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WATCHFUL WAITING OR CUT TO CURE?

Experts debate treatment of pancreatic cystic neoplasms.

ARTICLES BY
Horacio J. Asbun, MD;
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In this issue

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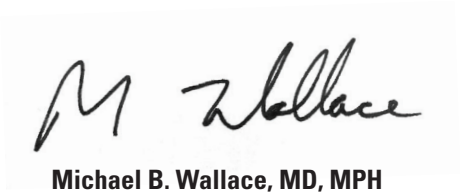
Note From the Editor

This issue of *AGA perspectives* is a very special one for me. First, our feature article focuses on management of pancreatic cystic neoplasms, a condition that I tackle every week with my own patients. It presents a paradigm for many issues we now confront in gastroenterology; namely how to manage an early neoplasia that has an unknown natural history. As with many organs, from Barrett's esophagus, to small colorectal polyps, and even the breast and prostate, we are increasingly detecting early, indolent neoplasia. While this is generally a good thing, we must also adapt and refine our approach from the "war on cancer" approach with aggressive therapy for all, to a more nuanced approach of risk-based therapy. In this issue, Professors Massimo Raimondo and Horacio Asbun from Mayo Clinic present the competing arguments for a conservative/observation approach versus an aggressive resection approach. As with most illnesses of this nature, the authors support a balanced, team-based approach.

I also bid a farewell to the *AGA perspectives*. My short tenure with the magazine comes with a new opportunity to be editor in chief of one of our major GI journals. I am very reassured to turn the journal over to Michael Camilleri, MD, AGAF, at Mayo Clinic. Dr. Camilleri is familiar to most, if not all, of our AGA membership as an outstanding clinician and investigator as well as the founding editor in chief of *Clinical Gastroenterology and Hepatology*. While AGA searches for a new permanent editor, *AGA Perspectives* will be in excellent hands.



Michael B. Wallace, MD, MPH
EDITOR

We welcome member feedback on all of the perspectives presented in this issue. Send your letters and comments to communications@gastro.org and include "*AGA Perspectives*" in the subject line.

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WATCHFUL WAITIN OR CUT TO CURE?

Experts debate treatment of pancreatic cystic neoplasms.

Massimo Raimondo, MD

Professor of Medicine, Division of Gastroenterology and Hepatology, Mayo Clinic, Jacksonville, FL

Dr. Raimondo is an AGA Institute Council Councillor and a member of the ACG Training Committee.

Watchful Waiting

Pancreatic cystic neoplasms are non-inflammatory cystic lesions found in 2.6 percent and up to 13.5 percent of the general population according to the radiology literature.[1] Their prevalence increases with age, particularly in individuals over 60 years old. In a study done at Mayo Clinic, Rochester, MN, the cumulative incidence of intraductal papillary mucinous neoplasms (IPMN) was two per 100,000 inhabitants, whereas the prevalence was 26 per 100,000.[2] No clear data exists with regard to the epidemiology of serous cystadenomas and mucinous cystic neoplasms which along with IPMNs represent the most common pancreatic cystic neoplasms encountered in clinical practice.

The majority of patients are diagnosed with small (< 1 cm) pancreatic cystic neoplasms that are asymptomatic. According to the most recent guidelines put together by an expert panel of pancreatologists, conservative management is offered to patients who

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Cutting Is the Cure

Over the past 20 years, there has been no significant improvement in the overall prognosis of pancreatic cancer. Marked improvements in imaging studies, however, have allowed us to detect cystic neoplasms at an earlier stage, prior to them becoming malignant. In resected specimens, invasive intraductal papillary mucinous neoplasm (IPMN) has been shown to have similar poor survival as invasive ductal adenocarcinoma, and one should not miss the opportunity to prevent the conversion of a premalignant cystic neoplasm to an invasive stage.[1]

In an accumulative review of published literature on IPMN in 3,568 patients, the mean frequency of malignancy for main duct IPMN (MD-IPMN, n=843) was 61.6 percent with a mean frequency of invasive IPMN of 43.1 percent.[2] In the same group of patients, the mean frequency of malignancy for resected branch duct IPMN (BD-IPMN, n=2027) was 25.5 percent and the mean

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Dr. Asbun has no conflicts to disclose.


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WATCHFUL WAITING

... this approach makes sense as pancreatic surgery still carries a high morbidity ...

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are asymptomatic, have small lesions usually smaller than 3 cm in size and have no worrisome features on cross-sectional imaging and/or on endoscopic ultrasound. In clinical practice, this approach makes sense as pancreatic surgery still carries a high morbidity particularly for pancreas head resections, despite reduction in mortality rates.

The carcinoembryonic antigen (CEA) test, which measures the amount of this protein that may appear in the blood of some people who have certain kinds of cancers, has been used in cystic fluid obtained by endoscopic ultrasound fine-needle aspiration to discriminate between mucinous and serous cystic lesions, with an accuracy of almost 80 percent. However, intracystic CEA according to a recent meta-analysis does not discriminate between benign and malignant pancreatic cystic neoplasms.[3] The GNAS gene is mutated in two-thirds of pancreatic juice and cystic fluid of patients with IPMNs and it is absent in serous cystadenomas and mucinous cystic neoplasms. Therefore, when positive, it could help to identify patients with IPMN. Similar to CEA, GNAS does not predict prognosis because it does not discriminate between benign and malignant IPMNs. Other markers tested in pancreatic specimens (juice, tissue and cystic fluid) such as miRNA, DNA methylation markers and proteomics appear promising, but they are not applicable for routine practice yet.

For small and asymptomatic pancreatic cystic neoplasms, a good quality cross-sectional imaging or endoscopic ultrasound to rule out a true mural nodule is appropriate as baseline. In these instances, the risk of malignancy is exceedingly low and patients can be followed conservatively.

The more we follow and study patients with small cystic neoplasms, the more we realize that the majority of these lesions will not increase in size and will remain asymptomatic. This is the case in our transplant patient population on immunosuppression.[4] Seventy-three patients out of 4,409 transplanted patients were followed for a median 27 months (range 4 to 106 months). Median cyst size was 13 mm. Cyst size remained stable in 55 patients (75 percent), increased in size (median increase 7 mm) in 15 (21 percent) and decreased in size in three (4 percent). Consensus indication for resection developed in only two patients: one patient developed main pancreatic duct involvement (main pancreatic duct 8 mm) after 14 months of follow up; this patient has not had surgery yet. The other patient developed a mural nodule after 31 months of follow up. EUS-FNA revealed high-grade dysplasia that was confirmed at surgery.

Knowledge of the natural history of pancreatic cystic neoplasms is of paramount importance because it helps us to identify patients who may not require any treatment either endoscopic or surgical. For example, it is well accepted by gastroenterologists and surgeons that asymptomatic (<2 cm) serous cystadenomas do not require any treatment.

In the absence of available molecular markers that can predict prognosis in pancreatic cystic neoplasms, we should abstain from treating small, asymptomatic cystic lesions for which the treatment (alcohol + chemotherapy ablation and/or surgery) could be worse than the disease.

A recent meta-analysis nicely clarified the role of individual cyst features and the risk of malignancy in IPMN. It turns out that cyst size larger than 3 cm was the single most valuable criterion in patients' malignant IPMN with odds ratios far greater than the presence of mural nodule, main pancreatic duct size and presence of symptoms.[5] Unfortunately, as acknowledged by the authors, this study considered only patients who had surgery with surgical pathology available. Though valuable, the results of this meta-analysis cannot be applied to asymptomatic patients who are actively followed up in practice and who have not been operated on.

An important study by Kwok *et al.* was presented in Chicago at Digestive Disease Week® 2014.[6] The authors hypothesized that patients with high comorbidities are more likely to experience non-pancreas cancer mortality than suffer pancreas

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frequency of invasive cancer was 17.7 percent. There is no question that resection provides the best chance for cure and avoids the lifelong surveillance and the potential anxiety caused by the presence of a pancreatic lesion in these patients. On the other hand, the same improvements in imaging studies that allow us to act more promptly have created a challenge by uncovering a large number of asymptomatic pancreatic small cystic neoplasms for which it is unclear whether they should undergo surgical resection; and if so, when is the best timing for it. Hence the debate: to cut or to observe.

For the purpose of this point-counterpoint, it may be beneficial to draw attention to what — in today's management of pancreatic cystic neoplasms — is not debatable:

1. The management of these lesions should be approached in a multidisciplinary fashion. The old mode of practice, in which a single physician (usually the surgeon), would make an independent decision, should now be obsolete. All of these patients, and in particular the ones in whom the decision to operate is not clear, should be assessed in a multidisciplinary fashion. The benefit of this approach is evident and recommended in the literature.[3] Furthermore, the actual landmark publications on the subject have originated from a multispecialty group analysis as demonstrated by the international consensus guidelines.[2]

2. While there has been no significant improvement in the long-term survival of pancreatic cancer patients over the past several decades, there has been a marked decrease in morbidity and mortality in pancreatic surgery. Significant improvements in surgical technique and perioperative care have allowed for a decrease in 30-day mortality for pancreaticoduodenectomy to less than 5 percent in experienced hands. Furthermore, if not for their baseline pancreatic cancer diagnosis, patients undergoing pancreaticoduodenectomy usually recover to a long-term good quality of life and the bad "post-Whipple" reputation no longer holds true for the large majority of patients. The introduction of the minimally invasive approach to pancreatic resections has further improved the results of surgical treatment. Several independent studies as well as meta-analysis[4,5] have shown that laparoscopic distal pancreatectomy has definite advantages over its open counterpart,

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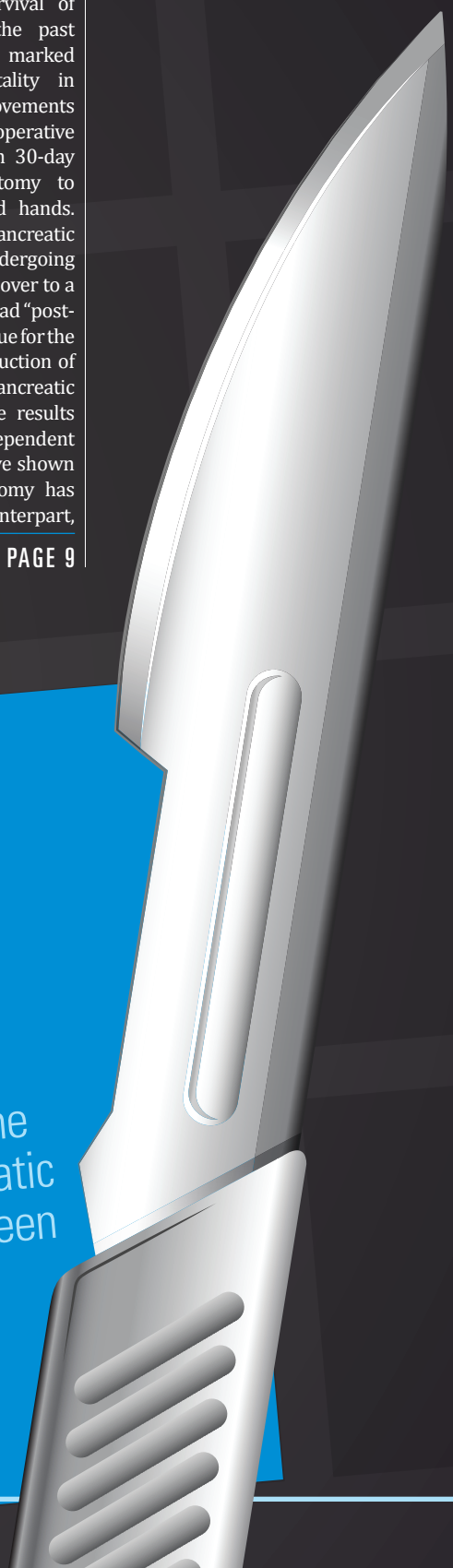
CUTTING IS THE CURE

While there has been no significant improvement in the long-term survival of pancreatic cancer patients, there has been a marked decrease in morbidity and mortality in pancreatic surgery.



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cancer death. They presented the results of a retrospective longitudinal cohort study in patients with cystic pancreatic neoplasms (including those with high-risk cyst features) diagnosed between 2006 and 2010 in view of a low versus high Charlson Comorbidity Index — a widely used validated system. In a multivariate analysis, Charlson score greater than or equal to three was associated with highest risk of non-pancreas cancer mortality (Hazard Ratios 8.8 [95 percent CI 5.7, 13.7]) compared to individual cystic features. Among patients with "high-risk" cyst features, those with Charlson score greater than or equal to three had 19.4 percent mortality form non-pancreas cancer mortality related death versus 3.2 percent among patients with Charlson less than three (log rank, p<0.0001). Therefore, comorbidities should be considered in all patients with high-risk cyst features before surgical decision making.

In conclusion, as we gather more information about the natural history of pancreatic cystic neoplasms, we should be more mindful and gauge our medical and surgical decision making based on evidence. In the end, we should always bear in mind the concept of "*Primum Non Nocere,*" and while accumulating more evidence, watchful waiting remains the best strategy. ■

The more we follow and study patients with small cystic neoplasms, the more we realize that the majority of these lesions will not increase in size and will remain asymptomatic.

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and should be considered the procedure of choice for the majority of patients. Laparoscopic pancreaticoduodenectomy done in experienced centers has shown at least the same, if not better results.[6] Nevertheless, given its complexity, further studies are needed before laparoscopic pancreaticoduodenectomy can be considered the procedure of choice for all institutions.

3. Location, location, location. The location of the lesion is a crucial factor when debating if surgery or observation should be followed in a patient in which either of the two choices is not readily clear. A small lesion in the distal tail of the pancreas can usually be approached laparoscopically with low morbidity and a short hospital stay with patients promptly returning to their normal activities. In select patients, it is not unusual that a spleen-preserving procedure can be accomplished. On the contrary, a lesion located in the head of the pancreas will usually require a pancreaticoduodenectomy. Even if approached laparoscopically, the procedure is of a large magnitude and has a more significant impact on the patient's life.

4. Age is also an important factor to consider in the decision to cut. Mucinous cystic neoplasms (MCN) have shown to be low grade at the time of detection with a prevalence of cancer of 17.5 percent.[7] It is felt that asymptomatic lesions that are less than 4 cm in size and present no suspicious characteristics can be observed. However, MCNs are most common in middle-aged woman and, in these relatively young patients, surgical resection is a definitive solution that weighs against the need for lifelong follow-up, further eliminating the cost and apprehension commonly associated with it. The annual risk of malignancy for BD-IPMN is 2 to 3 percent.[2] Therefore, giving the accumulative risk of malignancy, patients younger than 65 years of age with a BD-IPMN lesion greater than 2 cm, should be considered for surgical resections when fit for surgery.

Cystic neoplasms should be approached in a multispecialty fashion.

5. Treat the patient not the x-ray. The large majority of patients with asymptomatic cystic neoplasm in whom observation is recommended will understand the benefits of avoiding surgery and tolerate the small risk associated with observation. There will be a subset of patients, however, that the presence of a pancreatic lesion and the need for long-term surveillance and follow-up will cause significant worry. A family history of pancreatic cancer will add to the anxiety. For these patients, the perceived risk can be a significant detriment in their quality of life. If reassurance efforts by the physician are not successful this factor may be the deciding reason to proceed with surgery in those patients in whom the decision is not readily clear.

In summary, cystic neoplasms should be approached in a multispecialty fashion. There are current guidelines that help us decide when surgery is clearly indicated and when observation is clearly indicated. However, there is a sizeable group of in-between patients in whom it would be reasonable to consider either of the two approaches. For these patients, the decision should be consider individually and when in doubt, surgery will be the definitive curative treatment — especially for those patients with lesions in the tail of the pancreas treated at high-volume centers. ■

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Impact of CDC Recommendations on Age Cohort-Based Screening for HCV in Primary Care

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Dr. Vargas serves as the chair of the AASLD Ethics Committee.

The field of hepatology finds itself at a pivotal moment in its history. We have long recognized hepatitis C virus (HCV) as a masterful foe that evaded many efforts to stop the slow devastation that it yields without successful treatment. Because most hepatologists today rely on the miracle of liver transplantation to rescue our patients from cirrhosis and its complications, we are uniquely positioned to encounter the common and frustrating clinical scenario of the patient who arrives at the diagnosis of HCV the same day it is revealed that cirrhosis is already well-established. Since the onset of my clinical efforts more than 20 years ago, I have toiled with a long, challenging therapy anchored on the use of interferon which, pegylated or not, limited my ability to incite enthusiasm even in the most motivated of patients. We are now entering a hopeful era when we will eliminate interferons as a base for our treatment approach and broaden the spectrum of patients we can treat safely. With this promise in front, the question can be fairly asked: how will we define our success?

We have long known that a vast majority of our potential patients have no idea that they can be at risk for a viral infection that is insidious and costly to manage once it has played out its course. The valuable data gleaned from the National Health and Nutrition Examination Survey (NHANES) places the national (excluding homeless and institutionalized people) prevalence of HCV infection at 1.5 percent. Adjusting for those not accounted for in the surveys, we estimate that 4.5 to 5 million Americans may be infected with the virus. One may ask, if these numbers are known, why is there a problem? The sad truth is among those infected, 45 to 85 percent are not even aware of their "at-risk" status and thus lack the motivation to seek screening. Strategies to test those who were covered by the risk-based approach of the 1998 CDC recommendations have, not surprisingly, been less than effective. Some reports place the prevalence of HCV testing in these groups as low as 17 percent. This is why the current CDC recommendation to include non-risk-based, one-time testing of adults born between 1945 and 1965 is an important step to address this deficiency at a timely point in history.[1]

Using NHANES results and CDC surveillance data, recommendations have been issued to test the baby-boomer generation. CDC noted increases in non-A, non-B hepatitis (read HCV before we had identified it) that steadily increased from 1965 to the late 1980s when HCV was identified. Analysis of birth cohort sets that revealed the disproportionate distribution of HCV infections among surveyed individuals led to the selection of the currently recommended birth cohort.

We have long known that a vast majority of our potential patients have no idea they can be at risk for a viral infection that is insidious and costly to manage once it has played out its course.

We need to know that the incidence of HCV in this baby-boomer cohort is 3.25 percent, and that 76.5 percent of all HCV-infected Americans are found in this birth cohort of the American population.

The CDC recommendation arrived at the same time as the impressive headlines of new, potentially all-oral direct antiviral regimens claiming fantastic viral responses in the range of 85 to 95 percent in phase II and early phase III data. It is difficult to contain the excitement of seeing interferon-free options for even my sickest patients come to light, coupled with a recommendation to bring the largest group in society to benefit from treatment to recognition and education about the effective treatments available to them. The U.S. Preventive Services Task Force was convinced, after initial misgivings, to give birth cohort screening an important "B" grade ranking, communicated by the publication of several papers confirming that sustained viral response to HCV treatment leads to less cirrhosis, less hepatocellular carcinoma and decreased demand for expensive care such as liver transplantation.[2] Ultimately, this means a decrease in deaths due to HCV.

Does this mean that the work of hepatology is done? My answer is a resounding NO! We have to recognize that however effective, treatment of 5 million Americans will not be easy. Many do not have access to care. Importantly, those incarcerated may return to society with unrecognized disease, unrealized medical coverage, and they will remain a seedbed for future infection. Recent reports from CDC reveal both that injection drug use may be leading to a new wave of infections in younger populations and increased incidence of HCV in men who have sex with men who are infected with HIV. For those patients who are willing to be treated presently, the cost of therapy may exceed $100,000. Success will be defined by how we overcome all those challenges and advocate for our patients, support our primary care colleagues, and expand the pool of HCV treating clinicians to fully help the enormous need. ■

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BUILDING A COHORT TO STUDY THE IMPACT OF DIET ON THE GUT MICROBIOME

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Dr. Chan is the chair of the AGA Institute Research Policy Committee. He is a consultant to Pfizer Inc., Pozen Inc. and Bayer HealthCare.

There is an exploding interest in the scientific, lay and medical community about the gut microbiome, consisting of several pounds of bacteria, archaea, fungi and viruses in each adult, and its role not only in digestive diseases, but disorders as diverse as the metabolic syndrome and diabetes.[1] An individual's gut microbial profile develops over childhood to reach relative stability by adulthood, characterized by a personalized core of colonizing microbes that continue to fluctuate over time.[2] The major determinants of these adult states are not yet known, with influences proposed to include host genetics, early childhood exposures and both short- and long-term dietary patterns.[3] Diet alters the composition and function of this microbiome, and the microbiota in turn ferments and metabolizes dietary components. However, it remains unclear what components of short-term or long-term diet have greater impacts

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on gut microbiota composition and function. This fundamental question has motivated my interest as a gastroenterologist and clinical epidemiologist to pursue investigation in this exciting new frontier of science. My hope is that understanding whether and how dietary patterns and constituents influence the microbiome will provide a step toward modifying it therapeutically to avoid "unhealthy," disease-linked or otherwise dysbiotic states.

To date, my scientific focus has been in the role of long-term diet and lifestyle factors in relation to the etiopathogenesis of digestive diseases such as colorectal cancer and IBD.[4] To build upon this work, I hope to leverage the exciting methodological developments that have recently become available in characterizing the human microbiome to understand whether some relationships currently identified between long-term diet, lifestyle and chronic digestive diseases may be mediated by changes in gut microbial composition or function. Although several pioneering studies of the relationship of diet to the gut microbiome have already been conducted, they have primarily been limited to relatively short-term controlled feeding studies or conducted in cohorts with small numbers of individuals, yielding conflicting results.[5-8]

[Our AGA-funded research] will provide one of the first opportunities to associate key dietary factors and environmental characteristics with the microbiome on a population scale.

Thus, to help fill this knowledge gap, my team at Harvard Medical School/Massachusetts General Hospital was fortunate to receive the first AGA-Elsevier Gut Microbiome Pilot Research Award from the AGA Research Foundation to support our efforts to investigate the gut microbiota within the Health Professionals Follow-Up Study (HPFS), a prospective cohort of 51,529 male U.S. health professionals that has provided us biennially updated information on diet, lifestyle and medical diagnoses.

Over a one-year period in 2012–13, nearly 700 men within the HPFS underwent a lifestyle validation study in which detailed biometric measurements, physical activity records and food frequency questionnaires designed to assess both long-term dietary patterns and short-term dietary recall were collected at multiple timepoints. With the additional support of AGA, we are able to successfully collect stool specimens using a validated home self-collection method from 412 men enrolled in the MLVS concurrent with assessment of dietary intake. These data, as well as information on a range of other lifestyle characteristics (e.g.,

Dr. Chan's research was funded in part by the 2013 AGA-Elsevier Gut Microbiome Pilot Research Award.

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Learn about AGA's Center for Gut Microbiome Research and Education at **www.gastro.org/microbiome**.

geographical location, medication use and disease diagnoses), will provide one of the first opportunities to associate key dietary factors and environmental characteristics with the microbiome on a population scale.

Over the next year, we will pursue 16S and shotgun metagenomic and metatranscriptomic sequencing of these stool specimens to deeply characterize both the community structure as well as function of the gut microbiome of this uniquely valuable cohort. We will apply a cutting-edge microbial profiling and computational analysis pipeline to focus on the influence of diet on specific candidate organisms, genes and pathways associated with digestive diseases. Ultimately, we hope that detecting the influence of diet on microbiota shifts will strengthen the case for causality for diet-disease relationships, facilitate the use of microbial composition as an intermediate biomarker to assess efficacy of dietary interventions to promote health, and elucidate molecular targets for disease prevention and therapy. Importantly, we anticipate this work will form a foundation for scaling our stool collection protocol to broader, population-based cohorts. This will offer an unprecedented opportunity to prospectively characterize the gut microbiome in relation to chronic conditions, including digestive diseases such as gastrointestinal cancer, IBD and functional bowel disorders. ■

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GI Practice Thought Leader Becomes AGA President

John I. Allen, MD, MBA, AGAF, of Yale University School of Medicine, will continue his service to the American Gastroenterological Association (AGA) and the broad GI community throughout the coming year in his new role as president of the AGA Institute. Dr. Allen's term began at the conclusion of Digestive Disease Week® (DDW) 2014.

During his presidency, Dr. Allen plans to continue AGA's tripartite mission of research, clinical practice and education. All three pillars will be supported by robust advocacy and networking with national organizations that create health-care law, regulations and policies. Important research endeavors include the growing endowment for research support targeted especially at investigators beginning their academic career (AGA Research Foundation) and the Center for GI Innovation and Technology. AGA education will transform into new, exciting modalities that speak to both beginning and advanced-career gastroenterologists.

"[Dr. Allen's] vision for AGA is shaped by his personal experiences as a physician, clinical researcher, teacher and patient," said Robert A. Ganz, MD, a longtime colleague of Dr. Allen's from Minnesota Gastroenterology, P.A. "He recognizes that the specialty of GI faces enormous challenges and is unwavering in his commitment to support AGA members in this new era of health-care delivery."

Anticipating the coming changes in health care, Dr. Allen has led the AGA in developing a series of programs under the "Roadmap to the Future of GI," designed to provide a portfolio of tools that directly help practitioners thrive in a period of great change in health care. The goals of the Roadmap are to deliver high-quality care, demonstrate quality and maximize revenue.

Over the past decade, Dr. Allen has served AGA in increasing capacities. In 2007, Dr. Allen was selected to chair the AGA Institute Clinical Practice Committee, a committee responsible for all aspects of clinical practice, including quality measures and practice management. In 2009, Dr. Allen was nominated and elected to be a community practice councillor to the AGA Governing Board.

"During his tenure, [Dr. Allen] was one of the hardest working, productive and valuable members of the board, leading crucial efforts in practice-related initiatives," said Loren A. Laine, MD, AGAF, professor of medicine, Yale School of Medicine, and past president, AGA Institute. "It was no surprise, and well-deserved, when [Dr. Allen] was elected vice president in 2012, with succession to president in 2014."

AGA Institute outgoing president, Anil K. Rustgi, MD, AGAF, passes the gavel to incoming president, Dr. John I. Allen, during the AGA Business Meeting at DDW® 2014.

Dr. Allen graduated with honors from Rice University in Houston, TX, in 1973, and the University of New Mexico Medical School, Albuquerque, in 1977, completing internship, residency and gastroenterology specialty training at the University of Minnesota, Minneapolis. Dr. Allen then spent 10 years as faculty in the department of medicine at University of Minnesota.

From 1991 through 2013, Dr. Allen helped build Minnesota Gastroenterology into a large single-specialty gastroenterology practice in the Twin Cities of Minnesota and develop their nationally known quality improvement program.

On April 1, 2013, Dr. Allen assumed the role of clinical chief of the section of digestive diseases and a professor of medicine at Yale University School of Medicine, New Haven, CT.

Dr. Allen and his wife Carolyn, an advanced endoscopy nurse, have two grown children: Jennifer and Josh. ■

To learn more about Dr. Allen's unique and broad perspective on all aspects of GI care, read the *Gastroenterology* article profiling his upbringing, education, career and accomplishments.

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AGA RESEARCH FOUNDATION

Treatment of Autoimmune Pancreatitis

WHEN TO OFFER IMMUNOMODULATORS OR RITUXIMAB

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Drs. Chari and Hart have no conflicts to disclose.

Autoimmune pancreatitis (AIP) is the pancreatic manifestation of a multi-organ syndrome currently referred to as IgG4-related disease. AIP has a characteristic response to steroid therapy that is unique among pancreatic diseases. Although there are no data from randomized controlled trials, steroids are currently accepted as the mainstay of treatment for induction of remission in AIP. There are several variations in dosing and duration of steroid treatment, but irrespective of the regimen initial response rates approach 100 percent. Despite an initial treatment response, up to 50 percent of individuals will have a disease relapse during follow-up. There are several options for treating relapses, including readministration of high-dose steroids with or without maintenance treatment (either low-dose steroids or a steroid-sparing immunomodulator). Additionally rituximab (RTX) appears to be effective in many for both induction and maintenance of remission.

It is important to emphasize that AIP is by definition a steroid-responsive disease. Therefore, we do not advocate for the use of non-steroid treatments in individuals who are not responsive to high doses of steroids. In those situations, alternative diagnoses (namely malignancy) must be reconsidered prior to escalating medical treatment. Conversely, patients who initially respond to steroids, but become dependent on high doses to maintain disease remission ("steroid dependent") are appropriate candidates for additional treatment. Also, due to the potential, albeit small, risk for serious drug-related toxicities, providers must be familiar with drug monitoring.

Our initial treatment for AIP consists of a course of high-dose steroids for four weeks followed by a taper over the next eight weeks. Since not all patients with AIP develop a relapse, we do not think that maintenance treatment with an immunomodulator (or low-dose steroids) is necessary for everyone. We do recommend considering maintenance therapy for those with relapsing disease. Since the majority of patients with AIP are diagnosed at an advanced age, we have generally used a steroid-sparing immunomodulator (typically azathioprine or 6-mercaptopurine) to avoid potential long-term steroid-related complications. One subset of patients for whom we consider starting maintenance treatment at the time of diagnosis for the group with disease involving the biliary tract proximal to the intrapancreatic portion of the common bile duct (i.e., IgG4-related sclerosing cholangitis). A more aggressive treatment strategy for these subjects is justified due to their very high risk for disease relapse, which can rapidly progress to secondary biliary cirrhosis. In brief, we consider a steroid-sparing immunomodulator for those with relapsing disease or who have IgG4-related sclerosing cholangitis at the time of diagnosis.

Despite early reports of the successful maintenance of remission of disease with an immunomodulator, at our institution up to half of patients are intolerant or "resistant" to immunomodulators with unsatisfactory disease control due to either the inability to taper off

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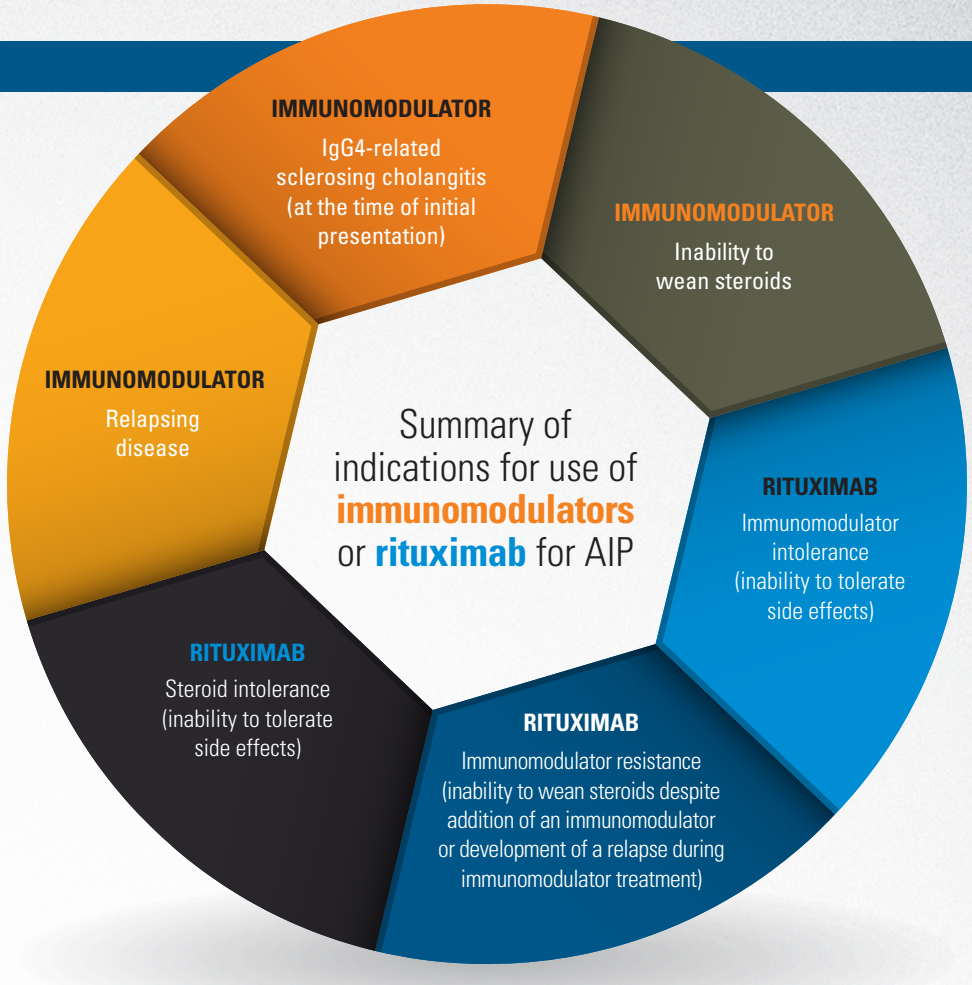

Reserve RTX for patients who cannot tolerate steroids or are refractory to immunomodulators; we do not generally recommend it as a first-line agent.

steroids or development of a relapse during treatment with the immunomodulator.[1] Our experience using immunomodulators is similar to that observed in patients with inflammatory bowel disease with about 25 percent of patients requiring drug discontinuation due to treatment-limiting side effects. Depending on the side effect we consider substitution of an alternative thiopurine (6-mercaptopurine) or class-switching to mycophenolate mofetil. Although the subset of patients with immunomodulator resistance or intolerance represent only a small subset of our tertiary AIP referral population (approximately 10 percent), these difficult-to-treat patients can suffer significant morbidity and an alternative treatment approach is required.

We have been using RTX, an anti-CD20 monoclonal antibody, with promising results in these difficult-to-treat patients.[1] Aside from high-dose steroids, RTX is the only agent that has been demonstrated to induce disease remission as monotherapy, so RTX is also a viable option for individuals who are unable to tolerate high-dose steroids (e.g., steroid-induced psychosis). The dosing frequency and total number of doses for treating AIP has not been determined, but response rates are very high regardless of the protocol used. One major issue with RTX is the high cost of administration, particularly in comparison to steroids and other medical alternatives. Thus, it is most appropriate to reserve RTX for patients who cannot tolerate steroids or are refractory to immunomodulators, and we do not generally recommend it as a first-line agent.

In summary, AIP is by definition a steroid-responsive disease. Despite the lack of controlled treatment data, steroids are accepted as the mainstay of induction treatment. There is currently no consensus regarding the optimal strategy for maintenance of disease remission. Although the data remain preliminary, we feel that immunomodulators (azathioprine, 6-mercaptopurine) can be considered in those who initially respond to high-dose steroids, but cannot be weaned from steroids without disease recurrence or who have a relapsing disease course. We consider using RTX for individuals who are unable to tolerate treatment with an immunomodulator or develop a relapse during treatment. For individuals who cannot tolerate high-dose steroids, RTX is the only alternative medical treatment option. The use of advanced medical treatment options in AIP remains under evaluation, and we expect these strategies will continue to evolve as additional data become available. ■

NUTRITION IN ACUTE PANCREATITIS

MOVING FULL CIRCLE

OR MOVING FORWARD?

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Dr. Windsor has no conflicts to disclose.

Acute pancreatitis is a common reason for acute hospital admission and in the absence of any specific treatment the management remains supportive. Little support is required for self-limiting mild disease, but the management of severe and critical disease is based on supporting failing organ systems in intensive care units. And while it is true that there are a number of specific interventions at our disposal, (including analgesia, fluid resuscitation, enteral nutrition, endoscopic bile duct clearance, antibiotics, drainage of infected collections, removal of infected pancreatic necrosis and cholecystectomy) none of them specifically target outcome-determining pathophysiology, except perhaps enteral nutrition.

Nutritional therapy in acute pancreatitis has passed through a number of eras. Over the early part of the last century patients were allowed to eat and drink during attacks of acute pancreatitis. More recently the dogma of pancreas rest became entrenched as a fundamental tenet of acute pancreatitis management. In practice, this meant avoidance of any fluid or food intake by mouth and usually nasogastric tube drainage of the stomach. Starvation was thus practiced on the pretext that any stimulation of the pancreas might exacerbate the severity of acute pancreatitis and lead to a worse outcome. A critical examination finds the evidential base for this approach inadequate, but the practice of starvation until pain and ileus had resolved was widely practiced.

The scientific development of parenteral nutrition (PN) addressed two concerns. It countered the catabolic effects of acute pancreatitis, including the anergy associated with protein malnutrition, and it avoided stimulation of the pancreas. Systematic reviews of studies comparing parenteral with enteral nutrition revealed that the enteral approach was superior with reduced infective complications and mortality.[1] A more appropriate appellation for this era of

> While there are a number of specific interventions at our disposal for treating acute pancreatitis, none of them specifically target outcome-determining pathophysiology, except perhaps enteral nutrition.

PN for pancreas rest might be the era of "gut neglect," for the GI tract is an end-organ that itself requires targeted support in order to maintain its barrier and other functions.

Even with the evidence establishing the primacy of enteral nutritions there were still vestiges of concern about the need for pancreatic rest, insisting that delivery of nutrition should be beyond the duodenum. But more recent studies have shown that nutritional support can be delivered safely and effectively into the stomach in the majority of patients.[2] Parenteral nutrition has now assumed a supplemental role, being indicated when the enteral route cannot be used to deliver calculated nutritional requirements. And the nasojejunal route is only indicated when nasogastric or nasoduodenal feeding fails.

The era of normal diet, starvation, parenteral support, enteral support into the jejunum, enteral support into stomach, raises questions about what the future holds for nutritional support in acute pancreatitis. Allowing ad libitum or volitional oral intake in mild to moderate acute pancreatitis appears safe, even before the loss of pain and the return of normal serum pancreatic enzyme levels.[3] It is likely that there will be an increasing trend toward patient controlled intake, the inclusion of specific oral supplements and nasal tube feeding restricted to those at risk of intolerance.

Although the field may appear to have come full circle, moving forward to optimal individualized oral and enteral feeding will require answers to some key questions. There is a need to determine the balance between giving "too much too soon" (which might promote non-occlusive mesenteric ischemia, especially if there is persisting splanchnic vasoconstriction with inadequate fluid resuscitation) and giving "too little too late" (which might promote intolerance to enteral nutrition, especially if there is significant villous atrophy, enterocyte loss and mural inflammation). There is still much to learn about how to determine the optimal start time for oral and enteral nutrition, the rate of escalation, and the best response to feeding intolerance. There is also the need to optimize the composition of nutritional support. While intravenous (but not enteral) glutamine supplementation appears to reduce the risk of mortality and infectious complications,[4] the delivery of other pharmaco-nutrients represents an untapped opportunity. And it is time to formally evaluate the concept of gut rousing (in contrast to pancreatic rest and gut neglect) which postulates that the timely administration of appropriate gut directed therapies will prevent or mitigate gut dysfunction.[5] The future role of advanced enteral nutrition in acute pancreatitis is likely to be expanded to deliver specific treatments to counter the systemic effects of toxic gut derived mesenteric lymph and to manipulate the microbiome to modulate the disease course. ■

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Developing a Fellowship Curriculum in Women's Gastrointestinal Health

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Drs. Chokshi and Devuni have no conflicts of interest.

Sex and gender differences exist across all facets of health and disease, and gastroenterology is no exception (see Table 1). Despite increased attention to women's GI health in recent years, challenges remain in integrating this important topic into fellowship training. Developing a curriculum in women's GI health can be an exciting and rewarding task, especially with a clear framework for how to proceed.

When establishing a women's GI health curriculum, several factors must be taken into account. First, adequate training in this topic extends beyond gastroenterology. This undertaking is a multidisciplinary effort and should include, if possible, representatives in such fields as obstetrics and gynecology, urology, surgery, nutrition, oncology, physical therapy, psychiatry, radiology, primary care, and geriatrics. Communication and collaboration by the women's health faculty can enhance the experience for trainees. That said, key faculty members within the gastroenterology division are essential to leading the initiative. Next, curricular development requires a clear plan and objectives. These can be based on the Gastroenterology Core Curriculum developed by AGA, ACG, AASLD and ASGE, which clearly describes goals for training in general women's digestive health as well as specific health and disease states, including pregnancy.[1] In addition, specific topics can also be promoted, such as corresponding digestive differences in men and/or differences in the lesbian, gay, bisexual and transgender populations. Performing a needs assessment at one's own institution may be a helpful way to begin.

WOMEN - CONTINUED ON PAGE 22

Table 1. Gender Differences in GI Diseases

GENDER-BASED DIFFERENCE	EXAMPLES
Diseases more commonly seen in women	IBS Primary biliary cirrhosis Autoimmune hepatitis
Diseases less commonly seen in women	Barrett's esophagus Esophageal adenocarcinoma Hepatocellular carcinoma
Pregnancy-related diseases (unique to pregnancy)	Hyperemesis gravidarum Acute fatty liver of pregnancy Intrahepatic cholestasis of pregnancy
Pregnancy-related diseases (not unique to pregnancy)	GERD Constipation Gallstone disease
Diseases that can affect fertility	IBD Celiac disease
Decreased female compliance with recommendations	Colorectal cancer screening

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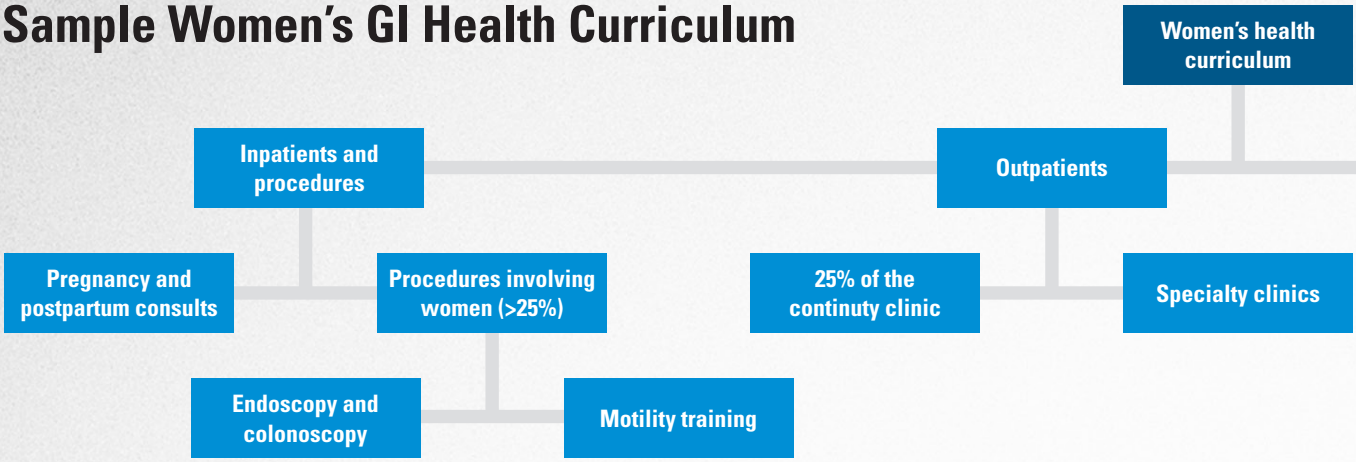
Teamwor

Sample Women's GI Health Curriculum



WOMEN - CONTINUED FROM PAGE 20

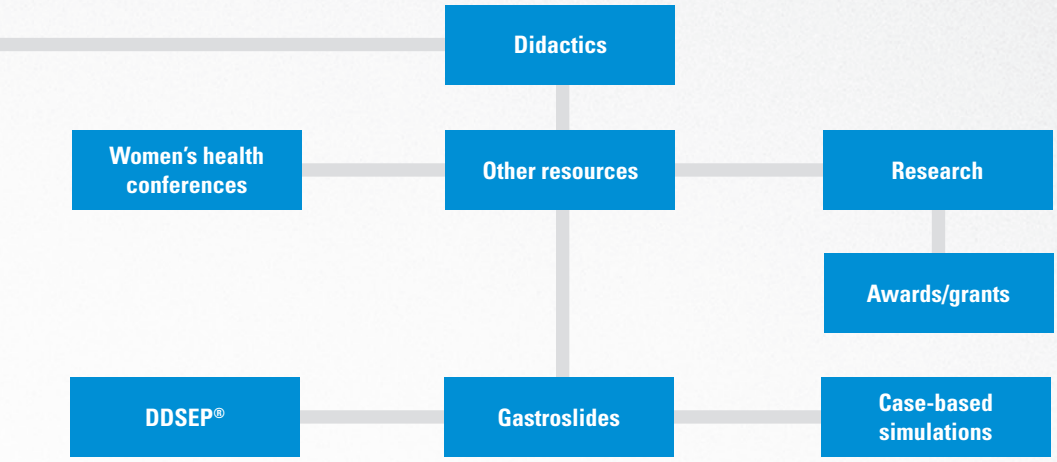
Learning objectives should be both didactic and clinical so that the curriculum can be built upon both goals. Didactic sessions can include core lectures from faculty across specialties, small group conferences, simulations and/or Web-based modules. Clinical training should focus on inpatient and outpatient care of women at all stages along with procedural training, including endoscopy and manometry.

How exactly an institution integrates women's health into the GI curriculum depends heavily on the resources available. According to the GI Core Curriculum, at least 25 percent of all patients seen in each of the clinical settings, including continuity clinic and procedures, must be women.[1] This can prove difficult in certain settings, such as a VA hospital, so care should be taken to increase exposure in different ways. Conversely, trainees with access to a women's hospital may get the added experience of seeing pregnancy consults and/or working with postpartum patients on pelvic floor care. Each institution must assess its own needs and utilize its resources to the fullest. At our institution, adding women's GI health to the curriculum has occurred alongside the development of a women's GI health clinic and an endoscopy day dedicated to female patients and providers. Thus, along with monthly didactic sessions and motility study interpretation, fellows rotate through these weekly sessions. Some institutions have been able to organize full women's GI health rotations and even dedicated fellowship tracks, complete with various specialty clinics, inpatient consults, anorectal motility training, didactic sessions and research time. Again, these training opportunities depend on availability of expertise and other resources that help guide curriculum development (see algorithm above).

How exactly an institution integrates women's health into the GI curriculum depends heavily on the resources available. According to the GI Core Curriculum, at least 25 percent of all patients seen in each of the clinical settings, including continuity clinic and procedures, must be women.

Various teaching aids are at our disposal to "fill the gaps" of our institutions where needed. AGA includes topics in women's digestive health and disease as part of its Digestive Diseases Self-Education Program® (DDSEP)[2] and Gastroslides[3] curricula. These resources provide background, PowerPoint slides and test questions that can be easily integrated into didactic sessions. In addition, collections of women's health-related studies can be supplemented by these resources to enhance the breadth of the trainees' exposure. Case-based simulations provide clinical scenarios that may be missing at a given institution. Currently, researchers at the University of Wisconsin Health Center, headed by Sumona Saha, MD, are working to build a module of cases based on the women's digestive health section of the GI Core Curriculum that incorporates scores and real-time feedback for learners (personal communication with Dr. Saha). When complete, these simulations will likely have far-reaching effects on the quality of the women's GI health education for our fellows.

With the foundation of the curriculum in place, attention can move toward competency assessment and scholarship. Assessment of fellows can come in various forms. Trainees' competency should be assessed in clinical settings, possibly using mini-clinical examination or objective structured clinical examination formats, as well as during procedures. Questionnaires and/or board-type questions can be



For more on this topic

Read Dr. Chokshi and Devuni's full article in the Mentoring, Education and Training Corner of *Gastroenterology*.

given both before and after rotations to evaluate progress. Fellows should also have opportunities for scholarly advancement in women's GI health. Critical appraisal of the literature in women's health topics can be included in the form of journal clubs and other didactic sessions. Opportunities for original research should be encouraged, as should involvement with faculty projects. At some institutions, NIH sponsors a K12 career development award for junior faculty called Building Interdisciplinary Research Careers in Women's Health (BIRCWH). The goal of BIRCWH is to increase the number and skills of clinical investigators in women's health through mentorship with other women's health researchers. Knowledge of programs like this one can empower our fellows to seek grants and move forward as academic gastroenterologists with a focus on women's GI health.

We know there are clear differences in women's digestive health and disease compared to men, and this disparity provides us with a unique opportunity to improve the education of our trainees. Assessing institutional resources and collaborating between disciplines can initiate this undertaking of creating a curriculum, and supplemental resources are available. These efforts strengthen fellowship education and can serve as a backbone for the academic and clinical advancement of women's gastrointestinal health. ■

The Future of Hepatology Training: PATHWAYS TO CERTIFI

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Dr. Salgia has no conflicts to disclose.

It is no surprise that the field of hepatology is evolving. Even prior to the approval of new antiviral regimens for hepatitis C, the demands on hepatologists for managing patients with chronic liver disease has never been higher. For a relatively young field, hepatology has seen growth in many areas over the past two decades, including the management of viral hepatitis, growing referrals for the management of cirrhosis and liver transplant evaluations, and the management of hepatocellular carcinoma. Important to the management of these diseases is liver transplantation. With more than 6,000 liver transplants performed annually in the U.S., and five-year survival exceeding 70 percent, these patients require long-term care from specialists trained in transplant hepatology. But this raises a concern shared by many — how do we increase the number of hepatologists qualified to care for the growing burden of chronic liver disease?

The current gastroenterology fellowship training model mandates five months of clinical hepatology and acquisition of knowledge in transplantation. This is sufficient for gastroenterology board certification. Currently, a fourth year of ACGME-accredited fellowship training is required in advanced and transplant hepatology to be board eligible for transplant hepatology. Based on my experience in training and as a transplant hepatologist, the standard GI fellowship training is currently insufficient for practice as a transplant physician. I highly recommend a dedicated training period committed to acquiring the skills to care for transplant recipients and complicated patients with chronic liver disease. Yet the reality for many fellows is that the burden of medical school debt and deferment of full-time salary as training status is continued makes the choice of an extra year of training unappealing.

In order to deal with the current and projected manpower shortage of hepatologists, ABIM has created an approved GI-transplant hepatology pilot fellowship program. Select trainees would be eligible

FUTURE - CONTINUED ON PAGE 26


CATION

Step-by-Step guide to applying for the GI-transplant hepatology combined pilot program:

1

Determine your interest and commitment to transplant hepatology/ advanced hepatology career during the first year of fellowship.

2

Inform your GI program director (PD) about your interest, and make sure your program has an ACGME-accredited transplant hepatology fellowship. If not, your program should apply for this first.

**Note: not all GI fellowships are eligible for a TH fellowship.*

3

Work with your PD to modify your first and second year of fellowship to complete all GI competency requirements.

4

Apply to the pilot program in March of your second year of fellowship. Obtain application materials from your transplant hepatology program director.

5

Approval is on a case-by-case basis.

FUTURE - CONTINUED FROM PAGE 24

to spend their third year of fellowship training in transplant hepatology. To qualify, an ACGME-accredited GI fellowship program would need to have (or apply for) an affiliated accredited transplant hepatology fellowship. Presently there are 41 ACGME-accredited transplant hepatology fellowship programs. A fellow interested in the combined pilot program would express interest early-on in fellowship training to the program director, and apply to the pilot program in March of his or her second year of fellowship. The goal is for the fellow to achieve competencies both in GI and transplant hepatology by the end of year three of fellowship and be able to certify for both ABIM specialty boards.

Obviously this goal requires modification to the current GI training schedule. Fellows interested in the pilot program should complete the vast majority of GI training in the first two years, and limit their hepatology experience to only two-to-three months rather than the currently required five months (see figure). The focus during the third year of training would be on hepatology and transplant. In order to maintain GI competency, it is recommended to continue with attendance at a blend of conferences, and to participate in GI call and continuity clinic. However, the rest of the time is focused on transplant training including pre-transplant and post-transplant management in the inpatient and outpatient settings, perioperative management, transplant immunology, and pathology. Evaluation is similar to GI fellowship with milestones specific to transplant hepatology training that will be based on recommended assessments in the Next Accreditation System.

> In order to deal with the current and projected manpower shortage of hepatologists, ABIM has created an approved GI-transplant hepatology pilot fellowship program.

It is my belief that this option is likely to attract more trainees to the field of transplant hepatology, yet it is not for every interested candidate. For example, those committed to a career in research may not have sufficient time during their combined training program to adequately pursue their research interests. Other trainees may need additional time beyond their second year of fellowship to decide their future career pathway. The fourth year of dedicated transplant hepatology training will likely still have a role and be available for these fellows. Time will tell whether the demand will still exist for the additional year of training. Presently the ABIM pilot program can approve up to 10 fellows per year, and it remains.

The decision to complete transplant hepatology training within a three-year combined training program or a fourth year of training is up to the individual trainee and offers an exciting new option for GI training. As we evaluate our current system and modify it, we can attempt to meet the growing demands of patient care in hepatology. ■

International Consensus Guidelines on the Management of Pancreatic Mucinous Neoplasms

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Dr. Tanaka receives research support from Olympus. He is also the auditor of the Japanese Society of Gastroenterology and the Japan Gastroenterological Endoscopy Society.

Recently, intraductal papillary mucinous neoplasm (IPMN) of the pancreas has been drawing increasing attention. International consensus guidelines (ICG) on the management of IPMN and mucinous cystic neoplasm of the pancreas, published in 2006 (Sendai),[1] have been revised in 2012 (Fukuoka).[2] The most prominent changes proposed in the Fukuoka guidelines are a lowered threshold (>/= 5 mm) of the size of the main pancreatic duct and branch duct to increase the sensitivity of the diagnosis of main duct-IPMN (MD-IPMN) and branch duct-IPMN (BD-IPMN), respectively, and the use of two-phase criteria for the preoperative presumption of malignancy, i.e., worrisome features to warrant thorough examinations by endosonography and high-risk stigmata of probable malignancy to indicate surgical resection.

The morphological classification of IPMNs of the Fukuoka guidelines retained mixed type along with BD type and MD type. The mixed-type IPMN looks like an advanced form of BD-IPMN and is characterized by MD dilation (>5 mm) and a higher frequency of malignancy, similar to MD-IPMN. The classification has been changed to be able to rely on radiographic features rather than histological findings, because the classification is important in preoperative therapeutic decision-making.

The revised Fukuoka guidelines recommend resection of all MD-IPMNs just as did the Sendai guidelines. Major changes in the Fukuoka guidelines exist in the indication for resection of BD-IPMNs. Although the Sendai guidelines advocated resection of BD-IPMNs with at least one of five criteria for suspected malignancy ("Sendai criteria"), i.e., positive pancreatic juice cytology, the presence of mural nodules, cyst size greater than 3 cm, dilation of the main pancreatic duct and abdominal pain, the adequacy of the size criterion was controversial, since only 13 to 22 percent of resected BD-IPMNs greater than 3 cm without mural nodules were malignant. To avoid unnecessary surgical intervention the Fukuoka guidelines moved the size criterion from high-risk stigmata to a category of worrisome features (Figure 1).

The histological subclassification of IPMNs into gastric, intestinal, pancreatobiliary and oncocytic type has been introduced in the Fukuoka guidelines. Most BD-IPMNs were of the gastric type, while MD-IPMNs were usually of intestinal type. The prognosis of BD-IPMNs is better than that of MD-IPMNs, and hence the histological subtypes are correlated with the prognosis. On the contrary, invasive carcinoma derived from intestinal-type IPMNs shows a better prognosis than invasive carcinoma derived from nonintestinal types, i.e., gastric, pancreatobiliary, oncocytic and nonclassifiable types. Thus, the histological subtypes would be of considerable interest to predict the prognosis, if determined preoperatively by immunohistochemical staining or molecular marker determination of the pancreatic juice or fluid samples aspirated from BD-IPMNs. This is a future point currently under intensive investigation.

BD-IPMNs observed without resection need continuous surveillance in terms of their malignant change and the development of distinct pancreatic ductal adenocarcinoma (PDAC). The malignant change of BD-IPMNs received full consideration in the Sendai guidelines and the adequacy of the Sendai criteria to predict the malignant change has been documented well, except for the size criterion revised in the Fukuoka guidelines as mentioned above. The development of distinct PDAC in the pancreas harboring IPMNs was just briefly mentioned in the Sendai guidelines, and given more detailed and well-evidenced consideration in the Fukuoka guidelines. A distinct PDAC may occur even in the remnant pancreas after partial pancreatectomy for noninvasive or invasive IPMNs.

Evidence indicates a relatively high prevalence of PDAC in patients with BD-IPMNs: 1.9 to 9.3 percent.[3] The yearly incidence is reported to be 0.41 to 1.1 percent per year.[3] Worsening diabetes and high levels of serum CA19-9 are suggested to predict the presence of PDAC. Patients who develop PDAC tend to be older and have a smaller BD-IPMN and main pancreatic duct compared to those who do not develop PDAC. However, the exact incidence or pathogenesis of concomitant PDAC is not known. Concomitant PDACs tend to be smaller and less extensive than ordinary PDAC, reflecting the early detection.

The optimal interval and diagnostic modality of surveillance of BD-IPMN remain to be determined. CT and MRCP are usually performed alternately every six months, but the adequacy of this strategy is unclear. The Fukuoka guidelines suggest that the interval of surveillance can be lengthened after two years of no change in small BD-IPMNs; however, continued six-month surveillance is also recommended for the early diagnosis of concomitant PDAC. Endosonography is more sensitive to observe such a PDAC as well as malignant changes in BD-IPMN, although this technique is more invasive, more expensive and more examiner-dependent. The Japan Pancreas Society is currently conducting a large-scale prospective surveillance study to elucidate the optimal interval and modality of surveillance of BD-IPMN. ■

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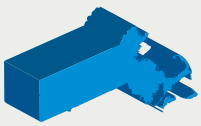
GEORGIA

Southeast Georgia Physician Associates-Gastroenterology, part of the Southeast Georgia Health System physician practice network, seeks board-certified/eligible physicians of gastroenterology who desire physician-based, inpatient/outpatient practices to join our three-physician team in Brunswick/St. Simons Island, Georgia. Our hospital-owned office group requires expertise in therapeutic endoscopy; ERCP and EUS preferred, not required. These include an option to teach medical students through an academic appointment at Georgia Regents University, if desired. Call: one in four weekends, and one in four weeknights. Office hours: 8 a.m. to 4 p.m. We offer competitive income, production incentives and comprehensive benefits. Please email CV to **Sube Lawrence**, Physician Recruiter, at slawrence@sghs.org.

SOUTHEAST GEORGIA HEALTH SYSTEM



MASSACHUSETTS

STAFF SCIENTIST. Experienced basic or translational scientist at the level of assistant professor or higher, with the ability to attain extramural funding. Areas of research desired include: the association between obesity and malignancy; the impact of obesity on the gastrointestinal tract and liver. Candidates should have an MD and/or PhD degree or equivalent.

An Equal Opportunity Employer.

Send CV and references via email to linda.neville@bmc.org or mail to:

Hemant K. Roy, MD,
Chief, Section of Gastroenterology,
Boston Medical Center and Boston University School of Medicine
650 Albany Street, X 504
Boston, MA, 02118

MARYLAND

Join a Leader in Integrated Healthcare Delivery — KAISER PERMANENTE

The Mid-Atlantic Permanente Medical Group, PC (MAPMG) located throughout the metropolitan Washington, DC, and Baltimore areas is currently interviewing candidates for our Gastroenterology Department in LARGO, MARYLAND.

The Kaiser Permanente medical care program is the largest and most experienced integrated healthcare system in the country. Established over 50 years ago, our programs continue to receive national awards of excellence. The Mid-Atlantic Permanente Medical Group is a physician-owned and managed multi-specialty group with over 1000 physicians serving 500,000 patients at 30 medical centers located throughout the Washington, DC and Baltimore metro areas.

Living and working in the Mid-Atlantic Region offers you all of the convenience of two major metropolitan areas with easy access to the Chesapeake Bay, Shenandoah Mountains, and Atlantic Ocean. The region is great for families: the local public schools are considered among the finest in the country. Best of all, you are just minutes away from the cultural, historical, and entertainment venues of our nation's capital.

Here are just some of the reasons why our 1,000 physicians joined the Mid-Atlantic Permanente Medical Group:

- physician-led and driven practice
- built in referral base from large multi-specialty group
- multi-specialty support
- collegial atmosphere
- affiliation with top hospitals
- reasonable, predictable schedules

Please apply online at http://physiciancareers.kp.org/midatl and email CV to cooper.j.drangmeister@kp.org.

Place GI Position Listings and Activity Announcements

For as little as $82.50, you can place a classified ad of 100 words or less in AGA's weekly email newsletter, *AGA eDigest*, or AGA's bimonthly magazine, *AGA Perspectives*. If you place ads in both *AGA Perspectives* and *AGA eDigest*, you will receive a 10 percent discount. Advertising in either includes a free online classified listing. Learn more by contacting Rachel Steigerwald at 301-272-1603 or email communications@gastro.org. The deadline for the August/September 2014 issue is July 11, 2014.

Upcoming Research Funding Opportunity

The AGA Research Foundation will award $1.5 million in research funding to support young researchers in gastroenterology and hepatology.

August 2014 Deadline

- AGA-R. Robert & Sally Funderburg Research Award in Gastric Cancer ($100,000): **Aug. 29**

Apply online at **www.gastro.org/foundation**.

AGA RESEARCH FOUNDATION

Government Gastroenterology Locum Tenens Opportunities Available!

Tired of waiting on licensure? Want the flexibility of working locums without the hassle of getting a new state license? Next Medical has small business set aside status with government facilities. Our classification can provide Next Gastroenterologists an advantage on certain government locums. Locums include VA facilities, IHS, Air Force Bases, Outpatient Clinics and more...

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- Malpractice insurance with tail is provided
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Call today for more info at 877-480-6398 ext. 206 and ask for Christa
or visit us at www.nextmedicalstaffing.com