AGA Perspectives

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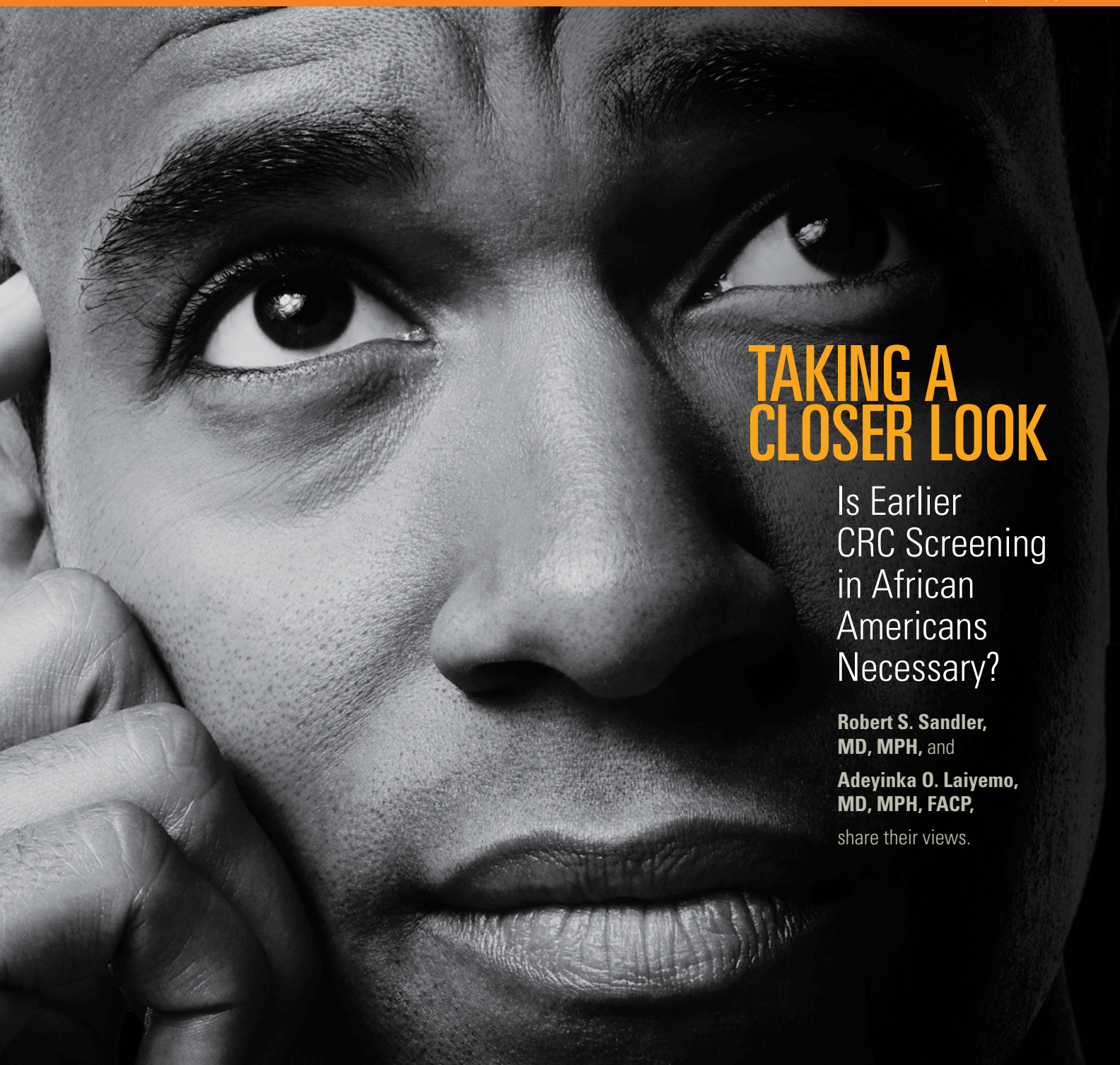

TAKING A CLOSER LOOK

Is Earlier CRC Screening in African Americans Necessary?

Robert S. Sandler, MD, MPH, and **Adeyinka O. Laiyemo, MD, MPH, FACP,** share their views.

AGA Perspectives

In this issue

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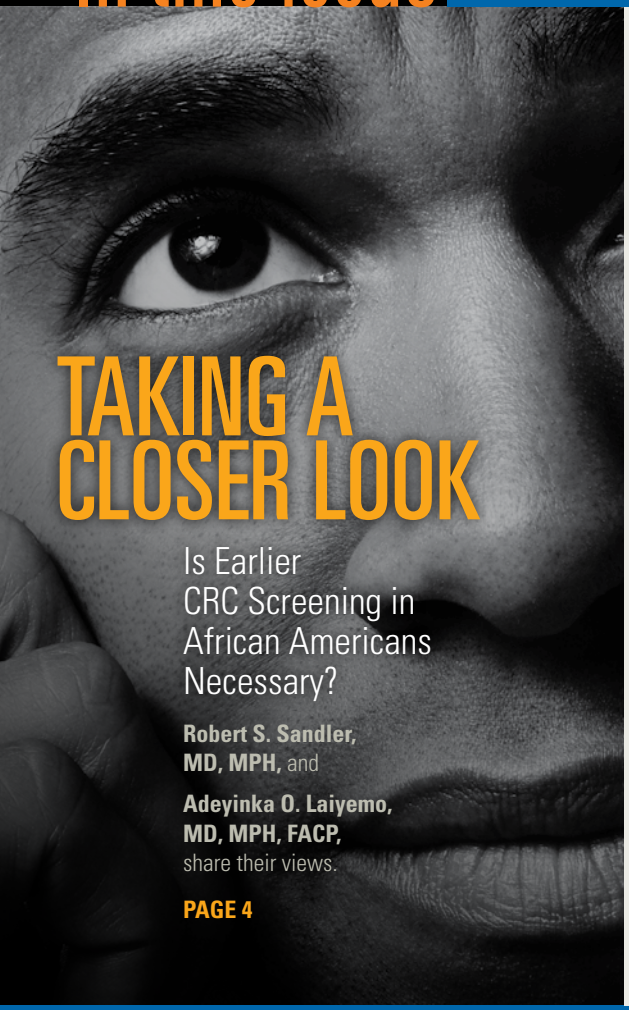

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Note From the Editor

Dear readers, by the time this issue of *AGA Perspectives* reaches you DDW® 2013 will be over and I will have completed my term as editor of this publication. Going forward the editorship will no longer be the job of the AGA councillor-at-large. We are very fortunate that Dr. Michael Wallace has agreed to serve as the editor of *AGA Perspectives*.

The June-July 2013 issue focuses on the disparities that exist in digestive diseases ranging from the underlying biology of diseases, the clinical presentations, access to care, and amongst those who provide clinical care or do research in the field. To start, we address the controversial topic of whether screening for colorectal cancer in African Americans should start at an earlier age. I was sitting next to Dr. Robert Sandler at an AGA meeting last fall when the topic came up and to my surprise he said he would argue against the notion. Of course, once Bob explained his perspective it made good sense. You can read his arguments against early screening while Dr. Adeyinka O. Laiyemo provides a compelling point of view on why screening should be offered earlier in this month's point-counterpoint.

When I started my GI training, inflammatory bowel disease (IBD) was thought to affect only whites, but this is no longer true. Dr. Amar Deshpande examines the role that genetics and environment play in the increasing prevalence of IBD in diverse populations in the U.S. and worldwide. My UCSD colleagues Drs. Julio Gutierrez and Jesus Rivera-Nieves make the case for balancing the discrepancies in the race or ethnicity of providers of digestive diseases care and those who are being cared for in the U.S. now and in the future. As Maria Abreu, MD, reports the AGA is striving to increase the numbers of young clinicians and investigators from underrepresented minorities to enter careers related to digestive diseases. Dr. Jeanette Keith discussed the disparities related to obesity while Dr. Deborah Procter reports her experiences volunteering doing missionary work in this issue's International Corner. For all of us with smart phones or tablets Dr. Ashish Atreja introduces us to top apps for gastroenterology!

I appreciate your support of *AGA Perspectives* during my time as editor and I look forward to the exciting new ideas that Mike has planned.

Sheila E. Crowe, MD, AGAF
EDITOR

"It is my great pleasure to take on the new role of editor for *AGA Perspectives* and continue the fantastic job of my predecessor, Dr. Sheila Crowe. This journal fills an important niche in exploring emerging trends in our field. We will keep our readers informed of what's new, exciting and emerging, from science, to practice, to endoscopy and training."

— Michael B. Wallace, MD, MPH

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

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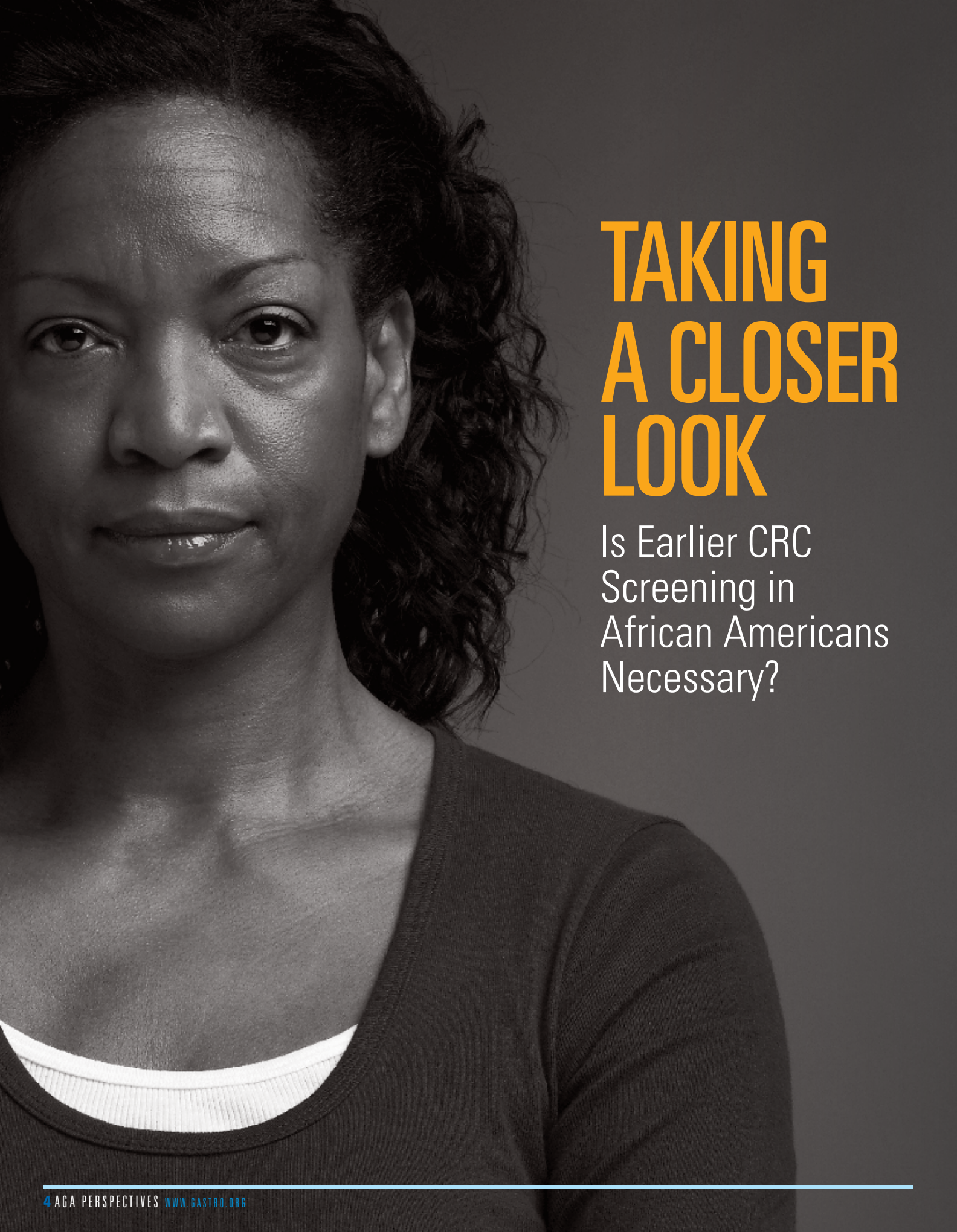

TAKING A CLOSER LOOK

Is Earlier CRC Screening in African Americans Necessary?

WE SHOULD SCREEN AFRICAN AMERICANS EARLIER: IT IS A RECALIBRATION ISSUE

It is well established that African Americans are more likely to be diagnosed with and die from colorectal cancer (CRC) when compared to all other race-ethnicities in the U.S. What is controversial is what to do to eliminate this public health problem. In my opinion, only a comprehensive approach can be effective.[1]

Adeyinka O. Laiyemo, MD, MPH, FACP
Assistant Professor of Medicine, Howard University

Dr. Laiyemo had no relevant conflicts to disclose.

Role of putative risk factors for colorectal cancer

Many studies have identified some risk factors for CRC such as low socio-economic status, cigarette smoking, alcohol ingestion and obesity. A higher prevalence of these risk factors has been postulated to contribute to the higher burden of CRC among African Americans. Although this explanation is plausible, important questions are raised due to the fact that these risk factors — including lower health-care access and lower CRC screening uptake — are also prevalent among the Hispanic population,[2] which consistently has lower risk of CRC when compared with non-Hispanic whites and non-Hispanic blacks.

Access versus utilization versus biology

African Americans have lower access to preventive care services including CRC screening due to lack of health-care insurance or having "less desired" health-care coverage or receiving care from safety net hospitals with long waiting times. Furthermore, when compared with non-Hispanic whites, African Americans are less likely to utilize health-care resources among Medicare beneficiaries and within the equal access Military Medical Systems and Veterans Affairs facilities. These suggest that health-care access and utilization factors may be the underpinning etiology of CRC disparity by race. However, other studies have reported that African Americans are more likely to present with advanced stage CRC even when CRC screening and

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WE SHOULD NOT SCREEN AFRICAN AMERICANS EARLIER: THE GUIDELINES ARE UNCLEAR

Robert S. Sandler, MD, MPH
Division of Gastroenterology and Hepatology, University of North Carolina

Dr. Sandler is a consultant for POZEN Inc.

The good news about colorectal cancer (CRC) is that the incidence and the mortality have been decreasing progressively since the early 1970's. The bad news is that CRC remains the second leading cause of cancer death in the U.S. with an estimated 51,690 deaths in 2012. Risks for developing and dying from CRC are not equally distributed by race. Both the incidence and mortality of CRC are greater in African Americans, who also develop the disease at a younger age than whites. In order to have the greatest impact, however, I would argue against a policy of screening African Americans at an earlier age. Screening African American earlier just does not make sense.

What do the guidelines recommend?

Unfortunately, guidelines have reached different conclusions. The guidelines developed jointly by the American Cancer Society and the U.S. Multisociety Task Force, of which AGA is a part, recommend that screening start at age 50 for everyone[1] as do guidelines from the U.S. Preventive Services Task Force. The American College of Gastroenterology,[2] influenced in part by Agrawal *et al.*,[3] recommend screening African Americans starting at age 45. The Institute for Clinical Systems Improvement similarly suggests age 45 for African Americans. The American College of Physicians (ACP), after reviewing the aforementioned guidelines, inexplicably recommended that screening start at age 40 for African Americans.[4] There is clearly no consensus among the guidelines, suggesting that there is no definitive "right" answer.

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WE SHOULD SCREEN AFRICAN AMERICANS EARLIER: IT IS A RECALIBRATION ISSUE

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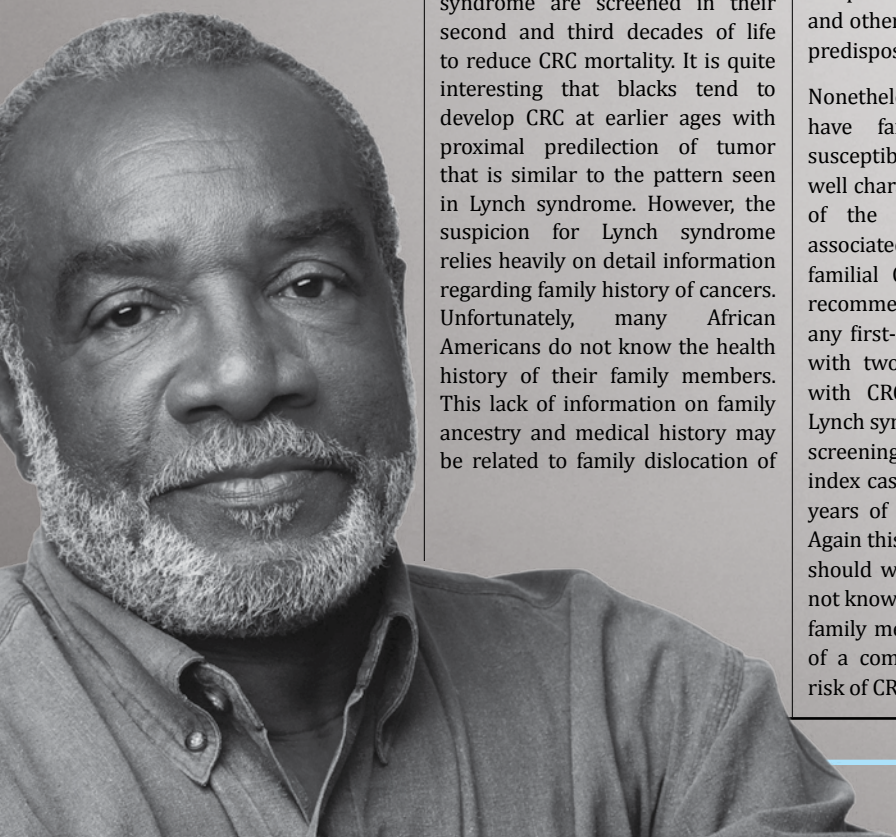
treatment are covered benefits, are more likely to present at younger ages and are more likely to present with proximal CRC. These studies suggest underlying biological differences. Perhaps, CRC disparity by race is due to a combination of these factors.

Knowledge of family history of cancer

The strongest risk factor for the development of CRC is genetic susceptibility. Although approximately 70 percent of CRC are sporadic, these CRC may actually be due to unidentified inherited defects. Nonetheless, the remaining 30 percent of CRC have familial predisposition, but well characterized syndromes such as Familial Adenomatous Polyposis syndrome (FAP) and Lynch syndrome account for only 5 percent of these.

> ... given the lack of knowledge of family health history among African Americans, it is imperative to begin CRC screening earlier than 50 years of age among this high-risk population.



Families with FAP and Lynch syndrome are screened in their second and third decades of life to reduce CRC mortality. It is quite interesting that blacks tend to develop CRC at earlier ages with proximal predilection of tumor that is similar to the pattern seen in Lynch syndrome. However, the suspicion for Lynch syndrome relies heavily on detail information regarding family history of cancers. Unfortunately, many African Americans do not know the health history of their family members. This lack of information on family ancestry and medical history may be related to family dislocation of the old and lack of stability in the family dynamics among African Americans in the present day. Therefore, it is not surprising that there is paucity of data among African Americans with regards to the prevalence of Lynch syndrome and other inherited conditions that predispose to CRC.

Nonetheless, 25 percent of CRC have familial tendencies with susceptibility patterns that are not well characterized. Our recognition of the increased risk of CRC associated with this nonsyndromic familial CRC is the rationale for recommending that subjects with any first-degree relative and those with two second-degree relatives with CRC (other than FAP and Lynch syndrome) should begin CRC screening 10 years earlier than the index case in the family or at forty years of age, whichever is earlier. Again this begs the question, "What should we do for subjects who do not know the health history of their family members, but are members of a community with the highest risk of CRC mortality?"

Proffering practical solutions

While dietary and lifestyle factors have been associated with increased risk of CRC, there is little evidence to suggest that dietary changes and lifestyle modification actually reduce CRC risk among those with increased susceptibility to the disease. Comprehensive dietary change and fiber supplementation did not affect adenoma recurrence in the Polyp Prevention Trial and Wheat Bran Fiber Study. The use of non-steroidal anti-inflammatory drugs and aspirin as chemopreventive agents is hampered by unfavorable risk-benefit ratio. Only screening with fecal occult blood testing and flexible sigmoidoscopy reduced CRC mortality in randomized trials. Moreover, African Americans generally have lower socio-economic status, have more challenges obtaining and consuming fresh fruits and vegetables, and tend to live in neighborhoods with minimal recreational facilities for physical activities.

Within the Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial (the only CRC screening trial with a large number of blacks), we noted that when compared with non-Hispanic whites, non-Hispanic blacks were less likely to undergo the trial sponsored flexible sigmoidoscopy and were less likely to undergo diagnostic colonoscopy following an abnormal sigmoidoscopy in which a polyp or mass was found.[3] Although we did not find any racial difference in prevalence of colorectal neoplasia among compliant participants at baseline, CRC incidence and

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WE SHOULD NOT SCREEN AFRICAN AMERICANS EARLIER: THE GUIDELINES ARE UNCLEAR

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How great is the risk for African Americans?

Data from the Surveillance Epidemiology and End Results (SEER) Registry can help determine the potential impact of screening. SEER meticulously collects incidence and mortality data on about 28 percent of the U.S. population. While CRC mortality is higher for African Americans, a number of factors impact mortality including access to medical care, delay in seeking care, differences in treatment and tumor biology. Incidence of cancer would therefore be a better measure to gauge the potential impact of screening. The incidence of CRC by age, race and gender is shown in Figure 1.

> ... to have the greatest impact on erasing disparities we would focus efforts on screening African Americans after age 50, not before.

From the figure there are three important conclusions. First, although the risk for African Americans at age 45 is higher than for whites, the risk for all groups is low and the lines on the graph are nearly superimposable (the absolute difference in rates is small). Secondly, the risk for CRC for all groups increases strikingly after age 50, which explains recommendations to start CRC screening at age 50. Thirdly, the risk for African Americans deviates most from whites after age 50. It is after age 50 where there are the highest rates and the greatest disparities for African Americans. Therefore, to have the greatest impact on erasing disparities we would focus efforts on screening African Americans after age 50, not before.

Number needed to screen

Using the most recent SEER data from 2005-2009, the incidence rate for black men age 45-49 is 39.8 per 100,000 compared to a rate for white men of 30.8, a relative increase of 29 percent. The relative increase for black women is 43 percent. Given these higher relative risks, let's suppose we decided to start screening African Americans at age 45. As shown in Figure 2, we would need to screen 2,512 African American men or 2,816 African American women to detect one cancer. If we waited until age 50, the

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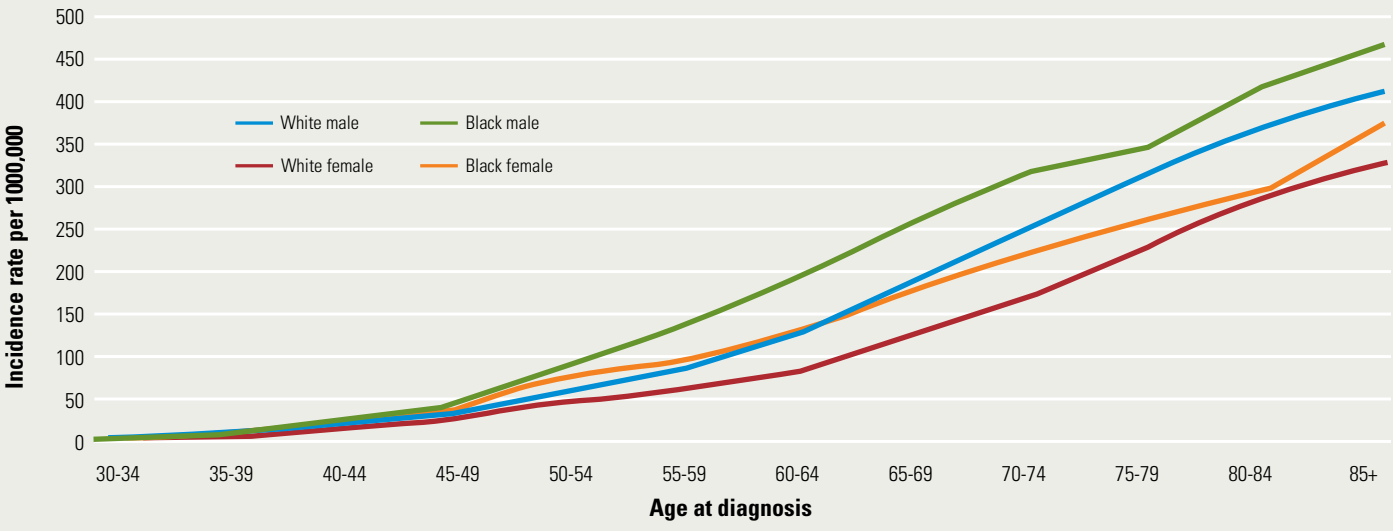
Figure 1: Age-specific SEER incidence rates, 2005-2009.



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mortality were higher among blacks in both screen and usual-care arms when compared to whites within the same randomization assignment. However, while the distal CRC mortality among blacks in the usual-care arm was twice that of whites in the usual-care arm, blacks in the screen arm had similar distal CRC mortality as whites, but significantly higher proximal CRC mortality. While this finding suggests that screening may ameliorate CRC disparity, it underscores important differences in susceptibility by race.

improving CRC screening and early detection of malignancy needs to be at the core of any pragmatic approach to reduce the burden of CRC among African Americans.

Therefore, improving CRC screening and early detection of malignancy needs to be at the core of any pragmatic approach to reduce the burden of CRC among African Americans. However, given the lack of knowledge of family health history among African Americans, it is imperative to begin CRC screening earlier than 50 years of age among this high-risk population. This should be done in conjunction with improving access, encouraging utilization of health-care resources and promoting family health discussions. This will serve as a recalibration of risk among African Americans in the next one or two generations to identify the subset of African American families at increased risk in order to establish a "new beginning" for them. We need uniformity in the recommended starting age of screening for African Americans, whether 40[4] or 45[5] years, to avoid confusion among care providers.

REFERENCES

1. Laiyemo AO. In search of a perfect solution to ensure that "no colon is left behind". *Dig Dis Sci.* 2012 Feb;57(2):263-5.

2. Bolen JC, Rhodes L, Powell-Griner EE, Bland SD, Holtzman D. State-specific prevalence of selected health behaviors, by race and ethnicity--Behavioral Risk Factor Surveillance System, 1997. MMWR CDC Surveill Summ. 2000 Mar 24;49(2):1-60.

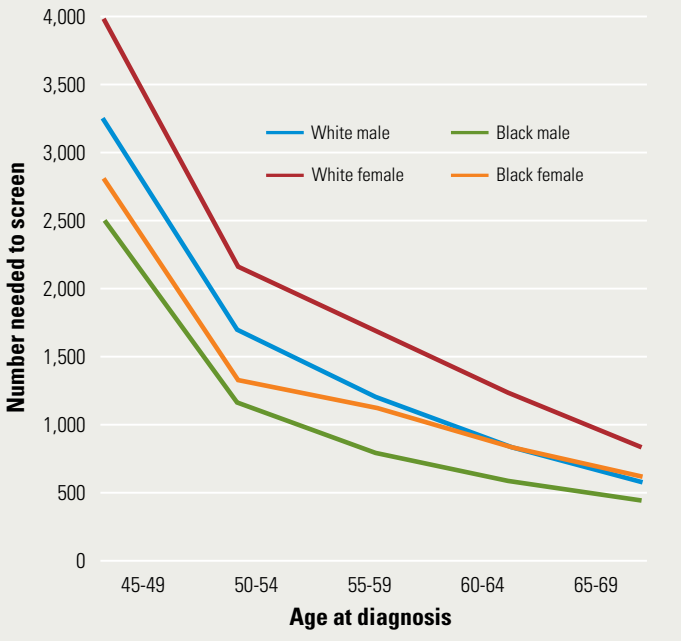
3. Laiyemo AO, Doubeni CA, Pinsky PF, *et al.* Race and Colorectal Cancer Disparities: Healthcare Utilization versus Different Cancer Susceptibilities. *J Natl Cancer Inst.* 2010;102(8):538-46.

4. Qaseem A, Denberg TD, Hopkins RH Jr, *et al;* Clinical Guidelines Committee of the American College of Physicians. Screening for colorectal cancer: a guidance statement from the American College of Physicians. *Ann Intern Med.* 2012 Mar 6;156(5):378-86. Erratum in: *Ann Intern Med.* 2012 Jul 17;157(2):152.

5. Rex DK, Johnson DA, Anderson JC, Schoenfeld PS, Burke CA, Inadomi JM; American College of Gastroenterology. American College of Gastroenterology guidelines for colorectal cancer screening 2009 [corrected]. *Am J Gastroenterol.* 2009 Mar;104(3):739-50.

Figure 2

Number needed to screen to detect one cancer by age, race and sex.



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number needed to screen to detect one cancer is 1,140 for men or 1,305 for women — less than half. If we started screening African Americans at age 40 as recommended by the ACP, the number needed to screen for men is an astonishing 4,630 for men and 5,181 for women!

The point is simply that we could have a far greater impact on overall cancer incidence by focusing our efforts on those at higher risk, specifically those over age 50. A complex microsimulation model that individualized screening by gender and race found only marginal effects on lifetime costs and outcomes by starting screening in African Americans at an earlier age than whites.[5] The authors raised the possibility that complex guidelines might confuse providers and consumers and decrease adherence thereby offsetting any benefits of individualized screening based on race.

Are we doing a good job with screening?

Data from the Behavioral Risk Factor Surveillance System of the CDC from 2010 indicate that only 60.3 percent of African Americans have been screened for colorectal cancer compared to 66.1 percent for whites. This represents a substantial improvement since 2005 when the rate for African Americans was 43.9 percent. There are also data, largely from whites, showing that we do a poor job getting patients with advanced adenomas back for surveillance exams.[6] Doing a better job with screening and surveillance exams could have a more important impact on incidence and mortality than a change in the starting age for screening.

Conclusion

There is no doubt that the incidence of colorectal cancer in African Americans is greater than whites and that they develop the disease at a younger age. I would certainly not discourage a 45 year old African American interested in screening. However, I would also not change the guidelines. Instead I would focus efforts on African Americans over age 50 where we could have far greater impact on erasing disparities and decreasing the burden of CRC.

REFERENCES

1. Levin B, Lieberman DA, McFarland B, Andrews KS, Brooks D, Bond J, Dash C, Giardiello FM, Glick S, Johnson D, Johnson CD, Levin TR, Pickhardt PJ, Rex DK, Smith RA, Thorson A, Winawer SJ. Screening and surveillance for the early detection of colorectal cancer and adenomatous polyps, 2008: a joint guideline from the American Cancer Society, the US Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology. *Gastroenterology* 2008;134:1570-1595.

2. Rex DK, Johnson DA, Anderson JC, Schoenfeld PS, Burke CA, Inadomi JM. American College of Gastroenterology guidelines for colorectal cancer screening 2009 [corrected]. *Am J Gastroenterol* 2009;104:739-750.

3. Agrawal S, Bhupinderjit A, Bhutani MS, Boardman L, Nguyen C, Romero Y, Srinivasan R, Figueroa-Moseley C. Colorectal cancer in African Americans. *Am J Gastroenterol* 2005;100:515-523.

4. Qaseem A, Denberg TD, Hopkins RH, Jr., Humphrey LL, Levine J, Sweet DE, Shekelle P. Screening for colorectal cancer: a guidance statement from the American College of Physicians. *Ann Intern Med* 2012;156:378-386.

5. Lansdorp-Vogelaar I, van BM, Zauber AG, Boer R, Wilschut J, Winawer SJ, Habbema JD. Individualizing colorectaloscopy screening by sex and race. *Gastrointest Endosc* 2009;70:96-108, 108.

6. Schoen RE, Pinsky PF, Weissfeld JL, Yokochi LA, Reding DJ, Hayes RB, Church T, Yurgalevich S, Doria-Rose VP, Hickey T, Riley T, Berg CD. Utilization of surveillance colorectaloscopy in community practice. *Gastroenterology* 2010;138:73-81.

Genetic Variations and Environmental Exposures Influence the Pathogenesis of Inflammatory Bowel Disease

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Dr. Deshpande has served on the speakers' bureaus for UCB Inc. and Abbott Laboratories.

Inflammatory bowel disease (IBD) affects approximately 1 million Americans and millions of others worldwide. Its geographic clustering through Western Europe and North America has led to the long-standing belief that non-whites were unlikely to develop IBD and that much of what determines propensity to develop the disease is heritable. However, there is an increasing prevalence of IBD and other autoimmune diseases in non-white races and numerous ethnic groups, likely in part due to improved sanitation across the world. These data have made it clear that more than just genetics is involved in the pathogenesis of IBD and that the environment is a critical component.

Actually, IBD likely represents a spectrum of diseases that involve the complex interplay of genetics, the mucosal immune system, the microbiome, diet and a myriad of environmental factors. So we wondered whether the phenotype of IBD is different across ethnic groups? And if so, is this due to genetics, environmental exposures or the interplay between the two? I submit that IBD phenotype is influenced by (race and/or) ethnicity. Yet, while some of this influence is driven by genetics, there are environmental differences between ethnic groups that account for varying presentations as well.

Several studies examined the phenotypic differences in IBD across ethnicities. For example, it has been reported that black Americans with Crohn's have different disease distribution and need for surgery compared with Hispanics and non-Hispanic whites (NHW). There are also differences in the frequencies of extra-intestinal manifestations across ethnicities in the U.S. Studies from other continents further delineate phenotypic differences across races. What has always been hard to tease out in these studies is the relative contributions of genetics and environment, both dietary and socio-economic. In addition, the definitions of race and ethnicity are inconsistent, usually boiling down to self-report, which leads to issues with consistency of data.

With the advent of genome-wide association studies, we are now able to catalog ever-expanding single-nucleotide polymorphisms (SNPs). While 15 years ago we were only starting to discover the specific genetic abnormalities associated with IBD, a recent paper described 163 loci associations. We hope that these SNPs will provide a better understanding of the genetic basis of ethnic differences in IBD. A great example of the use of this technology is the IL28B SNP in patients with hepatitis C; the prevalence of the CC and TT alleles in blacks, whites and Asians has provided us greater insight into the disparities in response to interferon-based hepatitis C therapies across ethnicities. We expect to soon find that some of the ethnic differences in IBD phenotype and treatment could also be explained by some of the SNPs found in IBD.

We have a large cohort of Hispanic patients followed at our Crohn's and Colitis Center at the University of Miami and we have had the opportunity to closely study ethnic differences in this group. We recently published data showing differences between Hispanics and NHW with regard to age of diagnosis, IBD subtype, rate of surgery and types of medications used. Although this suggests a possible genetic basis for the phenotypic differences phenotype may also be influenced by migration patterns. In unpublished data we have calculated a genetic load based on known SNPs and found no difference in the burden of SNPs between Hispanics and NHW with IBD. Those with a higher load presented with IBD at an earlier age, driven mostly by U.S.-born Hispanics and NHW rather than by foreign-born Hispanics. This suggests that differences are not uniquely genetic (Hispanic versus NHW) but also environmental (born in the U.S. versus abroad). Foreign-born Hispanics were also older at diagnosis and more likely to have ulcerative colitis compared with U.S.-born Hispanics and NHW. In addition U.S.-born Hispanics more closely resembled the NHW cohort in terms of age of diagnosis and propensity towards Crohn's disease. The resemblance of Hispanic phenotypes to those of NHW in just one generation is far too rapid to be explained by genetic changes alone. Thus, this is our most compelling data that some of the phenotypic differences between ethnicities must be environmental, with different diets, sets of exposures and intestinal microbiota in the U.S. compared with those of their countries of origin.

Access to medical care and utilization of medical services become important when discussing observations regarding disease phenotype as some ethnicities are unevenly represented across socio-economic strata. At our university's IBD referral clinic and adjacent county safety-net clinics, uninsured patients were less likely to receive immunomodulators and biologics. But when Hispanics and non-Hispanics were compared controlling for clinic attended, there was no difference in medical therapy. We also have soon-to-be-published data that will describe equal rates of IBD surgery in Hispanics and non-Hispanics when accounting for access to care. So perhaps some of the differences seen in IBD patients across ethnicities are representative of socio-economic status and utilization of health care rather than ethnicity alone.

In our studies with U.S.- and foreign-born Hispanics, we have observed the contribution of genetics and the environment, the latter including both local factors (e.g. diet, microbiome and toxins) as well as more global features (e.g. socio-economic). Thus, both genetic variations amongst populations and environmental exposures are critical in determining the phenotypic and treatment response differences in IBD across ethnicities. As we learn more through epidemiologic, genetic and microbiome studies, we will be able to better define the role each of these factors play on the pathogenesis of IBD. ■

Arguing for Increased Diversity In Gastroenterology: Shaping the Next Generation of Gastroenterologists

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University of California San Diego

Dr. Gutiérrez had no relevant conflicts to disclose.

Jesús Rivera-Nieves, MD, AGAF

University of California San Diego
Chair, AGA Underrepresented Minorities Committee

Dr. Rivera-Nieves had no relevant conflicts to disclose.

The face of medicine has begun to change in the last few decades with greater participation of women in the field. However, this change has not kept pace with the dramatic demographic changes in our country over the same period. Gastroenterology is likely further behind as, of the 4,742 AGA domestic physician members who have indicated their ethnicity (there are 10,282 total), only 424 have self-identified as African American or Hispanic.

Minorities are the fastest growing segments of our population and, by 2050, the number of non-Hispanic whites in the U.S. is expected to dip below 50 percent for the first time in history (see Figure 1). National efforts have attempted to increase the pipeline of underrepresented minorities (URMs) into the health sciences, but this pipe carries just a trickle of black and Hispanic students (see Figure 2) and many more are lost, before reaching positions in competitive subspecialties such as gastroenterology and hepatology. When these students arrive at medical school they find few minority role models and mentors, since the number of URM faculty members has remained essentially flat for several decades.

Although no data exists on the ethnic diversity of GIs in the U.S., extrapolation from domestic AGA members who identify their race as African American or Hispanic make up only 4.4 and 4.5 percent, respectively. The reason for the low rates of minorities in our field is unclear; however, it has long been noted that when minorities choose medical professions they are most likely to become primary care physicians[1] and reciprocally less likely to enter subspecialties. While the debate on diversity in medicine will continue, we as a community need to assign our own value to increasing diversity to our field.

Health disparities in gastroenterology

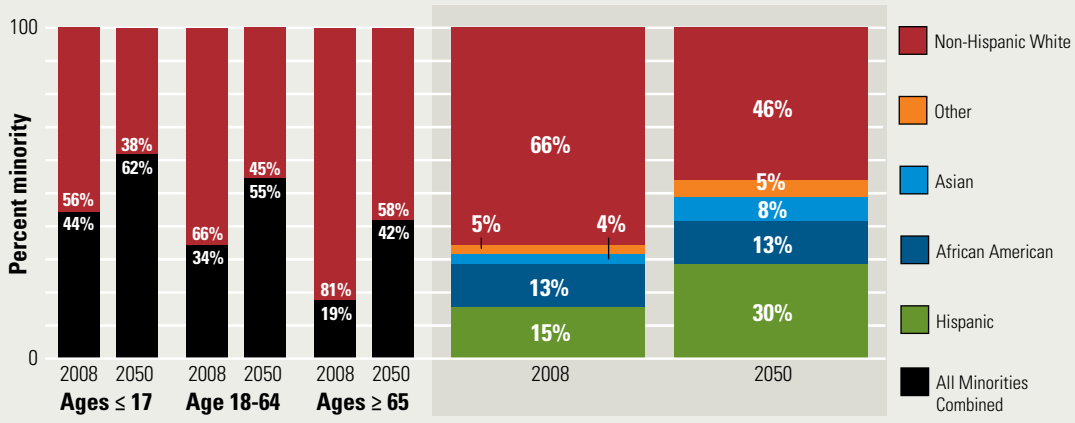
Conditions treated and diagnosed by the GI are common and sometimes epidemic within some of our minority communities. African Americans are more likely than Caucasians to present with colorectal cancer before age 50, have higher incidence rates and have decreased survival after diagnosis.[2] Non-Hispanic blacks are twice as likely to have anti-hepatitis C antibodies than whites.[3] Hepatitis B continues to be an epidemic amongst Asian-born,[4] while Latinos are twice as likely to die of cirrhosis compared with Caucasians.[5]

Talking tough?

Asking why diversity might be important to our field at a dinner party can generate as much controversy as gun control or abortion. From our perspective there is much to gain by finding intelligent minority students interested in a career in GI, especially as minority students will be the majority in just two decades. For a more diverse future in gastroenterology, AGA members, GI fellowship program directors and division chiefs should work together to recruit and retain minorities and provide them with adequate mentoring, so that they are successful and serve as role models and mentors to future generations of physicians.

A diverse GI community may be more inclined to address and broaden research questions in health disparities in our field and improve the health and well being of our minority (soon to be majority) population. Minority physicians attract race/ethnic concordant patient encounters, which increases patient satisfaction.[6] URMs are also significantly more likely to practice in underserved communities than their white counterparts.[7] Others contend that adding diversity to a team facilitates productivity by fostering a more creative and innovative workforce. Minority doctors may influence other physicians by

Figure 1: Racial and ethnic changes in the U.S. population between 2008 and 2050.



REFERENCES

1. Palepu A, Carr PL, Friedman RH, Ash AS, Moskowitz MA. Specialty choices, compensation, and career satisfaction of underrepresented minority faculty in academic medicine. *Acad Med* 2000;75:157-160.

2. Agrawal S, Bhupinderjit A, Bhutani MS, *et al.* Colorectal cancer in African Americans. *Am J Gastroenterol* 2005;100:515-23; discussion 514.

3. Armstrong GL, Wasley A, Simard EP, McQuillan GM, Kuhnert WL, Alter MJ. The prevalence of hepatitis C virus infection in the United States, 1999 through 2002. *Ann Intern Med* 2006;144:705-714.

4. Centers for Disease Control and Prevention (CDC). Screening for chronic hepatitis B among Asian/Pacific Islander populations--New York City, 2005. *MMWR Morb Mortal Wkly Rep* 2006;55:505-509.

5. Yoon YH, Yi HY, Thomson PC. Alcohol-related and viral hepatitis C-related cirrhosis mortality among Hispanic subgroups in the United States, 2000-2004. *Alcohol Clin Exp Res* 2011;35:240-249.

6. Komaromy M, Grumbach K, Drake M, *et al.* The role of black and Hispanic physicians in providing health care for underserved populations. *N Engl J Med* 1996;334:1305-1310.

7. Grumbach K, Mendoza R. Disparities in human resources: addressing the lack of diversity in the health professions. *Health Aff* (Millwood) 2008;27:413-422.

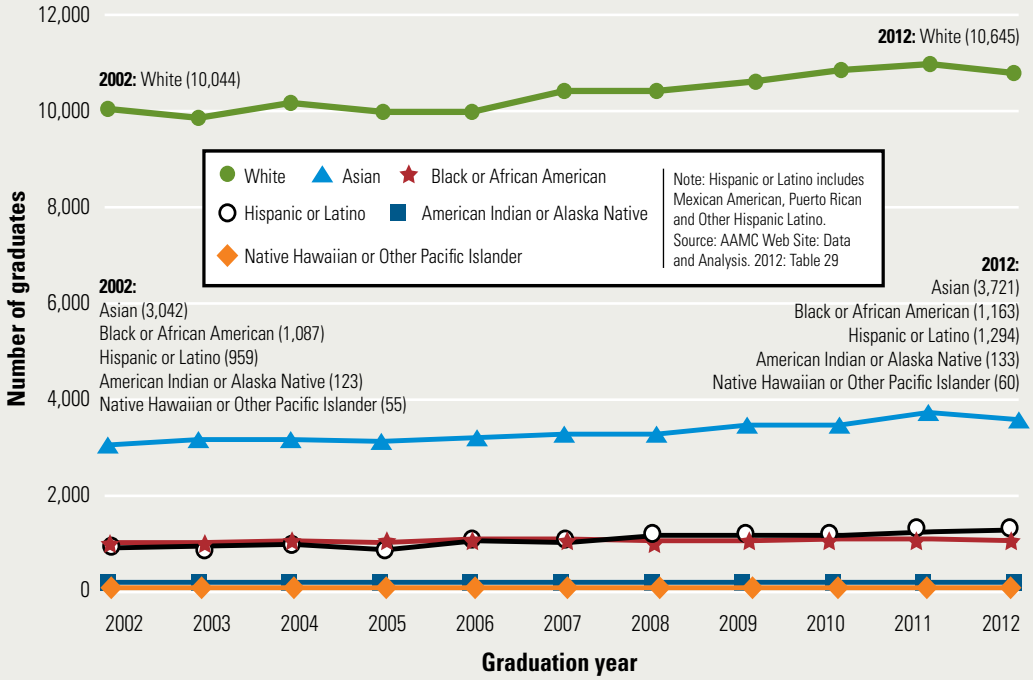
exchanging cultural mōrēs. Yet perhaps the most compelling argument is the predicted physician shortfall in the next decade. As we look for young physicians, the fastest growing segments of the population could provide capable individuals willing to care for our growing aging population.

Investing in the future

AGA and ASGE are sponsoring a series of events to educate minority students and residents on the benefits of a career in gastroenterology. During the upcoming meeting of the Latino Medical Student Association, we will introduce minority students to GI, through a didactic session followed by a hands-on endoscopy session. It will be a chance for us to seek out mentees and engage the next generation of San Diego physicians with the exciting tools of our specialty. The number of minority GIs is too small for us to address this problem alone, thus we need all of the AGA membership to recognize the value of diversity and jointly support our efforts. We have much to gain and definitely nothing to lose. ■

Figure 2

Race and/or ethnic composition of medical schoool graduates between 2002 and 2012.



Classifieds

MONTANA

Benefis Hospitals, one of America's top 100 hospitals, is seeking a second employed gastroenterologist to join an established GI practice in Great Falls, Montana to assist in serving the community of Great Falls and north central Montana.

Applicants must be board certified and ERCP trained. This opportunity is available because one independent GI physician retired and a second exited his hospital practice creating an urgent need. The gastroenterologists who remain cannot absorb the retiring physician's busy practice with volumes of roughly 130 follow-up endoscopy cases monthly along with daily consults. There is an open opportunity for endoscopic ultrasound, a service not currently provided in Great Falls.

The endoscopy unit includes six endoscopy suites and one bronch lab. It is designed as an ASC and all patients are managed within the unit with occasional procedures in the OR, primarily pediatric patients.

The office practice is located in the new Benefis Medical Professional Building which is connected to the hospital for easy access.

Work Hours and Call Coverage:

The retired physician saw six to seven consult patients daily, with half-day office hours. There are no weekend clinic hours. Physicians currently take their own call during the week and rotate weekends. Hospital call schedule is one in four allowing time to enjoy the Great Falls lifestyle.

Procedures (performed by retiring gastroenterologist):

Approximately 2,000 procedures a year

- 1,200 colonoscopies (12-14 scopes a day)
- 600-700 EGDs
- 75 ERCPs
- 40 flexible sigmoidoscopies
- 30-40 PEG tube placements

Endoscopy FACTS:

- Olympus equipment
- Endoscopy suites and one bronchoscopy suite
- 10 bed recovery unit
- Experienced and helpful staff of RNs and techs

Compensation and Benefits:

This opportunity is an employed position. We offer a nationally competitive compensation based on a productivity model and our comprehensive benefits include paid vacation, retirement plan, generous CME, relocation assistance and malpractice.

If interested, please contact:

Abby Meschberger, Physician Recruiter
Email: abbymeschberger@benefis.org
Phone: 406-731-8889 or 800-648-6620
Fax: 406-731-8890
Website: www.benefis.org

DEXILANT WORKS A SECOND SHIFT TO HELP SHUT DOWN ACID PUMPS

Conclusions of comparative efficacy cannot be drawn from this information.

96% OF 24-HOUR PERIODS REMAINED HEARTBURN FREE IN A 6-MONTH STUDY[1]

Overall treatment Median percentage of 24-hour heartburn-free periods of the maintenance of healed EE study vs 29% with placebo. Secondary efficacy endpoint, $p<0.0025$.[1,2]

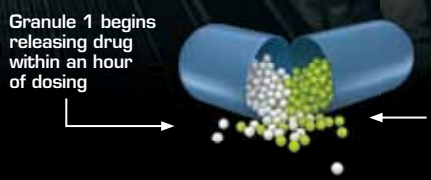
DEXILANT 30 mg (n=132); Placebo (n=141)

DEXILANT 30 mg provides effective maintenance of EE healing

- 66% of patients remained healed over 6 months with DEXILANT 30 mg (n=125) vs 14% with placebo (n=119; $p<0.00001$). Study primary endpoint.[1,2]

Results of a 6-month, multicenter, double-blind, placebo-controlled, randomized study of patients who had successfully completed an EE study and showed endoscopically confirmed healed EE. Based on crude-rate estimates, patients who did not have endoscopically documented relapse and prematurely discontinued were considered to have relapsed.

DDR DEXILANT WORKS WITH A DUAL DELAYED RELEASE FORMULATION



Artistic rendition of granules.

Indications for DEXILANT (dexlansoprazole)

- Healing all grades of erosive esophagitis (EE) for up to 8 weeks
- Maintaining healing of EE and relief of heartburn for up to 6 months
- Treating heartburn associated with symptomatic non-erosive gastroesophageal reflux disease (GERD) for 4 weeks

Important Safety Information

- DEXILANT is contraindicated in patients with known hypersensitivity to any component of the formulation. Hypersensitivity and anaphylaxis have been reported with DEXILANT use.
- Symptomatic response with DEXILANT does not preclude the presence of gastric malignancy.
- PPI therapy may be associated with increased risk of *Clostridium difficile* associated diarrhea.
- Long-term and multiple daily dose PPI therapy may be associated with an increased risk for osteoporosis-related fractures of the hip, wrist, or spine. Patients should use the lowest dose and shortest duration of PPI therapy appropriate to the condition being treated.
- Hypomagnesemia has been reported rarely with prolonged treatment with PPIs.
- Most commonly reported adverse reactions were diarrhea (4.8%), abdominal pain (4.0%), nausea (2.9%), upper respiratory tract infection (1.9%), vomiting (1.6%), and flatulence (1.6%).
- Do not co-administer atazanavir with DEXILANT because atazanavir systemic concentrations may be substantially decreased. DEXILANT may interfere with absorption of drugs for which gastric pH is important for bioavailability (e.g., ampicillin esters, digoxin, iron salts, ketoconazole). Patients taking concomitant warfarin may require monitoring for increases in international normalized ratio (INR) and prothrombin time. Increases in INR and prothrombin time may lead to abnormal bleeding and even death. Concomitant tacrolimus use may increase tacrolimus whole blood concentrations. DEXILANT may increase serum levels of methotrexate.

Please see adjacent brief summary of prescribing information for DEXILANT.

References: 1. DEXILANT (dexlansoprazole) package insert, Takeda Pharmaceuticals America, Inc. **2.** Metz DC, Howden CW, Perez MC, et al. *Aliment Pharmacol Ther.* 2009;29:742-754.

DEXILANT
dexlansoprazole
30 MG | 60 MG DELAYED RELEASE CAPSULES

Two releases. One pill.

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Visit DexilantHCP.com today!

BRIEF SUMMARY OF FULL PRESCRIBING INFORMATION
DEXILANT (dexlansoprazole) delayed-release capsules for oral use

INDICATIONS AND USAGE

DEXILANT is indicated for:

- healing of all grades of erosive esophagitis (EE) for up to 8 weeks
- maintaining healing of EE and relief of heartburn for up to 6 months
- the treatment of heartburn associated with symptomatic non-erosive gastroesophageal reflux disease (GERD) for 4 weeks

CONTRAINDICATIONS

DEXILANT is contraindicated in patients with known hypersensitivity to any component of the formulation. Hypersensitivity and anaphylaxis have been reported with DEXILANT use *[see Adverse Reactions]*.

WARNINGS AND PRECAUTIONS

Gastric Malignancy
Symptomatic response with DEXILANT does not preclude the presence of gastric malignancy.

***Clostridium Difficile* Associated Diarrhea**
Published observational studies suggest that PPI therapy like DEXILANT may be associated with an increased risk of *Clostridium difficile* associated diarrhea, especially in hospitalized patients. This diagnosis should be considered for diarrhea that does not improve *[see Adverse Reactions]*.

Patients should use the lowest dose and shortest duration of PPI therapy appropriate to the condition being treated.

Bone Fracture
Several published observational studies suggest that PPI therapy may be associated with an increased risk for osteoporosis-related fractures of the hip, wrist or spine. The risk of fracture was increased in patients who received high-dose, defined as multiple daily doses, and long-term PPI therapy (a year or longer). Patients should use the lowest dose and shortest duration of PPI therapy appropriate to the conditions being treated. Patients at risk for osteoporosis-related fractures should be managed according to established treatment guidelines *[see Adverse Reactions]*.

Hypomagnesemia
Hypomagnesemia, symptomatic and asymptomatic, has been reported rarely in patients treated with PPIs for at least three months, in most cases after a year of therapy. Serious adverse events include tetany, arrhythmias, and seizures. In most patients, treatment of hypomagnesemia required magnesium replacement and discontinuation of the PPI.

For patients expected to be on prolonged treatment or who take PPIs with medications such as digoxin or drugs that may cause hypomagnesemia (e.g., diuretics), health care professionals may consider monitoring magnesium levels prior to initiation of PPI treatment and periodically *[see Adverse Reactions]*.

Concomitant use of DEXILANT with Methotrexate
Literature suggests that concomitant use of PPIs with methotrexate (primarily at high dose; see methotrexate prescribing information) may elevate and prolong serum levels of methotrexate and/or its metabolite, possibly leading to methotrexate toxicities. In high-dose methotrexate administration, a temporary withdrawal of the PPI may be considered in some patients *[see Drug Interactions]*.

ADVERSE REACTIONS

Clinical Trials Experience
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The safety of DEXILANT was evaluated in 4548 patients in controlled and uncontrolled clinical studies, including 863 patients treated for at least 6 months and 203 patients treated for one year. Patients ranged in age from 18 to 90 years (median age 48 years), with 54% female, 85% Caucasian, 8% Black, 4% Asian, and 3% other races. Six randomized controlled clinical trials were conducted for the treatment of EE, maintenance of healed EE, and symptomatic GERD, which included 896 patients on placebo, 455 patients on DEXILANT 30 mg, 2218 patients on DEXILANT 60 mg, and 1363 patients on lansoprazole 30 mg once daily.

Most Commonly Reported Adverse Reactions
The most common adverse reactions (≥2%) that occurred at a higher incidence for DEXILANT than placebo in the controlled studies are presented in Table 2.

Table 2: Incidence of Adverse Reactions in Controlled Studies

Adverse Reaction	Placebo (N=896) %	DEXILANT 30 mg (N=455) %	DEXILANT 60 mg (N=2218) %	DEXILANT Total (N=2621) %	Lansoprazole 30 mg (N=1363) %
Diarrhea	2.9	5.1	4.7	4.8	3.2
Abdominal Pain	3.5	3.5	4.0	4.0	2.6
Nausea	2.6	3.3	2.8	2.9	1.8
Upper Respiratory Tract Infection	0.8	2.9	1.7	1.9	0.8
Vomiting	0.8	2.2	1.4	1.6	1.1
Flatulence	0.6	2.6	1.4	1.6	1.2

Adverse Reactions Resulting in Discontinuation
In controlled clinical studies, the most common adverse reaction leading to discontinuation from DEXILANT therapy was diarrhea (0.7%).

Other Adverse Reactions
Other adverse reactions that were reported in controlled studies at an incidence of less than 2% are listed below by body system:
Blood and Lymphatic System Disorders: anemia, lymphadenopathy
Cardiac Disorders: angina, arrhythmia, bradycardia, chest pain, edema, myocardial infarction, palpitation, tachycardia
Ear and Labyrinth Disorders: ear pain, tinnitus, vertigo
Endocrine Disorders: goiter
Eye Disorders: eye irritation, eye swelling
Gastrointestinal Disorders: abdominal discomfort, abdominal tenderness, abnormal feces, anal discomfort, Barrett's esophagus, bezoar, bowel sounds abnormal, breath odor, colitis microscopic, colonic polyp, constipation, dry mouth, duodenitis, dyspepsia, dysphagia, enteritis, eructation, esophagitis, gastric polyp, gastritis, gastroenteritis, gastrointestinal disorders, gastrointestinal hypermotility disorders, GERD, GI ulcers and perforation, hematemesis, hematochezia, hemorrhoids, impaired gastric emptying, irritable bowel syndrome, mucus stools, oral mucosal blistering, painful defecation, proctitis, paresthesia oral, rectal hemorrhage, retching
General Disorders and Administration Site Conditions: adverse drug reaction, asthenia, chest pain, chills, feeling abnormal, inflammation, mucosal inflammation, nodule, pain, pyrexia
Hepatobiliary Disorders: biliary colic, cholelithiasis, hepatomegaly
Immune System Disorders: hypersensitivity
Infections and Infestations: candida infections, influenza, nasopharyngitis, oral herpes, pharyngitis, sinusitis, viral infection, vulvo-vaginal infection
Injury, Poisoning and Procedural Complications: falls, fractures, joint sprains, overdose, procedural pain, sunburn
Laboratory Investigations: ALP increased, ALT increased, AST increased, bilirubin decreased/increased, blood creatinine increased, blood gastrin increased, blood glucose increased, blood potassium increased, liver function test abnormal, platelet count decreased, total protein increased, weight increase
Metabolism and Nutrition Disorders: appetite changes, hypercalcemia, hypokalemia
Musculoskeletal and Connective Tissue Disorders: arthralgia, arthritis, muscle cramps, musculoskeletal pain, myalgia
Nervous System Disorders: altered taste, convulsion, dizziness, headaches, migraine, memory impairment, paresthesia, psychomotor hyperactivity, tremor, trigeminal neuralgia
Psychiatric Disorders: abnormal dreams, anxiety, depression, insomnia, libido changes
Renal and Urinary Disorders: dysuria, micturition urgency
Reproductive System and Breast Disorders: dysmenorrhea, dyspareunia, menorrhagia, menstrual disorder
Respiratory, Thoracic and Mediastinal Disorders: aspiration, asthma, bronchitis, cough, dyspnoea, hiccups, hyperventilation, respiratory tract congestion, sore throat
Skin and Subcutaneous Tissue Disorders: acne, dermatitis, erythema, pruritis, rash, skin lesion, urticaria
Vascular Disorders: deep vein thrombosis, hot flush, hypertension

Additional adverse reactions that were reported in a long-term uncontrolled study and were considered related to DEXILANT by the treating physician included: anaphylaxis, auditory hallucination, B-cell lymphoma, bursitis, central obesity, cholecystitis acute, dehydration, diabetes mellitus, dysphonia, epistaxis, folliculitis, gout, herpes zoster, hyperlipidemia, hypothyroidism, increased neutrophils, MCHC decrease, neutropenia, rectal tenesmus, restless legs syndrome, somnolence, tonsillitis.

Other adverse reactions not observed with DEXILANT, but occurring with the racemate lansoprazole can be found in the lansoprazole prescribing information, ADVERSE REACTIONS section.

Postmarketing Experience
The following adverse reactions have been identified during post-approval of DEXILANT. As these reactions are reported voluntarily from a population of

uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Blood and Lymphatic System Disorders: autoimmune hemolytic anemia, idiopathic thrombocytopenic purpura
Ear and Labyrinth Disorders: deafness
Eye Disorders: blurred vision
Gastrointestinal Disorders: oral edema, pancreatitis
General Disorders and Administration Site Conditions: facial edema
Hepatobiliary Disorders: drug-induced hepatitis
Immune System Disorders: anaphylactic shock (requiring emergency intervention), exfoliative dermatitis, Stevens-Johnson syndrome, toxic epidermal necrolysis (some fatal)
Infections and Infestations: Clostridium difficile associated diarrhea
Metabolism and Nutrition Disorders: hypomagnesemia, hyponatremia
Musculoskeletal System Disorders: bone fracture
Nervous System Disorders: cerebrovascular accident, transient ischemic attack
Renal and Urinary Disorders: acute renal failure
Respiratory, Thoracic and Mediastinal Disorders: pharyngeal edema, throat tightness
Skin and Subcutaneous Tissue Disorders: generalized rash, leukocytoclastic vasculitis

DRUG INTERACTIONS

Drugs with pH-Dependent Absorption Pharmacokinetics

DEXILANT causes inhibition of gastric acid secretion. DEXILANT is likely to substantially decrease the systemic concentrations of the HIV protease inhibitor atazanavir, which is dependent upon the presence of gastric acid for absorption, and may result in a loss of therapeutic effect of atazanavir and the development of HIV resistance. Therefore, DEXILANT should not be co-administered with atazanavir.

DEXILANT may interfere with the absorption of other drugs where gastric pH is an important determinant of oral bioavailability (e.g., ampicillin esters, digoxin, iron salts, ketoconazole).

Warfarin

Co-administration of DEXILANT 90 mg and warfarin 25 mg did not affect the pharmacokinetics of warfarin or INR. However, there have been reports of increased INR and prothrombin time in patients receiving PPIs and warfarin concomitantly. Increases in INR and prothrombin time may lead to abnormal bleeding and even death. Patients treated with DEXILANT and warfarin concomitantly may need to be monitored for increases in INR and prothrombin time.

Tacrolimus

Concomitant administration of dexlansoprazole and tacrolimus may increase whole blood levels of tacrolimus, especially in transplant patients who are intermediate or poor metabolizers of CYP2C19.

Clopidogrel

Concomitant administration of dexlansoprazole and clopidogrel in healthy subjects had no clinically important effect on exposure to the active metabolite of clopidogrel or clopidogrel-induced platelet inhibition. No dose adjustment of clopidogrel is necessary when administered with an approved dose of DEXILANT.

Methotrexate

Case reports, published population pharmacokinetic studies, and retrospective analyses suggest that concomitant administration of PPIs and methotrexate (primarily at high dose; see methotrexate prescribing information) may elevate and prolong serum levels of methotrexate and/or its metabolite hydroxymethotrexate. However, no formal drug interaction studies of high-dose methotrexate with PPIs have been conducted *[see Warnings and Precautions]*.

USE IN SPECIFIC POPULATIONS

Pregnancy

Teratogenic Effects

Pregnancy Category B. There are no adequate and well-controlled studies with dexlansoprazole in pregnant women. There were no adverse fetal effects in animal reproduction studies of dexlansoprazole in rabbits. Because animal reproduction studies are not always predictive of human response, DEXILANT should be used during pregnancy only if clearly needed.

A reproduction study conducted in rabbits at oral dexlansoprazole doses up to approximately 9 times the maximum recommended human dexlansoprazole dose (60 mg per day) revealed no evidence of impaired fertility or harm to the fetus due to dexlansoprazole. In addition, reproduction studies performed in pregnant rats with oral lansoprazole at doses up to 40 times the recommended human lansoprazole dose and in pregnant rabbits at oral lansoprazole doses up to 16 times the recommended human lansoprazole dose revealed no evidence of impaired fertility or harm to the fetus due to lansoprazole.

Nursing Mothers

It is not known whether dexlansoprazole is excreted in human milk. However, lansoprazole and its metabolites are present in rat milk following the administration of lansoprazole. As many drugs are excreted in human milk, and because of the potential for tumorigenicity shown for lansoprazole in rat carcinogenicity studies *[see Nonclinical Toxicology]*, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use

Safety and effectiveness of DEXILANT in pediatric patients (less than 18 years of age) have not been established.

Geriatric Use

In clinical studies of DEXILANT, 11% of patients were aged 65 years and over. No overall differences in safety or effectiveness were observed between these patients and younger patients, and other reported clinical experience has not identified significant differences in responses between geriatric and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

Renal Impairment

No dosage adjustment of DEXILANT is necessary in patients with renal impairment. The pharmacokinetics of dexlansoprazole in patients with renal impairment are not expected to be altered since dexlansoprazole is extensively metabolized in the liver to inactive metabolites, and no parent drug is recovered in the urine following an oral dose of dexlansoprazole.

Hepatic Impairment

No dosage adjustment for DEXILANT is necessary for patients with mild hepatic impairment (Child-Pugh Class A). DEXILANT 30 mg should be considered for patients with moderate hepatic impairment (Child-Pugh Class B). No studies have been conducted in patients with severe hepatic impairment (Child-Pugh Class C).

OVERDOSAGE

There have been no reports of significant overdose of DEXILANT. Multiple doses of DEXILANT 120 mg and a single dose of DEXILANT 300 mg did not result in death or other severe adverse events. However, serious adverse events of hypertension have been reported in association with twice daily doses of DEXILANT 60 mg. Non-serious adverse reactions observed with twice daily doses of DEXILANT 60 mg include hot flashes, contusion, oropharyngeal pain, and weight loss. Dexlansoprazole is not expected to be removed from the circulation by hemodialysis. If an overdose occurs, treatment should be symptomatic and supportive.

CLINICAL PHARMACOLOGY

Pharmacodynamics

Serum Gastrin Effects

The effect of DEXILANT on serum gastrin concentrations was evaluated in approximately 3460 patients in clinical trials up to 8 weeks and in 1023 patients for up to 6 to 12 months. The mean fasting gastrin concentrations increased from baseline during treatment with DEXILANT 30 mg and 60 mg doses. In patients treated for more than 6 months, mean serum gastrin levels increased during approximately the first 3 months of treatment and were stable for the remainder of treatment. Mean serum gastrin levels returned to pre-treatment levels within one month of discontinuation of treatment.

Enterochromaffin-Like Cell (ECL) Effects

There were no reports of ECL cell hyperplasia in gastric biopsy specimens obtained from 653 patients treated with DEXILANT 30 mg, 60 mg or 90 mg for up to 12 months.

During lifetime exposure of rats dosed daily with up to 150 mg per kg per day of lansoprazole, marked hypergastrinemia was observed followed by ECL cell proliferation and formation of carcinoid tumors, especially in female rats *[see Nonclinical Toxicology]*.

Effect on Cardiac Repolarization

A study was conducted to assess the potential of DEXILANT to prolong the QT/QT_c interval in healthy adult subjects. DEXILANT doses of 90 mg or 300 mg did not delay cardiac repolarization compared to placebo. The positive control (moxifloxacin) produced statistically significantly greater mean maximum and time-averaged QT/QT_c intervals compared to placebo.

NONCLINICAL TOXICOLOGY

Carcinogenesis, Mutagenesis, Impairment of Fertility

The carcinogenic potential of dexlansoprazole was assessed using lansoprazole studies. In two 24-month carcinogenicity studies, Sprague-Dawley rats were treated orally with lansoprazole at doses of 5 to 150 mg per kg per day, about 1 to 40 times the exposure on a body surface (mg/m^2) basis of a 50 kg person of average height [1.46 m^2 body surface area (BSA)] given the recommended human dose of lansoprazole 30 mg per day.

Lansoprazole produced dose-related gastric ECL cell hyperplasia and ECL cell carcinoids in both male and female rats *[see Clinical Pharmacology]*.

In rats, lansoprazole also increased the incidence of intestinal metaplasia of the gastric epithelium in both sexes. In male rats, lansoprazole produced a dose-related increase of testicular interstitial cell adenomas. The incidence of these adenomas in rats receiving doses of 15 to 150 mg per kg per day

(4 to 40 times the recommended human lansoprazole dose based on BSA) exceeded the low background incidence (range = 1.4 to 10%) for this strain of rat.

In a 24-month carcinogenicity study, CD-1 mice were treated orally with lansoprazole doses of 15 to 600 mg per kg per day, 2 to 80 times the recommended human lansoprazole dose based on BSA. Lansoprazole produced a dose-related increased incidence of gastric ECL cell hyperplasia. It also produced an increased incidence of liver tumors (hepatocellular adenoma plus carcinoma). The tumor incidences in male mice treated with 300 and 600 mg lansoprazole per kg per day (40 to 80 times the recommended human lansoprazole dose based on BSA) and female mice treated with 150 to 600 mg lansoprazole per kg per day (20 to 80 times the recommended human lansoprazole dose based on BSA) exceeded the ranges of background incidences in historical controls for this strain of mice. Lansoprazole treatment produced adenoma of rete testis in male mice receiving 75 to 600 mg per kg per day (10 to 80 times the recommended human lansoprazole dose based on BSA).

A 26-week p53 (+/-) transgenic mouse carcinogenicity study of lansoprazole was not positive.

Lansoprazole was positive in the Ames test and the *in vitro* human lymphocyte chromosomal aberration assay. Lansoprazole was not genotoxic in the *ex vivo* rat hepatocyte unscheduled DNA synthesis (UDS) test, the *in vivo* mouse micronucleus test or the rat bone marrow cell chromosomal aberration test.

Dexlansoprazole was positive in the Ames test and in the *in vitro* chromosome aberration test using Chinese hamster lung cells. Dexlansoprazole was negative in the *in vivo* mouse micronucleus test.

The potential effects of dexlansoprazole on fertility and reproductive performance were assessed using lansoprazole studies. Lansoprazole at oral doses up to 150 mg per kg per day (40 times the recommended human lansoprazole dose based on BSA) was found to have no effect on fertility and reproductive performance of male and female rats.

PATIENT COUNSELING INFORMATION

See FDA-Approved Medication Guide

To ensure the safe and effective use of DEXILANT, this information and instructions provided in the FDA-approved Medication Guide should be discussed with the patient.

Inform the patient to watch for signs of an allergic reaction as these could be serious and may require that DEXILANT be discontinued.

Advise patients to immediately report and seek care for diarrhea that does not improve. This may be a sign of *Clostridium difficile* associated diarrhea *[see Warnings and Precautions]*.

Advise the patient to immediately report and seek care for any cardiovascular or neurological symptoms including palpitations, dizziness, seizures, and tetany as these may be signs of hypomagnesemia *[see Warnings and Precautions]*.

Advise the patient to tell their health care provider if they take atazanavir, tacrolimus, warfarin and drugs that are affected by gastric pH changes *[see Drug Interactions]*.

Advise the patient to follow the dosing instructions in the Medication Guide and inform the patient that:

- DEXILANT is available as a delayed-release capsule.
- DEXILANT may be taken without regard to food.
- DEXILANT should be swallowed whole.
- Alternatively, DEXILANT capsules can be administered as follows:
  - Open capsule;
  - Sprinkle intact granules on one tablespoon of applesauce;
  - Swallow immediately. Granules should not be chewed.
  - Do not store for later use.

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DEX006 R19 _BS L-LPD-0912-3

Journal Editors' Picks

CGH JUNE

The Evaluation and Treatment of Hemorrhoids: A Guide for the Gastroenterologist
By Robert A. Ganz

Chemoembolization and Radioembolization for Hepatocellular Carcinoma
By Riad Salem, *et al.*

Statins Are Associated With Reduced Risk of Esophageal Cancer, Particularly in Patients With Barrett's Esophagus: A Systematic Review and Meta-analysis
By Siddharth Singh, *et al.*

Safety and Efficacy of Endoscopic Mucosal Therapy With Radiofrequency Ablation for Patients With Neoplastic Barrett's Esophagus
By William J. Bulsiewicz, *et al.*

Sustained Clinical Benefit and Tolerability of Methotrexate Monotherapy After Thiopurine Therapy in Patients With Crohn's Disease
By Margien L. Seinen, *et al.*

GASTRO JUNE

Cause-Specific Mortality of People With Barrett's Esophagus Compared With the General Population: A Population-Based Cohort Study
By Masoud Solaymani-Dodaran, *et al.*

Comorbidities Affect Risk of Nonvariceal Upper Gastrointestinal Bleeding
By Colin John Crooks, *et al.*

Prevalence of Germline *PTEN, BMPR1A, SMAD4, STK11,* and *ENG* Mutations in Patients With Moderate-Load Colorectal Polyps
By Joanne Ngeow, *et al.*

Incidence, Presentation, and Outcomes in Patients With Drug-Induced Liver Injury in the General Population of Iceland
By Einar S. Björnsson, *et al.*

Acute-on-Chronic Liver Failure is a Distinct Syndrome That Develops in Patients With Acute Decompensation of Cirrhosis
By Richard Moreau, *et al.*

CGH JULY

Avoiding and Defending Malpractice Suits for Postcolonoscopy Cancer: Advice From an Expert Witness
By Douglas K. Rex

Serrated Colon Polyps as Precursors to Colorectal Cancer
By Seth Sweetser, *et al.*

Safety and Efficacy of Teduglutide After 52 Weeks of Treatment in Patients With Short Bowel Syndrome Intestinal Failure
By Stephen J.D. O'Keefe, *et al.*

Association Between Reduced Levels of Alkaline Phosphatase and Survival Times of Patients With Primary Sclerosing Cholangitis
By Lina Lindström, *et al.*

The Resurgence of Serum Alkaline Phosphatase as a Surrogate Biomarker for Prognosis in Primary Sclerosing Cholangitis
By Jayant A. Talwalkar, *et al.*

GASTRO JULY

Recurrence of Esophageal Intestinal Metaplasia After Endoscopic Mucosal Resection and Radiofrequency Ablation of Barrett's Esophagus: Results From a U.S. Multicenter Consortium
By Milli Gupta,*et al.*

Radiofrequency Ablation (RFA) and Endoscopic Mucosal Resection for Dysplastic Barrett's Esophagus and Early Esophageal Adenocarcinoma: Outcomes of UK National HALO RFA Registry
By R.J. Haidry, *et al.*

Remission of Barrett's Esophagus With Early Neoplasia Five Years After Radiofrequency Ablation With Endoscopic Resection: A Netherlands Cohort Study
By K. Nadine Phoa, *et al.*

New Oral Anticoagulants Increase Risk for Gastrointestinal Bleeding: A Systematic Review and Meta-analysis
By I. Lisanne Holster, *et al.*

Can We Make a Difference In The Obesity Epidemic?

Jeanette N. Keith, MD

Decatur Gastroenterology Associates, AL

Dr. Keith is a consultant for Abbott Laboratories, Bristol-Myers Squibb, Hospira, Merck, Pfizer, Sanofi Aventis and UCB.

It is well documented that there is an obesity epidemic in the U.S.[1, 2] Second, obesity portends a worse outcome for many gastrointestinal disorders including gastroesophageal reflux disease (GERD) and colorectal cancer.[3] Finally, gut flora and gut hormones appear to regulate body weight.[4] Thus, in this era of pay-for-performance and the need for optimizing patient satisfaction scores, there is an increasing need to address obesity in our GI practices. However, the lack of training and limited reimbursement keeps many gastroenterologists from incorporating medical weight management into our practices. During medical school, my class received approximately two hours of didactics related to nutrition in medicine. As a fourth year student, I spent a month shadowing a gastroenterologist whose practice included clinical nutrition, which shaped my career. However, as a resident, I used very little of the information learned during my senior year elective, despite caring for numerous obese patients.

It was my brush with death due to status asthmaticus during my GI fellowship and the need for long-term steroid therapy that motivated me to pursue additional training in clinical nutrition. Following my hospital discharge on high-dose prednisone, I gained 85 pounds in four months, despite all my efforts to control my weight. Suddenly and painfully, for the first time in my life, I could truly empathize with my patients. This experience was further complicated by receiving conflicting recommendations for the optimal diet from dietitians and colleagues alike. It was from this vantage point that I began my personal search for the best method to improve my health and to gain a greater understanding of obesity in order to become a more effective clinician.

Race, ethnicity and culture have a direct impact on effectiveness in medical weight management. "Ideal body weight" should be considered in a cultural context.[5] For example, in African American, Native American and Hispanic cultures, a patient's desired weight may be greater than what is considered the ideal body weight. In contrast, for my Asian and Afro-Caribbean patients, their desired weight may be lower than ideal. Consequently, years lost due to obesity-related complications occur at a lower BMI for Asians and a higher BMI for African Americans and Hispanics.

In designing weight loss programs for our patients, it is important to have measurable, achievable goals based upon lifestyle, access to food, socio-economic status and education level for both rural and urban populations. Furthermore, it is essential to understand patients' motivation for participating in the program. It is the patient's "why" that keeps them going when weight management becomes difficult. I experienced this first hand as it was my "why" that motivated me to lose the 85 pounds that I gained while on steroids. Subsequently, as director of a medical weight management program that specialized in caring for bariatric patients, I was amazed to learn that 40 percent of my younger obese patients had never cooked a meal from start to finish. They lived in multi-generational homes where they worked and their parents cooked while caring for their children or they ate out. Many also did not have access to fresh fruits and vegetables living in "food deserts". Bariatric surgery, while effective, was not an option for many due to lack of insurance. Therefore, we needed simple, directed steps capable of achieving lasting behavioral changes for our patients.

"Ideal body weight" should be considered in a cultural context. Years lost due to obesity-related complications occur at a lower BMI for Asians and a higher BMI for African Americans and Hispanics.

I have effectively incorporated evidence-based strategies into my GI practice. First, BMI is measured at each visit. Second, if the BMI is greater than 25 or the weight is increasing, we discuss motivation levels for weight loss and identify modifiable dietary habits by assessing typical meal patterns. The goal is to determine where a 500 calorie/day deficit can be made: reducing fried and fatty food, limiting simple carbohydrates, increasing fruits and vegetables and/or controlling portion sizes. Third, I ask my patients to identify one new positive dietary change they would be willing to make to each visit and track their progress. Last, I encourage them to choose one new activity to add to their daily schedule as at least one hour of physical activity per week reduces colon cancer risks.[6] When counseling a patient, a target weight with the lowest risk of obesity-related complications within a patient's cultural context is used. In less than five minutes per visit, medical weight management in the GI practice can achieve 10 percent weight loss reducing the risk for common chronic GI disorders, especially for high-risk minority populations. ■

REFERENCES

1. Flegal KM CM, Ogden CL *et al.* Prevalence and trends in obesity among US adults, 1999-2008. *JAMA* 2010;303:235-41.

2. Center for Disease Control. Difference in prevalence of obesity among black, white and hispanic adults. United States 2006-2008. www.cdc.gov/mmwr/preview/mmwrhtml/mm5827a2.htm#tab1. Accessed June 11, 2010.

3. Wise LA RL, Palmer JR *et al.* Anthropometric risk factors for colorectal polyps in African-American women. *Obesity* 2008;16:859-68.

4. Jayasena CN BS. Role of gut hormones in obesity. Endocrinol Metab *Clin N Am* 2008;37:769-87.

5. Fontaine KR RR, Wang C *et al.* Years of life lost due to obesity. *JAMA* 2003;289:187-93.

6. Sanchez NF SB, Saab S, *et al.* Physical activity reduces risk for colon polyps in a multiethnic colorectal cancer screening population. *BMC Research Notes* 2012;5:312-319.

Increasing Diversity In GI One Young Mind at a Time

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I have had the privilege of being involved in several projects that we hope will change the face of the future of gastroenterology. We know from studies that patients prefer to see physicians that they feel connected to by race and ethnicity. Gastroenterology is a more intimate specialty, and it is my impression that patients prefer to discuss their problems with a physician who shares a similar background in culture in order for them to best express themselves. There is no perfect place to start enticing young, smart, creative minds into gastroenterology. The AGA has made a commitment on various levels to increase the opportunities for young people to develop a taste for gastroenterology.

For several years, the AGA has sponsored a program titled "Investing in the Future". This program has been sponsored by the AGA Underrepresented Minorities Committee and its goal is to expose students, in particular minority students, to a career in gastroenterology. In the last two years, members of the committee in collaboration with the ASGE have spoken at several historically black medical colleges to share some of the highlights of being a gastroenterologist and to offer tips for getting into fellowship programs. Typically, these are information sessions are run by an AGA or ASGE faculty member along with a fellow from a local GI fellowship program, who can provide insight into the application process for becoming a GI fellow. In this way, we believe that we can both expose students to the field, but also give them tools to be successful in applying.

In addition to that program, the AGA has been involved in student research fellowship awards, and one of the exciting developments is that AGA was granted a competetive NIH grant to bolster this program further for underrepresented minorities. In particular, the grant will allow the AGA to provide a stipend for students to work during the summer with a mentor. The stipend will cover lodging and travel for the students as well as a stipend for expenses. In this way, we hope to stimulate an interest in gastroenterological research and make it more likely for these students to be ultimately successful in getting into a GI training program. Although this award was just granted and this is the first year of the process, the young people who have applied for these awards have been superb. The applicants have ranged from college students from Africa who have already set themselves apart by their accomplishments, to the child of Cuban immigrants attending Harvard College. The applicants have all been of the highest caliber.

The other half of that equation is the quality of the mentors. The mentors represent a wide swath of research interests as well as a wide geography from the East Coast to the West Coast. In this way, we hope to fill the needs of all the potential applicants. The mentors are all, in addition, individuals who have a commitment to improving the pipeline of underrepresented minorities.

Finally, the AGA Underrepresented Minorities Committee sponsored education and research at DDW to highlight some of the health-care disparities, and more importantly to help guide underrepresented minority trainees in their quest for a successful career, whether that be in academia or in private practice. Some might wonder whether there is anything unique to underrepresented minorities with respect to the challenges we all face. It is my belief that until we improve the representation of minorities present in the U.S. within our field of gastroenterology, we should strive to do everything possible to make these individuals successful. ■

MOBILE APPS AND GASTROENTEROLOGY

Some of the top mobile apps relevant to the GI practitioner.

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So you have a smartphone and/or touch tablet (like iPad). **Now what?**

This article highlights some of the most useful mobile applications (apps) relevant to GI practitioners and trainees.[1] The success of apps is a result of an intuitive interface that allows for the ready reference of information with as few clicks as possible.[2] This article provides examples of top apps in each of the functional categories mentioned. Most of the apps listed below support iOS (Apple) as well as Android platforms and are either free or inexpensive.[3,4]

1

Prescription drug reference

Drug pharmacopia are one of the most popular and widely used apps. Pharmacopia apps provide a point-of-care prescription drug reference tool and an interaction checker (sometimes with additional cost). Examples are:

- **Epocrates:** Comes with both paid and free lite versions.
- **Micromedex:** A lesser-known app, but with most features in the free version.
- **Lexicomp:** Requires subscription for most users.
- **Monthly Prescribing Reference (MPR):** A commonly used drug reference.

2

Medical calculators

These are essential especially for trainees in various specialties. They contain common medical and GI formulas (i.e. MELD score) and assist with drug dosing (i.e. steroid conversions). Examples are:

- **MedCalc 3000:** One of the most popular calculators (comes with a price).
- **Archimedes:** Provides specialty-focused calculators (free and paid versions).
- **Calculate by QxMD.** Basic version is free.

3

One-stop shop content

These all-inclusive apps provide access to varied resources such as the latest news, drug references, disease references, etc. Examples are:

- **Medscape:** Often ranked as the top free medical app. The drug reference section is popular and includes herbal drug references and an interaction checker. Medscape allows users offline access to its content, which is crucial for those times when the Internet is unavailable.
- **Skyscape:** This can be thought of as collection of apps including medical calculators (Archimedes), medical news alerts, practice guidelines, access to paid textbooks and drug reference (RxDrugs). Some of the apps require a one-time payment.

There is a lot to explore from the hundreds and thousands of apps currently available.

4

Access medical records

Many electronic health record vendors have their own apps that allow basic views of medical records that can serve as a very effective "rounding list". In addition, some vendors have personal health record apps that are handy when trying to elicit information from patients about their medication list and past history. Examples include Epic Haiku and Canto.

5

Literature

There are many apps that will allow you to browse through the latest medical and non-medical news. While review of general news apps (like CNN) or RSS feed readers (like Google Reader) is beyond the scope of this article, examples of medical news-specific apps are:

- **Docwise:** A personal magazine for physicians that provides access to medical journals, news and topics in one place. The app has the ability to track relevant topics for you and save them for offline reading.
- **Medpage Today:** One of the best known online medical news services that also provides continuing medical education activities within the app. Recently, MedPage Today has expanded its services to become a one-stop shop content app.
- **Journal apps:** Many journals (including *JAMA*, *NEJM*, *Gastroenterology* and *CGH*) have their own apps where you can get free tables of contents, abstracts and the full text of some articles.

6

Guidelines and best practices

These specialized medical apps provide custom recommendations based on guidelines and best practices. Examples are:

- **U.S. Preventive Services Task Force (USPSTF) electronic Preventive Services Selector:** Provides basic screening and public health information (from USPSTF) based on patient's demographics.
- **Best Practice:** From BMJ Group.
- **AGA Instant Recommendations for IBD Quality:** This new app provides instant recommendations for the management of patients with inflammatory bowel disease (IBD). The app asks six yes-or-no questions then uses national IBD quality measures to deliver quick, concise and actionable recommendations for treatment at the point of care.

7

Patient communication and education

Even though not a medical app, many providers use Google Translate to allow instant translation of English to other languages to allow communication with their patient. While not a substitute for trained medical translators (especially for informed consent, etc.), this app provides an easier and hassle-free way to start conversations. In addition, some one-stop shop apps provide content for patient education, though many of them are not designed to be used primarily by patients.

8

Cloud-based storage and retrieval of content

One of the most interesting developments has been the advent of apps that allow your content to be stored online in the cloud, which can be accessed from smartphones, tablets or desktop browsers. While many of these apps cannot be recommended for patient or research data, they do offer invaluable tools to enhance productivity (such as accessing your latest presentations or manuscripts from home, office or during travel). Examples are: Google Docs, Microsoft Skydrive, DropBox, Box and Evernote.

9

Stay connected

Social media is increasingly used for outreach and brand promotion. Most organizations have strict guidelines on what is acceptable to post on social media, so vigilance is required before adopting these apps for your practice. Examples are Facebook, Twitter, YouTube and LinkedIn apps.

10

A whole lot more!

There is a lot to explore from the hundreds and thousands of apps currently available.[3, 4] Some of the commonly used apps (outside clinical practice) provide access to emails, maps and real-time directions using in-built GPS, picture and video recording, games, and streaming media (like YouTube, podcasting). Detailed review of apps will be available at **http://egastro.org/blog**.

One of the most interesting developments has been the advent of apps that allow your content to be stored online in the cloud...

REFERENCES

1. Franko OI, Tirrell TF. Smartphone app use among medical providers in ACGME training programs. *J Med Syst.* 2012;36:3135-9.

2. Ozdalga E, Ozdalga A, Ahuja N. The smartphone in medicine: a review of current and potential use among physicians and students. *J Med Internet Res.* 2012;14:e128.

3. Apple app store. Available at https://itunes.apple.com/. Accessed March 1, 2013

4. Google Android store. Available at https://play.google.com/store. Accessed March 1, 2013

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Missionary Work

It's About More Than Doing Endoscopies

Tears were running down my cheeks as four six-year-old girls took turns (well, not really turns, more or less at the same time) showing off their newly acquired reading skills to me at Copprome Orphanage in Honduras on my most recent visit there the week before Christmas 2012. This was in contrast to these same little girls who five months previously barely knew their letters and would wander aimlessly lost in their first grade classroom with 35 other children, with little hope of learning to read. How had I been so lucky as to be a part of this amazing transformation?

It all started over 20 years ago when I was newly married and we happened to hear an Episcopal priest talk about his work in an orphanage. Having no children of our own yet, we decided to sponsor a child. Little did I know that this night would be a turning point in my life. Over the next 12 years the sponsorship kept going, I finished my fellowship, took my first job, had two boys and always wanted to visit Honduras.

Enter another fateful moment … we had moved to Yale and I did a colonoscopy on a patient that required a three-week inpatient stay because of complications (yes, a lawyer). His sister-in-law led dental trips to Honduras and we quickly established a rapport (I wasn't sued). The next thing I knew, I was on a plane with three medical students leading the medical arm of a brigade. It wasn't always easy — in fact I spoke no Spanish and had never done this before. I more or less panicked the first night there after we had set up our clinic and were expecting to see over 1,000 patients over the next five days. I told my dentist friend that I really didn't think I could do this. To which she responded, "Just do the best you can." I thought … well, I can do that. I can do my best. That first visit our medical team did evaluate 1,182 patients. Surprisingly, few rare tropical diseases — mostly diabetes, hypertension and URIs, etc. In other words, the same general medical conditions we see in the U.S.

Honduras Children's Project
www.honduraschildrensproject.org

CURE International
www.cure.org

There is a good public health-care system in Honduras; the issue is getting the people to it. You don't work, you don't get paid, so there is no concept of early detection, much less prevention. Our annual clinics went to rural areas close to the people; we took our own medicines and supplies and saw anyone who came in the door.

Now you might be asking, what would I do if I went on such a trip? The answer is just about anything, but be flexible. The second year, my then 12-year-old son accompanied us and he dispensed anti-parasite medicine — weighing patients and measuring amounts. It took my non-medical husband two more years, but when he finally did come the generators and lights worked better than they ever had before. And our younger son was now the 11-year old PIP dispenser.

We all get back to the basics and remember why we went into medicine in the first place.

A few years later, I invited my GI fellows to come and eventually four of them did, one twice. For me it's always fun to watch my fellows in very different circumstances than at Yale-New Haven Hospital (and I have to brag that they shine brightly!). On our trips, the weather is hot, the sun is strong and there are many bugs. The patients stand in long lines, are very grateful (and I don't mean as future donators) and never complain. From my fellows' viewpoint, they can practice in the field away from high-tech medicine and electronic medical records. We all get back to the basics and remember why we went into medicine in the first place. Since we take our own medicines and supplies, we dispense and take care of all issues in the field and refer that which we can't manage to the central clinics.

Now you might be wondering what the first part of this article has to do with the delivery of medicine in rural Honduras. Well, one thing leads to another, you meet like-minded people and I was introduced to Copprome. As we all spent more and more time with the kids, my older son realized that the only way to break the cycle of poverty was to ensure they received a good education. So two years ago, he founded the educational arm for Copprome, Honduras Children's Project. With his nonprofit, a teacher was hired and 14 children now go to a special education center. And through my tears as I listened to them reading, I realized that once again, I was experiencing a miracle — instead of only dreaming about reaching for the stars, these children were going to get a chance to realize their dreams. ■

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