Commonwealth Fund

Metro areas with the largest, smallest gender wage gaps in 2017

Female physicians earned 37% less than males in Charleston, S.C.



Note: Compensation surveys were completed by more than 65,000 physicians in 2016 and 2017.
Source: Doximity

Female physicians face enduring wage gap

BY RICHARD FRANKI
MDedge News

Male physicians make more money than female physicians, and that seems to be a rule with few exceptions. Among the 50 largest metro areas, there were none where women earn as much as men, according to a new survey by the medical social network Doximity.

The metro area that comes the closest is Las Vegas, where female physicians earned 20% less – that works out to $73,654 – than their male counterparts in 2017. Rochester, N.Y., had the smallest gap in terms of dollars ($68,758) and the second-smallest percent difference (21%), Doximity said in its 2018 Physician Compensation Report.

The largest wage gap on both measures can be found in Charleston, S.C., where women earned 37%, or $134,499, less than men in 2017. The other members of the largest-wage-gap club are as follows: Kansas City, Mo., and Nashville, Tenn., both had differences of 32%, and Providence, R.I., and Riverside, Calif., had differences of 31%, Doximity said in the report, which was based on data from "compensation surveys completed in 2016 and 2017 by more than 65,000 full-time, licensed U.S. physicians who practice at least 40 hours per week."

A quick look at the 2016 data shows that the wage gap between female and male physicians increased from 26.5% to 27.7% in 2017, going from more than $92,000 to $105,000. "Medicine is a highly trained field, and as such, one might expect the gender wage gap to be less prominent here than in other industries. However, the gap endures, despite the level of education required to practice medicine and market forces suggesting that this gap should shrink," Doximity said.

'Medicine is a highly trained field, and as such, one might expect the gender wage gap to be less prominent here than in other industries. However, the gap endures.'

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AGA Resource
In a recent issue of AGA Perspectives, Ellen M. Zimmermann, MD, AGAF, chair of the AGA Women's Committee, wrote about the need for transparent policies at institutions to help close the gender gap. Read more at http://ow.ly/43If30jTlEc.

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GI & HEPATOLOGY NEWS

THE OFFICIAL NEWSPAPER OF THE AGA INSTITUTE

Announcing the 2018 Section Research Mentor Award recipients

The AGA Institute Council Section Research Mentor Award acknowledges AGA members for their achievements as outstanding mentors in a specific area of research. We are pleased to announce the 2018 recipients who will be recognized by each of the 13 AGA Institute Council sections during Digestive Disease Week® (DDW) 2018. Congratulations to these exceptional mentors!

Basic & Clinical Intestinal Disorders
Gary D. Wu, MD

Cellular & Molecular Gastroenterology
Charalabos Pothoulakis, MD

Clinical Practice
Amnon Sonnenberg, MD, MSc

Esophageal, Gastric & Duodenal Disorders
Nicholas J. Shaheen, MD, MPH, AGAF

Gastrointestinal Oncology
Randall W. Burt, MD, AGAF

Growth, Development & Child Health
Deborah L. Gumucio, PhD

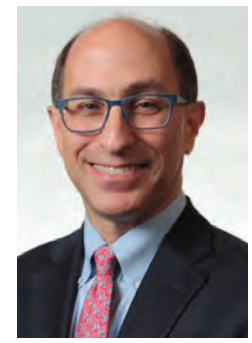
Imaging, Endoscopy & Advanced Technology
Michael B. Wallace, MD, MPH, AGAF

Immunology, Microbiology & Inflammatory Bowel Diseases
Claudio Fiocchi, MD

Liver & Biliary
Scott L. Friedman, MD

Microbiome & Microbial Diseases in the Gastrointestinal Tract
Jeffrey I. Gordon, MD

Neurogastroenterology & Motility
Richard W. McCallum, MD, AGAF



Obesity, Metabolism & Nutrition
Lee M. Kaplan, MD, PhD, AGAF

Pancreatic Disorders
Suresh T. Chari, MD

AGA hosted productive Capitol Hill meeting

Rep. Peter Roskam (R-Ill.), Chair of the Subcommittee on Health of the Ways and Means Committee, invited AGA and the Alliance of Specialty Medicine to participate in a policy roundtable to learn more about the issues facing physicians and their patients. Chairman Roskam recently took over the chair of the Health Subcommittee, which has prime jurisdiction over Medicare Part B issues when Rep. Pat Tieberi, R-OH, retired. The roundtable focused on regulatory issues that impact physician practices and their ability to provide timely care to patients.

AGA and the Alliance of Specialty Medicine thanked Chairman Roskam and Congress for the technical corrections to the Quality Payment Program (QPP) that were included as part of the bipartisan budget agreement passed earlier this year that will significantly improve physicians' ability to successfully participate in the Merit-based Incentive Payment System (MIPS) track. Because of the lack of opportunity for specialists like gastroenterologists to participate in advanced alternative payment models (APMs), most physicians will be participating in MIPS. Although Congress provided CMS with more flexibility in scoring for MIPS, we stressed to Chairman Roskam that MIPS reporting and scoring needs to be simplified to make it less administratively burdensome and costly for physicians. We also addressed the ongoing challenges regarding electronic health records (EHR) interoperability and the administrative and financial burdens it has on physician practices. This roundtable is part of one of AGA's top advocacy issues, urging the Centers for Medicare & Medicaid Services (CMS), other payors, and Congress to provide relief to physicians.

AGA also raised the issue of alternative payment models and gastroenterology's experience with developing bundles and episodes around common GI conditions. AGA stressed to Rep. Roskam the need for CMS to move forward piloting specialty payment models that have been approved by the Physician Technical Advisory Committee (PTAC) to test them in the Medicare population. The need for modernizing the Stark laws to enable physician practices to participate in alternative payment models was also discussed at the roundtable since the current Stark laws prohibit physician referral based on volume or value. AGA supports S. 2051/H.R. 4206, the Medicare Care Coordination Improvement Act, which would provide CMS with the regulatory authority to create exceptions under the Stark law for APMs and to remove barriers in the current law to the development and operation of such arrangements. The legislation would allow CMS to waive the Stark laws for physicians seeking to develop and operate APMs like what Congress allowed for accountable

AGA believes this legislation (S. 2051/H.R. 4206) is necessary for many of the innovative payment models developed by gastroenterologists to be implemented in the Medicare program.

Continued on following page

Protect the next generation of GI investigators

Investing in research is the only way we will identify new diagnostics and treatments. However, at this time of unparalleled scientific and clinical opportunity, promising early-stage investigators are leaving the field because of the instability of federal research funding.

Fortunately, the AGA Research Foundation has a proven track record of funding young investigators whose work advances the field of gastroenterology. The foundation provides a key source of funding at a critical juncture in a talented investigator's career.

"My work focuses on exploring hydrogen pyroxide transport through aquaporin-3 channels and the effects this has on wound repair and mucosal immune function in the intestine. The results will help us to better understand how these proteins work in the gut and will lead to new ways of combating inflammation and infection," says Jay Thiagarajah, MD, PhD, 2017 AGA Research Scholar Award recipient.

Help the AGA continue to build a community of investigators through the AGA Research Foundation.

Your donation to the AGA Research Foundation can fund future success stories by keeping young scientists working to advance our understanding of digestive diseases.

Donate today to help protect the GI research pipeline. Make a tax-deductible donation at www.gastro.org/donateonline.

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Courtesy Dr. Jay Thiagarajah

Dr. Jay Thiagarajah, 2017 AGA Research Scholar Award recipient.

Continued from previous page

care organizations (ACOs). AGA believes this legislation is necessary for many of the innovative payment models developed by gastroenterologists to be implemented in the Medicare program.

Prior authorization addressed

Prior authorization was also a major topic raised with Rep. Roskam and how it impacts all physicians regardless of where they practice. We emphasized how tremendously burdensome prior authorizations is to physicians and physician practices, and gave examples of how it often interrupts and/or delays delivery of patient care.

AGA and the alliance recommended that payors make prior authorization requirements and criteria transparent and easily accessible.

We also recommended that CMS standardize and streamline prior authorization processes by Medicare Advantage and Part D plans. We also encouraged the committee to conduct oversight hearings to investigate prior authorization and utilization management practices by Medicare Advantage Organizations and Part D plans.

AGA and the alliance will continue to work with Rep. Roskam and the committees of jurisdiction to find solutions to lessen the regulatory burden on physicians that take time away from providing care to patients.

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AGA Fellows application period now open

The application period for the 2019 AGA Fellowship is now open. The AGA Fellows program recognizes long-term AGA members for their superior work in clinical private or academic practice and in basic or clinical research. Members whose professional achievements demonstrate personal commitment to the field of gastroenterology and meet the AGA Fellows program criteria are encouraged to apply.

Learn about joining this community of excellence and to how to apply online at www.gastro.org/fellowship. AGA Fellows receive:

- The privilege of using the designation "AGAF" in professional activities.
- An official certificate and pin denoting your status.
- A listing on AGA's website alongside esteemed peers.
- And more.

Apply and gain international recognition for your achievements when you become an AGA Fellow.

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Psychotherapy helps patients with chronic digestive disorders

New AGA Clinical Practice Update explains benefits of psychogastroenterology for patients.

Patients with chronic digestive disorders can better cope with their symptoms and the effects on their daily lives when they receive support from mental health professionals specializing in psychogastroenterology, according to a new AGA Clinical Practice Update, published in the April issue of Gastroenterology (gastrojournal.org). Gastroenterologists who integrate brain-gut psychotherapies, including cognitive-behavior therapy (CBT) and gut-directed hypnotherapy, into their practice can help patients better understand and manage any psychiatric comorbidities and coping skills, which will help reduce patient symptom burden and health care resource utilization.

Patients with chronic digestive disorders can better cope with their symptoms and the effects on their daily lives when they receive support from mental health professionals specializing in psychogastroenterology.

These therapies are optimally delivered by mental health professionals specializing in psychogastroenterology, a field dedicated to applying effective psychological techniques to GI problems.

According to best practice advice, to help promote the use of brain-gut psychotherapies in routine GI care, gastroenterologists should:

1. Routinely assess health-related quality of life, symptom-specific anxieties, early-life adversity, and functional impairment related to a patient's digestive symptoms.
2. Master patient-friendly language on the following topics: the brain–gut pathway and how this pathway can become dysregulated by any number of factors; the psychosocial risk, perpetuating and maintaining factors of GI diseases; and why the gastroenterologist is referring a patient to a mental health provider.
3. Know the structure and core features of the most effective brain–gut psychotherapies.
4. Establish a direct referral and ongoing communication pathway with one to two qualified mental health providers and assure patients that he or she will remain part of their care team.
5. Familiarize themselves with one or two neuromodulators that can be used to augment behavioral therapies when necessary.

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For first-line constipation therapy, stick with the leader

The AGA recommends PEG laxatives (like MiraLAX) as a first-line constipation treatment[1]

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Start with MiraLAX for proven relief of occasional constipation.

*Survey of 300 consumers, 2017.

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Reference: 1. Clinical decision support tools. American Gastroenterological Association website. http://campaigns.gastro.org/algorithms/constipation/index.html. Accessed May 12, 2017.

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Polyethylene Glycol 3350, Powder for Solution, Osmotic Laxative

Doctor recommended, patient approved

It is worth treating acute infection

HCV *from page 1*

Dr. Terrault said she interprets that to mean, "The guideline leaves it open to us," and she personally treats acute HCV "very frequently." In addition to describing when and how, she highlighted several other special populations for which emerging treatment data point to major clinical benefit of acute HCV treatment coupled with excellent safety, including patients with end-stage renal disease, liver transplant recipients, and injectable drug users.

Treatment of acute HCV

Dr. Terrault deems treatment of acute HCV warranted in circumstances in which there is significant danger of transmission from the acutely infected individual to others. For example, health care providers with a needlestick HCV infection, injecting drug users, and men with acute HCV/HIV coinfection. She also treats acute HCV in patients with underlying chronic liver disease.

"Clearly, I wouldn't want those individuals to have any worsening of their liver function, so I would treat them acutely," explained Dr. Terrault, professor of medicine and director of the Viral Hepatitis Center at the University of California, San Francisco.

She cited as particularly impressive the results of the SWIFT-C trial presented by Suzanna Naggie, MD, of Duke University, Durham, N.C., at the 2017 AASLD annual meeting. In this modest-size, National Institutes of Health–sponsored, multicenter study of HIV-infected men with acute HCV coinfection, the sustained viral response (SVR) rate with 8 weeks of ledipasvir/sofosbuvir (Harvoni) was 100%, regardless of their baseline HCV RNA level.

"I think this is remarkable. They cleared virus quite late and yet they went on to achieve HCV eradication. It highlights how little we really know about the treatment of individuals in this phase and that relying on HCV RNA levels may not tell the whole story. I think this is important data to suggest maybe when we treat acute hepatitis C we can use a shorter duration of treatment for that population. There are also other small studies testing 8 weeks of treatment in non–HIV-infected individuals with acute hepatitis C in which they also showed very high SVR rates," the hepatologist said.

Copanelist Steven L. Flamm, MD, said that when he encounters a patient with acute HCV he, too, is prepared to offer treatment – he finds the available supporting evidence sufficiently compelling – but he often encounters a problem.

"Sometimes I'm blocked by insurance companies because this isn't officially approved," noted Dr. Flamm, professor of medicine and chief of the hepatology program at Northwestern University, Chicago.

"You're right," Dr. Terrault commented, "we have to make a pretty compelling argument to the insurer as to why we're treating. But 'treat to prevent transmission to others' usually is successful in our hands."

HCV in patients with end-stage renal disease

The product labeling for sofosbuvir (Sovaldi) says the drug's safety and efficacy haven't been established in patients with severe renal impairment or end-stage renal disease. However, a small multicenter study presented at the 2017 AASLD meeting demonstrated that 12 weeks of ledipasvir/sofosbuvir achieved a 100% SVR rate in patients with genotype 1 HCV and severe renal impairment, including some on dialysis, with no clinically meaningful change in estimated glomerular filtration rate or any signal of cardiac arrhythmia.

"They saw no meaningful safety signals," according to Dr. Terrault. "This, I think, is initial reassuring information that we were all very much waiting for."

"In general, I think glecapravir/pibrentasvir [Mavyret] has become the go-to drug for patients who have renal dysfunction because it's a pangenic regimen, it doesn't require use of sofosbuvir, and there's no dose adjustment. But I would say you could encounter situations where you might want to use sofosbuvir, and for me that situation is typically those direct-acting, antiviral-experienced patients who have failed other therapies and you really need to use sofosbuvir/velpatasvir/voxilaprevir [Vosevi] as your last or rescue therapy," the hepatologist continued.

HCV in liver transplant recipients

"In the years before the direct-acting antivirals, treating transplant patients was always very challenging," Dr. Terrault recalled. "They had very low response rates to therapy. That's all gone away. Now we can say that liver transplant recipients who require treatment have response rates that are the same as in individuals who have not had a transplant. These patients are now being treated earlier and earlier after their transplant because you can do it safely."

She pointed to a study presented at the 2017 AASLD meeting by Kosh Agarwal, MD, of Kings College London. It involved 79 adults with recurrent genotypes 1-4 HCV infection post–liver transplant who were treated with sofosbuvir/velpatasvir (Epclusa) for 12 weeks with a total SVR rate of 96%.

"The nice thing about sofosbuvir/velpatasvir is there are no drug-drug interactions with immunosuppressive drugs. Now it's very easy to take care of these patients," Dr. Terrault observed.

The other combination that's been studied specifically in liver transplant recipients, and in kidney transplant recipients as well, is glecapravir/pibrentasvir. In the MAGELLAN-2 study of 100 such patients with genotypes 1-6 HCV, the SVR rate was 99% with no drug-related adverse events leading to discontinuation.

Persons who inject drugs

The Centers for Disease Control and Prevention and the World Health Organization want HCV eradicated by 2030. If that's going to happen, physicians will have to become more comfortable treating the disease in injectable drug users, a population with a high prevalence of HCV. Several studies have now shown that very high SVR rates can be achieved with direct-acting antiviral regimens as short as 8 weeks in these individuals, even if they are concurrently injecting drugs.

"There is increasing evidence that we should be doing more treatment in persons who inject drugs. Many of these individuals have very early disease and their response rates are excellent," according to Dr. Terrault.

Moreover, their reinfection rates "are not outrageous," she said: 1% or less in individuals who stopped injecting drugs decades prior to anti-HCV treatment, 5%-10% over the course of 3-5 years in those who continue injecting drugs after achieving SVR, and about 2% in those on methadone substitution therapy. "These are very acceptable levels of reinfection if our goal is to move toward elimination of hepatitis C in this population," she said.

She reported having no financial conflicts regarding her presentation.

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Obesity increases risk of acute on chronic liver failure

BY JEFF CRAVEN
MDedge News

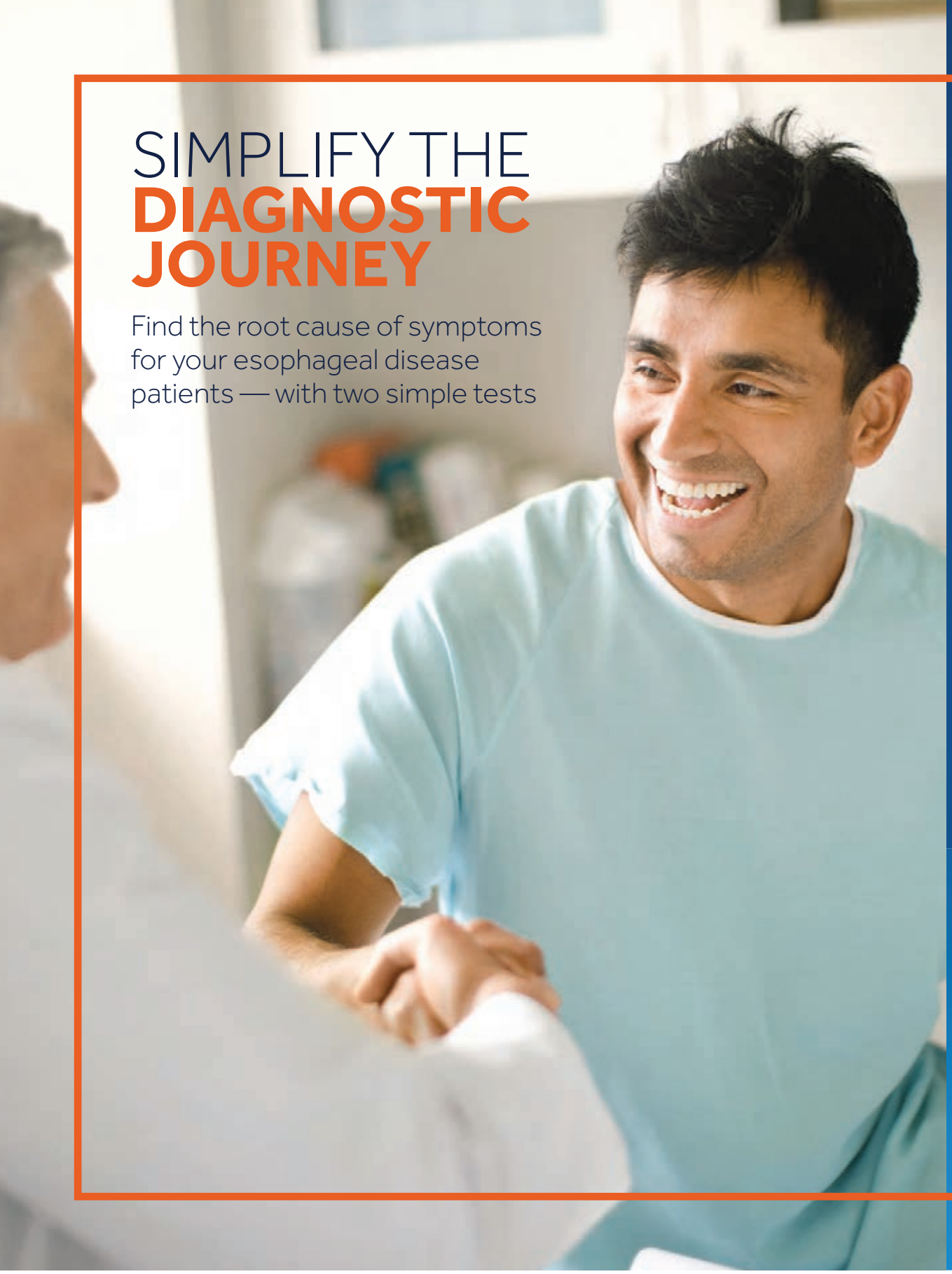
Class III obesity was significantly, independently associated with acute on chronic liver failure (ACLF) in patients with decompensated cirrhosis, and patients with both class III obesity and ACLF also had a significant risk of renal failure, according to a recent retrospective analysis of two databases published in the Journal of Hepatology.

Vinay Sundaram, MD, from Cedars-Sinai Medical Center in Los Angeles, and his colleagues evaluated 387,884 patients who were in the United Network for Organ Sharing (UNOS) during 2005-2016; were class I or II obese (body mass index 30-39 kg/m^2), class III obese (BMI greater than or equal to 40), or not obese (BMI less than 30); and were on a wait list for liver transplantation.

They used the definition of ACLF outlined in the CANONIC (Consortium Acute on Chronic Liver Failure in Cirrhosis) study, which defined it as having "a single hepatic decompensation, such as ascites, hepatic encephalopathy, variceal bleed, or bacterial infection, and one of the following organ failures: single renal failure, single nonrenal organ failure with renal dysfunction or hepatic encephalopathy, or two nonrenal organ failures," and confirmed the results in the Nationwide Inpatient Sample (NIS) databases by using diagnostic coding algorithms to identify factors such as hepatic decompensation, obesity, and ACLF in that study population.

Dr. Sundarem and his colleagues identified 116,704 patients (30.1%) with ACLF in both the UNOS and NIS databases. At the time of liver transplantation, there was a significant association between ACLF and class I and class II obesity (hazard ratio, 1.12; 95% confidence interval, 1.05-1.19; *P* less than .001) and class III obesity (HR, 1.24; 95% CI, 1.09-1.41; *P* less than .001). Other predictors of ACLF in this population were increased age (HR, 1.01 per year; 95% CI, 1.00-1.01; *P* = .037), hepa-

Continued on page 20



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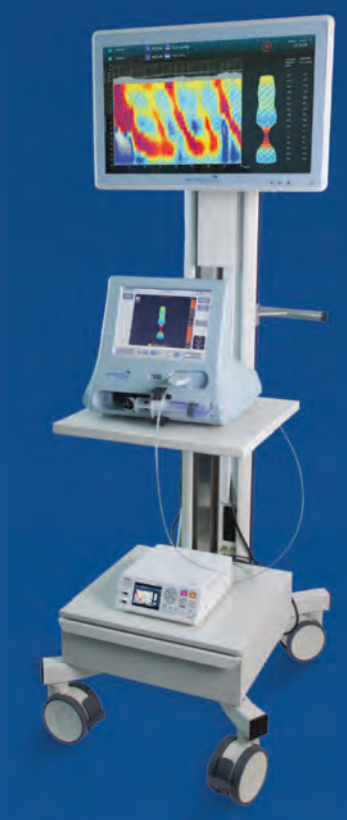

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Hepatic adenoma assessment: Wait more to avoid over-tx

BY ANDREW D. BOWSER
MDedge News

LAS VEGAS – For women with larger hepatic adenomas, current guidelines suggest reassessment 6 months after oral contraceptive withdrawal to determine whether resection is warranted. However, emerging data show reassessing at that time may lead to overtreatment, according to Laura M. Kulik, MD, professor of medicine (gastroenterology and hepatology), radiology and surgery (transplantation), Northwestern University, Chicago.

"There's been some controversy that 6 months may be too short," Dr. Kulik said at the inaugural Perspectives in Digestive Diseases meeting held by Global Academy for Medical Education.

Unlike other benign liver lesions, hepatic adenomas can hemorrhage and transform to hepatocellular carcinoma (HCC). Current guidelines from the European Association for the Study of the Liver state that larger lesions (i.e., 5 cm or greater on baseline imaging) are associated with a higher risk of complications. According to one systematic review cited in the document, almost all cases of hemorrhage or spontaneous rupture occur in lesions 5 cm or larger.

Oral contraceptive use has been associated with a 30- to 40-fold increase in hepatic adenoma incidence, according to the guidelines.

All men with hepatic adenomas should undergo resection or curative treatment, the guidelines say, since they have a significantly higher risk of HCC.

By contrast, women with hepatic adenomas larger than 5 cm should discontinue oral contraceptives – which may lead to tumor regression in some cases – and should be reassessed 6 months later with contrast-enhanced MRI; if the lesion is still greater than 5 cm at that time, they should be considered for resection or curative treatment, the guidelines say.

However, authors of a retrospective cohort study have challenged that advice, suggesting that a 6-month follow-up may not always be long enough to see adequate tumor regression (HPB 2017 Apr;19[Suppl 1]:S3).

In the study, researchers from Erasmus MC University Medical Center, Rotterdam, the Netherlands, reviewed records for patients who were diagnosed with a hepatic adenoma of at least 5 cm and followed for at least 6 months after oral contraceptives were stopped. Of that group, 104 underwent surgical treatment for a lesion larger than 5 cm, while the remaining 86 were conservatively treated. The researchers found that, in the conservatively treated group, 61 lesions (71%) regressed below the 5-cm cutoff after a median of 85 weeks (95% confidence interval, 52-110 weeks), with larger lesions taking significantly longer to regress.

Based on those findings, the investigators said the 6-month cutoff may lead to overtreatment, and that for some patients with particularly large tumors, it may be justified to wait up to 24 months.

"They do caution that beta-catenin mutated adenomas should probably be removed without waiting longer because of the risk of developing cancer."

Dr. Kulik reported disclosures related to Bayer, BMS, BTG, and Eisai. Global Academy and this news organization are owned by the same parent company.

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HBV therapy: Indefinite or FINITE for e-neg patients?

BY ANDREW D. BOWSER
MDedge News

LAS VEGAS – Current guidelines recommend indefinite continuation of antiviral therapy in chronic hepatitis B patients who are hepatitis B e-antigen (HBeAg) negative. But emerging data suggest that this may not always be the case.

"It's very provocative data, though not at the guideline level," W. Ray Kim, MD, said in a presentation at the inaugural Perspectives in Digestive Diseases meeting held by Global Academy for Medical Education.

"There are patients who really have begged to go off treatment because they are sick of taking the medication for year after year after year," said Dr. Kim, professor of medicine, gastroenterology and hepatology, Stanford (Calif.) University.

In light of new data, taking them off medication might be "something to consider" in noncirrhotic patients if they are completely suppressed, have normal ALT, and have a low level of quantitative hepatitis B surface antigen (HBsAg), Dr. Kim told attendees.

The most current Association for the Advancement of the Study of Liver Diseases guidelines state that, unless there is a competing rationale, antiviral therapy should be continued indefinitely for noncirrhotic adults with HBeAg-negative immune-active chronic hepatitis B.

They do also say that treatment discontinuation "may be considered" for individuals with proven loss of HBsAg. "However, there is currently insufficient evidence to definitively guide treatment decisions for such persons," the guidelines say.

Evidence has emerged since those guideline statements were written. Most recently, German investigators published results of the FINITE study showing some long-term responses after stopping tenofovir disoproxil fumarate (TDF) in noncirrhotic, HBeAg-negative patients.

In that prospective, controlled study, 62% of patients who stopped TDF therapy (n = 13) stayed off therapy to week 144 of treatment follow-up. Four of the patients achieved HBsAg loss, and median HBsAg change was $-0.59\log_{10}$IU/mL vs. $0.21\log_{10}$IU/mL in patients who stayed on TDF therapy.

Investigators said that result demonstrated the potential of stopping long-term TDF treatment and seeing either HBsAg loss or sustained virologic response. Before that, a retrospective study from investigators in Taiwan showed that age plus level of HBsAg were associated with HBV relapse after entecavir treatment in HBeAg-negative patients. According to investigators, those results suggested HBsAg levels could be used to guide timing of entecavir cessation.

If antiviral therapy is stopped in an HBeAg-negative patient, that patient should be monitored every 3 months for a year for recurrent viremia, ALT flares, and hepatic decompensation, Dr. Kim said..

Even before stopping, "there are a number of factors to consider, including biological relapse, flare, hepatic decompensation," he said.

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Dr. Kim reported serving as a consultant to Gilead.

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Continued from page 18

titis C virus (HR, 1.25; 95% CI, 1.16-1.35; *P* less than .001) and hepatitis C combined with alcoholic liver disease (HR, 1.18; 95% CI, 1.06-1.30; *P* = .002). Renal insufficiency was similar among the three groups, with increasing obesity class associated with a greater prevalence of renal failure.

"Given the heightened risk of renal failure among obese patients with cirrhosis, we suggest particularly careful management of this fragile population regarding diuretic usage, avoidance of nephrotoxic agents, and administration of an adequate albumin challenge in the setting of acute kidney injury," the researchers wrote. They encouraged "an even greater emphasis on weight reduction" for class III obese patients. They noted the association between class III obesity and ACLF is likely caused by an "obesity-related chronic inflammatory state" and said future prospective studies should seek to describe the inflammatory pathways for each condition to predict risk of ACLF in these patients.

They reported having no financial disclosures.

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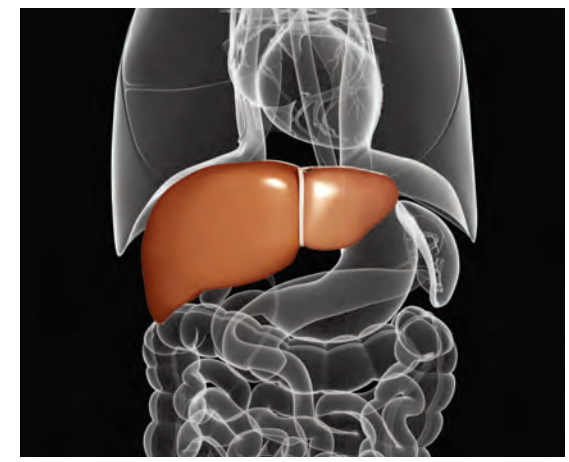
SOURCE: Sundaram V et al. J Hepatol. 2018 Apr 27. doi: 10.1016/j.jhep.2018.04.016.



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New drugs provide new options in HCC

BY ANDREW D. BOWSER
MDedge News

PHILADELPHIA – Recent approvals and investigations of treatments for advanced hepatocellular carcinoma (HCC) are encouraging, Nikolaos Pyrsopoulos, MD, MBA, AGAF, said at Digestive Diseases: New Advances, jointly provided by Rutgers and Global Academy for Medical Education.

"I am excited, because a few years ago, there was only one [Food and Drug Administration]–approved medication," Dr. Pyrsopoulos, division director for gastroenterology and hepatology at Rutgers New Jersey Medical School, Newark, said in an interview. "We are on the cusp where new compounds not only are being tested, but they are being approved."

In one of the most recent developments, the multikinase inhibitor cabozantinib significantly improved the primary endpoint of overall survival versus placebo in HCC patients in the randomized phase 3 CELESTIAL trial.

Median overall survival in CELESTIAL was 10.2 months for cabozantinib versus 8.0 months for placebo (P = .0049), according to the published report.

"It is very encouraging," Dr. Pyrsopoulos said of the cabozantinib results in a presentation on advances in HCC that he gave at the conference.

In one of the most recent developments, the multikinase inhibitor cabozantinib significantly improved the primary endpoint of overall survival versus placebo in HCC patients in the randomized phase 3 CELESTIAL trial.

For years, the only FDA-approved treatment for advanced HCC was sorafenib. In the randomized phase 3 SHARP trial, published in the New England Journal of Medicine in 2008, patients receiving the multikinase inhibitor had a median survival of 10.7 months, versus 7.9 months for placebo (P less than .001).

In April 2017, the FDA approved regorafenib for patients with HCC previously treated with sorafenib. In the randomized phase 3 RESORCE trial, published in The Lancet in 2017, median overall survival was 10.6 months for regorafenib-treated patients versus 7.8 months in the placebo group. Investigators reported that regorafenib improved overall survival with a hazard ratio of 0.63 (P less than .0001).

More agents are under investigation, including lenvatinib, another multikinase inhibitor. In results of a phase 3 randomized trial presented at the 2017 meeting of the American Society of Clinical Oncology, lenvatinib was noninferior to sorafenib in overall survival, with treatment-related adverse effects such as hypertension and diarrhea that were expected based on previous experience with the drug.

Cancer immunotherapy is making inroads into HCC. Just a few months after approving regorafenib, the FDA granted approval to nivolumab, a PD-1 inhibitor, for patients with HCC previously treated with sorafenib.

Dr. Pyrsopoulos highlighted another checkpoint inhibitor, tislelizumab. In January, BeiGene announced the initiation of a global phase 3 trial of this anti-PD-1 antibody versus sorafenib as first-line treatment of patients with unresectable HCC.

Although cancer immunotherapy holds great promise for HCC and other cancers, the treatments are associated with unique immune-related adverse events (irAEs) including immune-related hepatitis that may require corticosteroid treatment, according to Dr. Pyrsopoulos.

Dr. Pyrsopoulos reported disclosures related to AbbVie, Bayer, Genfit, Gilead Sciences, Hologic, Merck, Prometheus, Shire, and Vital Therapies.

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Advanced adenoma on colonoscopy linked to increased colorectal cancer incidence

BY ANDREW D. BOWSER
MDedge News

Advanced adenomas found on diagnostic colonoscopy were associated with increased risk of developing colorectal cancer, while nonadvanced adenomas were not, according to long-term follow-up results from a large screening study.

The findings come from a post hoc analysis of the Prostate, Lung, Colorectal, and Ovarian (PLCO) cancer screening trial that enrolled 154,900 individuals, of whom 15,935 underwent colonoscopy following an abnormal flexible sigmoidoscopy screening result.

With a median of 13 years of follow-up, the incidence of colorectal cancer was 20.0 per 10,000 person-years for patients who had advanced adenoma found on colonoscopy, according to a report on the study published in JAMA. By comparison, colorectal cancer incidence was 9.1 and 7.5 per 10,000 person-years for nonadvanced adenoma and no adenoma, respectively.

"By demonstrating that individuals diagnosed with an advanced adenoma are at increased long-term risk for subsequent incident CRC, these findings support periodic, ongoing surveillance colonoscopy in these patients," wrote Benjamin Click, MD, of the division of gastroenterology, hepatology, and nutrition, University of Pittsburgh, and his coauthors.

'By demonstrating that individuals diagnosed with an advanced adenoma are at increased long-term risk for subsequent incident CRC, these findings support periodic, ongoing surveillance colonoscopy in these patients.'

Compared with patients who had no adenoma, those with advanced adenoma were significantly more likely to develop colorectal cancer (rate ratio, 2.7; 95% confidence interval, 1.9-3.7; P less than .001). By contrast, there was no significant difference in risk of colorectal cancer for patients with nonadvanced adenoma and no adenoma (RR, 1.2; 95% CI, 0.8-1.7; P = .30).

Risk of death related to colorectal cancer was also significantly increased for patients with advanced adenoma versus no adenoma, and again, the investigators said, no such difference in mortality was found when nonadvanced adenoma was compared with no adenoma.

The PLCO screening study enrolled men and women aged 55-74 years beginning in 1993, with follow-up continuing until Dec. 31, 2013.

Small, nonadvanced adenomas are commonly found in colonoscopy, occurring in approximately 30% of patients, the investigators said. In the United States, when patients have one to two nonadvanced adenomas, they are typically advised to return in 5-10 years, the researchers noted. However, evidence is lacking in terms of who should return in 5 years, as opposed to 10 years.

"If appropriately powered prospective trials were to replicate these findings, demonstrating no significant difference in cancer incidence between participants with 1 to 2 nonadvanced adenoma(s) and no adenomas, colonoscopy use could be reduced by a large extent, as a surveillance examination at 5 years would not be needed," the study authors said.

The National Cancer Institute Division of Cancer Prevention supported the study. One author reported receiving grant support from Medtronic.

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SOURCE: Click B et al. JAMA. 2018;319(19):2021-31.

AGA Resource
Adequate prep is essential for a high-quality colonoscopy. Help your patients prepare by sharing resources from AGA's GI Patient Center at https://www.gastro.org/practice-guidance/gi-patient-center/topic/colonoscopy.

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Technical, judgment errors cited

Malpractice *from page 1*

colonoscopy cases, 21% of esophagogastroduodenoscopy cases, and 0% of endoscopic ultrasound cases, according to the study published in the April 24 Journal of Clinical Anesthesia.

Of all 58 claims, the mean payment was $99,754. When restricted to only claims that resulted in payment (22 cases), the mean payment rose to $275,510, and the median payment was $7,170. No significant difference existed in the percentage of cases that resulted in payment between high-, middle-, and low-severity cases.

The most common contributing factors to the alleged anesthesiology-related adverse events were lack of technical skill, clinical judgment errors, communication mishaps, and documentation problems. Within the technical skill category, technical problems from a known complication, poor technique, and failure to resuscitate were frequent contributing factors. Within the clinical judgment category, failure to monitor the physiological status of the patient was the most common subcategory noted.

Oversedation was another possible contributing factor in 62.5% of the cases, investigators found. For the purposes of this study, oversedation was defined as unexpected changes in the physiological state of the patient and/or unplanned intubation for a patient undergoing monitored anesthesia care.

But the authors concluded that oversedation alone did not lead to liability for anesthesia providers practicing in the endoscopy suite; rather, it was allegations of technical and clinical judgment failures, such as the inability to recognize acute clinical deterioration or manage difficulty, that most often resulted in settlements to plaintiffs. The analysis also suggested that, even when adverse events occured in the endoscopy suite, anesthesiologists were less likely to be found liable when highly trained and well-equipped anesthesia providers were readily available.

The authors concluded that it is critical to have a well-prepared anesthesia provider when medically complex patients are undergoing endoscopic procedures.

The authors had no disclosures.

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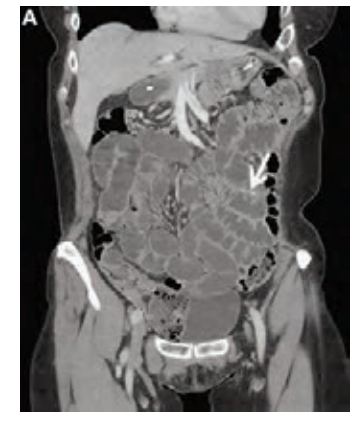
SOURCE: Stone AB et al. J Clin Anesth. 2018 Apr 24;48:15-20.

CLINICAL CHALLENGES AND IMAGES

What is your diagnosis?

By Guilherme Piovezani Ramos, MD, Seth Sweetser, MD, and John B. Kisiel, MD. Published previously in Gastroenterology (2016;151[1] e20-21.

A 63-year-old woman with a 6-year history of fibrostenotic ileocolonic Crohn's disease (CD) presented for evaluation after multiple hospitalizations for recurrent small-bowel obstruction (SBO). Treatment for CD included adalimumab and azathioprine. Before initiation of these medications, she had undergone a 30-cm ileal resection for partial SBO secondary to a fibroinflammatory ileal stricture. She had no other coexistent medical conditions. She denied nonsteroidal anti-inflammatory drug use, but did take acetaminophen for intermittent low-back pain. Family history was notable for a daughter with CD. The patient denied use of alcohol, tobacco, or illicit drugs.



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Over the past year, she has been hospitalized three times for partial SBOs that were treated conservatively. Her most recent hospitalization was 1 month ago, after which she was referred for assessment of inflammatory CD as the cause of recurrent SBO. She continued to complain of intermittent left lower abdominal pain after hospital discharge. Physical examination revealed a mildly distended abdomen with positive bowel sounds, tenderness to deep palpation in the lower quadrants, and no tympany to percussion or peritoneal signs. Laboratory evaluation, including complete blood count and basic metabolic profile, was unrevealing. Inflammatory markers, including erythrocyte sedimentation rate and C-reactive protein, had been within normal limits over the past year. On review of the abdominal computed tomographic images performed during the episodes of partial SBO, there was a transition point localized on the left lower quadrant; no mural enhancement or bowel wall thickening was seen.

Reevaluation with noncontrast CT of the abdomen showed resolution of previous acute obstruction. An enteroclysis tube was then placed and a second set of images demonstrated a curvilinear density in the left lower quadrant (Figure A, arrow), in the area of prior obstructions, which was not present on previous imaging studies.

What is the most likely cause of her recurrent SBOs?

The answer is on page 28.

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Quick quiz answers

Q1. Correct answer: C

Rationale
This patient is presenting early post–liver transplant with severe hepatic dysfunction. This severity of enzyme elevation is concerning for an underlying hepatic artery thrombosis. The next appropriate diagnostic test for this patient is a hepatic ultrasound with Doppler to assess hepatic artery patency. CMV infection does not typically occur within the first month post–liver transplant and would not be expected to cause this degree of elevation in the liver enzymes. Performance of liver biopsy, MRCP, or ERCP would not reveal the underlying etiology and may result in delay in diagnosis.

Reference
1. Stange BJ, Glanemann M, Nuessler NC, et al. Hepatic artery thrombosis after adult liver transplantation. Liver Transplantation. 2003;9:612-20.

Q2. Correct answer: C

Rationale
This patient has long-standing diabetes with associated complications from prolonged hyperglycemia, with symptoms of delayed gastric emptying. The next best step would be to perform a gastric-emptying study or scintigraphy to confirm the diagnosis of diabetic gastroparesis. A dietitian consult will be necessary once gastroparesis is confirmed, since dietary modifications are the mainstay of treatment. Strict blood glucose control is necessary to prevent worsening gastrointestinal symptoms, and an evaluation by an endocrinologist is reasonable if gastroparesis is confirmed. A trial of metoclopramide may be necessary if gastroparesis symptoms are not controlled with dietary modifications, but it would not be first-line treatment in diabetic gastroparesis.

References
1. Camilleri M. Advances in diabetic gastroparesis. Rev Gastroenterol Disord. 2002;2:47-56.
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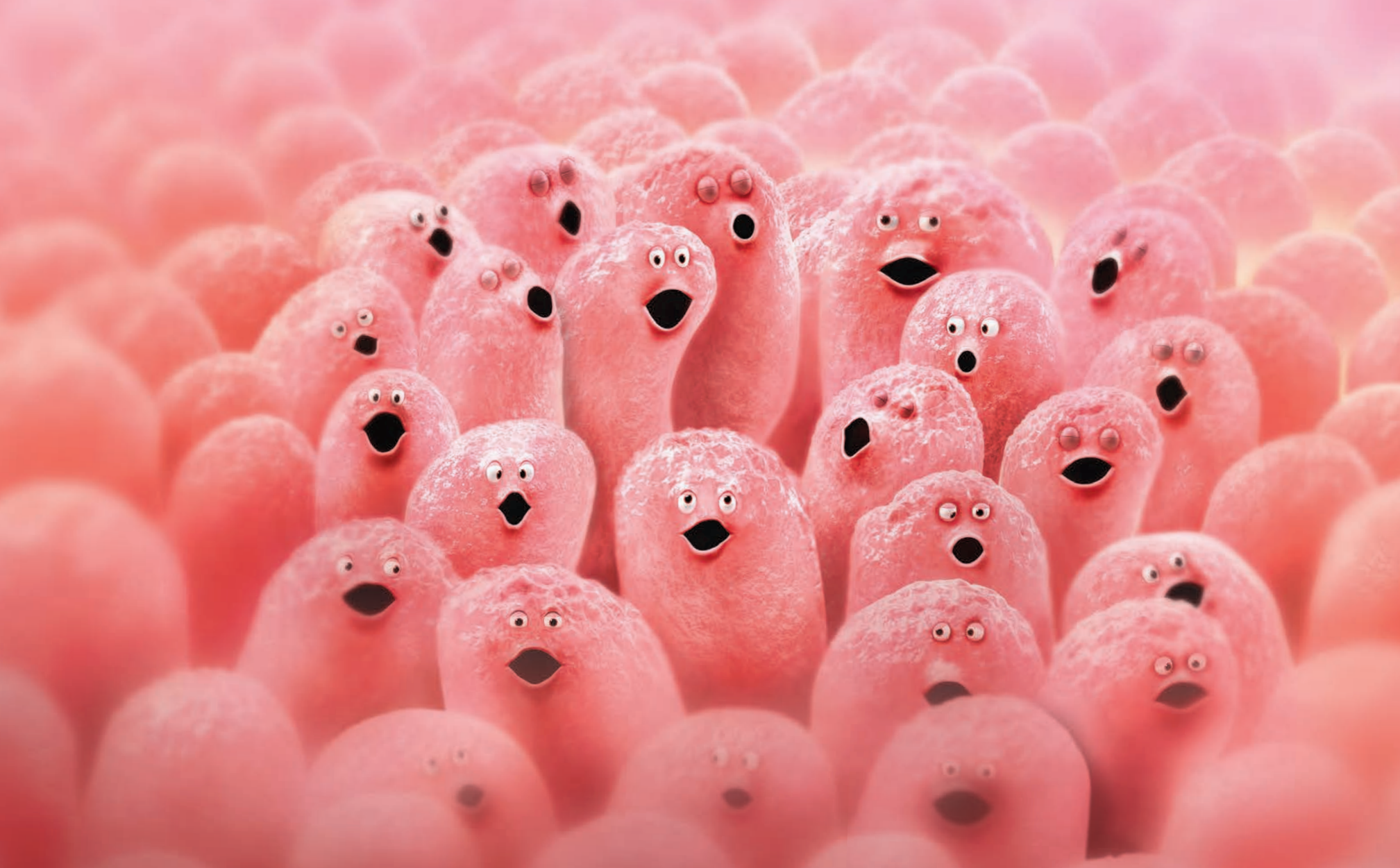

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**In the same study, 748 serum samples from 396 adult CD patients were divided into 2 cohorts: 335 samples from 278 patients were used to develop the Mucosal Healing Index (biomarker expression was modeled against endoscopic scoring CDEIS [Crohn's Disease Endoscopic Index of Severity] or SES-CD [Simple Endoscopic Score for Crohn's Disease]) and 412 samples from 118 CD patients were analyzed with endoscopic scoring for independent validation.[1]

References: 1. Vermeire S, D'Haens G, Hale M, et al. A novel serum test to describe the mucosal healing state by disease location in Crohn's disease patients. Presented at: World Congress of Gastroenterology; October 13-18, 2017; Orlando, FL. **2.** Kelly OB, Silverberg MS, Dulai PD, et al. Development and validation of a multi-marker serum test for the assessment of mucosal healing in Crohn's disease patients. Presented at: World Congress of Gastroenterology; October 13-18, 2017; Orlando, FL.

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May be better to eat the sugar

Sucralose *from page 1*

sucralose, or water as the control, finding that sucralose consumption resulted in a significant increase in blood flow to certain areas of the brains of study participants with obesity but not in lean individuals (2.10 mL/100 g per min vs. –.079 mL/100 g per min; *P* = .002).

Brandon Ge and his collaborators at the University of Southern California, Los Angeles, assessed changes in serum levels of hunger- and appetite-associated hormones. They also used functional magnetic resonance imaging (fMRI) to see how the various substances affected areas of the brain that are associated with appetite and satiety as well as reward circuit pathways. Finally, individuals in the study were allowed unrestricted access to food 90 minutes after consuming the study substance, and food intake was tracked and compared among participants.

MR. GE

Whether responses to caloric and noncaloric sweeteners are different between individuals with and without obesity has not been well established, though recent in vitro and in vivo studies have suggested an association.

"A proposed mechanism is that noncaloric sweeteners uncouple sweetness from calorie intake, which may impact neurophysiological regulators of feeding behavior," wrote Mr. Ge and his collaborators in an abstract presented at the annual meeting of the Endocrine Society. Still, the work attempts to fill a knowledge gap: "Little evidence, however, has determined the relationship between obesity status and neurophysiological and feeding responses to caloric and noncaloric sweetener consumption," they wrote.

Noncaloric sweeteners may uncouple sweetness from calorie intake, which may impact regulators of feeding behavior.

Of the 30 participants aged 19-24 years, 16 were female; half were lean, with a body mass index of 19-25 kg/m^2; the remainder met obesity criteria, with BMIs greater than 30 kg/m^2.

For the brain-imaging portion of the study, arterial spin labeling fMRI was used to examine blood flow in a number of predetermined regions of interest. These included the hypothalamus, amygdala, dorsal striatum, insula, and anterior cingulate cortex.

Participants had three scans, spaced at least 2 days apart and occurring after a 12-hour overnight fast. A scan with arterial spin labeling acquisition was taken before and 10 minutes after participants drank a 300-mL beverage consisting of just water, or either a 75-g glucose solution or 2 mmol/L sucralose.

Twenty-five of the participants had blood drawn at 0, 40, and 60 minutes after drinking the study beverage, to track levels of serum insulin, ghrelin, GLP-1, and peptide YY – all hormones that help regulate appetite and satiety.

Hormone levels for individuals who had the non–glucose beverages were similar, regardless of BMI. However, there were significant differences in cerebral blood flow between obese and nonobese participants. Mr. Ge, an undergraduate student, and his collaborators looked at the contributions of the individual brain structures to the significantly higher activation seen after sucralose consumption by the high-BMI participants. Individuals with obesity had significantly more activity in the amygdala than did the lean participants (*P* = .0088) after drinking the sucralose beverage; also, in lean individuals, hypothalamic activity decreased after sucralose consumption, while activity increased slightly in the high-BMI participants (*P* = .017).

Eating behavior after drinking the various beverages also differed depending on beverage type and BMI status. After the overnight fast and study beverage consumption, participants were offered unlimited access to a buffet-style meal. The beverage type had no significant effect on calorie consumption at the buffet for the lean study participants. However, obese individuals consumed significantly more calories than did lean individuals after ingesting sucralose (1,191 kcal vs. 731 kcal; *P* = .01). Caloric intake was not significantly different between the high- and low-BMI groups after consumption of water or glucose.

None of the study authors reported conflicts of interest.

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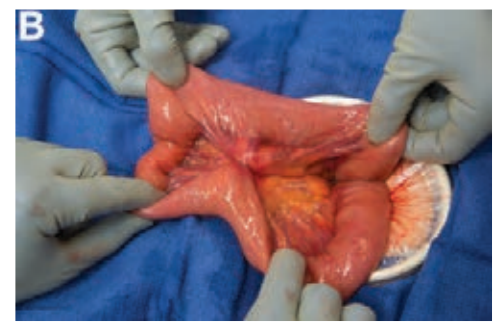
CLINICAL CHALLENGES AND IMAGES

The diagnosis

Answer to "What is your diagnosis?" on page 24: Recurrent SBO owing to contained perforation after accidental ingestion of a metal bristle of a barbecue grill brush

SBO may be caused by a variety of intrinsic or extrinsic lesions. Postoperative adhesions (60%) and malignant tumors (20%) are responsible for the majority of cases in the United States. CD accounts for approximately 5% of all SBOs.[1] The unusual root cause of our patient's SBO was unintentional ingestion of a foreign body.

The CT image in Figure A shows an extraluminal foreign body in the left lower quadrant, surrounded by soft tissue thickening which represents reactive granulation tissue. She underwent surgical exploration, which revealed a single adhesion from a loop of the midjejunum to the neighboring mesentery (Figure B) that, when lysed, uncovered a small metal fragment consistent with a wire bristle from a grill-cleaning brush (Figure C). On further history, she reported frequent outdoor residential food grilling and admitted to using a wire grill-cleaning brush. It is likely that she unintentionally ingested a metal bristle from a barbecue grill brush that was embedded in cooked food and penetrated through the small-bowel wall, causing an adhesive inflammatory reaction and subsequent recurrent SBO.



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Ingested foreign bodies are most frequently encountered in the pediatric population. Injury from inadvertent ingestion of wire grill-cleaning brush bristles is being reported with increasing frequency in adults.[2] Gastroenterologists should be aware of this type of foreign body injury to help prevent delay in diagnosis and ultimately treatment.

This case highlights several additional important points. First, the evaluation of SBO must begin with a broad differential diagnosis, even in a patient with established CD. Second, the bristles are small and difficult to visualize on imaging. After resolution of acute obstruction, diagnostic imaging should be performed without positive oral contrast agent, which can obscure subtle mucosal findings or in this case, a diminutive extraluminal foreign body. Finally, greater public awareness should be raised that bristles might dislodge from wire grill brushes and embed in cooked food.[3]

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Celiac disease: Can biopsy be avoided?

BY ANDREW D. BOWSER
MDedge News

LAS VEGAS – It may be only a matter of time before the "gold standard" small biopsy is no longer considered mandatory to make a diagnosis of celiac disease in adults, according to Joseph A. Murray, MD, AGAF, consultant in the division of gastroenterology and hepatology and department of immunology, Mayo Clinic, Rochester, Minn.

ANDREW D. BOWSER/MDEDGE NEWS

Dr. Joseph A. Murray suspects that soon biopsy may no longer be required to diagnose celiac disease.

"Right now, none of the adult societies support biopsy avoidance, but I predict that it will come to be," Dr. Murray said at the inaugural Perspectives in Digestive Diseases meeting held by Global Academy for Medical Education.

Biopsy, is being challenged in studies that examine alternative ways of making the diagnosis according to Dr. Murray. In one recently reported study, investigators at Royal Derby (England) Hospital suggested that clinicians could make a reliable diagnosis of celiac disease by looking at serum IgA-tissue transglutaminase antibody levels.

Those investigators retrospectively analyzed an unselected series of 270 adult patients and found that an IgA-tissue transglutaminase antibody cutoff of 45 U/mL, or 8 times the upper limit of normal, had a positive predictive value of 100%.

Biopsy avoidance remains controversial, however. In a published letter to the editor commenting on the Derby study, authors took issue with some of the statistical analysis and remarked that the study included some patients with Marsh 1 histology.

"Studies suggest that the majority of seropositive patients with Marsh 1 histology do not progress to develop villous atrophy while on a gluten-containing diet, raising the question whether all of them are truly celiac," they wrote.

The first society to endorse skipping the biopsy was the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition. In guidelines for the diagnosis of celiac disease, that group said a celiac diagnosis could be made based on symptoms, antibodies, and HLA in children with symptoms suggestive of the disease and high antibody levels.

"The data [are] now pretty good to support that approach in symptomatic children," Dr. Murray said. "If we apply these to adult patients, it's not bad, actually, partly because our biopsies aren't perfect." However, not all adult gastroenterology specialists agreed with the recommendations of the pediatric society. Guidelines from the British Society of Gastroenterology have stated that serology cannot replace biopsy, which "remains essential" for celiac disease diagnosis.

Global Academy and this news organization are owned by the same parent company.

Dr. Murray reported disclosures related to Ardent Mills, DBV Technologies, Evelo, GlaxoSmithKline, Johnson & Johnson, Immunogenix, Innovate, National Center for Complementary and Integrative Health, Takeda, Torax Medical, and UCB.

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AGA Resource
AGA offers celiac disease information for your patients in the GI Patient Center at https://www.gastro.org/practice-guidance/gi-patient-center/topic/celiac-disease.

Constipation on opioids? Follow these steps to ID true cause

BY ANDREW D. BOWSER
MDedge News

LAS VEGAS – For appropriate management of patients on opioids who develop constipation, one of the most important distinctions to make is whether the condition was caused by the pain treatment or was just exacerbated by it, according to Darren M. Brenner, MD, AGAF.

Because of the rampant use of opioids, the answer to that question is increasingly relevant to clinical practice, said Dr. Brenner, associate professor of medicine (gastroenterology and hepatology) and surgery at Northwestern University, Chicago.

"The key from a gastroenterologist and primary care perspective is to differentiate opioid-induced from opioid-exacerbated constipation because, realistically, treatment of the global symptom profile will provide the most effective outcomes and strategies for your patients," Dr. Brenner said at the inaugural Perspectives in Digestive Diseases meeting held by Global Academy for Medical Education.

Dr. Brenner described a concise algorithm (Curr Gastroenterol Rep. 2017 Mar;19[3]:12) for discerning these patient groups; he codeveloped the algorithm with meeting cochair Brooks D. Cash, MD, chief of the division of gastroenterology, hepatology, and nutrition at the University of Texas, Houston.

ANDREW D. BOWSER/MDEDGE NEWS

Dr. Darren M. Brenner proposes that the cause of pre-opioid constipation will help treat the opioid-induced version.

Step 1 in the algorithm is simply to ask patients whether they are constipated. "You should ask all of your patients who are on opioids if they have this problem," Dr. Brenner said. "A significant percentage of individuals using opioids will develop constipation."

According to the results of studies that Dr. Brenner summarized, up to 80% of patients taking opioids for chronic, noncancer pain will develop opioid-induced constipation, and more than 90% of opioid-taking patients with advanced illness will need laxatives. Clinicians might want to be skeptical then when patients on opioids reply "no" when asked whether they are constipated.

"From my own clinical experience, you will miss a third of your population that has constipation," Dr. Brenner said, noting that some patients will think of their condition in terms of incomplete evacuation or decreased stool frequency.

Step 2 of the algorithm, therefore, is to assess for signs and symptoms of functional constipation in all patients, regardless of whether they report the condition.

The recently published Rome IV diagnostic criteria included a new category for opioid-induced constipation. According to the new definition, opioid-induced constipation must include new or worsening symptoms, such as fewer than three solid bowel movements per week, and straining, blockage sensation, or manual maneuvers on at least 25% of bowel movements, among other symptoms listed in the report.

If patients do have constipation meeting these criteria, then step 3 of the algorithm is to determine whether the symptoms were present prior to taking opioids.

If onset of constipation is related to the start of opioid treatment, options may include prescribing peripherally acting mu-opioid receptor antagonists (PAMORAs). By contrast, onset unrelated to the start of opioids, also known as opioid-exacerbated constipation, may require treatment according to the underlying cause. For example, slow-transit constipation may respond to laxatives, while evacuation disorders may be treated with surgery, biofeedback, or physical therapy.

The hardest group to identify, according to Dr. Brenner, is individuals whose symptoms were so minor that they didn't even realize they had constipation symptoms prior to opioids.

Because treatment protocols for opioid-induced and opioid-exacerbated constipation are so different, "we must tease these people out," Dr. Brenner said.

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Dr. Brenner reported disclosures related to Allergan, Daiichi Sankyo, Ironwood Pharmaceuticals, Prius Medical, and others.

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White House pushes transparency in drug price plan

BY GREGORY TWACHTMAN
MDedge News

The White House is targeting greater price transparency and is looking at doctors to provide information about out-of-pocket costs as part of a broad initiative aimed at lowering the cost of prescription drugs.


MR. AZAR

The Trump administration believes it is a "right that, when you are sitting there with your doctor, you ought to be able to know what your out-of-pocket [cost] is for the drug you are going to be prescribed under your precise drug plan."

The information is critical, regardless of a patient's insurer, Alex M. Azar II, secretary of Health & Human Services, said at a press briefing.

Price transparency is a key theme to the broad package of proposals called American Patients First that the White House released May 11. The plan includes changes that can be made immediately as well as some upon which the administration will seek public comment, according to the plan.

Another tactic the administration is considering for quick action is requiring a drug's list prices to be included in all direct-to-consumer advertising.

The plan also calls for the banning of gag rules that prevent pharmacists from alerting patients when it would be cheaper to buy a prescribed drug without going through their insurance coverage, as well as moving certain drugs from Medicare Part B to Medicare Part D to improve the government's ability to negotiations for lower prices.

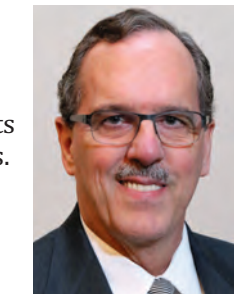
The overall strategy is laid out across four areas:

- Increasing competition through policy measures that prevent manufacturers from gaming the patent system and promoting innovation and competition among biologics.
- Improving negotiation abilities, including doing more with value-based purchasing; allowing for more substitution, especially in the case of single-source generics; and further examination of the competitive acquisition program for Part B.
- Providing incentives to manufacturers to lower their list prices.

PERSPECTIVE

Plan does not really address drug prices

I would like to provide some context for our story about the White House plan to lower drug prices. In mid-May, the White House rolled out a plan called "American Patients First" (https://www.hhs.gov/sites/default/files/AmericanPatientsFirst.pdf), a 44-page document that outlines a blueprint for price reduction. This document was released under the name of Alex M. Azar II, the Secretary of Health & Human Services. Mr. Azar is a second-generation immigrant, son of an ophthalmologist (Johns Hopkins University faculty) and is a Yale-educated lawyer who practiced with Kenneth Starr (Whitewater fame). He became a lobbyist, vice president for managed health services, and then president at Eli Lilly. His background is impressive, and he has more knowledge about the pharmaceutical industry than almost anyone. It should be noted that during his tenure at Eli Lilly, drug prices rose substantially.


DR. ALLEN

The pdf document lays out four challenges in the American drug market:

- High list prices
- Senior and government programs paying too much because of the lack of negotiating tools
- High and rising out-of-pocket expenses for patients
- Foreign governments free riding off of American investment and innovation.

There are four approaches listed:

- Improved competition
- Better negotiating
- Incentives for lower list prices
- Lowering out-of-pocket costs

You might wonder why we are the only country that does not negotiate drug pricing. In 2003, Congress passed a landmark bill to help seniors buy prescription drugs (Medicare Part D – Medicare Modernization Act). In that bill, there was a late addition that specifically barred the federal government from negotiating cheaper prices for medications. The bill essentially outsourced price management to insurance companies who adjudicate Medicare Part D. While the majority of politicians from both parties favor allowing the government to negotiate (Kaiser Family Foundation poll in 2015) no such bill has ever reached the floor of either house of Congress.

Other suggestions in this document include asking physicians to provide drug price information at point of service. I remember discussing this idea with pharmacists at the Minneapolis VA Medical Center in 1985 and concluding that the complexity of such an infrastructure was overwhelming. Another idea is to eliminate the byzantine system of rebates that drug manufactures provide to patients ("if you can't afford your medication, we can help"). I have personally witnessed pharmaceutical reps handing discount coupons for branded drugs to physicians who agreed to meet with them (to help patients). Anyone who has thought about this for more than 10 seconds understands that these maneuvers serve to mask real prices and secure patient loyalty to a specific drug.

It is time for physicians to get serious about drug pricing and how we are, at times, complicit in perpetuating such a system. It is telling that sector stock prices for both major pharmaceutical firms and pharmacy benefit companies dipped as President Trump began his speech but closed higher by the end of this announcement.

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• Lowering out-of-pocket costs.

Currently, there is no incentive to lower drug prices, Mr. Azar noted. He called out pharmacy benefit managers (PBMs) for financially benefiting from both manufacturers and the insurers they represent and said HHS is looking into banning financial compensation to PBMs from the manufacturers. He also said the agency will be releasing a request for information on the feasibility of doing away with rebates as a means of driving manufacturers to lower their prices.

PhRMA, the lobbying group representing pharmaceutical manufacturers, said in a statement that some of the changes related to Part D "could undermine the existing structure of the program that has successfully held down costs and provided seniors with access to comprehensive prescription drug coverage. We also must avoid changes to Medicare Part B that could raise costs for seniors and limit their access to lifesaving treatments."

The Pharmaceutical Care Management Association, the lobbying group for pharmacy benefit managers, also spoke out against the idea of eliminating rebates, noting in a statement that getting rid of them "and other price concessions would leave patients and payers, including Medicaid and Medicare, at the mercy of drug manufacturer pricing strategies. PBMs have long encouraged manufacturers to offer payers alternative ways to reduce net costs. Simply put, the easiest way to lower costs would be for drug companies to lower their prices."

The American Medical Association voiced support for the plan.

"The AMA is pleased the Trump administration is moving forward with its effort to address seemingly arbitrary pricing for prescription drugs," President David Barbe, MD, said in a statement "Physicians see the impact of skyrocketing prices every day as patients are often unable to afford the most medically appropriate medications – even those that have effectively controlled their medical condition for years. No one can understand the logic behind the high and fluctuating prices. We hope the administration can bring some transparency – and relief – to patients."

During a Rose Garden ceremony to introduce the initiative, President Trump said he is targeting foreign countries that require manufacturers to sell their products well below list prices as a condition of selling in their country, forcing Americans to absorb the research and development costs via higher prices for drugs.

"It's time to end the global free-loading once and for all," President Trump said. "I have directed U.S. Trade Representative Bob Lighthizer to make fixing this injustice a top priority with every trading partner."

One proposal President Trump campaigned on – giving the federal government the power to directly negotiate for drug prices – was not included in the plan.

"I am very disappointed that he has apparently dropped his support for allowing Medicare to negotiate the price of prescription drugs," Sen. Maggie Hassan (D-N.H.) said in a statement.

Also absent from the plan was a direct negotiation tactic for Part B drugs supported by Mr. Azar during his confirmation hearings.

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PRACTICE MANAGEMENT TOOLBOX:

New models of gastroenterology practice

BY JOHN I. ALLEN, MD, MBA, AGAF, AND NEAL K. KAUSHAL, MD, MBA

DR. ALLEN

DR. KAUSHAL

The variety of employment models available to gastroenterologists reflects the dynamic changes we are experiencing in medicine today. Delivery of gastrointestinal care in the United States continues to evolve in light of health care reform and the Affordable Care Act.[1] Within the past decade, as health systems and payers continue to consolidate, regulatory pressures have increased steadily and new policies such as electronic documentation and mandatory quality metrics reporting have added new challenges to the emerging generation of gastroenterologists.[2] Although the lay press tends to focus on health care costs, coverage, physician reimbursement, provider burnout, health system consolidation, and value-based payment models, relatively less has been published about emerging employment and practice models.

Here, we describe five new models of practice that have emerged in the past decade and have become viable choices for beginning and seasoned gastroenterologists alike.

Background

When the senior author graduated from fellowship in 1983 (J.I.A.), gastroenterology practice model choices were limited to essentially four: independent community-based, single-specialty, physician-owned practice (solo or small group); independent multispecialty physician-owned practice; hospital or health system–owned multispecialty practice; and academic practice (including the Veterans Administration Medical Centers).

In the private sector, young community gastroenterologists typically would join a physician-owned practice and spend time (2-5 years) as an employed physician in a partnership track. During this time, his/her salary was subsidized while he/she built a practice base. Then, they would buy in to the Professional Association with cash or equity equivalents and become a partner. As a partner, he/she then had the opportunity to share in ancillary revenue streams such as facility fees derived from a practice-owned ambulatory endoscopy center (AEC). By contrast, young academic faculty would be hired as an instructor and, if successful, climb the traditional ladder track to assistant, associate, and professor of medicine in an academic medical center (AMC).

In the 1980s, a typical community GI practice comprised one to eight physicians, with most having been formed by one or two male gastroenterologists in the early 1970s when flexible endoscopy moved into clinical practice. The three practices that eventually would become Minnesota Gastroenterology (where J.I.A. practiced) opened in 1972. In 1996, the three practices merged into a single group of 38 physicians with ownership in three AECs. Advanced practice nurses and physician assistants were not yet part of the equation. Colonoscopy represented 48% of procedure volume, accounts receivable (time between submitting an insurance claim and being paid) averaged 88 days, and physicians averaged 9,000 work relative value units (wRVUs) per partner annually. By comparison, median wRVUs for a full-time community GI in 1996 was 10,422 according to the Medical Group Management Association.[3] Annual gross revenue (before expenses) per physician was approximately $400,000, and overhead reached 38% and 47% of revenue (there were two divisions). Partner incomes were at the 12% level of the Medical Group Management Association for gastroenterologists (personal management notes of J.I.A.). Minnesota Gastroenterology was the largest single-specialty GI practice in 1996 and its consolidation foreshadowed a trend that has accelerated over the ensuing generation.

When one of the authors (N.K.K.) graduated from the University of California Los Angeles in 2017, the GI employment landscape had evolved considerably. At least five new models of GI practice had emerged: individual incorporation with a Professional Services Agreement (PSA), a clinician track within an AMC, large single-specialty group practice (partnership or employee), private equity–backed multistate practice, and locum tenens (Figure 1).

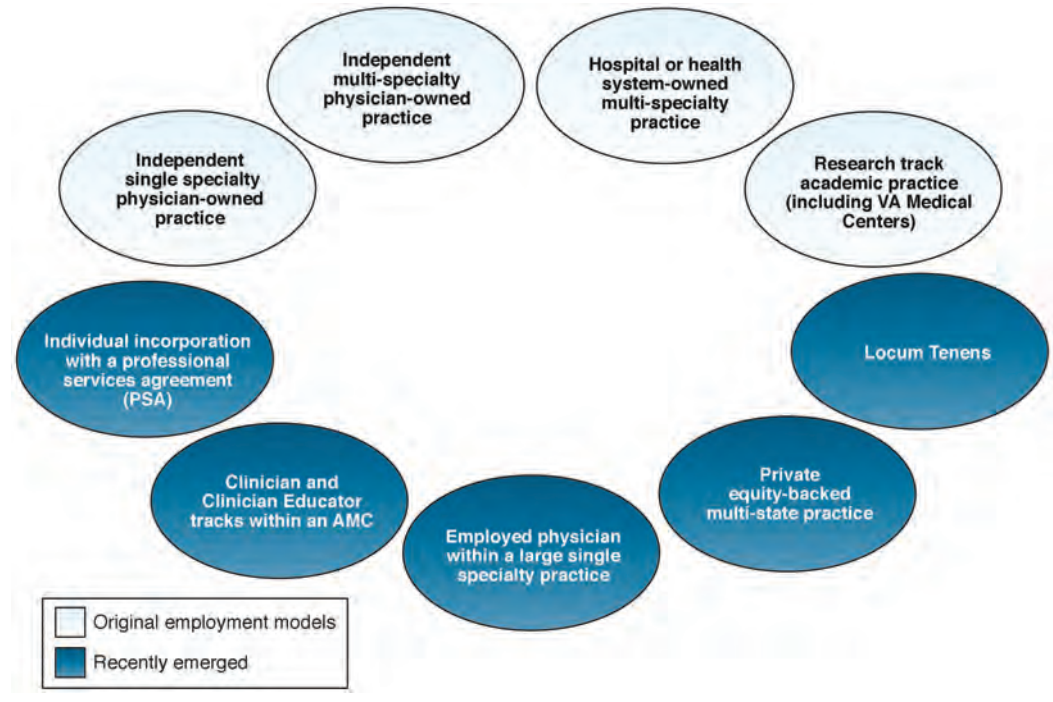

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Figure 1 Employment models (light blue) available in the 1980s and those that have emerged as common models in the last decade (dark blue).

Individual incorporation with a professional services agreement

For gastroenterologists at any career stage, the prospect of employment within a corporate entity, be it an academic university, hospital system, or private practice group, can be daunting. To that end, one central question facing nearly all gastroenterologists is, how much independence and flexibility, both clinically and financially, do I really want, and what can I do to realize my ideal job description?

An interesting alternative to direct health system employment occurs when a physician forms a solo corporation and then contracts with a hospital or health system under a PSA. Here, the physician provides professional services on a contractual basis, but retains control of finances and has more autonomy compared with employment. Essentially, the physician is a corporation of one, with hospital alignment rather than employment. For full disclosure, this is the employment model of one of the authors (N.K.K.).

A PSA arrangement is common for larger independent GI practices. Many practices have PSA arrangements with hospitals ranging from call coverage to full professional services. For an individual working within a PSA, income is not the traditional W-2 Internal Revenue Service arrangement in which taxes are removed automatically. Income derived from a PSA usually falls under an Internal Revenue Service Form 1099. The physician actually is employed through their practice corporation and relates to the hospital as an independent contractor.

There are four common variants of the PSA model.[4] A Global Payment PSA is when a hospital contracts with the physician practice for specific services and pays a global rate linked to wRVUs. The rate is negotiated to encompass

Continued on page 38

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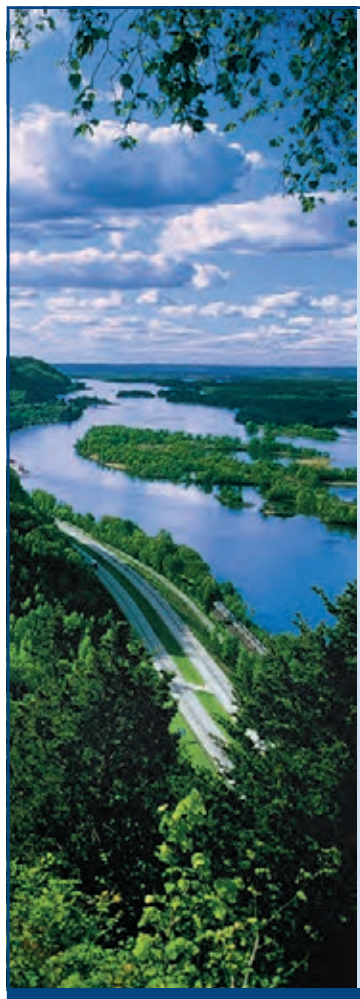

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Continued from page 36

physician compensation, benefits, and practice overhead. The practice retains control of its own office functions and staff.

In a traditional PSA, the hospital contracts with physicians and pays them based on RVU production, but the hospital owns the administrative part of the practice (staff, billing, collections, equipment, and supplies).

A practice management arrangement occurs when the hospital employs the physician who provides professional services and a separate third party manages the practice via a separate management contract. Finally, a Carve-Out PSA can use any of the earlier-described PSA arrangements and certain services are carved out under line-item provisions. For example, a hospital could contract with a private GI group for endoscopic services or night call and write a PSA expressly for these purposes.

Some notable benefits of the PSA are that physicians can maintain financial and employment independence from the hospital and have more control over benefits packages, retirement savings options, and health insurance. Physicians also can provide services outside of the hospital (e.g., telemedicine or locums tenens – described later) without institutional restrictions or conflicts. Finally, physicians benefit from tax advantages of self-employment (with associated business-related tax deductions) through their corporation. The potential downsides of a PSA contract are the subtle expansion of services demanded (known as scope creep) or the possibility of contract termination (or nonrenewal) by the hospital. In addition, medical training does not equip physicians with the knowledge to navigate personal and corporate finances, benefits packages, and tax structures, so the learning curve can be quite steep. Nevertheless, PSAs can be an innovative employment model for gastroenterologists who wish to preserve autonomy and financial flexibility. In this model, legal advice by an attorney skilled in employment law is mandatory.

Academic clinicians track

Until recently, clinically oriented academic faculty were channeled into the traditional ladder faculty model in which advancement was contingent on publications, national recognition, grant support, and teaching. As competition for market share has intensified among regional health systems, many AMCs have developed purely clinical tracks in which research, publication, and teaching are not expected; salaries are linked to clinical productivity; and income may approximate the professional (but not ancillary) income of a community gastroenterologist.

Various models of this arrangement exist as well. For example, clinicians can be employed within a group that has a board and management structure distinct from the faculty group practice, as in the case of the Northeast Medical Group at Yale New Haven Health System[5] and the University of Maryland Community Medical Group. In addition, clinicians can form an operating group separate from the faculty practice but as a controlled subsidiary (such as the University of Pittsburgh Community Medicine), separate operating group for primary care but specialists are employed within their respective departments (Emory Specialty Associates) or as a distinct clinical department within a faculty practice (University of California Los Angeles Medical Group Staff Physicians).

According to their website, when the Audax Group invests in a medical practice, they provide capital for substantial infrastructure support, business experience, and acumen, but retain medical practice leaders as their clinical decision makers.

Irrespective of the employment model, these clinicians essentially work similar to community gastroenterologists but within the umbrella of an AMC. For young faculty whose interest is not in research or teaching, this can be an attractive option that maintains a tie to a university health system. For a seasoned clinician in community practice, this is an option to return to an academic environment. Usually, productivity expectations within the clinician track approximate those of a community practice gastroenterologist, but again total compensation may not be as great because ancillary income streams usually are not available. We expect this AMC employment track to become more prevalent as universities expand their footprints and acquire practices, hospitals, and ambulatory facilities distant from the main campus.

Large single-specialty practice

Consolidation of independent practices has been evident for 20 years and has accelerated as physicians in smaller practices have aged and burdens of practice have increased. Now, most urban centers have large mega-sized practices or super groups that have grown through practice mergers, acquisitions, and successful recruitment. Large practices can be modeled as a single integrated corporation (with ancillary components such as an AEC or infusion center) or as individual business units that are grouped under a single corporate entity.[6]

Within these large and mega-sized practices, differing employment options have emerged in addition to the traditional partnership track. These include payment on a per-diem basis, annual salary, or a mix of both. As opposed to partnership, the employment track avoids responsibility for governance and corporate liability, although not individual liability, and usually does not involve after-hours call. An employed physician usually does not benefit from ancillary income that derives from AEC facility fees, infusion centers, and pathology and anesthesia services.

Private equity–backed practices

In June 2016, private equity entered the GI space with the investment of the Audax Group in a community GI practice based in Miami. The term private equity refers to capital that is not reported in public forums and comprises funds that investors directly invest into private companies or use to buy out public companies and turn them private.

According to their website, when the Audax Group invests in a medical practice, they provide capital for substantial infrastructure support, business experience, and acumen, but retain medical practice leaders as their clinical decision makers. They also bring proven expertise and economies of scale to resource-intensive aspects of a medical practice including information technology, regulation compliance, human resources, revenue cycle management, payroll, benefits, rents, and leases as examples. These components can be difficult to manage efficiently within independent medical practices, so many maturing practices are selling their practices to regional health systems. This multistate equity-backed medical practice is an alternative to health system acquisition, and may help physicians feel more in control of their practices and potentially share in the equity investment.

Take-away points

1. Multiple new models of gastroenterology practice have emerged in the last decade.
2. Many academic medical centers have developed a "clinicians track."
3. Community GI practices have evolved into large practices with several employment models.
4. Private equity has entered our specialty as an investment partner of a large community GI practice.

It is important to understand the employment structure and associations of any practice you are contemplating joining. The model devised by this group is meant to retain physician authority and responsibility while providing capital to support innovation and the development of needed infrastructure. Growth of market share and revenues can accrue back to physician owners. This is distinct from practices that are part of a health system in which there may be more of a corporate feeling and centralized governance.

Locum tenens

Locum tenens is a Latin phrase that means "to hold the place of." According to the website of a large locum tenens company (www.locumtenens.com), this practice model originated in the 1970s when the federal government provided a grant to the University of Utah to provide physician services for underserved areas in the Western United States. The program proved so successful that hospital administrators who had difficulty recruiting staff physicians began asking for staffing assistance.

Today, a substantial number of physicians at all stages of their careers are working as locum tenens. They work as independent contractors so that income taxes are not withheld and benefits are the responsibility of the individual. As with the PSA arrangement, a physician would meet with both an accountant and labor lawyer to establish him or herself as a corporate entity for tax advantages and limited liability from litigation.

Early-stage physicians who might be following a significant other or spouse to specific locations sometimes consider a locum tenens as a bridge to permanent positions. Late-stage physicians who no longer want to be tied to a small-group or solo practice

have become locum tenens physicians who enjoy multiple temporary employment positions nationwide. This pathway no longer is unusual and can be a satisfying means to expand employment horizons. As with all employment situations, due diligence is mandatory before signing with any locum tenens company.

Conclusions

The employment spectrum for gastroenterologists and other medical professionals has expanded greatly between the time the senior author and the junior author entered the workforce. Change is now the one constant in medicine, and medicine today largely is fast-paced, corporatized, and highly regulated. Finding an employment model that is comfortable for current physicians, whose life situations are quite diverse, can be challenging. but a variety of opportunities now exist.

Think carefully about what you truly desire as a medical professional and how you might shape your employment to realize your goals. Options are available for those with an open mind and persistence.

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