The NEW GASTROENTEROLOGIST

A Quarterly Supplement to GI & Hepatology News | Fall 2016

A Perspective on Fecal Microbiota Transplantation

Letter
FROM THE EDITOR

Bryson W. Katona is an instructor of medicine in the division of gastroenterology at the University of Pennsylvania.

Dear Colleagues,

The microbiome continues to be a fascinating area with applications not only in gastroenterology, but all of medicine. One area of microbiome research that has received significant attention over the past few years is fecal microbiota transplantation (FMT). In this issue of *The New Gastroenterologist*, Olga Aroniadis and Lawrence Brandt from Montefiore Medical Center/Albert Einstein College of Medicine provide a fantastic overview of FMT use for the treatment of *Clostridium difficile* infection.

Additionally, at the end of fellowship, the nuances of coding and billing often remain a mystery to most. This issue features a very useful summary of the basics of coding by Dawn Francis (Mayo Clinic – Jacksonville), which will certainly be a good review for all gastroenterologists. Also included is a great synopsis of pertinent financial books for gastroenterologists by Melvin Lau (Scott & White Healthcare/Texas A&M), as well as coverage of the AGA Tech Summit highlighting the important role of innovation within our field.

The AGA-AASLD Academic Skills Workshop is a great program designed for fellows and young career GIs who are interested in pursuing careers in academic medicine. In this issue, Patricia Jones (University of Miami) and Swathi Eluri (UNC Chapel Hill) give terrific perspectives on this workshop from the viewpoint of an early career faculty member and a fellow, respectively. Lastly, there are two additional articles that address workplace equality and the improving gender gap within our field as well as the differing working environments for physicians in different states.

In addition to the content of *The New Gastroenterologist* being delivered in print every quarter with *GI & Hepatology News*, it is also available via *The New Gastroenterologist* app as well as free online via www.gastro.org or www.gihepnews.com. Additionally, if you have any suggestions for future topics, or are interested in contributing an article to *The New Gastroenterologist*, please contact me (bryson. katona@uphs.upenn.edu) or Ryan Farrell (rfarrell@gastro.org).

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

The NEW GASTROENTEROLOGIST

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Bryson W. Katona, M.D., Ph.D.

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ON THE COVER

Frozen fecal material is being prepared.
Photo provided by OpenBiome

IN THIS ISSUE

DDSEP® eight

Digestive Diseases Self-Education Program

QUESTIONS

// Answers on page 31

Q1: An 18-year-old female college student has a 6-month history of vomiting, with an associated 15-pound weight loss during this time period. Her medical history is significant for gastroenteritis about 1 year ago and surgery for pyloric stenosis as an infant. She has no psychiatric history. Current medication includes an oral contraceptive. She describes the vomiting episodes as effortless regurgitation of food within 30 minutes of a meal. She also reswallows the food if she is in public. The vomiting occurs with almost every meal, either solid or liquid. An upper endoscopy, 4-hour gastric-emptying test by scintigraphy, and basic blood laboratory tests are performed. Upper endoscopy is normal with no retained food. She cannot complete the gastric-emptying test because she vomits the radiolabeled test meal. Her blood work demonstrates a normal fasting blood glucose and complete blood count.

What is the most likely etiology of her symptoms?
A. Recurrent small bowel obstruction
B. Adaptation to the belch reflex
C. Idiopathic gastroparesis
D. Bulimia

Q2: A 34-year-old man with ileocolonic Crohn's disease presents with symptomatic anemia. Staging of his disease reveals active ileal and right colonic disease. His hemoglobin is 9 g/dL with iron 20 mcg/dL, iron saturation 6%, and ferritin 25 ng/mL. You decide to administer intravenous iron replacement.

Which of the following regulators of iron assimilation plays the most significant role in determining the need for intravenous over oral iron replacement?
A. Divalent metal transporter 1 (DMT1)
B. Duodenal cytochrome B (DcytB)
C. Hephaestin
D. Hepcidin
E. Heme oxygenase

For more information about DDSEP© visit gastro.org/ddsep

News from the AGA

What Not to Do: 6 Tips for Early Career GIs

A recent report published by the Association of Medical Colleges provides a list of six of the most common behaviors that medical students and trainees should question before doing. Despite the focus on new physicians, these tips are applicable to GIs at any stage of their career.

Here are the six tips from the report:

- Don't suggest ordering the most invasive test or treatment before considering other, less invasive options.
- Don't suggest a test, treatment, or procedure that will not change the patient's clinical course.
- Don't miss the opportunity to initiate conversations with patients about whether a test, treatment, or procedure is necessary.
- Don't hesitate to ask for clarification on tests, treatments, or procedures that you believe are unnecessary.
- Don't suggest ordering tests or performing procedures for the sole purpose of gaining personal clinical experience.
- Don't suggest ordering tests or treatments preemptively for the sole purpose of anticipating what your supervisor would want.

The report and its corresponding study were designed as part of the Choosing Wisely Canada campaign. The campaign aims to create a conversation about the use of unnecessary tests and procedures between clinicians and patients. AGA participated in the U.S. version of the campaign; review AGA's GI-Specific Choosing Wisely List at www.choosingwisely.org/societies/american-gastroenterological-association/. Do you agree with the list or have any other tips to add? Share your thoughts with other AGA members in AGA Community (community.gastro.org).

Additional Resource for Trainees

Looking for additional tips to help you excel as a GI? Check out AGA's 10 Tips for New GI Fellows at http://www.gastro.org/trainees/tips-for-new-gi-fellows.

Save Thousands of Dollars on Your Student Loans

You and your family could save thousands of dollars by refinancing your student loans with CommonBond, AGA's affinity partner. Pay off your old student loan with a new one at a lower interest rate. Unlike refinancing your mortgage, refinancing student loans with CommonBond has no additional fees, no origination, prepayment, or refinancing fees.

CommonBond offers fixed, variable rate, and even hybrid student loans. They can even provide an estimate of your interest rates in minutes without affecting your credit score. Just answer a few questions about yourself and you could be on your way to saving thousands of dollars.

Visit http://studentloans.gastro.org to get started today. The CommonBond Care Team, based in New York City, is also available to answer any questions you may have. Call 800-975-7812 or email them at gastro@commonbond.com.

Webcasts Available: 2016 Academic Skills and Regional Practice Skills Workshops

The webcasts from the 2016 Academic Skills and Regional Practice workshops are now available as education assets on the AGA website. AGA members can view presentations anytime, from anywhere, to learn helpful career tips and guidance.

Access numerous presentations instantly on topics such as negotiating job contracts, giving a killer presentation, and the pros and cons of going into academic or private practice.

To see featured videos, visit gastro.org/trainees.

AGA Outlook

For more information about upcoming events and award deadlines, please visit http://www.gastro.org/education and http://www.gastro.org/research-funding.

Upcoming Events

Dec. 1, 2016

Digestive Disease Week® (DDW) 2017 Abstracts

Abstracts may be submitted for consideration to DDW® 2017 online beginning on Oct. 20, 2016. The submission site will close on Thursday, Dec. 1, 2016.

Dec. 8-10, 2016

2016 Advances in Inflammatory Bowel Diseases, Crohn's & Colitis Foundation's Clinical & Research Conference

The 2016 Advances in Inflammatory Bowel Diseases, Crohn's & Colitis Foundation's Clinical & Research Conference is designed for health care professionals and researchers who study and manage patients with IBD.

Orlando, FL

Dec. 14, 2016; Feb. 10; Feb. 11; Feb. 25, 2017

Practice Skills Workshops

These workshops are targeted to GI fellows, and will provide valuable insight and information into how to start a successful career in a variety of practice settings. They will be held at five separate locations.

New York, NY (12/14); Pinehurst, NC (2/10); Stanford, CA (2/11); Houston, TX (2/25); Chicago, IL

Feb. 3-4, 2017

AGA Women's Leadership Conference

This conference is the premier leadership development event tailor-made for female gastroenterologists.

Irving, TX

Feb. 19-22, 2017

Gastroenterology Updates in IBD and Liver Disease (GUILD) 2017

Guild 2017 teaches GIs ongoing education and insights to improve patient care and overall healthcare outcomes.

Maui, HI

May 6-9, 2017

DDW® 2017

Chicago, IL

Awards Application Deadlines

AGA-Elsevier Pilot Research Award
Deadline: Jan. 6, 2017

AGA-Elsevier Gut Microbiome Pilot Research Award
Deadline: Jan. 6, 2017

AGA-Medtronic Research & Development Pilot Award in Technology
Deadline: Jan. 6, 2017

AGA-Rome Foundation Functional GI and Motility Pilot Research Award
Deadline: Jan. 13, 2017

AGA Microbiome Junior Investigator Research Award
Deadline: Jan. 13, 2017

AGA-Pfizer Pilot Research Award in Inflammatory Bowel Disease
Deadline: Jan. 13, 2017

AGA-Caroline Craig Augustyn & Damian Augustyn Award in Digestive Cancer
Deadline: Jan. 20, 2017

AGA-June & Donald O. Castell, MD, Esophageal Clinical Research Award
Deadline: Jan. 20, 2017

AGA Investing in the Future Student Research Fellowship
Deadline: Feb. 3, 2017

AGA-GRG Fellow Abstract Prize
Deadline: Feb. 24, 2017

AGA-Moti L. & Kamla Rustgi International Travel Award
Deadline: Feb. 24, 2017

AGA Student Abstract Prize
Deadline: Feb. 24, 2017

AGA-AASLD Academic Skills Workshop: Fellow and Faculty Perspectives

By Patricia D. Jones MD, MSCR, and Swathi Eluri, MD, MSCR

Dr. Jones is an assistant professor in the department of medicine, hepatology division, and the Sylvester Comprehensive Cancer Center, University of Miami Miller School of Medicine, Miami; Dr. Eluri is a fellow in the department of medicine, division of gastroenterology and hepatology, University of North Carolina School of Medicine, Chapel Hill, NC. The authors have no conflicts of interest.

In March 2016, we had the opportunity to attend the Academic Skills Workshop sponsored jointly by the American Gastroenterological Association (AGA) and American Association for the Study of Liver Diseases (AASLD). Keith Lindor, MD, AGAF, FAASLD, and John Inadomi, MD, AGAF, were the chairs of this year's workshop. This one and a half day gathering was meticulously planned and provided us with lessons in manuscript preparation, grant writing, delivery of oral presentations, career pathways in academic medicine, and early funding opportunities, among other topics.

Fellow perspective (Swathi Eluri)

I attended the Academic Skills Workshop as a second-year fellow and found it to be an invaluable experience. It provided an opportunity to meet thought leaders in the field and peers from across the country. Attendees with similar interests were paired with mentors in tailored sessions that not only provided exchange of ideas on individual research proposals, but also time for faculty to share their personal experiences in academic medicine. There were common themes among their stories, such as being passionate about your work, planning ahead, choosing the right mentors, the ability to take risks, hard work, and luck.

For fellows like me, who are still early in their training, descriptions of the different institutional tracks and resources that are needed to enhance success provided a useful general foundation. Being cognizant of individual goals, wishes, and priorities can help identify the correct institutional track. In addition, knowing the resources needed for success in each track, such as access to a large patient base for a clinician or protected time for a researcher, is key to finding the right job and choosing the right institutional environment. Most importantly, being aware of the expectations in the chosen track can help create a focused plan to meet career milestones.

While careful planning and goal-setting is one piece of the puzzle, the importance of "choosing an area/niche" and "making oneself indispensable" was also stressed by Marcia Cruz-Correa, MD, PhD, AGAF. For many faculty members at the meeting, their particular niche had evolved or dramatically changed over the years but the pervading sentiment expressed was to be open to new opportunities and to veer away from a planned path if the time is right.

The importance of being passionate and excited about your work cannot be overemphasized and is the driving force for success. Hard work and dedication are also necessary as exemplified by a story from Hashem B. El-Serag, MD, MPH, about arduously composing his first publication in English when still learning the language. Finally, the most tangible lesson from the workshop was that success in academia is built upon

Courtesy AGA

From left: Patricia Jones, MD; Megan Adams, MD, JD; Marcia Cruz-Correa MD, PhD, AGAF; and Veroushka Ballester, MD.

Courtesy AGA

From left: John Inadomi, MD, AGAF; Patricia Jones, MD; and Keith D. Lindor, MD, AGAF.

developing and maintaining relationships. Whether it is the mentor-mentee relationship that is especially key in the early stages of career development, or collaborations between institutions or peers, academic medicine is a team sport. Recognizing this will not only help create a supportive network of colleagues but also friends.

Junior faculty perspective (Patricia Jones)

In my first year on faculty, I attended the Academic Skills Workshop and realized that, in order to succeed in academics, quality mentoring is essential. Mentors help you develop a relevant area of focus, avoid making costly mistakes, and may also sponsor and promote you on an institutional, regional, or national level. There is no "one-size fits all" mentoring relationship and the workshop featured many classic examples such as Barbara H. Jung, MD, AGAF, and John M. Carethers, MD, AGAF, who began working together when Barbara was a medical student and John was junior faculty. They have maintained this relationship, which has evolved through different career stages. At times, it may be necessary to seek mentors in different disciplines, as demonstrated by Donna Evon, PhD, a psychologist, and Michael W. Fried, MD, AGAF, FAASLD, a hepatologist. With time, these relationships can become collaborative and beautiful friendships. Also, you may find yourself in a position where you need additional mentorship besides what is available at your home institution. In that case, seek mentorship outside of your institution by networking strategically at conferences and participating on committees. Participation in national committees and special interest groups exposes you to others working in your area, opens up opportunities for collaboration, and may help advance your career.

Many of the lessons learned about networking and how to select the appropriate job were helpful not only for fellows but also for those who have already started their first junior faculty position. After negotiating for a position that provides sufficient protected time to develop your research program, you must ensure that your time is spent productively. One of the most important messages from the workshop was the importance of "focus."

For a successful career in academia, it is critical to develop a focused niche and center both research and clinical efforts, if possible, around that niche. In most academic positions, you will have 3-5 years to establish yourself and secure independent funding. Some early-career funding opportunities highlighted were through the National Institutes of Health, Veteran's Administration, Patient-Centered Outcomes Research Institute, Agency for Healthcare Research and Quality, foundational sources, and pharmaceutical industry–sponsored research. In the current funding environment, it is important to think broadly and market yourself appropriately. Also, many of the funding mechanisms desirable to early-career investigators have an expiration date (e.g., 5 years after completion of terminal training). Therefore, it is important to make a timeline of your goals and important dates to guide and keep you focused as you navigate the early years of your career.

"People think focus means saying yes to the thing you've got to focus on. But that's not what it means at all. It means saying no to the hundred other good ideas that there are. You have to pick carefully. I'm actually as proud of the things we haven't done as the things I have done. Innovation is saying no to 1,000 things."

Steve Jobs

There is some truth to the above quote and we discussed the importance of selective participation. In maintaining focus and protecting your time, it will be important to choose how to participate at the local, national, and international levels. On a local level, meet regularly with your division chief to ensure that you know, and are meeting, expectations. Your division chief should help you sift through local opportunities for participation and decide which are worth your time (e.g., administrative duties). It may be important to say yes simply because you do not know how your career might benefit.

Courtesy AGA

From left: Monica Konerman, MD; Joanne Miller Melia, MD; and Swathi Eluri, MD.

Courtesy AGA

From left: Donna Evon, PhD, at lectern; Michael Fried, MD, seated.

Concluding thoughts

One of the most valuable lessons learned is that failure is inevitable and none of us are immune to it; it is an important part of the process and should be used constructively to improve the research project, grant, or manuscript in question. The workshop faculty shared examples of failures that eventually paved the way to success and showed that establishing a career in academics is a long, and sometimes arduous, process. The importance of patience and perseverance should not be understated.

On behalf of the fellows and junior faculty members who were fortunate to have the opportunity to attend the Academic Skills Workshop, we would like to thank the esteemed workshop faculty who dedicated their time. Each one of us, regardless of our training stage, found this experience to be invaluable and is thankful for the connections made with other like-minded peers and faculty. And be sure to check out www.gastro.org in the coming months for information on the 2018 workshop! ■

For a successful career in academia, it is critical to develop a focused niche and center both research and clinical efforts, if possible, around that niche.

What's Your Diagnosis?

An enlarging liver in a young diabetic male

Published previously in Gastroenterology (2015;149:e8-10)

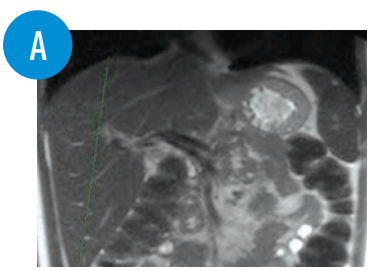
By Jason Xu, MD, Deepti Dhall, MD, and Vinay Sundaram, MD

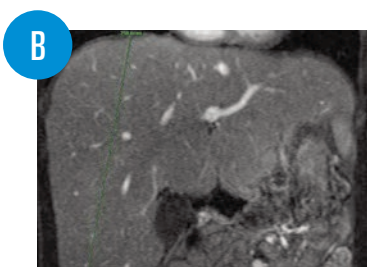
A 22-year-old man with history of type 1 diabetes mellitus, alpha-1-antitrypsin deficiency (ZZ phenotype), gastroesophageal reflux disease, hyperlipidemia, and depression presented to the hospital for increasing right upper quadrant pain and nausea for 2 weeks. The patient was a former heroin user and an active smoker, but denied significant alcohol use. The patient's home medications included insulin, atorvastatin, dexlansoprazole, paroxetine, buprenorphine, and trazodone. The patient had poorly controlled diabetes, requiring six hospitalizations for diabetic ketoacidosis within the last year.

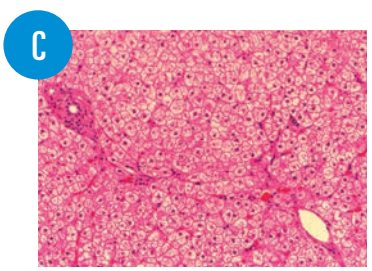
Physical examination revealed a soft, nondistended abdomen with diffuse tenderness and severe hepatomegaly without ascites, jaundice, spider angioma, or other stigmata of advanced liver disease. Laboratory studies showed an alanine aminotransferase of 223 U/L, aspartate aminotransferase of 331 U/L, alkaline phosphatase of 223 U/L, total bilirubin of 0.3 mg/dL, albumin of 3.4 g/dL, platelet count of 302 U/L, International Normalized Ratio of 0.9, and hemoglobin A_{1C} of 14.6%. Hepatitis B and C serologies were negative and the alpha-1-antitrypsin level was less than 60 mg/dL. MRI revealed a significantly enlarged liver with marked interval increase of 21.2 to 25.8 cm from 8 months prior. No focal hepatic lesions were identified. There was no intrahepatic or extrahepatic biliary ductal dilatation (Figures A, B). A core biopsy of the liver was performed showing hepatocytes are swollen with cleared cytoplasm (Figure C). Figures D and E show hepatocytes are strongly and diffusely positive for periodic acid–Schiff stain and largely negative for periodic acid–Schiff diastase stain, suggesting that the hepatocytes were swollen with glycogen that was digested with diastase. Periodic acid–Schiff diastase also highlights alpha-1-antitrypsin globules. ■

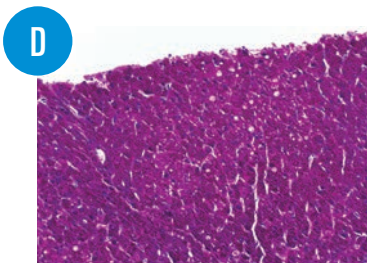
Based on the clinical scenario, imaging, and pathologic findings, what is the diagnosis?

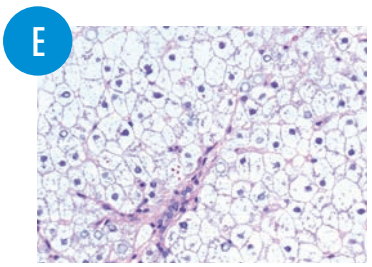
Dr. Xu is in the Department of Medicine, Dr. Dhall is in the Department of Pathology and Laboratory Medicine, and Dr. Sundaram is in the Department of Gastroenterology and Hepatology and Comprehensive Transplant Center, Cedars-Sinai Medical Center, Los Angeles.









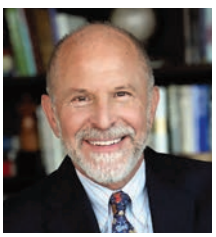


Courtesy AGA Institute

See ***The Answer*** on page 27

A Perspective on Fecal Microbiota Transplantation for *Clostridium difficile* Infection

By Olga C. Aroniadis, MD, and Lawrence J. Brandt, MD, AGAF, FASGE, MACG



Dr. Aroniadis is assistant professor of medicine and Dr. Brandt is professor of medicine and surgery in the division of gastroenterology, Montefiore Medical Center/Albert Einstein College of Medicine, Bronx, N.Y. Dr. Aroniadis and Dr. Brandt receive research support from OpenBiome.

Therapeutic transplantation of stool was first reported in the fourth century and has been used in veterinary medicine since the 17th century.[1] The first "modern" use of fecal microbiota transplantation (FMT) in humans was as a fecal enema for the treatment of pseudomembranous colitis in 1958[2], and its first use for *Clostridium difficile* infection (CDI), also by enema, was in 1983.[3] Currently, other routes of administration for fresh and frozen fecal product[4] include nasoenteric tube, esophagogastroduodenoscopy (EGD), colonoscopy, and most recently, oral capsules.[5-8] The Food and Drug Administration only sanctions FMT for the treatment of recurrent CDI or CDI that is severe or complicated and not responsive to conventional therapy;[9] use of FMT for any other indication requires it be performed under an FDA-approved application for an Investigational New Drug (IND).[10]

Composition and function of the intestinal microbiota

The mechanism by which FMT cures CDI is being slowly unraveled as we increase our understanding of the complex roles the intestinal microbiota play in health and disease.

The majority of our intestinal microbiota is anaerobic, and although more than 50 bacterial phyla have been described in the mammalian GI tract, only four predominate: Bacteroidetes, Firmicutes, Actinobacteria, and Proteobacteria. Further, two phyla account for over 90% of all bacteria in the human GI tract: Bacteroidetes and Firmicutes.[11] It is estimated that about 3,000 bacterial species reside in our GI tract, comprising as many as 10^{14} bacterial cells, a number 10 times greater than the number of cells in the human body.[12] Per gram of contents, there is a marked and progressive distal increase in the number of bacteria: 10^1 in the stomach, 10^3 in the duodenum, 10^4 in the jejunum, 10^7 in the ileum, and 10^{12} in the colon.[13] There is longitudinal heterogeneity of the microbial populations with a predominance of Firmicutes and Proteobacteria (notably *Helicobacter pylori)* in the stomach, Firmicutes and Actinobacteria in the small intestine, and Bacteroidetes and the *Lachnospirae* family of Firmicutes in the colon.[13]

The intestinal microbiota play a vital role in protecting our intestines against colonization by exogenous and endogenous pathogens by 1) competing for nutrients; 2) enhancing epithelial barriers to inhibit attachment of pathogens; and 3) modulating inflammation and the host immune system by activating intestinal macrophages,[14] neutrophils, innate lymphoid cells, T-helper cells, IgA-producing B cells and plasma cells,[14] to upregulate production of certain cytokines (IL-1b and IL-22), and mediate antigenic tolerance.[15,16]

Clostridium difficile infection

The pathogenesis of CDI is thought to begin with disruption of the normal balance of colonic microbiota, usually as a consequence of antibiotic use. Patients with RCDI exhibit decreased phylogenetic richness and a reduction of Bacteroidetes and Firmicutes phyla in their stool, compared with patients who have a single episode of CDI or with healthy controls.[17] FMT is thought to provide its therapeutic benefit by reestablishing a balanced microbiota with its attendant "colonization resistance." Indeed, the microbiota of the recipient's stool closely resembles that of the donor about 2 weeks after FMT, a change that persists for at least 4 months

Figure 1 A-C *Preparation of FMT material using patient-selected donor stool. The stool is transferred into a clean container, mixed with nonbacteriostatic saline, and then filtered through a gauze pad.*

after transplantation.[18] Another postulated mechanism whereby FMT prevents CDI recurrence involves secondary bile acids (deoxycholic and lithocholic acid), which inhibit the germination and growth of *C. difficile*. Fecal samples of patients with RCDI have high concentrations of primary bile acids (cholic acid and chenodeoxycholic acid), while secondary bile acids are nearly undetectable. In contrast, post-FMT fecal samples and non-CDI donor feces contain mostly secondary bile acids.[19] Indeed, one study has identified certain species, including *C. scindens*, that may play a primary role in maintaining resistance to CDI via the production of secondary bile acids.[20]

Most patients with CDI respond to standard treatment with metronidazole, vancomycin, or fidaxomicin, but with recurrence rates of 15%-30%.[21] Patients who have one recurrence have up to a 40% chance of a second recurrence, and after a second recurrence, up to 65% of patients will suffer a third.[22] Current literature on FMT for RCDI is comprised of single-center case series and case reports,[23-30] meta-analyses,[31,32] systematic reviews,[31,33,34] and randomized, controlled trials.[35-37] In all, about 92% of patients were cured of their RCDI, with a range of 81% to 100%. One multicenter long-term follow-up study of patients who underwent colonoscopic FMT for RCDI reported an astounding overall cure rate of 98%.[38] Patients in this study had symptoms for an average of 11 months before FMT and most (74%) reported prompt resolution of diarrhea within 3 days.[38] FMT via colonoscopy or enema is thought to be more successful for RCDI than FMT by EGD or nasoenteric tube; however, these methodologies have not been compared in head-to-head randomized controlled trials; the latter two routes give an overall resolution rate of approximately 80%.[39]

Three randomized controlled trials have evaluated FMT for RCDI.[35-37] The first was a small open-label trial that randomized patients to receive a short course of vancomycin followed by bowel lavage and FMT via nasoduodenal tube; a "standard" vancomycin regimen; or "standard" vancomycin regimen with bowel lavage.[37] Thirteen of 16 patients (81%) in the FMT group had resolution of RCDI after the first infusion. Two of the three remaining patients were cured after a second infusion with feces from a different donor (overall cure rate of 94%). Resolution of RCDI only occurred in 4 of 13 patients (31%) who received vancomycin alone and in 3 of 13 patients (23%) who received vancomycin with bowel lavage.[37]

The second trial was another open-label trial that randomized patients with RCDI to colonoscopic FMT versus vancomycin.[35] Significantly higher cure rates were reported in the FMT group, compared with the vancomycin group. Specifically, 18 of the 20 patients (90%) treated by FMT exhibited symptom resolution, compared with 5 of the 19 patients (26%) treated with vancomycin.[35]

The third trial comprised 44 patients treated in a randomized, placebo-controlled, blinded fashion with colonoscopic administration of either donor stool or the patient's own stool (autologous) at one of two sites (Brown Alpert Medical School, Providence, R.I., and Montefiore Medical Center, Bronx, N.Y.).[36] Overall, 91% and 63% of patients given donor or autologous stool, respectively, were cured of their RCDI. Interestingly, the percentages of cure differed at the two study sites with 90% and 43% cured in Rhode Island and 92% and 90% cured in New York after donor and autologous stool, respectively.[36] Reasons for this discrepancy are unclear, but differences in the patients treated at the New York site included a longer duration of disease, more recurrences, and more courses of fidaxomicin.[36]

Figure 2 A-B

The stool suspension is then drawn into catheter-tipped syringes.

Ten of 11 patients with CDI recurrence subsequently given open-label donor FMT remained symptom free.[36] Donor FMT restored normal microbial community structure with reductions in Proteobacteria and Verrucomicrobia and increases in Bacteroidetes and Firmicutes.[36] There were differences in the microbiome of the Rhode Island and New York study participants but none that accounted for the site difference in cure rates.[36] Detailed microbiome analyses from this trial are currently underway and perhaps will further explain how FMT effects cure in RCDI. FMT is currently recommended under the following conditions:[21]

1. At least three episodes of mild/moderate CDI and failure to respond to standard therapy;
2. At least two episodes of CDI resulting in hospitalization and significant morbidity;
3. Moderate CDI with no response to standard therapy for at least 1 week; and
4. Severe CDI with no response to standard therapy for 48 hours.[21]

Recurrence rates of CDI after successful FMT approximate 10%,[38,40,41] approximately two-thirds of which are precipitated by use of antibiotics for various infections such as pneumonia or urinary tract infection.[41] Prophylactic therapy with anti-CDI antibiotics, such as vancomycin, may be effective to prevent RCDI in patients who have received FMT and need antibiotics for treatment of non-CDI infections, but is not generally recommended at this time.[42] Probiotics do not seem to be effective for prophylaxis.[42]

FDA regulations

In May 2013, the FDA announced that feces used for FMT met the agency's definition of a drug/biologic substance and, thereafter, an IND application would be required to perform FMT. In July 2013, the FDA liberalized its ruling while maintaining discretionary oversight: Treating physicians could perform FMT for CDI, without an IND, in patients who had not responded to traditional therapy, provided the physician obtained appropriate informed consent, including acknowledgement that use of FMT is investigational and discussion of potential risks of FMT.[9] In March 2014, the FDA sought public feedback on draft guidance stipulating that the stool donor must be known to either the health care provider or the patient, and that the physician performing the FMT direct the donor and stool screening and testing. The draft was never enacted and the acting guidance remained the 2013 enforcement discretion. In February 2016, however, the FDA released a new draft guidance again addressing enforcement discretion regarding the IND requirements for the use of FMT to treat CDI. In particular, the FDA stated that stool biobanks may need to operate under an IND in order to arrange a more tailored regulatory scheme. The FDA has requested comments on the elements of a regulatory framework that would lend this oversight to the practice of stool banking. Once these comments are reviewed and synthesized, the FDA will disseminate its final regulatory mandate. The FDA still requires an IND for use of FMT to treat all other GI and non-GI diseases.

Figure 3

The stool suspension is then infused into the cecum via the accessory channel of a colonoscope, using a length of suction tubing that has a clamp on it to prevent retrograde passage of stool during syringe exchange.

FMT safety

It is not unusual for some transient GI complaints or altered bowel habits to occur for several days after FMT, including absence of bowel movements, abdominal cramping, gurgling bowel sounds, or increased feelings of gaseousness and bloating.[8,18,37] In a multicenter, long-term follow-up study, autoimmune disease (rheumatoid arthritis, Sjogren syndrome, idiopathic thrombocytopenic purpura, and peripheral neuropathy) developed in 4 of 77 patients who underwent FMT and were then followed for a minimum of 3 months; a clear relationship between the on-

Figure 4 A-E *Frozen fecal material preparation (courtesy of OpenBiome).*

set of autoimmune disease and FMT, however, was not evident.[38] Two cases of norovirus occurring after FMT have been reported,[43] however, it is unclear if these cases were a direct result of FMT, as in one case the donor had negative PCR for norovirus and in the other case, the donor was never tested. In a single case report, a woman, in whom CDI was successfully treated by FMT, reported a 34-pound weight gain, thereby developing new-onset obesity, after receiving stool from her daughter, who was healthy but overweight.[44] Death secondary to aspiration pneumonia was reported in an 80-year-old woman who underwent enteroscopic FMT for treatment of refractory CDI by infusion of a 100-150-mL fecal suspension into the distal duodenum over 12 minutes.[45]

The safety of FMT in immunocompromised patients was reported in a retrospective, multicenter study of 61 adult and 5 pediatric immunocompromised patients treated with FMT for refractory, recurrent, or severe CDI.[46] Patients were immunocompromised due to HIV infection, solid organ transplantation, oncologic conditions, immunosuppressive therapy for IBD, or other immunosuppressive medications or conditions. The overall CDI cure rate in this population was 89%, with an average follow-up period of 12 months. Ten (15%) patients experienced an adverse event within 12 weeks of FMT. Eight of these patients were hospitalized for various indications. Two deaths occurred within 12 weeks of FMT, one of which was the result of aspiration during sedation administered for colonoscopic FMT, while the other was unrelated to FMT. No patients experienced new infections or other diseases related to FMT. Three (9%) patients with IBD experienced a flare post-FMT. In another study of 12 patients with IBD who were on immunosuppressive therapy (for example, infliximab, azathioprine, 6-mercaptopurine, or oral glucocorticoids) and underwent FMT for treatment of IBD, transient abdominal bloating and distension in two (17%) patients were the only adverse events encountered.[47] At present, the long-term safety of FMT is unknown and remains the prime consideration. Larger numbers of prospective observations in controlled circumstances are needed. Recently, a national registry was funded which will follow 4,000 patients for 10 years post-FMT to assess long-term safety and adverse events.

The future

FMT is but the first step in a long journey to cure CDI. In an increasing number of instances, we are no longer using recipient-designated donors to donate stool (Figures 1-3) but rather frozen, highly filtered fecal material from healthy volunteer donors (Figure 4) that is thawed immediately

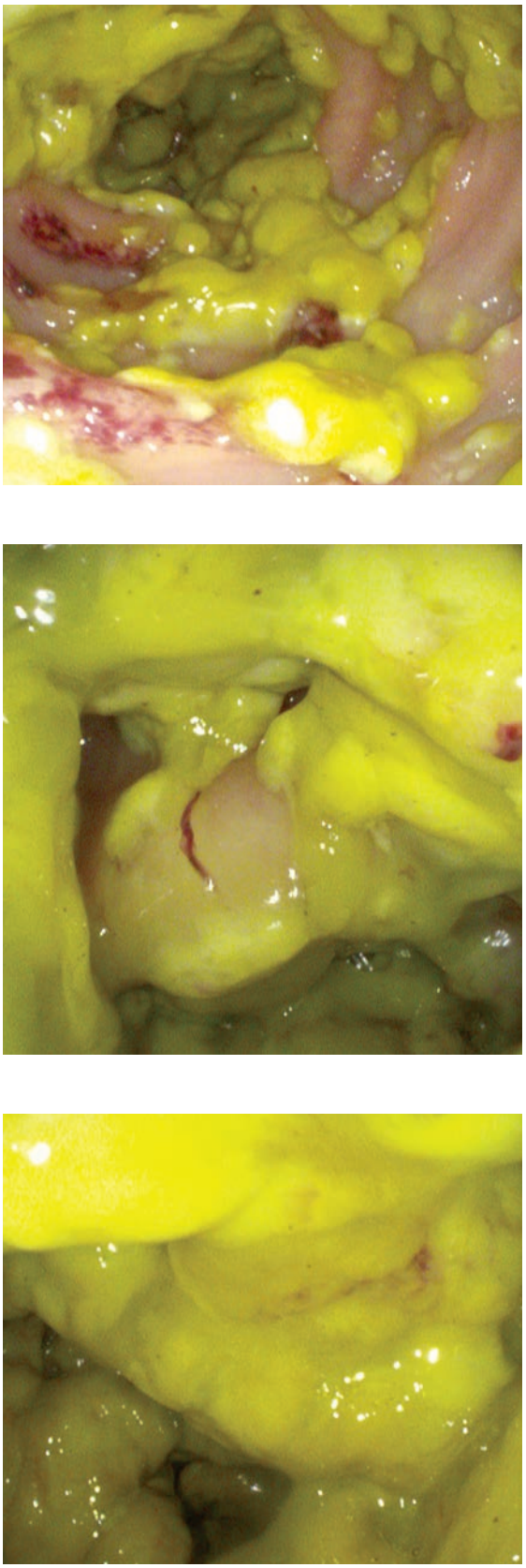


Figure 5 A-C *Endoscopy images of* Clostridium difficile *colitis.*

before use. In a recent trial from six Canadian medical centers, frozen stool was shown to be noninferior to fresh stool with response rates in intention-to-treat and per-protocol analyses of 75% and 70%, and 83.5% and 80.5%, respectively.[4] A large experience with stool banking and cryopreserved stool that then can be shipped for use at a distant location has also been very successful. OpenBiome, a nonprofit stool bank, presented at Digestive Disease Week® 2016 on the collective experience from 1,406 patients with CDI from 482 health care facilities in 49 states and 6 countries.[48] Overall success was reported in 82.4% of patients with RCDI and success was seen in 75.3% and 83.4% of patients treated by upper endoscopic route or colonoscopy, respectively.[48]

Data have shown that ingestion or infusion of a defined bacterial mixture can also cure CDI, obviating the need to use donor feces with its vast microbiological community. Infusion of a mixture of just six phylogenetically diverse bacteria were able to disrupt intestinal dysbiosis and resolve disease when given to mice with CDI.[49] In another study, a stool substitute consisting of 33 isolates obtained from intestinal bacterial cultures derived from a single healthy donor cured RCDI – with a follow-up of 6 months – in two patients in whom repeated standard antibiotics had failed.[50] Graham and colleagues used three species of *Bacteroides* (*B. ovatus, B. vulgatus,* and *B. thetaiotaomicron*) to cure one patient with RCDI.[51] Frozen capsules of stool-derived material have also been used successfully and given cure rates of 70%-100%.[5-8] These studies set the stage for a time in the not-too-distant future when a "designer" capsule of selected microorganisms, either alone or as part of a microbiotic community, with or without a possible microbiotic metabolic product, will be given to restore a balanced microbiota or correct an abnormality of commensal organisms thereby curing recalcitrant CDI.

FMT has been used to treat many other GI diseases including ulcerative colitis and Crohn's disease,[52-54] chronic constipation,[55,56] and irritable bowel syndrome with diarrhea.[57,58] The list of non-GI diseases shown to have an abnormal fecal microbiomic profile is large and growing and many of these diseases are reported to have been successfully treated with FMT with improvement in symptoms or even reported "cures." Such experiences need to be confirmed or refuted in a rigorous fashion by properly designed randomized and blinded clinical trials.

Conclusion

FMT is a highly effective therapeutic intervention for the treatment of RCDI with only few reported short-term adverse effects. At present, FMT has been shown to be efficacious for the treatment of RCDI using various routes of infusion. Although patient-selected donors were routine, there has been a movement toward using standard volunteer FMT donors. Employment of such stool-banked products is safe, enables rapid and convenient delivery, is cost saving, and eliminates redundant site-specific FMT protocols. On the horizon is development of products containing not stool, but an optimal species or number of species of intestinal bacteria that will enable rapid and safe treatment of a variety of GI and non-GI diseases. We now appreciate that a well-balanced and diverse community of bacteria is crucial to the health of the host and we are learning that to restore such a balance once it has been interrupted can result in cure of once debilitating and life-threatening diseases. While FMT and future modifications of microbiotic therapy are very exciting and likely to change the way we think about disease pathogenesis and treatment, safety must remain paramount and additional studies are required. ■

On the horizon is development of products containing not stool, but an optimal species or number of species of intestinal bacteria that will enable rapid and safe treatment of a variety of GI and non-GI diseases.

AGA resource

In August 2016, the AGA announced the funding of a new FMT National Registry by the National Institute of Allergy and Infectious Diseases at the National Institutes of Health (grant number R24AI118629). One of the primary objectives of this registry is to monitor the short- and long-term safety of FMT in the real world. With the support of multiple societies including Crohn's and Colitis Foundation of America (CCFA), Infectious Diseases Society of America (IDSA), and North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN), the FMT National Registry will bring us closer to better understanding the safety implications of this procedure. Please visit www.gastro.org/press_releases/aga-establishes-nih-funded-registry-to-track-fecal-microbiota-transplants for more information.

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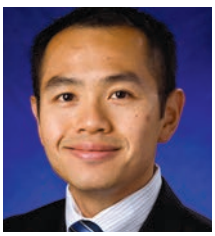
Turning Thousands into Millions: Five Books for Financial Success

By Melvin Lau, MD



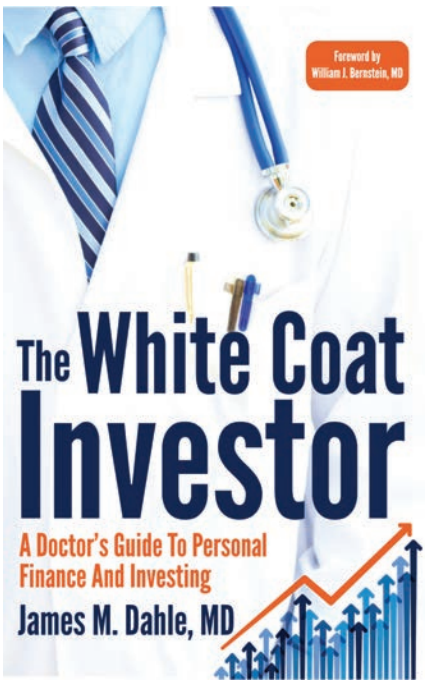
Dr. Lau is chief of the gastroenterology section, Baylor Scott & White Healthcare Austin/Round Rock, and assistant professor of medicine, Texas A&M University Health Science Center, Round Rock. All opinions belong to the author and he does not profit from the review of these books.

See one, do one, teach one. That was the motto during our training years. But when it comes to personal finance, there has been no one to "see," so we can't "do," and we definitely do not "teach." My experience, along with enormous feedback from others, confirms that even the best advice from financial advisors often needs to be supplemented. Furthermore, not all financial advisors have gastroenterologists' best interests at heart; our finances are unique and we generally command a large income. Listed below are several books that I have found to be useful in providing a firm financial foundation, not just for gastroenterologists but for all physicians.

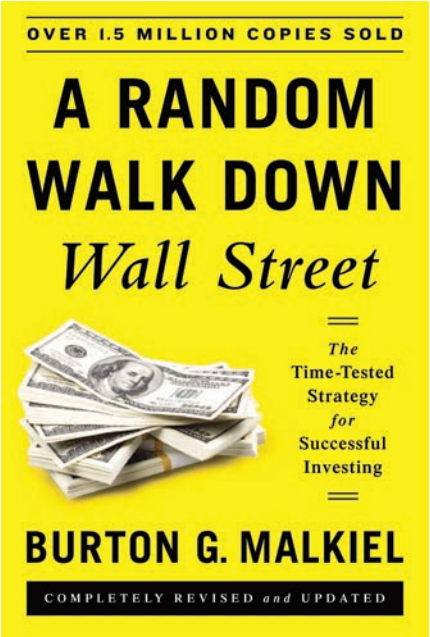
The White Coat Investor: A Doctor's Guide to Personal Finance and Investing

James M. Dahle, MD; 2014

If you only have time to read one financial book, this is it. It's a great starter for personal finances and addresses issues relevant to physicians, such as the abruptly higher salary of a young attending physician and the high student loans associated with our training. The author briefly touches on many topics so as to give the reader a broad overview of loans, investing, asset protection, and qualified retirement plans — including the backdoor Roth IRA. One issue of major importance for young physicians involves higher education loans coupled with higher interest rates and the likelihood of declining

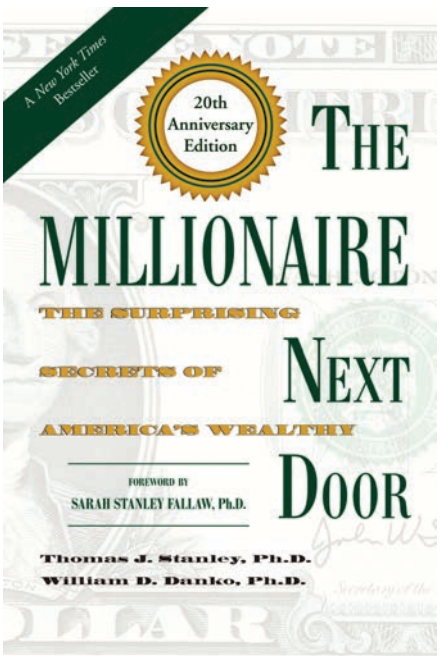


reimbursements. The author also has a helpful website (www.whitecoatinvestor.com), which offers additional information.



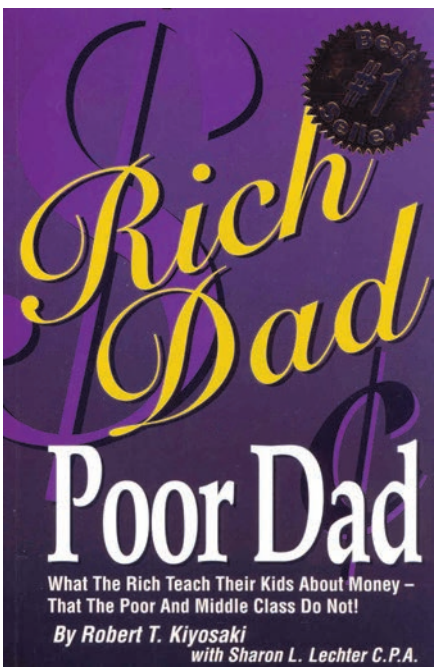
A Random Walk Down Wall Street: The Time-Tested Strategy for Successful Investing
Burton G. Malkiel; 2007

If you want to be serious about investing outside of retirement funds, this book is a "must read." The author touches on historical trends in the stock market, company stock valuation, and risk. He also provides an overview on how individual stocks are valuated based on two theories: Firm Foundation and Castle in the Air. The Firm Foundation theory values the stock of a company based on hard numbers, such as historical and current revenues and expenses (e.g., Coca Cola, Walmart). The Castle in the Air theory values the stock of a company based on the potential valuation of a company (e.g., Tesla). He further explains that there are patterns that indicate whether these stocks will improve or decline based on two competing analyses: fundamental versus technical. Fundamental analysis uses both Firm Foundation and Castle in the Air theories to help predict whether a stock is under- or overvalued. Technical analysis follows trends and patterns of a stock movement over a period of time to predict the future valuation. Although the author uses a fair amount of jargon, he admits to the unpredictability of the stock market (hence the title of the book) and the madness of crowds. He also includes interesting details about historical bubbles such as the "tulip-bulb craze" in the 1600s in Holland, the "south-sea" bubble in England in the 1700s, and the Florida real estate bubble in the 1920s.



The Millionaire Next Door: The Surprising Secrets of America's Wealthy
Thomas J. Stanley, PhD, and William D. Danko, PhD; 2010

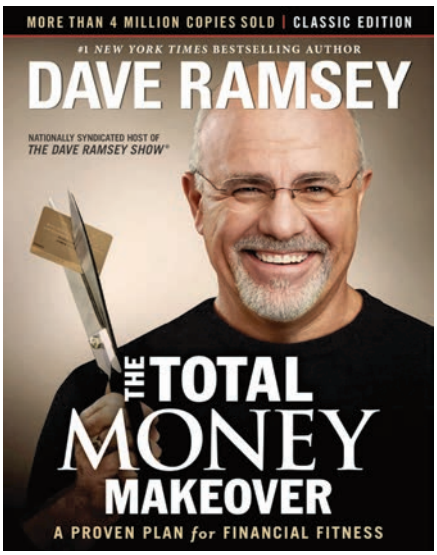
This New York Times bestseller has over 2 million copies sold. It summarizes 20 years of research and analysis of over 500 millionaires (via personal and focus group interviews) and 11,000 high–net worth individuals (via surveys). To the author's surprise, most millionaires live well below their means and allocate much of their time to building wealth. This is an important book for every physician, especially during the early attending years. Setting good spending habits early and not "keeping up with the Joneses" are pivotal lessons in this book. Additionally, there is an important chapter on the pitfalls of financially supporting adult children. As parents we desire our children to become financially independent and the author discusses how our "good intentions" can unfortunately subvert this goal.



Rich Dad Poor Dad: What the Rich Teach Their Kids About Money That the Poor and Middle Class Do Not!
Robert T. Kiyosaki with Sharon L. Lechter, CPA; 2011

Also a New York Times bestseller, this book focuses on real estate investing. The author stresses financial literacy and talks about getting out of the financial "rat race" by being creative and constantly

learning. This is an easy read for aspiring amateur entrepreneurs. The concept of a corporation (where taxes are paid only after all expenses are made) is fascinating since, as employed physicians, we are the exact opposite (our expenses are made with after-tax money). CME funds and flexible spending accounts are some instances where our expenses can be made with pre-tax money. The most important principle in this book is letting money work for you rather than you working for money. Kiyosaki implies that the reader needs to start a business outside of their "mundane" job, which offers just a paycheck. However, as physicians with higher earning potential, if we start early by saving and investing (with the power of compound interest), we can make money work for us just as easily without starting another business.



The Total Money Makeover: A Proven Plan for Financial Fitness
Dave Ramsey; 2013

The author runs a successful program called "Financial Peace University" in order to help people get out of debt. The book is basic, but speaks volumes to those middle-class Americans drowning in credit card debt, car loans, and student debt. Ramsey also includes helpful guidance about whether to invest or pay off their loans first. Somewhat counter-intuitively, Ramsey proposes paying off debt starting with the least amount first and the largest amount last. He asserts that the excitement of paying off the smaller amount first will encourage further commitment to save and eventually become debt free. This book is inspiring and practical when one is serious about being debt free.

Whether you are still in your fellowship training, early in your career, or established within the field, taking the time to learn about the various factors of financial success are critical to the security and future of you and your family. The above list of books, whether read separately or as a group, will help you make smart and informed decisions. ■

What Are the Best, Worst States for Physicians?

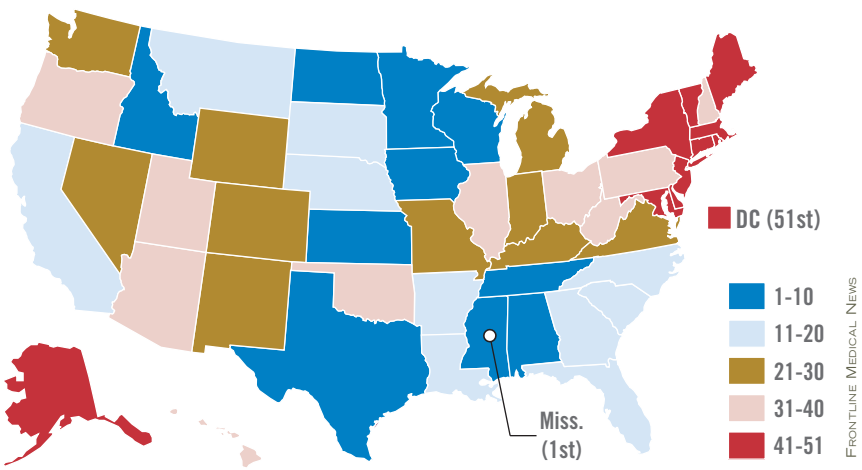
By Alicia Gallegos//Frontline Medical News

Should your future include a move to the South? A new report finds that Mississippi ranks as the best state to practice medicine, while the District of Columbia and New York are the least doctor-friendly areas in the United States.

The survey, conducted by personal finance website WalletHub, compares all 50 states and D.C. across 11 metrics, including physician starting salary, medical malpractice climate, provider competition, and annual wages – adjusted for cost of living. Data was derived from the U.S. Census Bureau, the Bureau of Labor Statistics, the U.S. Department of Health and Human Services, and the Missouri Economic Research & Information Center, among other sources.

View the entire WalletHub analysis here. ■

Ranked: Best and worst states for physicians, 2016



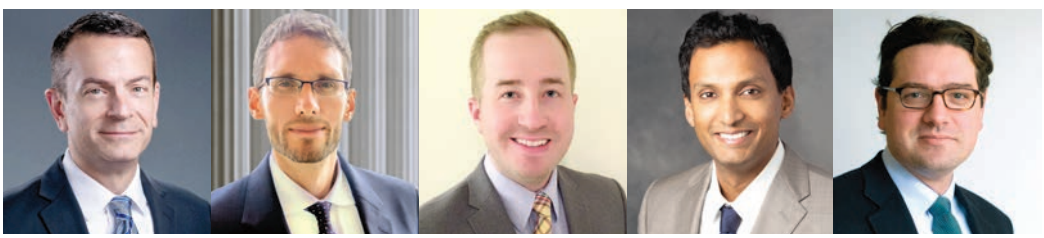
Note: State scores calculated using weighted averages for 11 relevant metrics, including physicians' mean annual wage and malpractice award payouts per capita.

Source: WalletHub

TRIFONENKO/THINKSTOCK

Tips from Digestive Health Innovators on the Different Paths to Success

By Kari Oakes // Frontline Medical News // From AGA Tech Summit



Dr. Stephen Drury, Dr. Christopher Thompson, Dr. Christopher Macomber, Dr. Sidhartha Sinha, Dr. Giovanni Traverso

Gastroenterologists are trained to be diagnosticians as well as proceduralists, who must use both their heads and their hands to solve problems. The specialty naturally lends itself to innovation, the focus of a daylong symposium sponsored by the AGA Center for GI Innovation and Technology.

Recently graduated gastroenterologists with an entrepreneurial streak can achieve their goals in private practice, as part of an academic department, or in industry with a bigger company or as part of a startup – and the choices aren't mutually exclusive. In presentations and subsequent interviews, innovators at the 1-day summit, held April 2 in Boston

and titled "How to Innovate in Digestive Health," shared experiences and lessons learned.

Among the organizers was Dr. Sidhartha Sinha, an instructor of medicine at Stanford (Calif.) University. "Innovation is really important for GI," said Dr. Sinha, himself a successful innovator. "Our field is broad and complex. ... The truth is we don't have optimal solutions for a lot of the core things that gastroenterologists focus on, such as inflammatory bowel disease, or functional disorders, or even cancer screening." He said, "It's important for people who are interested in innovation to get involved early. The path is long, it is hard, but it is very exciting, fun, and rewarding."

Early innovation brings perspective

Dr. Christopher Macomber is one such early innovator. Dr. Macomber, who holds both an MD and an MBA, has just finished his general surgery residency. He is also actively involved with two start-up companies, and first tapped his entrepreneurial side when he began an electronic medical records integration startup as a college undergraduate. That idea has reemerged as Mozaic Medical (http://mozaic-medical.com), currently a funded startup with software about to go live.

In medical school, he began a medical device start-up company. "It failed twice. But we're now into clinical trials," he said. This device is designed to use UV therapy to treat lupus erythematosus.

Dr. Macomber said he's found it challenging as a resident to maximize his training experience and still move entrepreneurial projects forward. As he wraps up training, though, he feels he's struck a balance: "I looked around at all the different job opportunities – academic, nonacademic." He has found a surgical group, he said, that is open to his continuing to pursue entrepreneurial work in parallel with his surgical practice.

One thing he thinks he'll bring to the table as a practicing surgeon and innovator is his global perspective. "A lot of things in our practice – robotics, endoscopy, laparoscopy – have shifted how surgery works, from big, invasive surgeries down to smaller ones. From a practice management standpoint, you really need to be on top of these things to see those issues coming."

Even smaller, less-disruptive innovations that streamline a process can be appealing to hospitals and practices. "Innovation extends beyond medical devices ... it can be process improvements, software, means of capturing data," he said. In fact, in terms of an innovative technology or process, "The more disruptive it is, the more challenging it can be to get to market," said Dr. Macomber.

Sometimes, finding unmet needs may be obvious, said Dr. Macomber. "You see them as you're going through your practice, because there are markers: high cost, low outcomes, inefficiency in a given process or procedure. ... You never really know where the innovation will be coming from, but it's up to the clinician to be watching for it, because you'll feel the effects before anybody else."

For innovators who want to build or maintain an active practice and to retain or refine their skills as clinicians and proceduralists, Dr. Macomber suggests finding a practice home that is receptive to the perspective a physician-innovator can bring. About his first postresidency position, Dr. Macomber said, "I'm really excited that I've found colleagues who support my drive to innovate."

Research can come first

An academic pathway that includes significant research training can also point the way to entrepreneurship in innovation. Dr. Giovanni Traverso was able to use his fellowship and postdoctoral period to explore interests in diverse fields; holding both an MD and a PhD, he was trained in molecular biology and genetics, so he explored options in those fields while in fellowship at Massachusetts General Hospital. In Boston, collaboration with MIT's Dr. Robert Langer, "a prolific innovator and inventor," taught him a lot about commercialization of technologies. "Spending time with Bob helped me learn how to push things forward," Dr. Traverso said. "Really, my interest in applied work was cemented by those early experiences. Mentors are extremely important."

Dr. Traverso has found that his dual clinician-researcher training carried through into later career interests. "There are a lot of people doing translational work, but for me, really getting things back to the patients was something I wanted to do."

Does one need to be a gastroenterologist to innovate in GI? Dr. Traverso said, "No, but it helps. Having a gastroenterologist as part of the team can help guide how we address some challenges."

An example can be found in addressing the "massive problem" of medication nonadherence: "50% of patients do not take drugs as they are prescribed," said Dr. Traverso. This problem is even bigger in the developing world, where only about 30% of patients are medication adherent. Increasing adherence may provide more positive impact than new drug development, in many cases, he said.

To address this, Dr. Traverso and his collaborators are developing a drug-eluting device that would be resident within the stomach for a period of time before disintegrating and then passing, eliminating the need for daily dosing of common medications. Perfecting a device that would not be subject to "the GI tract's incredible ability to achieve transit" required the expertise and advice of a gastroenterologist on the research team, said Dr. Traverso. The drug delivery device may have far-reaching implications: When mass drug delivery of the antiparasitic drug ivermectin is achieved in areas where malaria is endemic, the mosquito population drops markedly, "providing significant vector control," said Dr. Traverso.

"The message I would pass on is do not be shy in collaboration – in reaching out to folks," said Dr. Traverso.

The academic pathway has its merits

Dr. Christopher C. Thompson, professor of gastroenterology at Harvard Medical School, Boston, has been a successful entrepreneur while he's remained a faculty member. Dr. Thompson said that there's often a benefit to staying in academics, including access to collaborators, resources, and an infrastructure that can help with such matters as patent protection and legal filings. "You can take more risk if you're in academics," he said. "If you're at a leading academic center, you're more likely to be able to innovate with less concern about exposure and potential lawsuits than if you were in private practice trying to innovate." The career and economic security an academic appointment affords can make an innovator more comfortable with risk.

However, the decision to stay in academics can have a downside. Investors, said Dr. Thompson, can perceive the dual academic-innovator role as a lack of commitment to the success of the company, which can have a chilling effect on venture capital infusions. Also, others will need to be brought in to manage the company. "Often, this leads to early dilution," said Dr. Thompson. "And you have to hire people you really trust." Overall, it can be difficult to figure out where the boundaries lie between work with potential personal financial benefit, and patient care and research that's dedicated to the goals of the institution. Finally, time management may limit participation. "I think the best way to do this is to find a great team, and to stay as involved as possible," he said.

What's industry looking for?

Dr. Steven Drury left his career as a clinical pathologist to work for Covidien, now part of Medtronic, as its global medical director. Though he said goodbye to his practice reluctantly, he's seen rich benefits in being part of a bigger-picture look at how medical devices can benefit patients.

Dr. Drury spoke both about his own experiences, and about what a large company such as Medtronic is seeking when it assesses technology offered by a startup. Using the recent example of Covidien's acquisition of Beacon Endoscopic, Dr. Drury walked attendees through what Covidien liked about the product and company.

Some things were unique about Beacon, said Dr. Drury. "There was robust R&D early, leading to a platform of change. There was a solid pipeline of intellectual property." By selling early, with a full pipeline of intellectual property to come, Beacon could essentially take a shortcut, without having to capitalize development.

The benefits to Medtronic were also plentiful. The technology represented an immediate revenue stream in the GI space, expanding the company's global footprint. Also, Beacon represented a scalable business with little market development required. As a practical matter, this adaptation of an existing technique meant that there were no new codes or procedures, minimizing regulatory and institutional administrative hurdles.

Finally, the promise of Beacon's innovation pipeline is becoming a reality. After the 2015 release of the trademarked SharkCore™ technology, two more confidential devices are in the pipeline for 2017 and 2018 releases. These will move the core technology from the diagnostic to the therapeutic arena.

"Ultimately, it's about collaboration," said Dr. Drury. "Collaboration with industry can happen with or without acquisition," he said.

For attendees, the Beacon case study illustrated one of multiple pathways to successful commercialization of a good idea. Medtronic, said Dr. Drury, might be seeking various strengths from a product or idea, depending on the stage at which the investment's made. An early-stage start-up might be viewed more as a strategic investment, while a later-stage startup might be a wholesale acquisition.

The bottom line? It's about the patients, said Dr. Sinha. When innovators are judged, he said, "It won't be done by the amount of dollars raised, or patents filed, but by the number of patients that we actually impact and the lives we improve." ■

The bottom line? It's about the patients. When innovators are judged, "It won't be done by the amount of dollars raised, or patents filed, but by the number of patients that we actually impact and the lives we improve."

Reimbursement Basics in Gastroenterology

By Dawn L. Francis, MD, MHS

Dr. Francis is chair of clinical practice for the department of medicine, Mayo Clinic, Jacksonville, FL.

Payment for GI services is complex, but it is important to understand how it works as it is vital to your financial future, regardless of where you practice. Understanding reimbursement will allow you to select the most cost efficient setting for procedures, maximize your reimbursement, and avoid recoupments.

The overall reimbursement for the work you do is based on coding, coverage, and place of service (i.e., setting).

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Coding

Current Procedural Terminology (CPT) codes and Healthcare Common Procedure Coding System (HCPCS) codes are what physicians use to denote the services they provide to payors.

CPT codes are developed and maintained by the American Medical Association's (AMA) CPT Editorial Panel and describe medical procedures and services provided by physicians and other health care professionals.[1] Once new CPT codes are created, they are valued by the AMA/Specialty Society Relative Value Scale Update Committee (RUC). The RUC is a panel of experts including physicians from primary care and certain procedural specialties. They use a complex process that involves the specialty societies' recommendations about the value of work for CPT codes. The panel then provides value recommendations to the Centers for Medicare & Medicaid Services (CMS), more commonly known as Medicare.[2] Medicare is free to follow or not follow the RUC's recommendations for CPT codes. The RUC also periodically revalues existing codes; for example, the upper and lower GI procedural codes were revalued by the RUC from 2012 to 2014.[3] Medicare's final valuation for CPT codes is published each fall in the Medicare Physician Fee Schedule (MPFS).[4] Many commercial payors' fee schedules are based on the MPFS.

HCPCS codes are developed and valued by Medicare for products, supplies, and services not included in CPT.[5] Medicare can use HCPCS codes to meet specific programmatic needs. For example, Medicare created HCPCS codes G0105 (*Colon cancer screening; high risk*) and G0121 (*Colon cancer screening; not high risk*) for reporting outpatient colonoscopies for colorectal cancer screening on Medicare patients to allow administration of the colorectal cancer screening benefit.[6]

Coverage

Medicare pays for services that are "reasonable and necessary" for a variety of purposes. The agency covers certain services and procedures either nationally, under a national coverage determination (NCD) or locally, through the local coverage determination (LCD) process that describes coverage criteria.[7] Although private payors have their own coverage processes, they often look to Medicare when they create their own coverage decisions. If you provide a service or procedure that is not covered, your claim will be denied.

Medicare also covers certain preventive screening procedures, such as colonoscopy, under certain circumstances.[8] Failing to adhere to the rules will result in a denied claim. For example, Medicare covers screening colonoscopy every 10 years for beneficiaries who are asymptomatic and at average risk of developing colorectal cancer. Beneficiaries who are asymptomatic and receive another screening colonoscopy prior to the 10-year period in the absence of findings during the previous colonoscopy would result

"When a colonoscopy is performed on a Medicare patient, do you know how payment for the procedure is determined?"

"Is reimbursement different if the colonoscopy is performed in an ambulatory surgical center (ASC) versus the hospital?"

"When you perform a colonoscopy on a Medicare beneficiary, do you get paid the same amount if you remove a polyp with a snare vs. a biopsy forceps vs. using both?"

"Does Medicare reimburse differently based on what region of the country the procedure is performed?"

Courtesy Dawn L. Francis

in a denied claim.

Place of service and payment

Where a service or procedure is performed determines the payment for the physician and the facility. Each site has its own Place of Service (POS) code. The most common sites for gastroenterologists are the physician office (POS 11), the ASC (POS 24), and the hospital outpatient department (HOPD) (POS 19 – off hospital campus; POS 22 – on campus).

What is considered a physician office is not always clear. Medicare defines the office as a "location, other than a hospital, skilled nursing facility, military treatment facility, community health center, State or local public health clinic, or intermediate care facility, where the health professional routinely provides health examinations, diagnosis, and treatment of illness or injury on an ambulatory basis."[9] The office (POS 11) should be reported when services are performed in a "separately maintained physician office space in the hospital or on the hospital campus and that physician office space is not considered a provider-based department of the hospital."[10]

		Medicare [illegible]				
Diagnostic Endoscopy		Ambulatory Surgery Center	Outpatient Hospital		Physician Services	
CPT Code	Short Procedure Description	Facility Payment (National Medicare Average)	APC	Facility Payment (National Medicare Average)	Payment when Procedure is Performed in the Hospital or ASC (National Medicare Average)	Payment when Procedure is Performed in Office (National Medicare Average)
[illegible]	EGD	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	EGD biopsy	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	EGD ligation	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	EDG dilate strictr	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	ERCP	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	ERCP biopsy	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	ERCP duct stent placement	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	ERCP stent exchange w dilate	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	Colonoscopy thru stoma	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	Colonoscopy thru stoma biopsy	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	Flexible sigmoidoscopy	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	Flexible sigmoidoscopy biopsy	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	Colonoscopy	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	Colonoscopy biopsy	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	Colonoscopy lesion removal	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

Courtesy Dawn L. Francis

Figure 1. Payment for various endoscopic procedures based on CPT code, where procedure is performed and facility payment based on APC grouping.[11-13]

Physician office – The physician payment when procedures are performed in the office is higher than the ASC and HOPD because, in addition to physician work, it also includes the expenses related to maintaining a practice (practice expense) and liability insurance (malpractice) costs so there is no extra "facility" fee. The values for work, practice expense, and malpractice are adjusted to reflect the price variations around the country, and then the total is multiplied by the conversion factor ($35.80 in 2016) to arrive at the payment amount.[14] Your payment may be slightly more or less than those listed in the table above due to the geographic adjustments. For example, the 2016 Medicare National payment for colonoscopy in the office is $385.61; however, due to geographic adjustments, gastroenterologists in Nebraska receive $351.82 and physicians in Miami, FL receive $419.41.[11]

ASC – When a procedure is performed in the ASC, the physician payment includes only the physician work component and malpractice. A separate payment to the facility captures its costs. Each procedure covered in an ASC, including GI endoscopy procedures, is classified into an ambulatory payment classification (APC) group on the basis of clinical and cost similarity that includes most ancillary items and services with the primary service. Payments for procedures are established using a set of relative weights, a conversion factor, and adjustments for geographic differences in input prices.[15] All of the procedures in a particular APC group have the same facility payment (see Figure 1). This payment includes equipment. For example, if a patient has a colonoscopy with polypectomy, the facility payment is the same whether the polyp is removed with one snare and one biopsy forceps, or one snare; the latter situation will be a more favorable reimbursement and the former may lead to money loss.

Hospital outpatient – Similar to an ASC, when a procedure is performed in the HOPD the physician payment includes only the physician work component and malpractice. A separate payment to the facility captures its costs. Also like an ASC, HOPD payments are set for individual services using a set of relative weights, a conversion factor, and adjustments for geographic differences in input prices. Hospitals also can receive additional payments in the form of outlier adjustments for extraordinarily high-cost services and pass-through payments for some new technologies. The payment rate for each service is determined by multiplying the relative weight for the service's APC by a conversion factor. The relative weight measures the resource requirements of the service and is based on the geometric mean cost of services in that APC.[16]

Conclusion

Payment for services in gastroenterology, and all of medicine, is complex. Gastroenterologists need to be aware of payment implications regarding indications for the procedure, coding the procedure itself, and where the procedure is performed. Ultimately, payment policy favors doing the right thing for patients (such as not over-screening them for colon cancer) and using tools and resources efficiently. The new gastroenterologist would be well served to learn about payment for procedures and services as they make decisions about where and how they will practice. ■

Examples:

1. Colonoscopy in an ASC on an asymptomatic Medicare patient not at high risk for colon cancer. Two small (<10 mm) rectal hyperplastic polyps were removed on screening colonoscopy 5 years earlier. No polyps were found during the current examination.

Coding →	Coverage →	Place of service =	Medicare reimbursement
G0121 (Colorectal cancer screening; colonoscopy on individual not meeting criteria for high risk)	None - Medicare covers screening only once every 10 years for patients not at high risk for colon cancer[1]	ASC	$0

[1]https://www.medicare.gov/coverage/colorectal-cancer-screenings.html

2. EGD with biopsy in the ASC on a Medicare patient with abdominal pain and persistent dyspepsia.

Coding →	Coverage →	Place of service =	Medicare reimbursement
43239 (*Esophagogastroduodenoscopy, flexible, transoral, with biopsy, single or multiple*)	Yes - no LCDs, NCDs, or screening qualifications apply	ASC	Physician = ~$151.45 ASC = ~$416.80

3. Flexible sigmoidoscopy in the HOPD on a Medicare patient with diarrhea without evidence of bleeding.

Coding →	Coverage →	Place of service =	Medicare reimbursement
45330 (*Sigmoidoscopy, flexible, diagnostic, including collection of specimen(s) by brushing or washing, when performed [separate procedure]*)	Yes - no LCDs, NCDs, or screening qualifications apply	HOPD	Physician = ~$58.36 HOPD = ~$492.45

Courtesy Dawn L. Francis

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2. http://www.ama-assn.org/ama/pub/physician-resources/solutions-managing-your-practice/coding-billing-insurance/medicare/the-resource-based-relative-value-scale/the-rvs-update-committee.page
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7. https://www.cms.gov/Medicare/Coverage/DeterminationProcess/
8. https://www.cms.gov/Medicare/Prevention/PrevntionGenInfo/Downloads/MPS-QuickReferenceChart-1TextOnly.pdf
9. https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/PhysicianFeeSched/Downloads/Website-POS-database.pdf
10. https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/downloads/clm104c26.pdf
11. https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/PFSlookup/index.html
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13. https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/ASCPayment/index.html
14. http://www.medpac.gov/docs/default-source/payment-basics/physician-and-other-health-professional-payment-system-15.pdf?sfvrsn=0
15. http://www.medpac.gov/docs/default-source/payment-basics/ambulatory-surgical-center-services-payment-system-15.pdf?sfvrsn=0
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The Answer

From ***What's Your Diagnosis?*** on page 9

Liver biopsy demonstrated diffuse clearing of cytoplasm of the hepatocytes with strong periodic acid–Schiff positivity. There was no evidence of fibrosis, steatosis, inflammation, iron staining, or Mallory bodies. Combined with the clinical history of poorly controlled type 1 diabetes, these liver biopsy findings were consistent with glycogenic hepatopathy. Although the patient had alpha-1-antitrypsin deficiency, it was not believed to have contributed to his elevated liver enzymes because there were minimal scattered alpha-1-antitrypsin globules and no inflammation or fibrosis on biopsy. With better glycemic control, the patient's liver enzymes returned to normal levels. Unfortunately, the patient had a relapse because his diabetes again became uncontrolled.

Glycogenic hepatopathy is a disease process in which abnormal glycogen deposits in the liver, causing elevation of serum transaminases.[1] It is usually seen in patients with poorly controlled type 1 diabetes, with clinical signs and symptoms including abdominal pain, nausea, vomiting, and hepatomegaly. The key histologic findings of glycogenic hepatopathy are swollen and pale-staining hepatocytes on hematoxylin and eosin stains and extensive glycogen accumulation seen on periodic acid–Schiff stains. Other histologic features include prominent glycogenated nuclei, giant mitochondria, and scattered acidophilic bodies.[2] The marked accumulation of glycogen in hepatocytes is believed to cause hepatomegaly and leakage of transaminases.[3] Rapid enlargement of the liver results in stretching of the liver capsule and abdominal pain. ■

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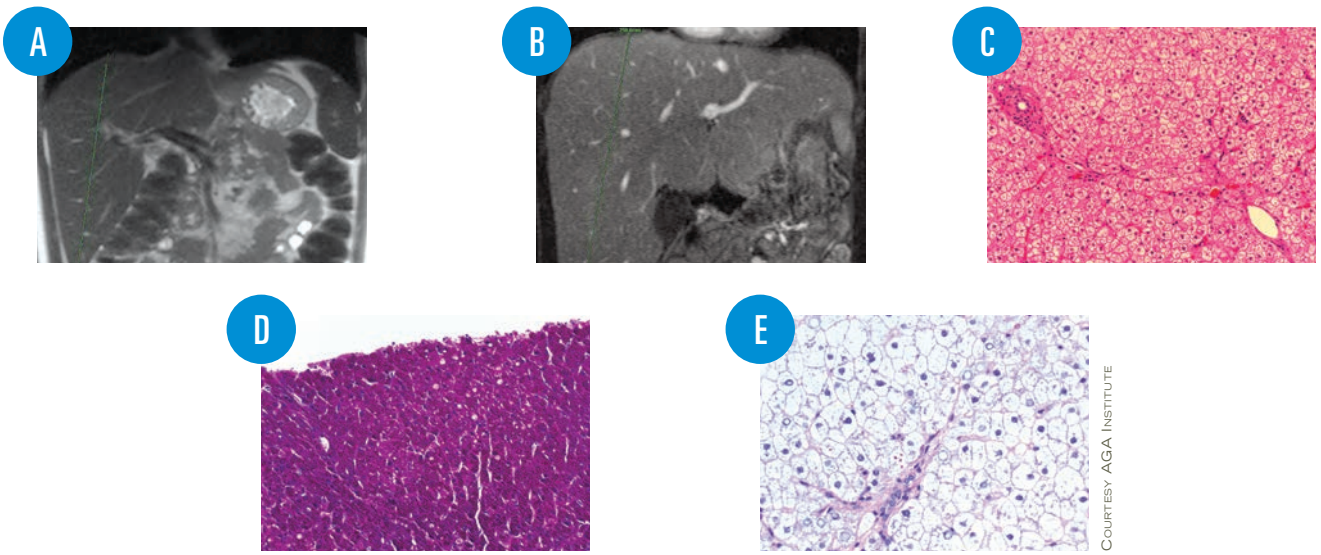

Courtesy AGA Institute

Gastroenterology's Gender Gap Has Narrowed Slightly – But More Work is Needed

By Amy Karon // Frontline Medical News // DDW

Dr. Zibing Woodward, Dr. Sunanda Kane, Dr. Jamile Wakim-Fleming, Dr. Kimberly Forde

Zibing Woodward, MD, is a female gastroenterologist – and in 2016, that still makes her unusual.

"In one fellowship program at which I interviewed, there were nine male faculty members and one female faculty member. She said that to succeed, you just have to become one of the boys," said Dr. Woodward, who recently completed her fellowship at Oregon Health & Science University and is now at the Oregon Clinic in Portland.

Only about 15% of U.S. gastroenterologists are women, according to the Association of American Medical Colleges. Ironically, that scarcity has fueled demand for female gastroenterologists, said Sunanda Kane, MD, MSPH, of the Mayo Clinic in Rochester, Minn. "There are good data to show that patients perceive that a woman will be 'gentler' with colonoscopy, and some will either wait longer or pay more for a woman to do their procedure," she said. "This is especially true for female patients."

Dr. Woodward's experiences led her to analyze the gender breakdown of faculty at 3-year GI fellowship programs across the United States. The results were striking. Not only did men tend to outrank women, but only 18% of program directors and 7% of division chiefs were female. Furthermore, 83% of programs with male division chiefs had male program directors, compared with only about half of programs with female division chiefs.

"[Some] men gastroenterologists do lack awareness about the gender gap, and there is an inherent bias in which they think women do not want to climb the career ladder, or be division chief or department chair, because they would rather focus on family obligations," Dr. Woodward said after presenting her findings at Digestive Disease Week® 2016. "I don't think anybody should make those assumptions. Women should be asked equally as men."

But promoting deserving female academics is only one step in closing gastroenterology's gender gap, Dr. Woodward and others said. Early-career women also need to connect with mentors, network, and strengthen leadership skills so they can compete on equal terms with men. Gastroenterology programs also need to take a hard look at how they can better accommodate women who have or want children.

Seeking mentors

Early-career mentoring helps determine long-term success. "When you seek promotion at an academic center, you have to include letters of support from people at other institutions who have worked with you in some fashion – national committees, collaborators on a research project, and so on," said Sharlene D'Souza, MD, who coauthored the analysis with Dr. Woodward and is an assistant professor of medicine at Oregon Health Sciences University, as well as the director of endoscopy at the Portland Veterans Affairs Medical Center.

The importance of mentoring underscores the need for diverse faculties, Dr. Kane added. "A faculty that has women at all ranks – assistant, associate, and full professor – is essential to helping female trainees fulfill their dreams and expectations. Women trainees feel left out and inadequately mentored about how to succeed in gastroenterology if there are no women to talk to."

But female trainees may have more "built-in" mentoring opportunities in medical school than during their internal medicine residency or gastroenterology fellowship, Dr. D'Souza said. Therefore, they need to understand the importance of mentors early on and proactively seek them out, she added.

The American Gastroenterological Association now has programs that match female trainees to mentors who can help with career development, Dr. Kane noted. Such efforts may be starting to pay off – in 2014-2015, 34% of first-year gastroenterology fellows were women, up from 27% in 2005-2006, according to the American Board of Internal Medicine's workplace survey.

But more work is needed. Ideally, fellowship programs should have their own mentorship programs for trainees, said Amy Oxentenko, MD, who is also at Mayo Clinic and has a long track record in medical education. Fellowship programs also should consider allowing fellows to have some say about who is on their advisory committee, Dr. Oxentenko said. "If a trainee is able to see that there are female faculty members who have been well supported in their careers within a gastroenterology division or department, that is often a very good surrogate for how they will be supported as a trainee."

"If a trainee is able to see that there are female faculty members who have been well supported in their careers within a gastroenterology division or department, that is often a very good surrogate for how they will be supported as a trainee."

Networking and building confidence

In addition to mentoring, networking before and during fellowship is vital, and starting early is important, Dr. Woodward emphasized. "I began considering gastroenterology during my fourth year of medical school. Looking back, I would have made more of an effort to network early on, both with my peers and with individuals in higher positions."

But traditional gender roles and expectations may deter some women from networking or competing for training opportunities, according to Dr. D'Souza. "When women ask for something and they are told 'no,' they think they had a bad idea. But when men ask and are told 'no,' they say 'why not?' As women, we need to be more persistent and to promote ourselves."

Dr. Woodward agreed. "As women, we are apologizing all the time, saying, for example, 'I am sorry I took this procedure or opportunity from you.' My male colleagues don't do that, so I gave myself permission to stop."

Attending networking sessions at conferences can help medical students and early fellows build confidence as well as professional relationships, Dr. Woodward and others said. "Male program directors also need to encourage women to network," added Jamile Wakim-Fleming, MD, of the Cleveland Clinic. "Men need to attend women's professional meetings in order to hear their concerns. Unless men attend women's meetings, progress will be slow."

But in the meantime, female gastroenterologists in community practice and academia are "taking things into their own hands in terms of networking," Dr. Woodward said. A new Facebook group for women in gastroenterology has attracted about 400 members, she noted. "We discuss clinical dilemmas, the challenges of being in practice, and the challenges of being a woman in GI."

As women physicians advance professionally, they must increasingly assert their clinical judgment and preferences. This can be discomfiting because it runs against conventional stereotypes, Dr. D'Souza said. "At some point, you have to get over worrying about other people's perceptions. It gets better with time, but a lot of young female faculty and trainees struggle with it."

She described asking senior female physicians if the tendency to question oneself fades with time. "They say they still experience it, but they have learned techniques and strategies that help them not show it and deal with it internally. They also stress the importance of having a strong network of friends and colleagues they can turn to if they do have self-doubt."

Case study

At the University of Pennsylvania Perelman School of Medicine, focused recruitment efforts have attracted female gastroenterology trainees and faculty in numbers well above the national average, said assistant professor of medicine Kimberly Forde, MD, MHS, who chairs the

Women in GI Committee there. About half of incoming gastroenterology fellows and 35% of gastroenterology faculty are now women, she said.

Part of this success stems from promoting women faculty to leadership positions throughout the university, Dr. Forde said. Beyond that, a variety of programs and activities at Penn aim to open gastroenterology to women. Each year, an accomplished female gastroenterologist visits campus to describe her research, teaching responsibilities, and tips for career success at an annual professorship and dinner.

"Men need to attend women's professional meetings in order to hear their concerns. Unless men attend women's meetings, progress will be slow."

The grand rounds series also hosts speakers on women's health, unconscious bias, and other topics related to recruiting women and minorities, Dr. Forde said. Additionally, women faculty from other academic institutions participate in research seminars and network with medical students, fellows, and faculty.

To foster leadership skills, the committee and the gastroenterology division at Penn also have sponsored participants chosen for the Association of American Medical Colleges professional development seminars for early-career women faculty, as well as the AGA Women's Leadership Conference, Dr. Forde said. "We also cohost a professional development series that focuses on topics such as career development, grant writing, and presenting or discussing research at national conferences. Such activities target all junior faculty and support a positive institutional culture," she said.

In pursuit of work-life balance

Gastroenterology remains heavily procedure based, which can deter women who have children or want them, experts noted. "There is the potential for having to work after hours to perform emergency on-call procedures, which would be disruptive to family life," Dr. Kane said. "A lot of women go into hepatology for this reason."

There are other problems, too. Heavy lead suits, which must be worn during certain endoscopies, "pose a challenge for pregnant women," said Dr. Wakim-Fleming. "Women would have to plan their family around this."

Once again, mentors can help, said Dr. Forde. "Meeting people in the field who have developed strategies for succeeding in gastroenterology shows that there can be balance between work and home. However, it should also be noted that a balance may not always be achieved – sometimes one of these spheres will overshadow the other, and the timing of a career apex may not be traditional. Nevertheless, with good time management skills and a genuine love of the work being done, the challenges of work-life balance seem less pressing."

Gastroenterology programs would be well advised to do some self-reflection on these topics, Dr. Wakim-Fleming said. "Any program that is not totally focused on physicians' productivity and understands the responsibilities of women outside of work will permit maternity leave, space for breastfeeding, and day care on site," she said. "Program directors need to be understanding of family values, permit part-time schedules, and give adequate maternity leave."

Dr. Oxentenko agreed. "Women who choose to start a family during training need to be shown that they will be supported," she said. "Offering flexibility for maternity leave or absence if a woman delivers a child during training would certainly be a positive. We may see more female residents entering gastroenterology if they see that they do not have to choose between their career or family, that they can effectively have both." ■

AGA programs for women

AGA offers a number of programs designed to support women in gastroenterology, including:

- **Women's Leadership Conference (Feb. 3-4, 2017)**
This 1.5-day conference is sponsored by the AGA Institute Women's Committee and is targeted toward both early-career and experienced women gastroenterologists in North America. The program focuses on essential supervisory and leadership skills that will help women advance their career in all practice settings.

- **Annual Women in GI Luncheon (DDW® 2017)**
This annual gathering showcases AGA's activities and commitment to women. It provides the opportunity for the 150 women gastroenterologists in attendance to exchange information, network, and hear from prominent women who are in GI leaders in the field.

DDSEP® eight ANSWERS

Digestive Diseases Self-Education Program

// From page 3

Q1: Answer: B

The patient clinically has rumination syndrome or an adaptation to the belch reflex, with effortless regurgitation, with voluntary reswallowing of the regurgitated material. Recurrent small bowel obstruction is less likely as the pattern of regurgitation is with almost every meal, within minutes, and does not follow the typical pattern of a bowel obstruction. Idiopathic gastroparesis is less likely as the pattern of regurgitation is not consistent with gastroparesis; in addition, she is not diabetic. She has no psychiatric history and there are no findings suggestive of bulimia.

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Q2: Answer: D

Objective: Appraise the relative roles of different regulators of iron homeostasis in the context of chronic inflammation. Iron deficiency is a common finding in IBD. When iron stores are depleted, the two most common routes of replacement are oral and intravenous. The decision as to the route of replacement is based in part on severity and acuity of iron deficiency as well as symptoms.

The principal regulator of iron homeostasis is hepcidin. In states of iron deficiency, hepcidin decreases, allowing for more transport of absorbed iron from the enterocyte into systemic circulation; conversely, states of iron overload lead to increases in hepcidin, resulting in breakdown of the basolateral enterocyte membrane transporter ferroportin, thereby trapping iron in the enterocyte and decreasing systemic availability.

In the setting of chronic inflammation, hepcidin increases, limiting iron bioavailability when taken orally; further, when the chronic inflammation is in the gut, there is impaired absorption across the apical enterocyte membrane. These compounding effects significantly impair oral iron assimilation in the setting of active IBD. Therefore, the best route of administration, particularly when the iron deficiency is severe and the patient is symptomatic, is intravenous.

There are some data suggesting that oral iron is capable of meeting iron needs in less severe cases of iron deficiency, but it more often leads to drug discontinuation due to side effects.

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