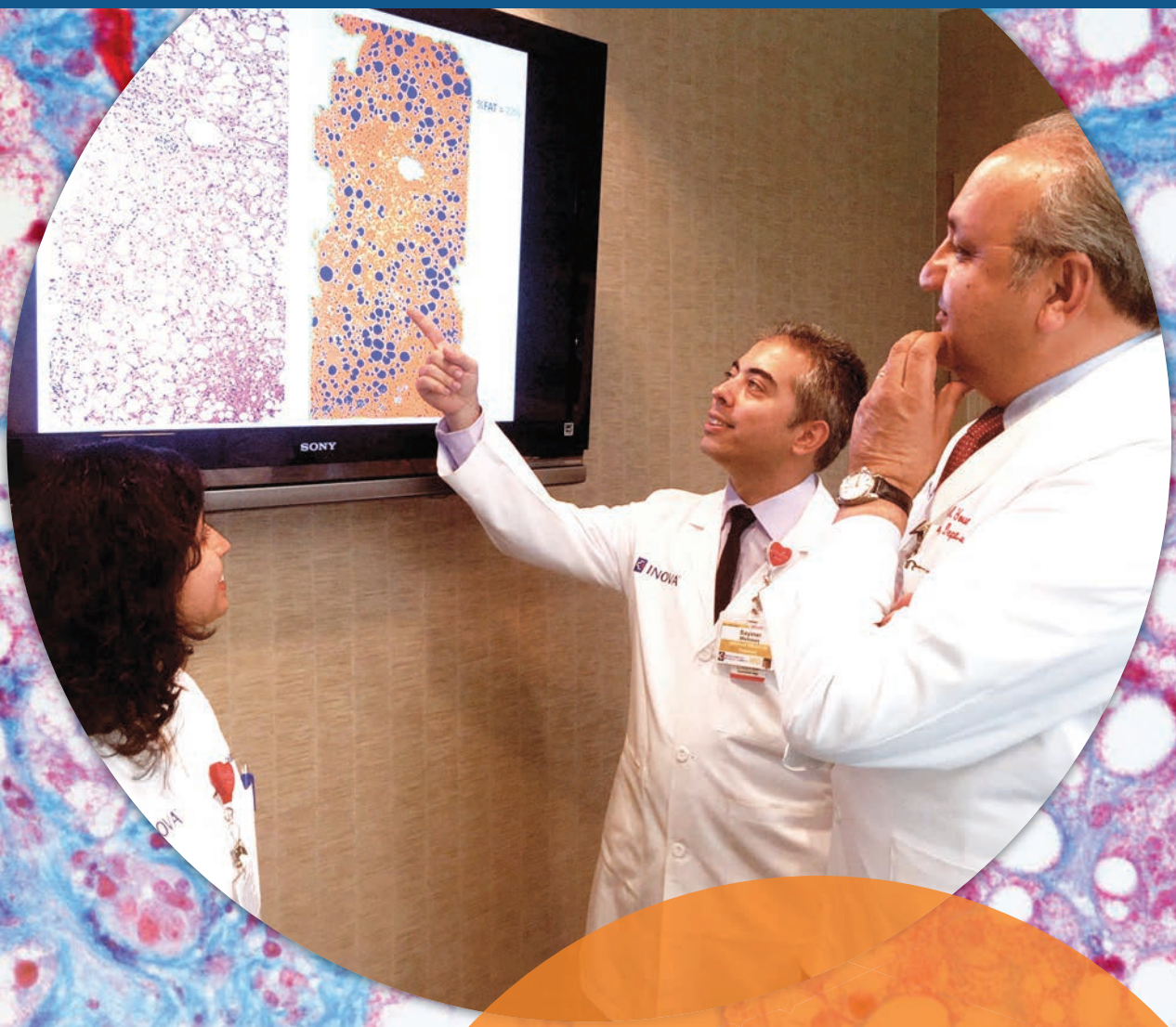
The NEW GASTROENTEROLOGIST

INSIGHTS FOR FELLOWS & YOUNG GIs A Quarterly Supplement to GI & Hepatology News | Summer 2016



Nonalcoholic Fatty Liver Disease

An Increasingly Recognized Chronic Liver Disease 16

Letter
FROM THE EDITOR

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

Dear Colleagues,

With the rising rates of obesity and metabolic syndrome in the United States, nonalcoholic fatty liver disease (NAFLD) has become an increasingly prevalent condition in our society, which makes knowledge in this area critical for all gastroenterologists. In this issue of *The New Gastroenterologist*, Mehmet Sayiner, Pegah Golabi, and Zobair M. Younossi from the Inova Health System in Virginia provide a terrific overview of NAFLD that looks at the current state of this condition and provides a glimpse into future diagnostic modalities and therapies.

Also in this issue is an eye-opening account of a medical trip to Haiti by Ranjeeta Bahirwani (Baylor University) as well as two perspectives on the AGA's recent involvement in the American Gut Project by Michael A. Schumacher (Children's Hospital, Los Angeles) and Faris El-Khider (Cleveland Clinic). In addition, there is an incredibly useful article about writing effective abstracts by the new Editor in Chief of *Gastroenterology*, Richard Peek (Vanderbilt University), which will surely come in handy given the fast-approaching abstract deadline for DDW® 2017.

There is coverage of two recent AGA events with pertinence to the young GI community: James Kimbaris (Temple University) provides an account of his experience at one of the recent Regional Practice Skills Workshops that was held in Philadelphia. Finally, as insurance is such an important topic for young career gastroenterologists and for our profession as a whole, this issue has an overview covering the essentials of obtaining and maintaining a disability insurance policy.

As we at the AGA strive to make *The New Gastroenterologist* an interesting and useful resource for all young career GIs, I truly appreciate the feedback and suggestions that many of you have provided over the last year. Please email me (bryson.katona@uphs.upenn.edu) or Ryan Farrell (rfarrell@gastro.org) if you have any suggestions or if you are interested in contributing to future issues of *The New Gastroenterologist*.

Sincerely,
Bryson W. Katona, M.D., Ph.D.
Editor in Chief

The NEW GASTROENTEROLOGIST

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

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ON THE COVER
(From left) Dr. Pegah Golabi, Dr. Mehmet Sayiner, Dr. Zobair M. Younossi

Photo provided by Ms. Deena Hellaji

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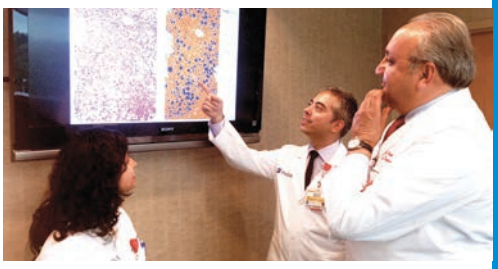

DDSEP® eight
Digestive Diseases Self-Education Program

QUESTIONS // Answers on page 21

Q1: A 47-year-old man with a history of chronic diarrhea presents with black, tarry stools for 2 days. Laboratory evaluation shows: hemoglobin 8.9 g/dL (normal: 14-17), platelets 201 x 10^3/microL (normal: 150-350), blood urea nitrogen 40 mg/dL (normal: 8-20), creatinine 0.8 mg/dL (normal: 0.7-1.3), calcium 12.5 mg/dL (normal: 9-10.5). An upper endoscopy reveals LA grade C esophagitis and a 1-cm clean-based ulcer in the duodenal bulb. Gastric biopsies show no *H. pylori* on H&E stain. He denies any history of NSAID or aspirin use.

What would be the most appropriate next step in management?
A. Repeat upper endoscopy in 6 weeks
B. Transfuse 1 unit packed red blood cells
C. Obtain fasting serum gastrin level
D. Sucralfate slurry four times daily

Q2: A 56-year-old woman with a history of scleroderma presents for evaluation of recurrent episodes of bloating, excess flatulence, mild nausea, and watery diarrhea for the past 5 months without associated weight loss, gastrointestinal bleeding, or fevers. She had a normal screening colonoscopy 2 years ago, and an upper endoscopy for evaluation of reflux and dyspepsia 5 years ago, which was only notable for a small sliding hiatal hernia. Laboratory testing reveals hemoglobin of 10.9 g/dL with an MCV of 106 fL. Stool studies are negative for occult blood, fecal calprotectin is not elevated, but a Sudan stain is positive.

Which of the following is the best next step?
A. *Helicobacter pylori* stool antigen testing
B. Tissue transglutaminase antibody testing
C. Colonoscopy with random biopsies
D. Hydrogen breath testing
E. Magnetic resonance enterography

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

News from the AGA

Early-Career GIs: Make Your Voices Heard

Have you seen the conversations happening in our members-only networking forum, AGA Community?

Since launching this spring, the forum has included numerous topics spanning the GI landscape. Some of the 100+ discussion threads focus on such areas as career transitions, de-identified patient cases, reimbursement, Digestive Disease Week,® and women in GI. Members can use AGA Community to network and gather information by responding to discussion threads or creating their own.

One recent post (http://community.gastro.org/FellowsAdvice/) solicited advice and tips from early-career GIs for incoming fellows. The post asks, "If you could go back, what are some things you wish you knew when first starting a fellowship?"

To jump in and share your advice for new fellows, or to start your own discussion thread, visit AGA Community at http://community.gastro.org/home.

Attention Trainee, Student, and Medical Resident Members: It's Time to Renew

If you are a current AGA medical resident, student, or trainee member, please renew today to ensure the continuation of your career-enhancing benefits for the upcoming membership year — July 2016 through June 2017. The deadline for renewal is Aug. 31, 2016.

While renewing, please also be sure to update your member profile and communications preferences at http://www.gastro.org/my-aga to help us better serve you.

Additionally, if you are completing your GI fellowship this summer, you can enjoy a few months of free membership. A reduced rate invoice for 2017 full membership will be due by the end of this year.

If you have any questions, please contact AGA Member Relations & Constituency Programs at member@gastro.org or 301-941-2651.

Interesting Stats: MACRA's GI Impact

CMS released the long-awaited proposed rule implementing the Medicare Access and CHIP Reauthorization Act (MACRA) earlier this year. We had an opportunity this summer to comment on the rule and advocate for changes, before the final version is released later this year.

The most important thing you can do now is to become more familiar with the programs under MACRA and begin to prepare for the changes it will mean for your practice. Here are a few interesting stats on the potential impact for GIs:

- CMS will roll out the comprehensive Merit-based Incentive Payment System (MIPS) and incentivize the use of alternative payment models (APMs). Services provided beginning on Jan. 1, 2017, will directly impact reimbursement provided in 2019, the first year in which the MIPS program and APMs are effective.
- CMS expects that 1,849 gastroenterologists will be excluded from MIPS. These GIs will be excluded because they participate in alternative payment models or see fewer than 100 Medicare Part B–eligible patients and bill less than $10,000 to Medicare.
- CMS projects the majority of GIs (61.5%) who participate in MIPS will receive a bonus. Positive payment adjustments are projected to be about $34 million for GIs. Unfortunately, this increase would be partially offset by negative payment adjustments for 38.3% of GIs. Nearly 60% of colorectal surgeons are also expected to receive a positive adjustment.
- The larger the practice, the more financial upside. According to CMS data, the likelihood of receiving an upward performance adjustment increases as the practice size increases. Among practices with two to nine eligible MIPS clinicians, only 29.8% are expected to receive a positive adjustment. This number increases to 81.3% for practices with 100 or more. Solo practitioners will be hit hardest by MIPS, with 87% likely facing a negative adjustment totaling a loss of $300 million for solo practices across all specialties.

Read more about the latest MACRA updates and how they will affect GIs on www.gastro.org/MACRA.

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

Aug. 19–21, 2016
2016 James W. Freston Conference: Intestinal Metaplasia in the Esophagus and Stomach – Origins, Differences, Similarities and Significance
Chicago, IL

Sept. 15-16, 2016
AGA Advocacy Day 2016
This year's event will focus on NIH funding and MACRA implementation.
Washington, DC

Oct. 27-28, 2016
AGA Drug Development Conference: Clinical Endpoints in Upper GI Disorders
Join the AGA Center for Diagnostics and Therapeutics in bringing more effective GI therapeutics to the market.
Washington, DC

Nov. 1, 2016
ABIM® Gastroenterology Certification Exam

Nov. 2, 2016
ABIM® Transplant Hepatology Certification Exam

Dec. 1, 2016
Digestive Disease Week® (DDW) 2017 Abstract Submission Deadline
Abstract submission will open in late October 2016. Check http://www.ddw.org for more details.

May 6-9, 2017
DDW® 2017
Chicago, IL

Awards Application Deadlines

Research Scholar Award
Deadline: Aug. 26, 2016

AGA-Takeda Pharmaceuticals Research Scholar Award in Inflammatory Bowel Disease
Deadline: Aug. 26, 2016

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

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

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Disability Insurance for the Young Physician and the Importance of the Future Insurance Option

By Michael R. Mazzarella

Mr. Mazzarella is president of Physicians Consulting Group, LLC, Collegeville, Pa.
email: pcgmrm@gmail.com. physiciansconsultinggroup.com

Think of a pyramid when you think of the importance of disability insurance (Fig.1). In our firm's experience, most physicians have the same financial concerns: income protection, loan repayment, mortgage/rent, partnership buy-in, child's education, retirement, etc. All are considerable obligations and are dependent upon your ability to work. When looking at the pyramid, the foundation must be your ability to earn income. If you cannot, you must have disability insurance to replace what you have lost. It's difficult for a young physician to contemplate being faced with an injury or illness so severe that it changes the course of the career they worked so hard to establish, but that's exactly why disability insurance should be considered an important component of a comprehensive insurance and financial protection plan. As you transition from being a fellow to an attending physician, it is critical that your disability policy is structured to maximize your monthly benefit.

It's difficult for a young physician to contemplate being faced with an injury or illness so severe that it changes the course of the career they worked so hard to establish, but that's exactly why disability insurance should be considered an important component of a comprehensive insurance and financial protection plan.

Why should a physician purchase an individual disability insurance policy?

An individual will spend anywhere from 11 to 15 years in training to become a physician. If we assume you are age 32 when you become an attending and have a starting salary of $250,000, your income potential to age 65 is $8,250,000. Taking into consideration the time you have committed, your income potential, and the obligations you have assumed, it is imperative to purchase a comprehensive individual disability policy.

When should a physician purchase disability insurance?

You should purchase disability insurance as soon as financially possible. Disability insurance premiums are based on your age, benefit amount, and your specialty. If you purchase the policy using level rates, your monthly premium is locked in to age 65. Also, you want to take advantage of your good health so you have no difficulty qualifying for a policy.

Can fellows purchase individual insurance if their current employer provides group disability?

Yes. Most companies have special issue limits for fellows. No income documentation is required and your group disability benefit is not used in the calculation of how much individual disability insurance you can purchase.

What can you expect the premium to be?

Individual disability insurance policies typically cost 2% of your current income.

How long does the application process take?

The application process usually takes two to four weeks.

What are the steps in the application process?

This process typically includes completion of an application, a blood/urine test, and a personal history interview (e.g., medical questions, confirmation of occupation and residence, etc.).

Who owns the disability policy?

You do.

Will you be able to obtain coverage if you have a pre-existing condition?

Yes. Depending on the medical condition, most carriers will still offer you some type of coverage. For many medical conditions, a policy can be issued with an exclusion for the medical condition. An exclusion allows the carrier to provide coverage except for a disability that occurs from that pre-existing condition.

What will a typical recommended policy include for a gastroenterologist?

There are certain definitions and riders that a comprehensive disability policy should include:

The **Own Occupation** definition of disability means that solely due to injury or illness, you are not able to perform the material and substantial duties of your occupation. So, if you cannot perform the duties of a gastroenterologist, but decide to work in another occupation, the income from the new occupation will not reduce the monthly benefit that will be paid to you by your disability insurance policy. The Own Occupation definition should last for the policy's entire benefit period.

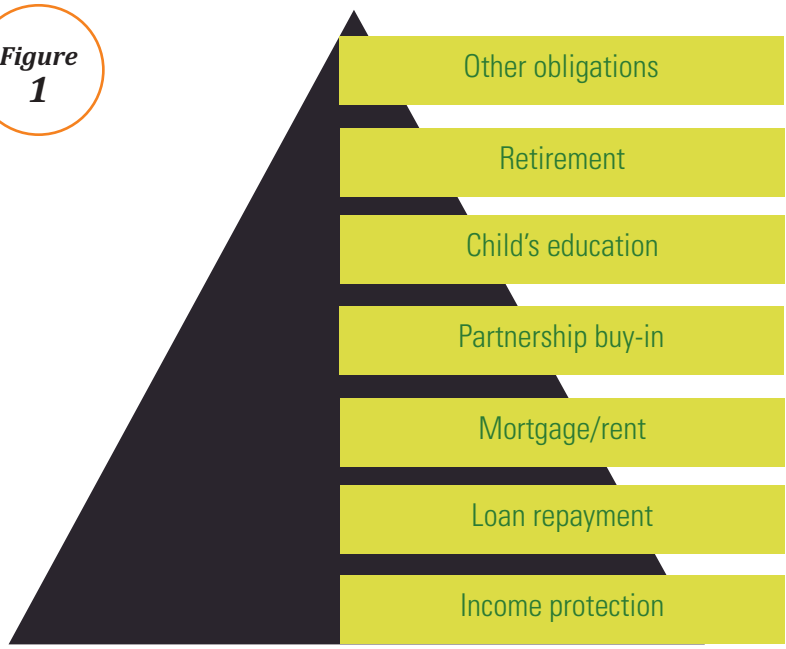
Future Increase Option (FIO) is critical for a young physician. It provides you with the ability to increase your disability coverage, regardless of your future health, as your income rises.

Additionally, your policy should have the **Automatic Increase Benefit**. This rider will also allow you to increase your benefit. However, it is not based on a rise in your income. The policy gives you the option to increase your policy at a 5% guaranteed rate during the first five policy years.

Cost of Living Adjustment is a rider that helps your benefit keep pace with inflation. After you have been disabled for 12 months, your monthly benefit will increase either on a compound or simple rate of interest, with no "cap" to age 65.

Residual Disability Benefit Rider: Under a residual disability provision an insured individual receives a percentage of their disability benefit based on the percentage of income loss the sickness or injury has caused. There are many disabilities that might allow you to continue working as a gastroenterologist on a limited basis, while suffering a loss of income. Adding the residual disability rider to your policy would allow you to continue receiving benefits proportionate to your loss of income.

Figure 1



Catastrophic Disability Rider (CAT): Catastrophic disability or catastrophically disabled means that, due to injury or sickness, you are: unable to perform two or more of the activities of daily living without human standby assistance; or cognitively impaired; or irrecoverably disabled. This benefit amount is in addition to your basic monthly benefit. The CAT rider is a relatively inexpensive rider to add and is an excellent way to substantially increase your monthly benefit should you become permanently disabled.

Of all the option riders recommended, the FIO rider is the most important for young physicians. It provides you with the ability to increase your disability coverage without evidence of insurability. This guarantees that any medical condition that develops after your original policy's purchase would be fully covered. From our experience, with assisting fellows for over 25 years, there are two critical times when the FIO rider is used. The first is when you have your signed contract to be an attending physician. Your income will increase substantially, so the FIO rider will enable you to increase your monthly benefit commensurately. The second is when you become a partner in your practice. If your policy was structured properly, when first purchased, your monthly benefit can reach a maximum of $17,000 if your income qualifies.

Once I have a disability policy, what do I need to do on a yearly basis to maintain my policy?

To maintain your disability insurance policy, your insurance broker should contact you on the policy anniversary to discuss with you your ability to raise your benefit if you financially qualify by either using a Future Insurability Rider or the Automatic Increase Benefit.

Disability insurance can be a complicated issue. The best decision a young physician can make is to employ the services of a professional insurance broker who specializes in assisting physicians with their disability insurance planning. The broker's expertise will enable him or her to structure an affordable disability policy for the fellow while also offering the flexibility to meet the changing needs of an attending physician. ■

What's Your Diagnosis?

An intriguing case of bright red blood per rectum

Published previously in Gastroenterology (2014;149:e1-2)

By Naseem Helo, M.D., Katherine Rhee, M.D., and Mohannad Dugum, M.D.

A 36-year-old man with a history of seizure disorder, mental retardation, and recurrent aspiration requiring percutaneous endoscopic gastrojejunostomy tube for feedings presented to the emergency room with bright red blood per rectum. He was also complaining of generalized abdominal pain. The patient was hemodynamically stable on presentation but the initial hemoglobin measurement was low at 6.5 g/dL and he was transfused 2 units of packed red blood cells. An abdominal radiograph showed moderate colonic gaseous distension with numerous cystic lucencies of various sizes throughout the colon (Figure A). Subsequently, CT of the abdomen showed numerous round pockets of gas within the walls of the ascending, transverse, and descending colon (Figure B). After this, a bedside sigmoidoscopy was performed revealing several small erythematous areas in the rectum without active bleeding and irregular mucosa with possible blebs in the descending colon (Figure C).

What is the diagnosis?

Dr. Helo is in the department of radiology, Loma Linda University Medical Center, Loma Linda, Calif.; Dr. Rhee is in the department of internal medicine, Medicine Institute, Cleveland Clinic, Cleveland; Dr. Dugum is in the division of gastroenterology, hepatology and nutrition, department of medicine, University of Pittsburgh. The authors disclose no conflicts.

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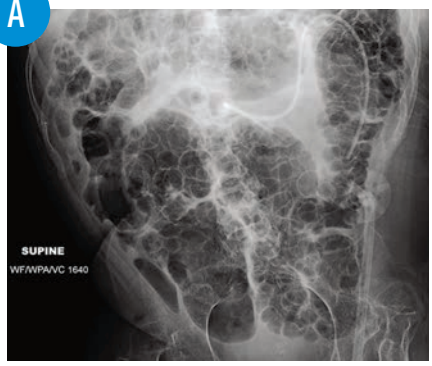

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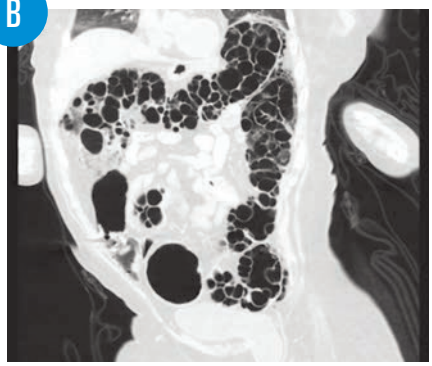

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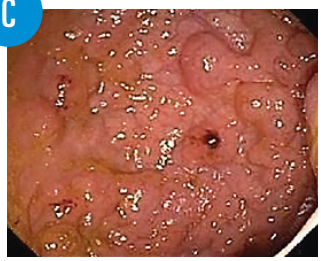

Courtesy AGA Institute

See ***The Answer*** on page 15

Hands Up for Haiti

By Ranjeeta Bahirwani, M.D.

Dr. Bahirwani is an assistant professor in the department of medicine at the Baylor University Medical Center, and also works at Texas A&M Health Science Center, College of Medicine, and Liver Consultants of Texas-Dallas.

As a transplant hepatologist, I am often astounded by the Herculean amount of time, effort, and resources spent keeping my patients alive. I am frequently overwhelmed by a sense of existential angst regarding the path I have chosen, but it is difficult to reconcile the quaternary care services I provide for my patients with most of the rest of the world, which struggles for access to basic health care. Unfortunately, access to medical care isn't a right, but a privilege, for the majority.

Perhaps this is why, when asked by a patient's husband, a church missionary, whether I would like to participate in a mission trip providing health care to a community of Haitians devastated by the massive 2010 earthquake, I didn't even blink before replying with a resounding yes! Of course, I had absolutely no idea what I was getting myself into at the time. I had been told that I would be part of a large crew headed to provide support to the locals. The idea seemed fabulous: one team of volunteers designated to teach Haitians how to farm; another – comprising women calling themselves "The Sewing Clan" – equipped with machines to teach women how to earn a living by stitching; and finally, a medical team to provide urgent, and limited, preventative care as required.

I was overwhelmed with anxiety at the prospect of practicing general internal medicine, which I had forgotten the day I passed my boards. I was reassured that I would be accompanied by other physicians and nurses with experience in relief efforts. As fate would have it, the other doctors committed to the trip backed out due to unavoidable circumstances and I was the sole physician heading the medical team. I was overcome with anxiety as I called MAP International (a global Christian health and relief organization) to order medications via their Global Essential Medicines and Supplies (GEMS) Medical Assistance Program. What medications would I need and how much? GEMS provides humanitarian aid organizations with low-cost, purchased and donated medication supplies from the World Health Organization Essential Drug List. Luckily, ordering was dummy-proof, as they offered "Mission Packs" including oral rehydration salts, a host of antibiotics, antipyretics, and vitamins. My joy was short-lived, however, as I noticed the five different kinds of ibuprofen and Tylenol available, including those for infants and children. Dear God, I would have to take care of children and infants? All I knew about medications for children was that aspirin can cause Reye's syndrome. My panic soon escalated as I realized how inept I was for this job. Is malaria endemic in Haiti? What about anti-helminthics? What is Cefaclor?

I had clearly underestimated the task ahead. Once we finally arrived to set up our clinic (a room in a local church), I was provided with two folding tables and three plastic chairs as furniture. My final crew comprised a cardiology nurse volunteer; the teenage daughter of a sewing team member; and a "pharmacy team" to dispense medications, led by the church pastor and his two assistants (husbands of the sewing crew). Maybe only a few will show up, I foolishly hoped, as flocks of eager locals came to greet their new visitors. I was introduced to our Creole translator, who knew just about everyone in the com-

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munity (God bless HIPAA), and we were put to task. I soon realized that each individual we met wanted to have an "issue," so they could be prescribed medication.

We dewormed everyone (treating one patient, I simultaneously pondered mebendazole's pregnancy category and wished desperately for Internet access; however, I did not even have a phone as electronic items were not permitted on the trip), handed out multivitamins and B-12/iron supplements, and addressed each individual's concern with our limited armamentarium of drugs. Every second person complained of GERD, a symptom I could thankfully handle, but of course we did not have enough omeprazole in stock. So those with mild GERD got five pills while those with more severe cases received 10. I was careful to prescribe Tylenol (instead of ibuprofen or aspirin) to my patients with back/knee pain and dyspepsia (and, of course, the few omeprazole pills I could spare). I gave children antibiotics and reassured concerned mothers (as well as myself) that their kids would feel better.

We had another issue that I soon realized was far from trivial: not only did I have to keep instructions simple with my makeshift pharmacists to ensure medications were prescribed correctly, I had to do the same with the patients! So mothers who had multiple children with upper respiratory infections were prescribed different doses of the same antibiotic to be given to each child based on size. I never imagined that I would need to ration infant Tylenol, but after day 1 and 200 patients, our limited medication supply was running out.

Over the next 2 days, we thought on our feet and made the best use of the drugs available. We sparingly prescribed antifungal ointment, antibiotics, vitamins, antihistamines, and antacids, yet no one left our clinic empty-handed or heavyhearted. Over 500 patients later, I wonder if I really helped any of the Haitians who walked into our clinic with eyes filled with hope and expectation and left with a handful of pills and a grateful smile. I certainly did not provide high-quality medical care; as I struggled with guilt over my limited capabilities, I was overwhelmed by the realization that no one expected anything more than a little attention and encouragement. When I look back on the experience of a lifetime, I have little doubt that every Haitian I met undoubtedly helped me. My existential angst was gone, well, at least temporarily. ■

I was overwhelmed by the realization that no one expected anything more than a little attention and encouragement. When I look back on the experience of a lifetime, I have little doubt that every Haitian I met undoubtedly helped me.

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Clearing the Fog for Your Career — Regional Practice Skills Workshop — Philadelphia

By James Kimbaris, M.D.

Dr. Kimbaris is a fellow in gastroenterology at Temple University Hospital, Philadelphia.

Photo courtesy Dr. James Kimbaris

(Left to right) Bryson Katona (Course Co-Director), James Kimbaris (2nd year fellow, Temple University), Laurel Fisher (Course Director), Gregory Berstein (2nd year fellow, Temple University).

The end of fellowship can be a scary yet exciting time for GI fellows. While some may stay in academia, others leave this umbrella for the first time to become a private practice physician or to pursue other career pathways. While program leadership can offer advice on certain career paths, the insular nature of any program can lead fellows to look for resources outside of their home institution. This year the AGA Institute, in conjunction with its Trainee and Young GI Committee, has taken the initiative to provide workshops meant to guide fellows through this process. Previous workshops have taken place in several locations, including Boston, New York City, Houston, and San Diego. As a current fellow training in Philadelphia, I was fortunate enough to attend our regional workshop, which was hosted by Dr. Laurel Fisher (director), Dr. Bryson Katona (co-director), and Dr. Tatyana Kushner (co-director) from the University of Pennsylvania. Attendees included several chiefs of gastroenterology, representatives of industry, a physician in private practice, and experts in health care innovation and compliance as well as 40 fellows from 10 different fellowship programs throughout the mid-Atlantic. Topics of interest included interviewing for, and evaluating, positions; deciding between a career in private practice, academia, or industry; and practicing in the context of evolving public policies such as the Affordable Care Act (ACA) and CMS cuts. In this article, I will review the highlights of several sessions to provide young physicians with some insight as they begin their careers.

A decision every fellow faces is staying in academia or entering private practice. Dr. Anthony Dimarino, chair of gastroenterology at Thomas Jefferson University, provided the address on "Life in Academics." He highlighted several important benefits of academic medicine including the ability to subspecialize within the field, perform research, and teach. He discussed the opportunity for close and frequent collaboration among specialties. While traditionally, a physician's lower salary in academics has deterred trainees, the pay gap between academics and private practice has decreased.[1] However, there are several challenges to having a successful career in academic medicine. The increasingly hostile grant-funding atmosphere has led to a push for increased clinical productivity. Another drawback addressed by the panel included the lack of autonomy that can exist in academia.

Dr. Oleh Haluszka, the former chief of gastroenterology at Temple University, offered advice on how to evaluate a job. He echoed Dr. Dimarino's thoughts regarding the pressure put upon academic clinicians for increased clinical productivity. He

further discussed the benefits of an academic career but also addressed the effect that the politics of academia can have on even the most talented of clinicians. In the end, he stressed the importance of fellows performing an honest self-assessment of themselves and of their goals prior to choosing a job.

While challenges in academia remain, the uncertainty of private practice in the current health care setting remains a point of trepidation amongst graduating fellows. Dr. Shivan Mehta, from the University of Pennsylvania, spoke on health care reform and provided an important reminder of the fluidity of a physician's business model. Current fellows have trained through ACA implementation as well as CMS cuts in colonoscopy reimbursement rates. There will be a decrease in the use of the fee-for-service model with an increased emphasis on quality metrics and pay for performance. While the decision to join a private practice and invest in an ambulatory endoscopy center may still be profitable, the business model and pay structure will almost certainly be different in 30 years when one would be leaving a practice.[2] These changes may have profound effects on smaller practices and continue to push for larger groups and hospital-owned practices.

The less traveled path of a career in industry was presented by Dr. Mark Sostek, executive director of global medicine development for AstraZeneca, who addressed the positives and negatives of a "Life in Industry." For gastroenterologists, options include working for device manufacturers, small biotech firms, and large pharmaceutical companies. Fellows considering a career in industry should carefully consider what type of position they might be interested in. For example, in pharmaceuticals, options for clinicians include involvement in drug development as well as medical affairs. A benefit of industry is an intellectually stimulating environment with a relatively predictable schedule, as compared to clinical medicine. However, most positions in industry typically require forgoing direct patient care while retaining knowledge and flexibility of different areas of therapy as business models will likely shift throughout their career. Fellows who may be interested in industry positions may choose to participate in industry-sponsored research to help lay the groundwork for a future career shift.

Understanding a contract is just as important as choosing a job. Throughout training, our contracts are boilerplate and rarely reviewed. It is especially important when entering private practice to understand the terms of the practice you are joining. David Schiller, J.D., LLM covered many important points including the compensation model, restrictive covenants, the path to partnership, and malpractice coverage including the importance of a tail (i.e., malpractice coverage for a period of time after the physician's employment has ended). Though most features are likely less negotiable in academics, terms of employment should still be understood and written clearly; this becomes especially important with inevitable changes in leadership.

Lastly, Dr. Asyia Ahmad, Chief of Gastroenterology at Drexel University, wrapped up the workshop with a thoughtful session on work-life balance. At the end of the day, most fellows need to balance their chosen career with a family. The challenge to achieve this balance starts early in training and does not become easier. Regardless of the decision to stay in academics, enter private practice, or go into industry, a work environment with supportive coworkers and partners is crucial to prevent burnout and have a long, successful career.

Regardless of the decision to stay in academics, enter private practice, or go into industry, a work environment with supportive coworkers and partners is crucial to prevent burnout and have a long, successful career.

In the end, fellows will have many options available once they graduate, and understanding personal priorities and goals will help them find the right job. Through the workshops created by the AGA Institute Trainee and Young GI Committee, fellows should feel more confident in their initial career decisions and any changes that come in the future. ■

References

1. Singh V, et al. Gastrointest Endosc. 2014;79:327-31.
2. Vicari J. Gastrointest Endosc. 2012;76:400-5.

The Answer

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

KAGANKIRIS/THINKSTOCK

The radiologic findings of numerous cystic lucencies within the walls of the colon and multiple round and smooth-surfaced elevated lesions on the sigmoidoscopy are classic for severe pneumatosis cystoids intestinalis (PCI).[1] PCI is a rare type of pneumotosis that was first described in the early 1700s and is described pathologically as gas within the submucosa or subserosa of the intestine.[2] The exact etiology of PCI is not understood fully. Several pathophysiologic mechanisms have been proposed including primary intestinal mucosal damage caused by surgical procedures or percutaneous placement of enteric feeding tubes. Other proposed causes include underlying malignancy, inflammatory bowel disease, long-term steroid treatment, graft-versus-host disease, infectious disease as well as radiotherapy and chemotherapy.[2,3] The exact cause of PCI in our patient is not entirely known, because multiple replacements of the gastrojejunostomy were shown consistently by fluoroscopic studies to be within the small bowel.

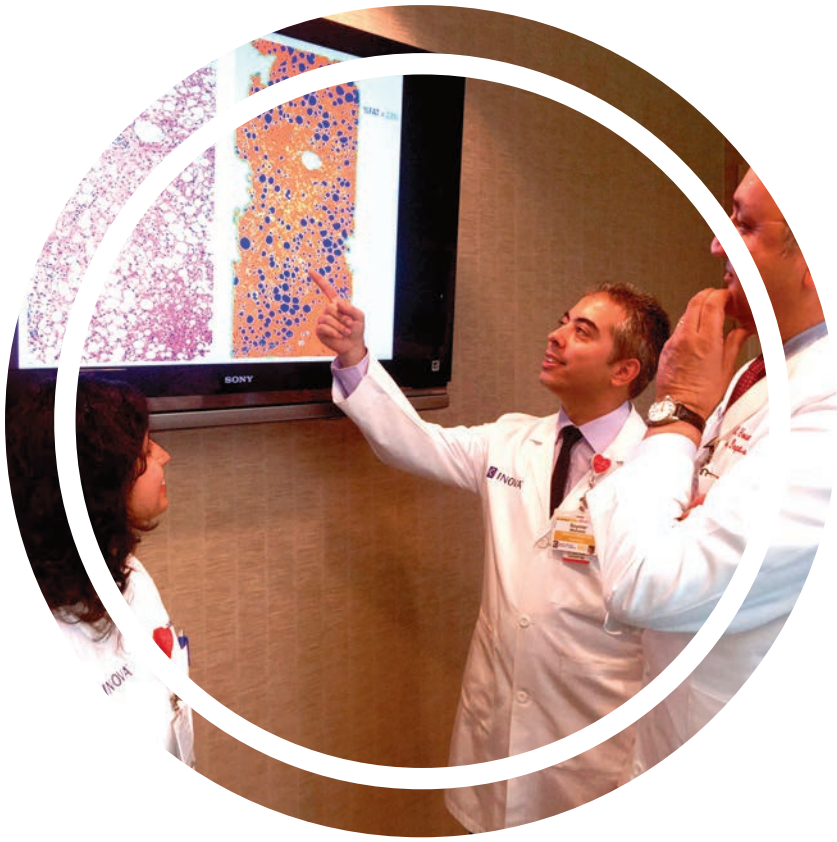
Patients with PCI can present with minor symptoms, such as abdominal pain, abdominal distention, nausea, vomiting, diarrhea, or bloody stool, but can also have more severe symptoms of intestinal obstruction and perforation.[2] The majority of PCI cases present as a radiologic finding without clinically substantial symptoms and are usually managed conservatively. Surgery should be reserved for cases of suspected bowel obstruction, perforation, or infarction.[2] Our patient was managed with packed red blood cells transfusions, and bowel rest without the use of antibiotics. The bleeding resolved over the next 2 days. A follow-up abdominal radiograph before hospital discharge showed minimal improvement of the pneumatosis. An abdominal radiograph done 8 weeks after this hospitalization showed near complete resolution of the PCI radiographic findings. ■

References

1. Ivanovic, A., et al. Gastrointestinal: the role of multidetector computer tomography in diagnosis of pneumatosis cystoides intestinalis. J Gastroenterol Hepatol. 2012;27:182.

2. Wu, L., et al. A systematic analysis of pneumatosis cystoids intestinalis. World J Gastroenterol. 2013;19:4973-8.

3. Zulke, C., et al. Acute pneumatosis cystoides intestinalis following allogeneic transplantation – the surgeon's dilemma. Bone Marrow Transplant. 2002;29:795–8.



Nonalcoholic Fatty Liver Disease: An Increasingly Recognized Chronic Liver Disease

By Mehmet Sayiner, M.D., Pegah Golabi, M.D., and Zobair M. Younossi, M.D., AGAF

Dr. Sayiner and Dr. Golabi are physician researchers at the Betty and Guy Beatty Center for Integrated Research, Inova Health System, Falls Church, Va.; and Dr. Younossi is also at the Betty and Guy Beatty Center for Integrated Research as well as the Center for Liver Disease, department of medicine, Inova Fairfax Hospital, Falls Church, Va. Dr. Younossi is the chairman of medicine at Inova Fairfax Hospital.

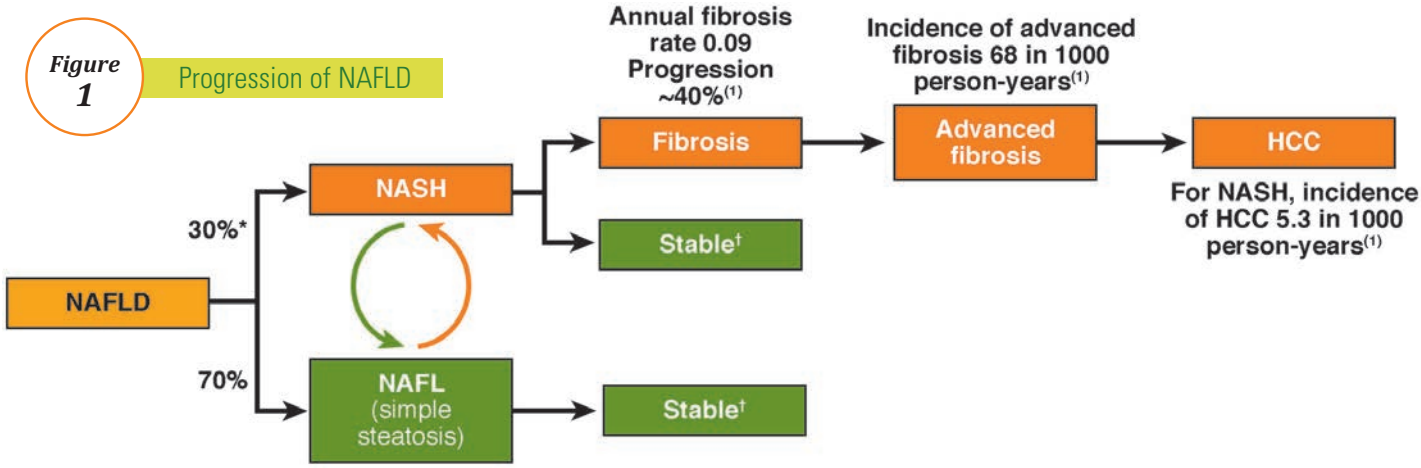


Figure 1 Progression of NAFLD

*NASH prevalence among NAFLD patients.
†Patients with NAFL and NASH are at risk for cardiovascular disease.
[1]Global Epidemiology of Non-Alcoholic Fatty Liver Disease-Meta-Analytic Assessment of Prevalence, Incidence and Outcomes. Younossi ZM *et al.* 2015.

Courtesy AGA

Nonalcoholic fatty liver disease (NAFLD) is considered to be the most common cause of chronic liver disease. NAFLD is defined by the presence of increased intrahepatic fat (more than 5% of total liver weight) detected by either histologic or radiologic assessment in the absence of secondary causes of fatty liver, such as excessive alcohol intake, certain medications, autoimmune or hereditary liver disease, and other causes of chronic liver disease.[1]

NAFLD covers a broad spectrum ranging from simple steatosis (nonalcoholic fatty liver or NAFL), which is usually nonprogressive, to nonalcoholic steatohepatitis (NASH). NASH is a complex liver disease modulated by numerous mechanistic pathways involving metabolic, genetic, environmental, and gut microbial factors. Patients with histologically proven NASH are at risk of progression to advanced fibrosis (stage 3 or 4), the stages of liver disease associated with the highest morbidity and mortality.[2] In fact, in patients with NAFLD, liver-related mortality is higher than the general population and cirrhotic NASH patients face the risk of developing liver failure or hepatocellular carcinoma (Figure 1).[3]

It is important to note that a number of patients with NAFLD have underlying impaired glucose tolerance, type 2 diabetes mellitus, hypertension, or dyslipidemia. In fact, NAFLD is considered the hepatic manifestation of metabolic syndrome.[4] Because of the increased prevalence of obesity and metabolic syndrome, NAFLD has reached epidemic proportions not only in the United States, but also in the rest of the world.[4] Although NAFLD is the most common cause of asymptomatic elevated transaminase levels, some NAFLD patients have normal liver enzyme levels.[4] This issue is important in establishing criteria to diagnose NAFLD in the general population.

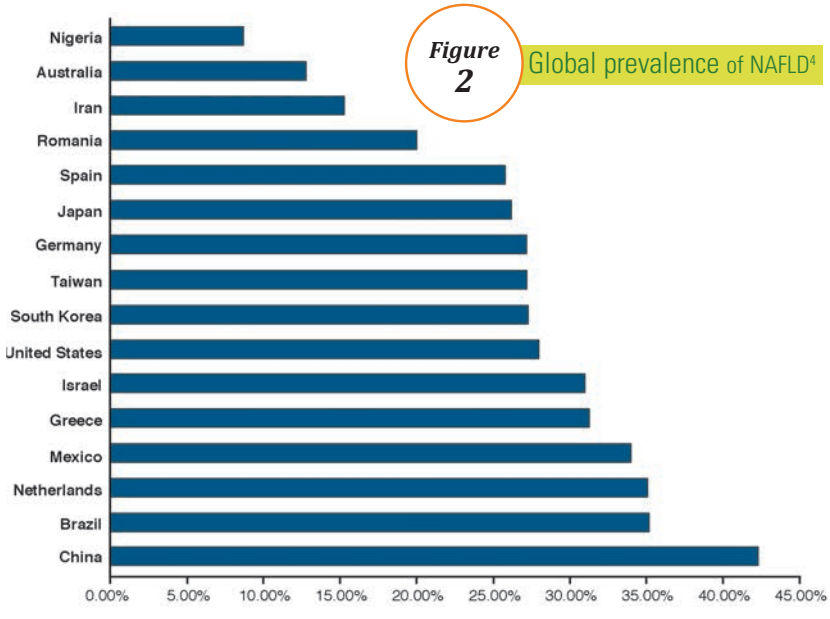


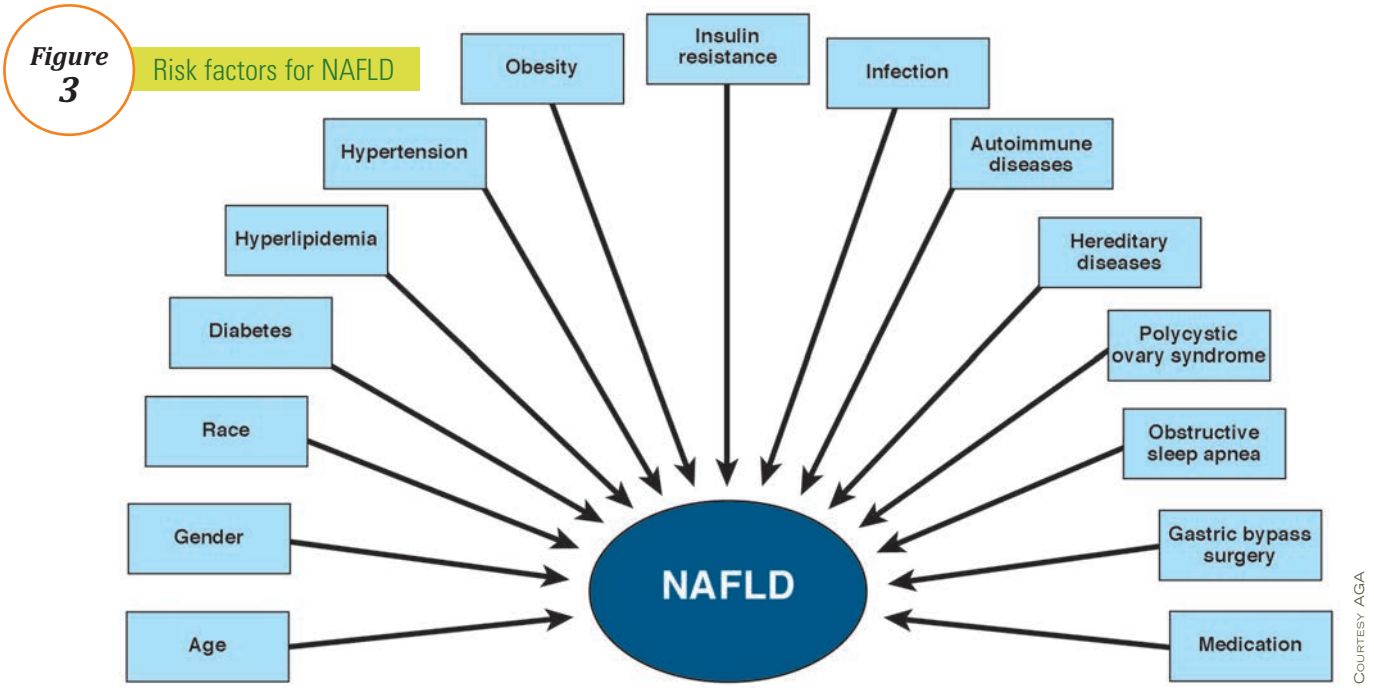
Figure 2 Global prevalence of NAFLD[4]

*Sayiner M et al. Epidemiology of Non-Alcoholic Fatty Liver Disease and Non-Alcoholic Steatohepatitis in the United States and the Rest of the World. Clin Liver Dis 2015. (doi:10.1016/j.cld.2015.10.001)

Courtesy AGA

Fundamentals

The true global incidence and prevalence of NAFLD and NASH, which is likely



to be underestimated, is not easy to establish because of the great differences among populations (Figure 2). A recent meta-analysis estimated that the global prevalence of NAFLD diagnosed by imaging is 25%. Also, among patients in North America with NAFLD diagnosis, NASH prevalence was 60.6% with a biopsy indication and 30% without a biopsy indication. These rates suggest that the overall prevalence of NASH in the general population may be between 1.5% and 6.5%.[1] It was also noted that the prevalence of NAFLD can be as high as 60% in patients with metabolic syndrome, 70% in diabetic patients, and exceeds 90% in morbidly obese patients.[5]

Age, sex, and ethnicity are nonmodifiable risk factors for NAFLD. In almost all populations, males have greater risk for NAFLD than females. Advancing age may affect the risk of NAFLD. In fact, NAFLD prevalence increases from younger to middle age while premenopausal women are relatively spared by NAFLD with increasing prevalence after the age of 50.[6] Ethnicity is another factor that could potentially affect the risk of NAFLD. Population studies in the United States revealed that the highest rates of NAFLD are seen in Hispanics, followed by whites, and then African Americans. Certain medications like glucocorticoids, amiodarone, tamoxifen, methotrexate, and isoniazid; some endocrinologic disorders like polycystic ovary syndrome and hypothyroidism; and certain surgical procedures like gastric bypass surgery are some other risk factors for NAFLD development (Figure 3).[7]

It is well known that insulin resistance plays a central role in the pathophysiology of both NAFLD and metabolic syndrome. In fact, the two-hit theory for the pathogenesis of NAFLD describes the intrahepatic lipid accumulation representing the first hit, followed by other "hits" from oxidative stress, endotoxins, cytokines, adipokines, and other pathways that could lead to NASH and its progression.[4] In patients with insulin resistance, hyperinsulinemia not only causes increased hepatic lipogenesis but also promotes lipolysis in adipose tissue, eventually causing an increased flux of free fatty acids from adipose tissue into hepatocytes. As hepatocytes accumulate lipid droplets, the liver becomes more susceptible to injury and subsequent progression to NASH. As stated above, NAFLD is associated with metabolic conditions such as type 2 diabetes mellitus, dyslipidemia, hypertension, polycystic ovary syndrome, and obstructive sleep apnea as well as some other metabolic conditions.[7] In fact, the presence of type 2 diabetes mellitus with NAFLD is associated with more progressive liver disease and a higher risk for mortality.[8] For example, the prevalence of NAFLD in type 2 diabetic patients ranges widely from 45% to 74% and presence of NAFLD worsens glycemic control in these patients. NASH and advanced fibrosis are often observed in diabetic patients who are asymptomatic and have normal liver enzymes.[7] There is a two- to fourfold higher risk of developing liver related complications in patients with diabetes and NASH, as well as increased mortality risk from cirrhosis.[6] Although the association is not as strong as it is with diabetes, hypertension may also be a risk factor for the development of hepatic fibrosis

among NAFLD patients. Furthermore, hypertriglyceridemia is an independent predictor of NAFLD. Studies have shown the association between NASH and increased non-HDL cholesterol levels, emphasizing that, most hyperlipidemic patients are likely to develop NASH.[6] Presence of one or more of these metabolic conditions increases not only liver-related morbidity and mortality from NASH, but also the risk of cardiovascular disease, which is the most common cause of death in patients with NAFLD.[8]

Recent innovations

One of the most recent innovations in NAFLD may be related to the development of noninvasive diagnostic modalities. Today, NAFLD and NASH are recognized globally and NASH has become the second most common indication for liver transplantation in the United States.[1] Ultrasound, computed tomography, and magnetic resonance imaging are good modalities to establish presence of fatty liver but are unable to distinguish NASH or stage of fibrosis.[9] Although ultrasound-based transient elastography has been used to assess hepatic stiffness in NAFLD, it is not fully validated as a screening tool for NASH in the U.S. population.[2] Magnetic resonance elastography offers the most accurate evaluation of hepatic parenchyma, but cost, duration, and availability limit its utility in clinical practice.[2] Beside these radiological modalities, biomarker panels are also used to assess fibrosis in patients with NAFLD. AST/platelet ratio (APRI) is a useful tool and can be calculated at the same time of patient visit. The specificity of an APRI score above 1 is 92.8% and can be used to exclude significant fibrosis.[2] The FIB-4 index combines age, platelet count, AST and ALT levels. Like APRI, the FIB-4 index is easy to use, calculations are simple, and the results are available immediately. The FIB-4 index has an area under receiver operating characteristic curve (AUROC) value of 0.85-0.87 for detecting advanced fibrosis.[2] NAFLD fibrosis score is an extensively validated tool and utilizes hyperglycemia, BMI, platelet count, albumin, AST/ALT ratio, and age. One advantage of this system is its ability to distinguish different stages of fibrosis, albeit there is a considerable proportion of patients with intermediate results.[2] FibroTest combines five biochemical markers: haptoglobulin, a_2-macroglobulin, apolipoprotein a1, total bilirubin, and gamma-glutamyl transferase. Similar to the FIB-4 index, FibroTest has an AUROC of 0.84 for advanced fibrosis.[2] These noninvasive scoring systems are useful in detecting or excluding advanced fibrosis and can spare a number of patients from undergoing liver biopsy.

As awareness of NAFLD increases, the impact of NAFLD on resource utilization has become an important issue. Recent studies revealed that the number of NAFLD patients seeking care in inpatient and outpatient settings has been increasing as well as the attendant annual hospital charges and payments.[10] Another study showed that after controlling for comorbid conditions, patients with NAFLD on ultrasound and elevated ALT levels experienced 26% higher health care costs than patients without NAFLD and normal ALT levels.[11] These data suggest that as the rate of obesity continues to rise, the economic impact of advanced liver disease related to NAFLD will be significant.

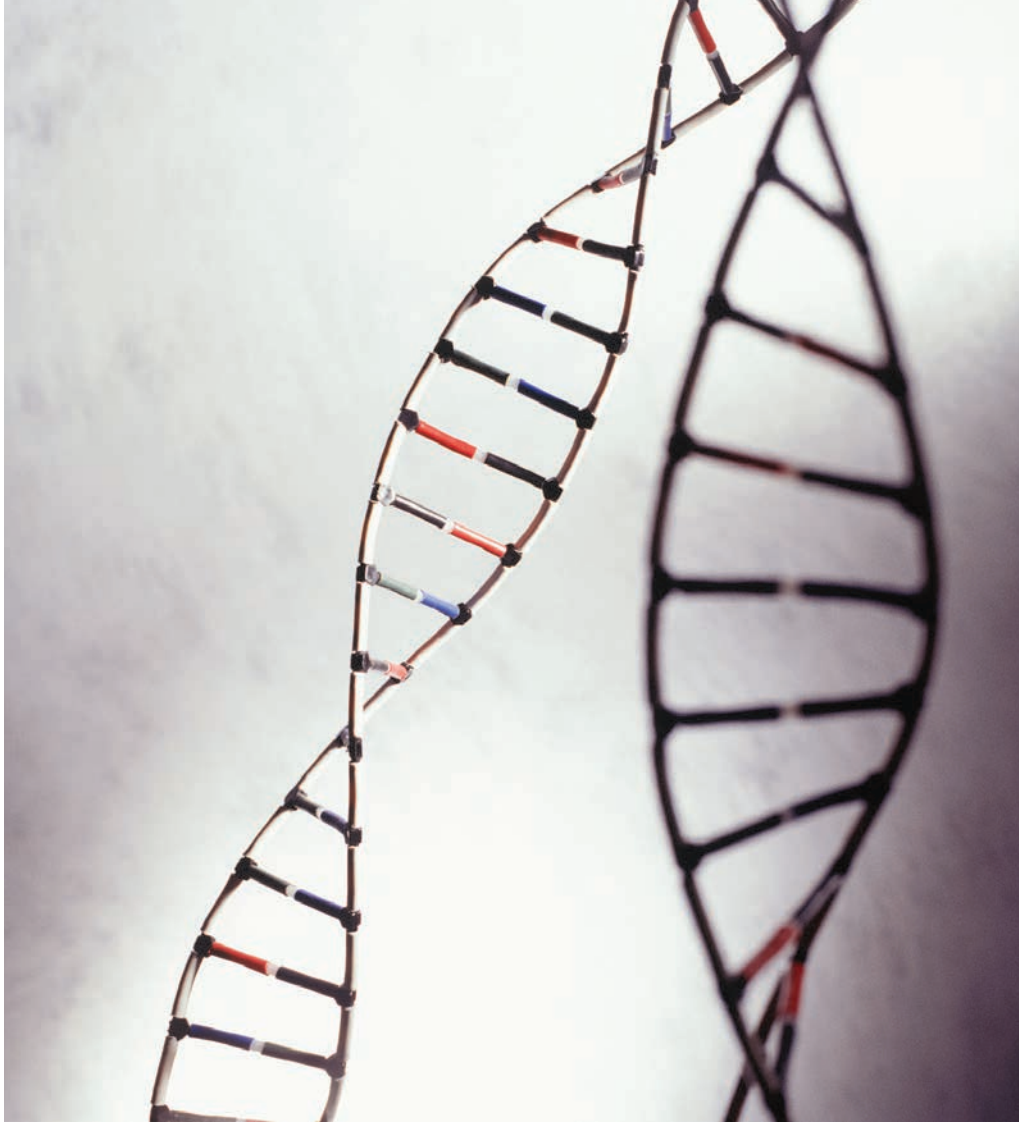
On the horizon

To date, pharmacologic treatments of NAFLD and NASH have targeted hepatic steatosis, insulin resistance, oxidative stress, inflammation, and fibrosis. In this context, orlistat, cannabinoid agonists, metformin, glitazones, statins, and fibrates have been tested in clinical trials. The diabetic drug classes of GLP-1 agonists, DPP-4 antagonists, and sodium-glucose transporter 2 antagonists are currently being investigated for primary treatment of NAFLD.[12] The PIVENS trial revealed that vitamin E was superior to placebo for the treatment of NASH but there was no benefit of pioglitazone over placebo.[13] In another trial, obeticholic acid, which is the farnesoid-X-nuclear receptor agonist, was found to improve the biochemical and histological features of NASH compared to placebo.[14] Beside these medications, lifestyle modification plays an important role in the treatment of NASH. It was shown in a recent study that the highest NASH resolution and fibrosis regression occurs in patients with weight losses greater than 10%.[15]

The PIVENS trial revealed that vitamin E was superior to placebo for the treatment of NASH but there was no benefit of pioglitazone over placebo.

In addition to the NAFLD's strong association with the metabolic syndrome, recent data suggest that heritable factors also play an important role in NAFLD pathogenesis.[16] The perception of the genetic input to NAFLD pathogenesis has increased substantially with the help of genome-wide association studies, which led to the identification of novel genes contributing to pathogenesis of NAFLD.[16] Using this

approach, a single nucleotide polymorphism of the patatin-like phospholipase domain containing three genes (rs738409) was found to be significantly associated with steatosis and the more progressive forms of NAFLD. Other polymorphisms of various genes have also been shown to be associated with increased risk of NAFLD, such as glucokinase regulatory protein and neurocan. In the last decade, family and twin studies have suggested that NAFLD may be heritable and we suspect that future studies will likewise uncover the genetic roots of NAFLD.[17] With advancements in genomics, proteomics, and metabolomics technologies, and the application of these platforms in the field of NAFLD, new noninvasive prognostic and diagnostic biomarkers are likely to be discovered in the near future.[18] Utilization of these platforms can not only help scientists identify biomarkers for the early diagnosis of NASH, but also identify potential targets for therapeutic interventions.



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Research opportunities

Although development of fibrosis in patients with NAFLD and NASH was historically believed to be an irreversible step in the path to cirrhosis, recent studies revealed that cirrhosis is a dynamic and reversible disease stage.[19] Scientists are now searching for novel therapeutic strategies that target specific steps in the process of fibrogenesis with the aim of reversing advanced fibrosis and cirrhosis.

Conclusion

Today, the cornerstones of the treatment of NAFLD are lifestyle interventions, which are effective not only for improving NAFLD, but also for the risk factors of metabolic syndrome and cardiovascular diseases. Nevertheless, lifestyle modifications are difficult to achieve and sustain. In addition to the above-mentioned pharmacologic agents, current studies are focusing on caspase inhibitors, PPAR alpha and delta, farnesoid-X-receptor agonists, and modulation of certain enzymes that play a role in preventing the inflammation that is associated with metabolic syndrome.[20] Although promising results have been carried out, more research is necessary for developing new regimens for patients with NASH. ■

References

1. Younossi Z.M., et al. Hepatology 2016;64:73-84.
2. Golabi P., et al.Expert Rev Gastroenterol Hepatol 2015;10:63-71.
3. Ong J.P., et al. Clin Liver Dis 2007;11:1-16, vii.
4. Sayiner M., et al. Clin Liver Dis 2016;20:205-14.
5. Musso G., et al. Ann Med 2011;43:617-49.
6. Lonardo A., et al. Dig Liver Dis 2015;47:997-1006.
7. Mishra A., et al. J Clin Exp Hepatol 2012;2:135-44.
8. Younossi Z.M., et al. Metabolism 2013;62:352-60.
9. Saadeh S., et al. Gastroenterology 2002;123:745-50.
10. Younossi Z.M., et al. J Clin Gastroenterol 2015;49:222-7.
11. Baumeister S.E., et al. Gastroenterology 2008;134:85-94.
12. Federico A., et al. World J Gastroenterol 2014;20:16841-57.
13. Sanyal A.J., et al. N Engl J Med. 2010;362:1675-85.
14. Neuschwander-Tetri B.A., et al. Lancet. 2015;385:956-65.
15. Vilar-Gomez E., et al. Gastroenterology. 2015;149:367-78.e5; quiz e14-5.
16. Chalasani N., et al. Gastroenterology 2010;139:1567-76, 1576 e1-6.
17. Dongiovanni P., et al. Curr Pharm Des. 2013;19:5219-38.
18. Younossi Z.M., et al. J Proteome Res 2010;9:3218-24.
19. Sohrabpour A.A., et al. Aliment Pharmacol Ther 2012;36:824-32.
20. Harrison S.A. Hepatology 2015;62:1652-5.

DDSEP® eight

Digestive Diseases Self-Education Program

ANSWERS

// From page 3

Q1: Answer: C

CRITIQUE

Factors raising suspicion for Zollinger-Ellison syndrome include recurrent peptic ulcer disease, multiple ulcers, post-bulbar ulcer, non–*H. pylori*/non-NSAID-related duodenal ulcer, diarrhea, erosive esophagitis, and family or personal history of MEN I. The patient in this question presents with duodenal ulcer without *H. pylori* or NSAID use, erosive esophagitis, and diarrhea, which raises suspicion for hypergastrinemia.

His laboratory evaluation also showed hypercalcemia, which may be due to hyperparathyroidism, a condition related to MEN I. The initial test to obtain when gastrinoma is suspected includes a fasting serum gastrin level. In follow-up of gastrin elevations, a gastric pH assessment should be performed and, depending on these results, a secretin stimulation test may be useful. Routine repeat upper endoscopy is not indicated after hemostasis of duodenal ulcer bleeding.

A restrictive transfusion strategy with a hemoglobin threshold of 7 g/dL has been shown to result in improved clinical outcome compared to a liberal transfusion strategy. While sucralfate may help the healing of duodenal ulcers, it is not the first-line therapy for long-term secondary prevention.

References

1. Roy PK, et al. Zollinger-Ellison syndrome. Clinical presentation in 261 patients. Medicine (Baltimore) 2000;79:379.

2. Murugesan SV, Varro A, Pritchard DM. Review article: Strategies to determine whether hypergastrinaemia is due to Zollinger-Ellison syndrome rather than a more common benign cause. Aliment Pharmacol Ther 2009;29:1055–68.

3. Villaneuva C, et al. Transfusion strategies for acute upper gastrointestinal bleeding. N Engl J Med. 2013;368:11-21.

Q2: Answer D

Objective: Identify the clinical presentation and risk factors for small intestinal bacterial overgrowth

Rationale: This patient likely has small intestinal bacterial overgrowth (SIBO) based on her symptoms, the steatorrhea with the positive Sudan stain for fat, and a slight anemia with an elevated MCV suggestive of B-12 deficiency secondary to the bacterial overgrowth. She also has scleroderma, a condition commonly associated with SIBO, because it impairs gastrointestinal motility.

While hydrogen breath testing may help establish the diagnosis of SIBO, there is variable sensitivity and specificity of the testing with false-positive and false-negative test results frequently occurring. An alternative strategy is to treat empirically with an accepted antibiotic regimen and assessing response after the course is completed.

References

1. Bures J, et al. Small intestinal bacterial overgrowth syndrome. World J Gastroenterol 2010;16:2978-90.

2. Abu-Shanab A, Quigley EM. Diagnosis of small intestinal bacterial overgrowth: The challenges persist! Expert Rev Gastroenterol Hepatol 2009;3:77-87.

3. Khoshini R, et al. A systematic review of diagnostic tests for small intestinal bacterial overgrowth. Dig Dis Sci 2008;53:1443-54.

Snapshots from the AGA Journals

Cell-based Strategy Curbs Constipation

May Cellular and Molecular Gastroenterology and Hepatology (doi: 10.1016/j.jcmgh.2015.12.010)

Key clinical point: Treatment at the nanomolecular level may become an alternative for various types of constipation.

Major finding: Oral doses of CFTRact-J027 normalized stool output and water content in a loperamide-induced mouse model of constipation with a 50% effective dose of approximately 0.5 mg/kg.

Data source: A proof-of-concept study in which a cell-based screen was performed for 120,000 drug-like, synthetic small molecules that were then tested in constipation-induced mice and control mice.

Disclosures: Dr. Cil and two coauthors are inventors on a provisional patent filing, with rights owned by the University of California, San Francisco. The study was funded in part by several grants from organizations including the National Institutes of Health and the Cystic Fibrosis Foundation.

Commentary

Dr. Wayne I. Lencer, AGAF, is chief of the division of gastroenterology, hepatology and nutrition and the Harry Schwachman Chair in Pediatric Gastroenterology at Boston Children's Hospital; and Longwood Professor of Pediatrics at Harvard Medical School, Boston. He has no conflicts of interest.

The article by Cil et al. describes the discovery and characterization of a small molecule (termed CFTR$_{act}$-J027), which is capable of opening the Cl- channel CFTR [the cystic fibrosis transmembrane regulator]. The paper shows that CFTR$_{act}$-J027 induces intestinal Cl secretion in the mouse by opening CFTR, and the authors suggest that the molecule may have clinical applications for the treatment of constipation in humans.

CFTR$_{act}$-J027 has several potential advantages, compared with other small molecules, in use for the treatment of constipation, including greater apparent potency and the chance for local (topical) activity.

Constipation-associated conditions such as constipation-predominant irritable bowel syndrome and opioid-induced constipation affect a large and growing proportion of the U.S. population. The discovery of CFTR$_{act}$-J027 is an important and timely advance toward increasing the therapeutic options for these disorders. There are still many hurdles to overcome before clinical application, but perhaps CFTR$_{act}$-J027, or another more refined compound that opens CFTR, will be found effective in treating constipation in humans. This would have a big impact. ■

Combo Birth Control Pills Increased Crohn's Disease Surgery

June Gastroenterology (doi: 10.1053/j.gastro.2016.02.041)

Key clinical point: Long-term use of combination oral contraceptives significantly increased the risk of surgery among women with Crohn's disease.

Major finding: Women who used combination OCs for more than 3 years were 68% more likely to need surgery than were nonusers.

Data source: A prospective national registry study of 4,036 women with Crohn's disease.

Disclosures: The study was funded by the Crohn's and Colitis Foundation of America, the National Institute of Diabetes and Digestive and Kidney Diseases, the American Gastroenterological Association, and the American College of Gastroenterology. Dr. Khalili reported receiving consulting fees from Abbvie. One coinvestigator reported consulting relationships with Bayer Healthcare, Pfizer, and Pozen. The other investigators had no disclosures.

Commentary

Millie D. Long, M.D., MPH, is assistant professor of medicine, University of North Carolina at Chapel Hill. Susan Hutfless, Ph.D., is assistant professor, director, Gastrointestinal Epidemiology Research Center, division of gastroenterology & hepatology, and department of epidemiology, Johns Hopkins University, Baltimore. Dr. Long and Dr. Hutfless have no relevant conflicts of interest.

Why should contraceptive choices matter to the gastroenterologist? Fifty percent of women diagnosed with inflammatory bowel disease (IBD) are diagnosed before age 30 (Gastroenterology 2004;126:1504-17). Contraception is routinely used by women with IBD who do not wish to become pregnant. For example, in one recent survey, 88% of women with IBD report current or prior use of hormonal contraception (Inflamm Bowel Dis. 2014;20:1729-33). In some instances, hormonal therapies can be used to improve "cyclical" gastrointestinal symptoms in women with IBD based on their self-report. Up to 60% of women with IBD report changes in GI symptoms surrounding menses. A total of 19% of women with IBD using estrogen-containing contraceptives reported that their symptoms were ameliorated by hormonal contraception. Interestingly, symptomatic improvement was reported in 47% of women using levonorgestrel (progestin) intrauterine devices (Inflamm Bowel Dis. 2014;20:1729-33).

Estrogen-containing oral contraceptives have also been linked to adverse outcomes. For example, estrogen-containing contraceptives are associated with an increased risk of venous thromboembolism (VTE) in the general population. Patients with IBD, particularly those who are smokers or who have recent hospitalization or active inflammation, are already at increased risk for VTE. As a rule, providers should assess VTE risk factors in IBD patients, including estrogen-containing oral contraceptive use, obesity, smoking, and active inflammation (Clin Appl Thromb Hemost. 2016 Feb 18. pii: 1076029616632906 [Epub ahead of print]). In those with these risk factors, the thrombotic risks of an estrogen-containing contraceptive likely outweigh the benefits. The current study by Khalili et al. provides another important potential risk of estrogen-containing contraception.

With the currently available data, progestin-only oral contraceptives (which have not been shown to increase VTE or surgical complication of Crohn's disease) or intrauterine devices with or without progestin should be considered in women with Crohn's disease as first-line contraceptive agents. Progestin-containing IUDs have nearly 100% effectiveness and fertility rapidly returns after discontinuation. Progestin-containing IUDs do not increase the risk of Crohn's disease complications.

While it is clear that the prescription for, or placement of, contraceptives is not within the purview of the treating gastroenterologist, the development of a collaborative relationship with a trusted gynecologist to help guide contraceptive choices in young women with Crohn's disease is of utmost importance. ■

Psychological Therapies Eased IBS for at Least 6-12 Months

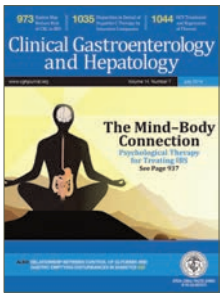
July Clinical Gastroenterology and Hepatology (10.1016/j.cgh.2015.11.020)

Key clinical point: A meta-analysis found that psychotherapy improved gastrointestinal symptoms in irritable bowel syndrome, with the effects persisting for at least 6-12 months.

Major finding: Immediately after treatment, the Cohen's d value was 0.69 (*P* less than .001), indicating a medium effect size. Cohen's d values were 0.76 and 0.73, respectively, at 1- to 6-month follow-up and at 6- to 12-month follow-up.

Data source: A systematic review and meta-analysis of 41 randomized controlled trials that included 2,290 patients with IBS.

Disclosures: The authors reported no funding sources and had no disclosures.



Commentary

Dr. Christopher V. Almario, division of gastroenterology, Cedars-Sinai Medical Center, Los Angeles. He has no relevant conflicts of interest to declare.

It is well established that psychological therapy is efficacious in managing irritable bowel syndrome (IBS), and it has an associated number needed to treat of four (Am J Gastroenterol. 2014 Sep;109:1350-65). A new meta-analysis from Laird and her colleagues revealed that the positive impact of psychotherapy on IBS symptoms persisted even 1 year after treatment.

While these findings are impressive and continue to support the use of psychotherapy in IBS, important issues remain. First, these results are based on data gathered in the highly controlled environment of randomized controlled trials (RCTs), and it is unclear whether they will translate to the "real world." RCT participants may be more willing to complete psychotherapy because they know they are being observed by research staff (referred to as the Hawthorne, or observer, effect). However, in real clinical practice, patients with IBS not subject to the Hawthorne effect may be less compliant with such therapies.

Other issues relate to the current limited adoption of psychotherapy in clinical practice. Factors contributing to the low uptake include variable third-party reimbursement and poor patient and provider acceptance (JAMA. 2015 Mar;313:949-58). Another factor is limited access to qualified psychotherapists. This is an area where telehealth and mobile apps can widen access, especially as Internet-delivered psychotherapy has been shown to be effective (Am J Gastroenterol. 2011;106:1481-91).

Given the high prevalence of IBS, along with the proven, persistent efficacy of psychological therapies in reducing IBS symptoms, efforts to increase both use of and access to these therapies in clinical practice are needed. ■

Tips and Advice for Writing Abstracts for Scientific Meetings

By Richard M. Peek Jr., M.D.

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Presenting an abstract at a scientific meeting is an exhilarating and rewarding benefit of training and represents a fundamental component in the career development of academic physicians. Above all, abstract presentations serve to disseminate your research findings, advance a specific field of investigation, and crystallize your reputation on a national level. Whether it be broad-based meetings such as Digestive Disease Week® (DDW) or focused meetings such as an AGA Freston, Federation of American Societies for Experimental Biology, Keystone, or Gordon Conference, abstract presentations provide opportunities to build nascent relationships with other investigators, network with colleagues, and garner critical feedback prior to submission of your research for publication. Interactions with leaders in the field can also serve as a nidus for future academic promotions and identifying new career opportunities. Insights and suggestions from content experts will undoubtedly strengthen your work and can often lead to new collaborations and scientific directions. Finally, from a pragmatic point of view, presenting at a national meeting may be the only way your department will fund your attendance!

A successful abstract requires considerable planning and forethought, and creating a scientific abstract is often the first step in the publication process. Publication of manuscripts and acquisition of grants are critical metrics in the promotion process and abstracts provide the opportunity to synthesize materials and organize data into an optimal format for manuscript submission. The reach goal should be a 1:1 ratio of abstracts submitted to papers published. In reality, however, this goal is infrequently achieved. One study determined that less than half of all abstracts presented at national meetings (45%) were ultimately published as papers.[1] My personal goal is to have a manuscript submitted within 1 year following an abstract presentation of that research.

Prewriting activities

Prewriting an exceptional abstract is not a task that can be left to the last minute so budget adequate time well before the deadline. This allows for multiple iterations and for coauthors to have time to read and make substantive, instead of cosmetic, critiques to the work. Many authors capitalize on the wisdom of individuals at their home institution whose expertise may not be directly aligned with the content of the abstract, which helps ensure the work will have broader appeal. Visit the website of the meeting you are planning to attend and follow

Chachamal/Thinkstock

the abstract instructions precisely. It is also helpful to review a subset of abstracts that were previously presented at your meeting of interest. Carefully consider the interests of the audience (and therefore, the abstract reviewers) and target those fields of interest as you develop the overall theme of the abstract. Finally, the most highly scored abstracts typically present fresh insights and new data and are not simply a repackaged version of a prior abstract;[2] in fact, DDW does not accept abstracts that were presented previously at a national meeting.

Reviewers have a very truncated period of time to review a large number of abstracts. For example, the abstract deadline for DDW is December 1 and reviewers typically have between 7-10 days to complete their reviews, hold teleconference calls to discuss abstract rankings, and construct tentative programs, all occurring at the busiest time of the year! For ease of review, use simple declarative sentences in the active voice to describe your findings. For clinical studies, use generic names for drugs and devices unless a specific brand is critical for the study. Be careful about the use of abbreviations unless you are certain that the audience and the reviewers are completely familiar with the terminology. If abbreviations are used, spell them out at the time of initial introduction. In terms of font style and size and line spacing, these are often legislated by the instructions for the abstract. If not, proportional fonts such as Arial or Times New Roman allow more words to be included. Do not, however, decrease the font size below 10-11 point or reduce line spacing to less than single space as this can infuriate an exhausted reviewer who may be reading your abstract at 11 p.m.

Individual components of your abstract

Title: This is where you can provide substantial curb appeal to the work. A clear and engaging title frequently sets the tone for how a reviewer will interpret and evaluate the work. Abstract titles are typically 10-12 words in length and include the scope of the work, the study design, and the goal. It is preferable to create a descriptive title rather than to state the results. Finally, an engaging title should be easy for reviewers and attendees outside of a particular niche to understand and should not contain unfamiliar abbreviations.

Authors and Affiliations: Authors are listed in order of their relative contributions with an exception being that the mentor or senior author is typically listed last. The first author is usually the person who conceived the study and did most of the work. Full names, credentials, and affiliations relevant to the study (e.g., departments and institutions) should be included. Finally, only include individuals who actually performed work on the project. Authorship is coming under increasing scrutiny and individuals included as authors should have played a defined role in the research.

Introduction/Background/Context/Aims (Why did you do this study?): I bold the name of each of the following components in order to distinguish them from each other. Because space is a limiting factor, only include 1-2 sentences of background that clearly sets the stage for your results. Abstracts

that contain a prodigious amount of background information can send a signal that the amount of actual data may be scant. Focus on clearly describing the gap that your research will address and then segue into the Specific Aims of the study. It is appropriate to also include a hypothesis but be rigorous and objective in conveying that your goal is not to prove that a particular hypothesis is true but instead to test whether it is true.[3]

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Methods (What did you do?): For abstracts, only convey a concise description of the methods and study design; details can be provided at the time of presentation. For clinical studies, important parameters to include are a description of the populations under study, whether a study was retrospective or prospective, whether there was randomization, the context of the study, and any measurements that were made.

Results (What did you find?): This is the most critical component of an abstract and it should include complete sentences that present real data described in units for all measurements (e.g., do not indicate that results will be presented). The primary outcome (even if it does not support your hypothesis or is negative data), relevant secondary outcomes, and relevant statistics including p values should all be included. Weaker abstracts include statements such as "the results demonstrated a trend toward significance" simply present the results and let readers draw their own conclusions. Many meetings allow the inclusion of a figure or a table, which can augment the visual appeal of your work; however, make sure symbols and font are legible, and only include these items if they convey your results more effectively. Frequently, abstracts are reduced in size for publication so if a figure or table is included, refer to previously published abstracts for suboptimal formatting to avoid.[3]

Conclusions/Implications: This section should include 2-3 sentences and focus on a brief description of the main outcomes without overstating the findings. Implications should reflect how the findings will impact other fields, clinical practice, policy, or subsequent research directions. Similar to the conclusions, avoid overstating the ramifications of your results.

Final actions before pushing the "Submit" button

Prior to submission, always review the Instructions to Authors to ensure that your abstract is absolutely concordant with the meeting guidelines. Proofread the final version several times yourself, and also have a colleague read the final version. Your goal is to have a grammatically perfect abstract with no misspelled words or typographical errors. I previously served on a Study Section and a grant being discussed had several grammatical errors prompting the primary reviewer to state that since the investigator was this sloppy with their grant preparation, we should more intensively question the rigor of the results. Although it seems unfair, you can avoid this with careful attention to detail and budgeting time before the deadline for final edits.

In conclusion, presenting scientific abstracts clearly benefits junior investigators, provides a wealth of opportunities, advances science, and serves as a nidus for publication of your research. Using clear declarative language, strictly adhering to abstract specifications for your meeting, and allowing adequate time for you and others to carefully proofread the work will help ensure an exceptional piece of work.

References

1. von Elm, E., et al. BMC Med Res Methodol. 2003;3:12.
2. Wood, G.J., et al. J Palliat Med. 2011;14:353-9.
3. Pierson, D.J. Respir Care. 2004;49:1206-12.

The American Gut Project – A Unique Learning Opportunity

By Faris El-Khider, M.D., M.S.

Dr. El-Khider is a gastroenterology fellow at the Cleveland Clinic's Digestive Disease Institute and is also in the department of pathobiology at the Cleveland Clinic's Lerner Research Institute.

"Is poop alive?" This question was asked in one of my first lab meetings as a GI research fellow. I didn't know how to accurately answer this question, given that up to half of our fecal biomass is composed of microbiota (represented by more than 5,000 bacterial taxa and other organisms).[1] Much of the work in our lab is related to gut microbiota in one way or the other, so when I saw the announcement on the AGA's website to participate in the American Gut Project (AGP), I knew that this would be a great way to learn more about the gut microbiome.

There have been many efforts to create a library for the trillions of organisms that make up the human microbiota. These organisms account for 1%-3% of body weight, and their collective genome – or "metagenome" – is estimated to be 100-fold larger than that of the human genome.[2] They can be isolated from the skin, mouth, genital tract, and gut and include bacteria, viruses, and fungi. In humans, the largest proportion of microbiota reside in the gut. This gut microbiome is not uniform; different parts of the gut have different anatomy and function as well as a markedly different microbial composition.[3] In addition, host factors have a tremendous influence on the microbial composition of the gut. The diversity of the gut microbiota is affected by diet, genetics, sleep habits, age, etc. The microbiome can also be affected by early-life events, and even events before birth through transmission of maternal commensal bacterial to the fetus.[4] On the other hand, the microbiome interacts with the host in a number of ways and microbiome-associated diseases range from *Clostridium difficile* colitis and inflammatory bowel disease (IBD) to obesity, atherosclerosis, fatty liver disease, and mental health disorders.[5]

One of the early efforts to link the microbiome and disease and to characterize the bacterial population of a healthy cohort was the Human Microbiome Project (HMP).[6] HMP was established by the National Institutes of Health in 2008 to examine the bacterial composition of stool samples from about 250 individuals, at up to three points in time. The AGP on the other hand is a donor-supported project where anyone can contribute by covering part of the cost. Underrepresented minorities are covered through other funding sources, including crowdfunding and donations. The project started in 2012 and paved the way to a better understanding of the microbiome of the general population through the mail-in submission of stool samples. This in turn markedly expanded recruitment and allowed AGP to study bacteria obtained from the stools of anyone living in the U.S.

The goal is to create a microbiome database and map that can be used to identify unhealthy and healthy microbiome states. Signing up takes just a few clicks and a stool collection kit with a unique identifier arrives in the mail in a few weeks. To date, more than 10,000 stool samples have been submitted and analyzed as part of the project.

The AGP relies on culture-independent methods for detecting bacteria by analyzing bacterial nucleic acids in stools. DNA isolated from a stool sample could be from human cells, bacteria and other organisms, or undigested food. The bacterial 16S ribosomal RNA (rRNA) gene has a specific signature that is shared by all bacteria and variations within its coding region can be used to differentiate between species. Using 16S rRNA sequencing, we can distinguish bacterial DNA from others. This process cannot determine the number of bacteria in the stool sample, but a relative abundance can be calculated so that the distribution of bacteria can be obtained. The process has limitations because it cannot reliably quantify adherent bacteria, or bacteria that are not annotated in current databases (sequences that are not linked to a name). Once a sample is received at the lab, individual bacterial taxa are identified using 16S rRNA sequencing and then scored using UniFrac,[7] an algorithm that scores microbial populations based on how similar they are. All data are free and available for researchers, clinicians, and patients.

As part of the Active Learning Session on the Microbiome at DDW® 2016, organized by the AGA Center for Gut Microbiome Research and Education, results from studies using data from AGP were presented.[8] These results highlight the dynamic nature of gut bacteria in relation to self-reported volunteer data. At the center of the AGP is a map representing the microbiome dissimilarity (or similarity) in the American population. Analyses show that there is increased microbiome diversity with alcohol consumption, BMI, and gender. There is an even stronger effect due to diet and age and hours of sleep at night. IBD patients have a largely distinct gut microbial composition compared with the general public and, as one would expect, IBD cohorts that are geographically different have overall distinct compositions. One clinical application is to create a map of an individual's microbiome changes over time, hence creating a projection of what a healthy microbiome should look like after (e.g., treatment for *C. difficile* colitis).

The AGP has already expanded into the British and Australian Gut Projects as well as Asian Gut planned for launch later this year. In addition, the team is planning on another even larger project where stool samples will be collected longitudinally over time to get a better understanding of the dynamics of gut microbiology.

Participating in AGP is certainly an unconventional and unique way to learn about gut microbiota and its effects on health and disease, and I will be looking forward to participating in future volunteer projects very soon. ■

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References

1. Dethlefsen L., et al. PLoS Biol. 2008;6:e280.
2. Levy M. et al. Genome Med. 2015;7:120.
3. Johnson L.R. Physiology of the Gastrointestinal Tract. 4th ed. Academic Press: San Diego, 2006.
4. Romano-Keeler J., Weitkamp J.H. Pediatr Res, 2015;77:189-95.
5. Dash S., et al. Curr Opin Psychiatry. 2015;28:1-6.
6. "Human Microbiome Project," 2016. Available: https://commonfund.nih.gov/hmp/index.
7. Lozupone C., Knight R. Appl Environ Microbiol. 2005;71:8228-35.
8. Molina J.A.N. Active Learning Session on the Gut Microbiome Digestive Disease Week® 2016.

The Gastroenterologist's Microbiota: Insights from the AGA Stool Sample Initiative

By Michael A. Schumacher, Ph.D.

Dr. Schumacher is a postdoctoral fellow in the division of gastroenterology at Children's Hospital, Los Angeles. mschumacher@chla.usc.edu

How much do you know about the bacteria that make up your gut microbiota? Experimental evidence accumulating from research labs around the world suggests that answering this question may soon have practical benefits to medical practice and patient care. Furthermore, access to this knowledge is rapidly becoming available to anyone willing to donate a sample.

It has been known for a long time that the intestinal tract is colonized by a large number of bacterial residents, but until recently there was limited understanding of the extent to which they contribute to overall health. In the past decade a number of microbiome projects, including the National Institutes of Health's Human Microbiome Project, have brought into focus the size and ecological diversity of gut bacteria. Importantly, these projects have catalyzed a multitude of studies aimed at understanding how an individual's microbiota is linked with health and disease, sometimes in surprising and unexpected ways.

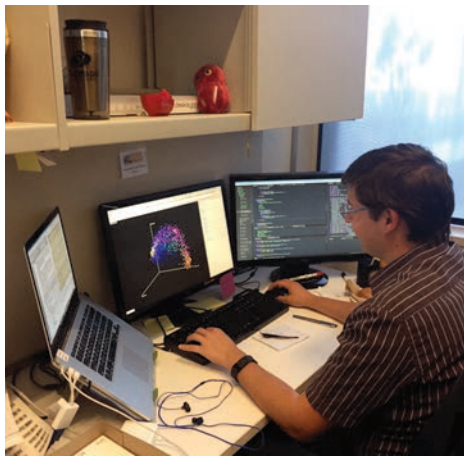
Emerging research from numerous labs is establishing the importance of maintaining a diverse community of bacteria in your gastrointestinal tract to support health and protection from a variety of ailments. Gut bacteria have been shown to impact the development of inflammatory disease,[1] metabolic disease,[2] cancer,[3] and obesity,[4] and these findings are just the beginning. Intriguing studies have also suggested that the impact of your gut residents may extend as far as direct influences on your mood.[5] With the potential for impact on a wide range of diseases and health outcomes, it is not difficult to see why so much attention is being devoted to this field to see how these findings may influence medicine.

The increased research focus and attention in this area has contributed to improvements in microbial sequencing technology and scalability of data collection/analysis. As costs of sequencing and obtaining data have reduced, the feasibility of identifying the microbial composition of large numbers of participants from many discrete populations is now possible. Why is this important? Because microbial diversity between individuals and between populations is high. The more data that can be obtained from diverse populations, the more insight can be obtained regarding how these complex communities and their interactions with the body influence health.

As the field of gastroenterology is at the forefront of this microbial revolution, the AGA and its Center for Microbiome Research and Education recently launched a stool sample initiative aimed at involving its members in this research. The goal? To characterize the microbiota of a strata of gastroenterologists and GI researchers by working with the American Gut Project (AGP) to analyze whether this population harbors any microbial trends. The AGP, spearheaded by Dr. Rob Knight at the University of California, San Diego, has been collecting stool samples for the past several years from a range of populations interested in learning more about their bacterial gut residents. These samples are analyzed by sequencing to characterize the presence and abundance of distinct microbial

American Gut Project fecal samples before processing.

An Illumina® sequencer, which sequences some of the bacterial DNA in the samples.



Courtesy Dr. Michael A. Schumacher

Analysis of the data; the more data collected, the more detailed the picture.

species in the gut.

So how does the AGP work? As a participant, your involvement is easy as you simply fill out a questionnaire about your background and dietary information, mail a stool sample to the AGP using a provided collection kit, and pay a fee ($99) to cover sequencing and analysis costs. (For the AGA initiative, these fees were reduced for nontrainee members or waived altogether for trainee member volunteers.) Once your sample arrives at the lab in San Diego, the bacterial DNA is extracted, and a portion of the 16S ribosomal RNA gene is amplified and sequenced on Illumina® machines, and the resulting sequences are analyzed. You will then receive an alert to obtain your results online. Clicking through the online portal provides a graphical summary and compares the percent make-up of your microbial phyla with others of similar diet, gender, age, and BMI. Eventually, you will be provided with a summary graphical representation that compares how similar your gut bacteria are to people of different nationalities or to microbial communities analyzed from other body sites. You also receive information on your four most abundant microbes, four most enriched microbes compared to the average population, and (most fun of all) the rare species that are present in your microbiome. For data-minded individuals, the raw sequencing data for your sample is available with a few extra clicks online.

Do gastroenterologists and other AGA members who work in the GI field develop a distinct microbial population? At DDW® 2016, an active learning discussion was held with AGA members and attended by many participants in the stool sample initiative. Dr. Lee Kaplan (Harvard Medical School), Dr. Rob Knight (UC San Diego), and Dr. Gary Wu (University of Pennsylvania) discussed the samples and analysis, and the next steps toward making this knowledge useful. The major findings revealed that AGA volunteer microbiotas are widely distributed and resemble a random sampling of the entire AGP population of healthy individuals and patients. So breathe a sigh of relief, gastroenterologists, your microbiome has likely not been drastically altered by your profession. How this information will become useful is the interesting question that labs around the world are now racing to address.

An intriguing finding from this explosion of research is that your gut microbiota, which begins to develop as soon as you are born, is malleable and shaped by a variety of factors. Individuals harbor a thriving bacterial community that matures throughout life, and responds to antibiotic insults, as well as dietary and lifestyle changes. As a result, distinct microbiotas are observed between many populations. What can we do with this information? This is the exciting part. Exactly how these different microbial communities impact health and disease and whether they can be precisely shaped for optimal health are actively being studied. There is hope that modifying your gut microbiota, perhaps through installation of defined microbial communities, may prevent antibiotic-associated predisposition to disease as well as prevent or treat inflammatory or metabolic diseases and even adverse health outcomes like obesity.

By embarking on this journey now, our field is setting the stage for a microbe revolution in medicine. Are we headed toward a future where defined microbial communities are introduced to patients to reinforce their microbial armor? Which species are providing this benefit and through what mechanism? In the (possibly near!) future, a patient may be tested for their microbial make-up and pose the question "what does it all mean and what can I do about it?" And there may actually be an answer. ■

References

1. Round J.L., Mazmanian S.K. Nat Rev Immunol. 2009;9:313-23.
2. Nicholson J.K., et al. Science 2012;336:1262-7.
3. Yoshimoto S., et al. Nature 2013;499:97-101.
4. Ridaura V.K., et al. Science 2013;341:1241214.
5. Bravo J.A., et al. Proc Nat Acad Sci. 2011;108:16050-5.

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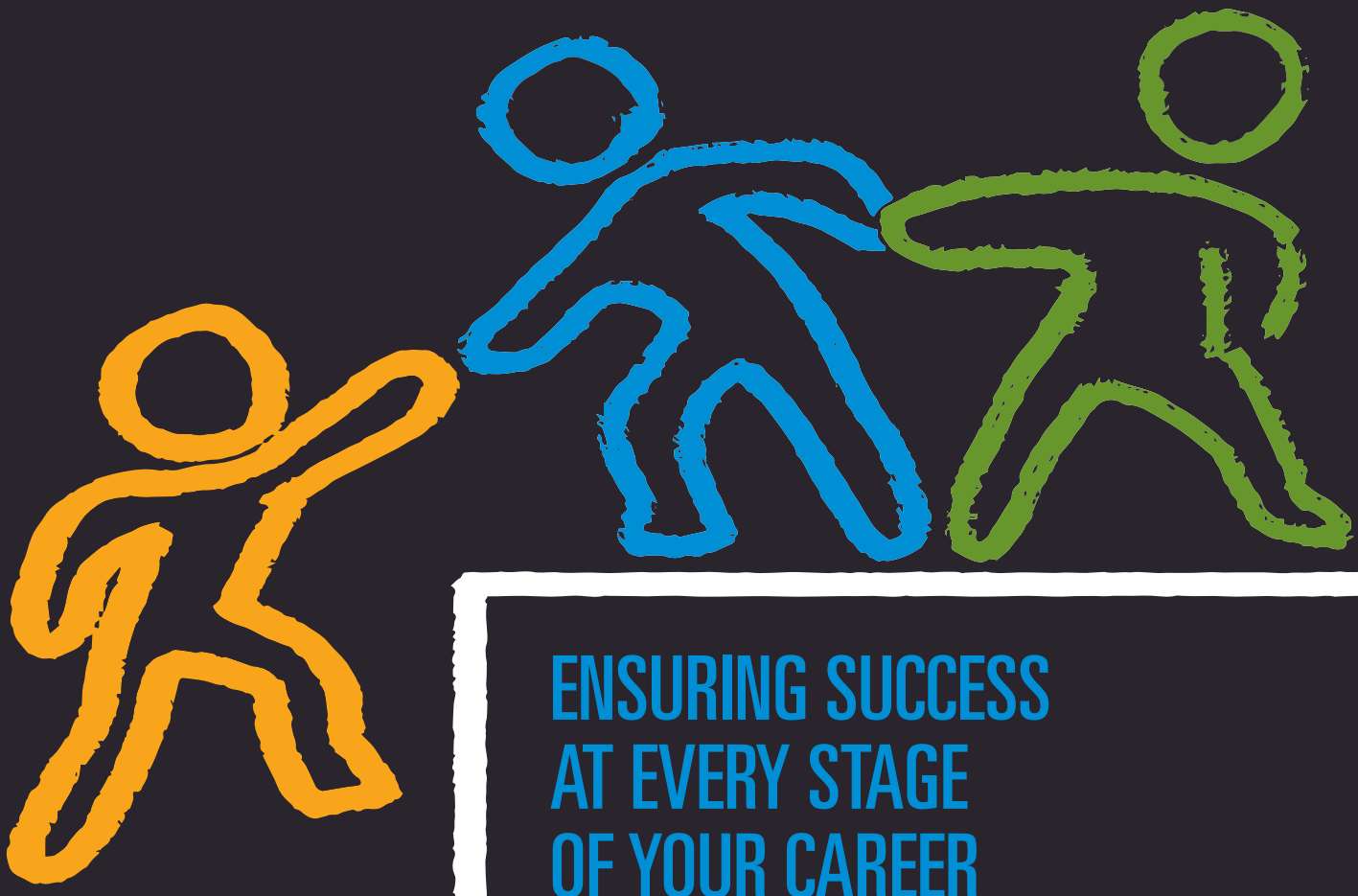

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