

# BEST OF ACG 2006

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**A**t the 2006 American College of Gastroenterology (ACG) meeting, new data were presented affecting every gastroenterologic specialty. Here, *Gastroenterology & Hepatology* summarizes some of the most important presentations, with expert commentary from opinion leaders in each area.

## Presentations in Irritable Bowel Syndrome

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### **Abstract 1218** Tegaserod: Rapid Onset of Action in Patients With Chronic Constipation

Lacy and colleagues analyzed pooled data from two placebo-controlled trials of tegaserod (Zelnorm, Novartis) for the treatment of chronic constipation patients, in order to measure the rapidity of response to therapy. Response was signified by complete spontaneous bowel movement (CSBM), defined as an associated feeling of complete evacuation, or spontaneous bowel movement (SBM), defined as a bowel movement achieved without the use of a laxative or enema within the preceding 24 hours. In order to be enrolled in either study, patients had to have, at baseline, less than three CSBMs per week and one of the following symptoms at least 25% of the time: straining, incomplete evacuation, or hard and/or very hard stools. Patients were treated with either tegaserod 6 mg twice daily or placebo, and data were analyzed for the intent to treat population. The authors found that

tegaserod treatment was associated with superior time to onset of CSBM versus placebo, as well as higher percentages of patients achieving CSBM or SBM within 24 and 48 hours. The majority of patients receiving tegaserod achieved CSBM within the first 24 hours of therapy and over 90% achieved SBM within 48 hours.

**BC** This abstract provides an indirect comparison to one of the main clinical features highlighted with another recently approved agent, lubiprostone (Amitiza, Takeda/Sucampo). One of the touted characteristics of lubiprostone is the speed of onset. It works very quickly, providing SBM within 24 hours of the first dose in about 63% of patients. Investigators working with lubiprostone presented similar data at this year's ACG meeting showing a 90% rate of SBM within 48 hours. The data from Lacy and associates summarized above show nearly identical findings for tegaserod, with regard to the rapidity of onset of SBM at both 24 and 48 hours. Although there is no head-to-head comparison between agents, the two studies do level the playing field with regard to how quickly these agents appear to work for patients with chronic constipation.

Another aspect of this abstract is the concept of a CSBM, which is different from what most other agents and therapeutic trials have examined. SBM, onset of bowel movement without the help of an enema or laxative, is an objective, numbers-driven outcome. CSBM addresses some additional quality issues, implying that patients feeling completely evacuated are therefore more satisfied with their defecation habits. That is a more rigorous endpoint to measure, and the fact that tegaserod was shown to be significantly statistically better than placebo at achieving it, even in this post-hoc analysis, provides additional proof of concept. We have had clinical experience with this drug for quite a few years, so we all recognize that it works. This study adds more evidence to the already strong base that tegaserod has demonstrated.

The third concept that this study hints at for discussion is whether or not tegaserod may be suitable for intermittent use. I think that an intermittent or on-demand approach could be justified as a potentially effective strategy based on these data, particularly in the

subset of patients with chronic constipation who perhaps respond a little too well to daily therapy.

### **Abstract 1270** Efficacy and Safety of Lubiprostone in a Subgroup of Constipation Patients Diagnosed with Irritable Bowel Syndrome with Constipation (IBS-C)

Johanson and colleagues pooled results of two placebo-controlled, 4-week, phase III trials of lubiprostone to evaluate efficacy in the treatment of constipation-predominant IBS (IBS-C). SBM frequency, stool consistency ratings, bowel straining, abdominal bloating and discomfort, and constipation severity assessments were compared between 45 placebo- and 46 lubiprostone-treated patients, in a subgroup characterized as having IBS-C. SBM rates were significantly higher among lubiprostone-treated patients (4.8–6 per week vs 2.8–4 per week for placebo) at all 4 weekly evaluations, and bowel straining scores were also consistently more favorable among lubiprostone-treated patients. Symptoms of abdominal bloating and discomfort were more improved among lubiprostone-treated patients at Weeks 3 and 4, and constipation severity ratings were significantly more improved at Weeks 1, 3, and 4. Nausea, the most common adverse event among lubiprostone-treated patients, was slightly more common than in placebo patients (35.6% and 28.4%, respectively).

**BC** This is the second report of lubiprostone use in patients with IBS-C. As noted above, we are seeing in this agent a corollary to research of tegaserod, but in the reverse order. Tegaserod was approved first for IBS and subsequently for chronic constipation. In the case of lubiprostone, the initial indication was for chronic constipation and now it is being examined for IBS. This is preliminary data but it is placebo-controlled and the investigators are finding that for SBMs, lubiprostone is superior to placebo at all data points in the initial 4 weeks. In addition, for some of the secondary measures, which for many patients are the most important symptoms of IBS (ie, abdominal bloating and abdominal pain), there was again improvement with lubiprostone compared to placebo. If the complete phase III results bear out these findings, and the observed differences are judged to be clinically significant with a favorable safety and tolerability profile, it is likely that we will have an alternative agent for use in constipation-predominant IBS in the reasonably near future. Lubiprostone, based on its mechanism of action and the knowledge of its effects on the gastrointestinal tract, will most likely be relegated to use in pure constipation-related illnesses such as chronic constipation and IBS-C. Tegaserod, though not indicated for IBS with mixed bowel form, is often used off-label in these patients

and there are some high-quality data showing that it does work in IBS-M patients. Some of this data is reported from phase III trials, and some from investigator-initiated studies. In a subset of patients with IBS-M, tegaserod can be effective, but patient selection must be conducted very carefully.

### **Abstract 1224** Rifaximin Is Superior to Other Antibiotics in Treating and Retreating Bacterial Overgrowth in IBS, Supporting a Lack of Bacterial Resistance Development

Lee and associates conducted a retrospective chart review to compare the efficacy of rifaximin (Xifaxan, Salix) versus other antibiotics to treat bacterial overgrowth and alleviate the associated symptoms of irritable bowel syndrome (IBS), as well as evaluating the efficacy of retreatment with rifaximin in this patient population. Charts were included for patients positive for Rome I IBS criteria seen between July 2004 and October 2005. Charts were examined to include any related antibiotic treatment, even if noted as part of pre-July 2004 patient history. Only patients with positive lactulose breath test and at least one follow-up visit and without a history of IBD or other gastrointestinal disease were included in analysis. The authors collected data on breath test results before and after treatment as well as clinical response, defined as a greater than 50% symptom improvement.

Of the 98 patient charts examined, 84 noted at least one course of rifaximin treatment. The median duration of patient treatment was 11 months. Clinical response was achieved in 69% of patients receiving an initial course of rifaximin compared to 38% for any occasion of neomycin use and 44% for all non-rifaximin antibiotics. Rifaximin was used as retreatment in 20 nonresponders to a first course of antibiotics and showed benefit in 75% of these patients. In 16 initially responsive patients with recurring symptoms, rifaximin was used as retreatment and all patients showed symptom improvement. A third course of rifaximin was used in 4 responsive but relapsing patients, again achieving response in the entire cohort. Retreatments were successful in 25% of patients administered doxycycline, augmentin, or neomycin. The authors concluded that IBS-related response to rifaximin was higher than with other antibiotics and that successful retreatment with rifaximin indicated a lack of development of bacterial resistance.

**BC** The concept of bacterial overgrowth and its role in the generation of IBS symptoms is currently the subject of much discussion. This is one of the first studies that has looked at the use of rifaximin compared to other antibiotics. It would be better to see a prospective, head-to-head

study of rifaximin compared to other antibiotics, but a retrospective review is the best alternative that we have right now. This study shows that patients who had IBS and evidence of bacterial overgrowth, when treated with rifaximin, achieved greater therapeutic benefit than those taking other antibiotics. In fact, rifaximin appears to work often as rescue therapy in patients that have failed other antibiotics. This abstract, taken in conjunction with the *Annals of Internal Medicine* article by Pimentel and associates (The effect of a nonabsorbed oral antibiotic [rifaximin] on the symptoms of the irritable bowel syndrome: a randomized trial. *Ann Intern Med.* 2006;145:557-563), which was recently published, solidifies the role of rifaximin as an effective antibiotic option for this group of patients. Another preferential attribute of rifaximin is its side-effect profile, which is negligible compared to placebo and certainly lower than many other antibiotics.

Although the retrospective nature of this study limits its applicability and the firm conclusions that can be drawn from the data, it does provide a logical stepping stone for a placebo-controlled trial or, more importantly, a comparative trial of rifaximin versus other antibiotics in a treatment-naïve group of patients with IBS, either with or without evidence of bacterial overgrowth. Many of us are now treating IBS patients with antibiotics, often without prior testing for small intestinal bacterial overgrowth, because such testing is unreliable and can be invasive. In a clinical trial setting, however, I would prefer to first look at a group with positive overgrowth testing in order to establish proof of concept.

### **Abstract 1232** Are Anti-Endomysial or Anti-Tissue Transglutaminase Antibodies Alone Sufficient To Screen for Celiac Sprue in Patients with the Irritable Bowel Syndrome?

Chey and coworkers sought to identify the most accurate and simple test to screen for the subset of IBS patients affected by celiac disease. Patients meeting Rome II non-constipated IBS criteria and healthy individuals scheduled to undergo colonoscopy for colorectal cancer screening were recruited at 4 US sites to undergo serological screening for celiac disease. Subjects agreeing to participate were tested for IgG and IgA anti-gliadin (AGA), anti-endomysial (EMA), and anti-tissue transglutaminase (TTG) antibodies. Total serum IgA levels were also measured. At the time of abstract publication, 323 IBS patients and 241 controls were enrolled in this ongoing trial. Of the IBS patients, 24 had at least one abnormal antibody test versus 7 of the healthy controls. Diagnosis of celiac disease was confirmed in 4 IBS patients and 2 controls. The authors concluded that celiac antibodies are significantly more prevalent among IBS patients but that biopsy-proven celiac disease is not. Further, no single antibody

test reliably identified all individuals with biopsy-proven celiac disease. If screening for celiac disease is pursued in patients with IBS, the authors recommend a panel of antibody tests, rather than EMA or TTG alone.

**BC** In this analysis, the investigators presented data from a trial that is attempting to determine, in a US population, if celiac disease is more common in IBS patients than in asymptomatic controls. The study is approximately 75% complete, and thus far they have not found any difference between IBS patients and controls with regard to the prevalence of histologically proven celiac disease. However, patients with IBS symptoms appear to be significantly more likely to have celiac-positive serologies, compared to asymptomatic controls. There are a number of studies that have shown that celiac disease is more common in patients with IBS symptoms but those studies are nearly all non-US studies, from areas where the populations are more homogeneous. This is the first prospective US study to have examined the same question and although there does not appear to be an increase in the histologic diagnosis of celiac disease in US IBS patients, these results are still intriguing.

The hypothesis that arises from these findings is whether or not, among IBS patients with positive celiac disease antibodies, there is a degree of gluten hypersensitivity that does not manifest as histologic enteropathy but is sufficient to promote the development of antibodies. The best way to prove this would be to observe these patients' IBS symptoms and celiac markers after embarking on a gluten-free diet. The next step for these investigators will be to treat this particular subset of patients, as well as a group of sprue antibody-negative IBS patients, with a gluten-free diet to see what happens to their IBS symptoms.

## Presentations in GERD

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### **Abstract 17** Prior Endoscopy Does Not Improve Long-Term Survival From Esophageal Adenocarcinoma Among United States Veterans

Rubenstein and colleagues conducted a retrospective analysis of Veterans Administration patients who had been diagnosed with gastroesophageal reflux and had subse-

quently developed esophageal adenocarcinoma (EAC), to determine whether esophageal endoscopy, when employed as a surveillance technique at least 1 year prior to EAC diagnosis, would affect overall patient survival. They examined 155 confirmed cases diagnosed between 1995 and 2003, and data were compiled for history of endoscopic surveillance, date of EAC diagnosis, cancer stage at diagnosis, course of therapy, and date of death. The researchers found that mortality was associated with increasing cancer stage at diagnosis, Charlson comorbidity index, and age. Patients with a history of endoscopic surveillance were more likely to be diagnosed at an earlier stage and to undergo surgical resection. These patients appeared to have better short-term survival but by 6-year follow-up, survival advantage was no longer present. The authors concluded that surveillance for EAC improved the stage at diagnosis and the likelihood of surgical resection for these patients but did not impart a long-term survival advantage.

**JR** The good news from this abstract is that it confirms that screening for dysplasia in our patients with Barrett esophagus (BE) does allow us to detect cancer at an overall earlier stage. The bad news is that esophageal cancer is still a gravely serious disease with poor long-term prognosis. As we accrue more data on this subject, we are finding that we need to do everything possible to prevent the development of BE. Further, as safer and more effective treatment techniques become available, we need to treat it, rather than simply watching these patients.

Currently available therapeutic options for BE, including photodynamic therapy and mucosal resection, are relatively complicated and dangerous. Thus, we reserve them for patients with high-grade dysplasia. If the data presented above are true, then our current surveillance techniques are not impacting long-term survival and watching BE in most cases is not enough. This is, however, a retrospective analysis of a very controversial issue. Regardless, it adds credence to the idea that we need to improve our therapies for BE and use them more aggressively.

The other related issue is that, across the board, BE patients have an increased risk of death when compared to an age-matched population, but they are not dying from esophageal cancer. They are more likely dying from cardiac disease because a significant fraction of patients with BE are also obese or they are smokers and thus have poor protoplasm. These issues need to be addressed in our BE patient populations as well.

#### **Abstract 22** Clinical Utility of the Bravo Capsule

Dukowicz and associates sought to validate the clinical utility of the Bravo pH monitoring capsule (Medtronic) through administration of a physician questionnaire, prior to capsule placement, that collected data regard-

ing indications for the test, patient symptoms, prior testing for the same symptoms, and current medication. Patients were studied either on or off medication at the physicians' request. A follow-up questionnaire was then administered to determine whether new information was garnered through Bravo monitoring and if the new information affected the course of treatment. Over a course of 6 months, 240 procedures were available for inclusion and 106 fully completed questionnaires were returned and included for analysis. The most common primary symptoms leading to referral were reflux (heartburn and regurgitation) in 65%, chest pain or chronic cough in 9%, dysphagia in 5%, and ear-nose-throat symptoms in 3%. Of the total patients evaluated, 91% had undergone prior testing, including endoscopy, barium swallow, and radiographic imaging, and 27% had undergone previous pH testing via either catheter or Bravo placement. Results of the current Bravo study provided new information in 75% of patients and changed diagnosis in 25%. In 64% of cases, a change in the course of disease management was made, including referral to surgery in 26% of patients, cessation of prior medication in 18%, increased medication dosage in 12%, and new medication in 12%. The authors concluded that use of the Bravo pH monitoring system provides new and useful information that affects course of treatment in patients with acid reflux symptoms.

**JR** The Bravo capsule is basically an old technology utilized in a more patient-friendly manner. The old, catheter-based systems of pH monitoring, where a tube was inserted up the nostrils, were associated with poor patient tolerance. In addition, patients who tested negative for reflux often did so due to the catheter affecting their ability to eat, exercise, or otherwise perform their normal daily activities.

The Bravo capsule, which is the size of a vitamin pill, can be attached to the lining of the esophagus. Some patients have discomfort, but the capsule allows them to move around. There is no tube hanging out of their noses. They can go to work, eat regularly, exercise, and sleep well. In addition, the Bravo capsule provides 48 hours of uninterrupted data. Therefore, it is not surprising that these researchers were acquiring useful information through Bravo.

#### **Abstract 24** Prevalence of Clinically Relevant Esophageal Mucosal Pathology in Subjects Who Self-Initiate Use of Prilosec OTC™ (Omeprazole 20 mg)

Shaheen and colleagues examined subjects self-initiating therapy for frequent heartburn with over-the-counter

(OTC) omeprazole (Prilosec OTC, AstraZeneca) to determine the prevalence of esophageal mucosal pathology (EMP) including erosive esophagitis, BE, stricture, ulcers, and esophageal carcinoma within this population. Patients were administered a questionnaire to obtain baseline demographic profiles and underwent endoscopy to detect mucosal pathology. Demographic characteristics among 1,024 intent-to-treat subjects were 45% men, 63% white, 32% Hispanic, with a mean age of 43 years and a mean body mass index of 28.7. Concomitant therapy, including antacids and OTC and prescription H<sub>2</sub> receptor antagonists, were employed by 33.2% of subjects. The researchers found that OTC omeprazole effectively controlled symptoms among patients who had heartburn 4–6 days per week (28%) or daily (32%) before initiating therapy, with subjects reporting no heartburn (29%) or heartburn once weekly or less (37%) during treatment. However, among the total cohort, approximately one third had clinically relevant EMP (see Table 1).

**JR** This study shows that we are going to run into problems with OTC proton-pump inhibitor (PPI) medications if patients are not seeing a physician. In this study, there were 22 people with short-segment BE, which is premalignant, and 1 person with cancer. If this study had not been done and these individuals had continued to take OTC medication without the care of a physician, there would have been at least 1 death related to that drug relieving symptoms and people thinking that they were safely and effectively treating benign disease. When omeprazole was first authorized for OTC use, it was only the second time a drug had gone OTC at full dose. This drug at this dose revolutionized the treatment of gastroesophageal reflux disease, and now it is available OTC. I do not believe that people read labels and package inserts carefully and heed the stated recommendation to see a doctor if symptoms persist for over 2 weeks. Further, manufacturers package this drug in 6- and 9-week batches that send a mixed signal regarding the appropriate course of treatment.

This study emphasizes the fact that there is a subgroup amongst these self-treating subjects, perhaps 10–15%, with Los Angeles Grade C or worse esophagitis. It shows that the drugs are effective but that a third of these people, who have more serious disease, could develop grave complications or even die because they waited 1, 2, 3, or even 4 years to seek care and get an endoscopy. Therefore, the packaging should more clearly state that symptoms may be associated with more serious disease and that taking these medications without the supervision of a physician could result in the development of esophageal cancer and possibly death.

**Table 1.** Prevalence of Esophageal Mucosal Pathology (EMP) in Subjects Who Self-Initiated Over-the-Counter Omeprazole Use

EMP	Prevalence, n (%)	95% Confidence Interval
Any EMP	343 (33.5)	30.6–36.4%
Any Erosive Esophagitis	311 (30.4)	
LA Grade A Erosive Esophagitis	170 (16.6)	
LA Grade B Erosive Esophagitis	95 (9.3)	
LA Grade C Erosive Esophagitis	39 (3.8)	
LA Grade D Erosive Esophagitis	6 (0.6)	
Barrett Esophagus	18 (1.8)	
Short Segment Barrett Esophagus	22 (2.1)	
Esophageal Stricture	32 (3.1)	
Esophageal Ulcer	6 (0.6)	
Esophageal Carcinoma	1 (0.1)	

### Abstract 52 XP19986 Decreases Reflux and Is Well Tolerated in GERD Patients

Castell and associates conducted a multicenter, randomized, double-blind, placebo-controlled crossover trial of the novel agent XP19986, a prodrug of R-baclofen, a gamma-aminobutyric acid-b agonist, to assess the tolerability and efficacy of this agent in controlling symptoms of gastroesophageal reflux disease (GERD). Patients with a history of GERD symptoms at least 3 times weekly and 20 or more reflux episodes on impedance monitoring over the course of 2 hours following a high-fat meal were enrolled in separate cohorts of 4 escalating doses of XP19986 or placebo. Patients received single doses in intervals ranging from every 4 to every 7 days. High-fat meals were consumed within 2–6 hours following each dose, and reflux episodes and R-baclofen levels were collected for 12 hours following dosing. GERD symptom frequency, vital signs, echocardiogram data, and clinical lab values were also collected throughout the study.

The primary endpoint for the trial was the total number of reflux events over the 12-hour monitoring period following XP19986 dosing. For the combined

10, 20, and 40 mg groups, the median number of reflux events during placebo treatment was 51, with a median of 7 fewer events in the corresponding XP19986-treated groups. XP19986 was well tolerated at all dose levels, with 1 incidence of fatigue, compared to 1 in the placebo group, and no nausea or headaches reported, compared to 3 incidences of each on placebo.

**JR** The next era in the treatment of reflux disease will focus on the mechanism of reflux rather than on acid. Acid is necessary to protect our gastroenterologic environment and kill bacteria. We only use PPIs to suppress acid because it is not meant to be in the esophagus. The root problem of reflux disease, however, is the valve relaxing at the wrong time. We need drugs that allow the valve to function more effectively without making it too tight, as can happen with surgical therapy.

The original problem with baclofen was that 25–30% of patients developed side effects, though it effectively decreased episodes of transient lower esophageal sphincter relaxation and both acid and nonacid reflux. This trial represents an attempt to develop new, more purified drugs derived from baclofen that have a better safety profile. In the future, these will be the drugs of choice for treating patients with nonerosive reflux disease.

### **Abstract 56** Eosinophilic Esophagitis: Prevalence and Predictive Factors

Prasad and colleagues assessed the prevalence of eosinophilic esophagitis in patients undergoing endoscopy for dysphagia and the clinical and endoscopic factors predictive of eosinophilic esophagitis. Consecutive patients presenting with dysphagia at the Mayo Clinic Rochester outpatient clinic between June 2005 and June 2006 were enrolled and completed the validated Mayo Dysphagia Questionnaire. During endoscopic examination, midesophageal biopsies were obtained in those patients with findings suggestive of eosinophilic esophagitis and no other clear etiology of their dysphagia. Biopsies were analyzed and eosinophilic esophagitis defined as the presence of more than 20 eosinophils per high-power field. Of the 376 patients included, 48% had no endoscopically evident cause for their dysphagia and 60% underwent midesophageal biopsy. The authors concluded that among patients with unexplained dysphagia, a substantial fraction can be diagnosed with eosinophilic esophagitis on biopsy. Furthermore, a history of food impaction and specific endoscopic features of rings, furrows, and mucosal fragility also suggest eosinophilic esophagitis.

**JR** Eosinophilic esophagitis is one of a series of diseases that have an allergic background, and we are not sure why

their prevalence is increasing. Others include asthma and various types of allergies. The increasing prevalence of eosinophilic esophagitis may well become a major cause of solid-food dysphagia in younger people. I agree with the authors in that any patient who has food impaction or unexplained solid-food dysphagia needs to be screened for eosinophilic esophagitis, which can sometimes be detected on endoscopy with the visualization of characteristic rings and furrows but often requires biopsy of both the distal and the proximal esophagus to confirm. Historically, younger patients who had solid-food dysphagia likely had Schatzki ring or a peptic stricture, but with rising prevalence, it is now just as likely that they have eosinophilic esophagitis.

For the last 10–15 years, many clinicians have recommended that biopsy should be performed only in cases of suspected BE or cancer. Eosinophilic esophagitis is changing our approach in that regard.

## Presentations in Endoscopy

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### **Abstract 2** Utilization and Acceptance of Wireless Esophageal Capsule Endoscopy for Evaluation of Self-Referred Subjects With Chronic Heartburn

Golding and associates examined the clinical utility of esophageal capsule endoscopy (ECE) in the screening of patients at risk for BE. Subjects (n=40) over the age of 50 with a minimum of 2 episodes of heartburn a week during the preceding 6 months were recruited to undergo ECE. Subjects were not under current gastroenterologic care and had not undergone upper endoscopy during the preceding 5 years. Erosive esophagitis was identified in 13 studies (32%). Three subjects had circumferential ulcerations. Subjects with normal studies reported more severe heartburn (33% vs 15%) and were more likely to use medications for relief of heartburn on most or all days (59% vs 46%) than those with esophagitis. Mucosal changes associated with BE were identified in 15 (38%) studies. Subjects with possible BE were more likely to

report heartburn of over 5 years' duration and nocturnal heartburn on most or all nights. The authors concluded that esophagitis and BE are common in adults self-referred for investigation of chronic heartburn. A possible approach for evaluation of patients with chronic GERD without warning symptoms could be the performance of ECE followed by upper endoscopy and biopsy in only those with positive findings.

**RS** This study was provocative in uncovering an incredibly high yield of patients with mucosal disease among responders to a newspaper advertisement. The abstract presented the findings as if 70% of patients had mucosal disease, and it is not clear whether there was overlap between the erosive esophagitis and BE populations. Regardless, it was a high level of abnormalities among a high risk population that was 62% male and 90% white. These findings makes a stronger case for screening people who are not under medical care. I think it is very common for people who have symptoms but who do not verbalize or reach the threshold for seeking care to volunteer for studies, resulting in a heightened frequency of disease.

The experience of scoping primary-care patients in order to screen is that only 36% with reported GERD symptoms have mucosal disease. Obviously, this is a small study with results that cannot be applied to the general population but it nonetheless provides an interesting window into the group of untreated people with GERD. Earlier studies conducted before the era of PPI therapy have examined patients buying antacids at a pharmacy, what I call a preclinical population, and found similar results. We also know that approximately 40% of people with BE do not have bothersome symptoms of reflux and the question becomes one of how to access this group who, if detected, would be candidates for endoscopic surveillance.

In Locke and associates' standardized, validated population-based study conducted at the Mayo Clinic (Prevalence and clinical spectrum of gastroesophageal reflux: a population-based study in Olmsted County, Minnesota. *Gastroenterology*. 1997;112:1448-1456), the majority of people with GERD had not sought medical attention. I think this dynamic has shifted in the past several years with so much direct-to-consumer advertising, making the results found by Golding even more surprising. This study does suggest that, in spite of all the public awareness campaigns that have been conducted by the gastroenterologic organizations, there is still an untapped group of people out there who need to be evaluated. An interesting adjunct to this study would be to develop a questionnaire to determine what was different about this population: when they had last seen a physician, whether their symptoms crossed

the threshold for seeking attention, whether they had seen or heard advertisements for GERD therapy on television. A number of questions might help to identify why these people are naive to medical care.

### **Abstract 5** Cost-Utility of Screening for Barrett's Esophagus With Esophageal Capsule Endoscopy Versus Conventional Upper Endoscopy

Rubenstein and colleagues developed a Markov model of hypothetical 50-year-old white men with symptoms of gastroesophageal reflux, constructed to calculate outcomes associated with BE and esophageal cancer. They included direct medical costs, costs of lost productivity, and patient preferences for health states, and followed patients until age 80 or death. The overall measure was of the incremental cost-effectiveness ratio, analyzed from a societal perspective. Secondary outcomes included life expectancy, quality-adjusted life expectancy, and proportion of cancer deaths averted. Analysis revealed screening by conventional upper endoscopy to prevent 60.4% of cancer deaths, at a cost of \$11,254 per quality-adjusted life year gained, when compared to no screening. ECE prevented 59.0% of cancer deaths and provided 2 fewer quality-adjusted days, at greater cost. The only scenario favoring ECE was one in which the patient and patient's driver earned a combined total of over \$153,423 annually, resulting in substantial lost productivity to society. The authors concluded that conventional endoscopy and ECE yield similar outcomes and are both cost-effective but that conventional endoscopy remains the preferred strategy for the management of BE and esophageal cancer surveillance.

**RS** These findings were surprising in that the conventional wisdom would lead one to believe that a less invasive test is more cost-effective. However, the capsules are very expensive, averaging approximately \$450 each. By comparison, in low reimbursement areas like Southern California and Arizona, \$450 covers the Medicare costs for both the professional and the facility fee associated with an upper endoscopy procedure.

This study shows that the expense of the capsule will need to be reduced in order for it to provide a viable alternative for general screening. New esophageal capsules are in development that either acquire more images or have better resolution in order to improve their sensitivity, which is important for a screening test. This, along with new swallowing methods that enhance image quality, will make the capsules more effective and though the price may not come down, they will provide more accuracy for the money.

### **Abstract 73** Accuracy of Esophageal Capsule Endoscopy (ECE) for Diagnosis of Barrett Esophagus (BE)—A Pooled Analysis

Sharma and coworkers conducted a meta-analysis of published literature comparing accuracy of ECE versus conventional endoscopy for the diagnosis of BE. Data from 5 trials (total N=339; 144 with BE) were extracted and pooled and calculations were made to compare sensitivity, specificity, positive and negative predictive values, and 95% confidence intervals. Results revealed ECE sensitivity of 81%, specificity of 87%, positive predictive value of 82%, and negative predictive value of 86% for diagnosis of BE. Based on these results, in hypothetical populations with Barrett prevalences of 10% and 15%, positive predictive value of ECE would be 40% and 52%, respectively; negative predictive values would be 98% and 96%, respectively. The authors concluded that ECE has acceptable test characteristics for the screening of BE in patients with diagnosed GERD but traditional endoscopy remains the gold standard and may undermine the ECE results.

**RS** This study collects the existing published experience with capsule endoscopy. The peer-reviewed experience shows that very few patients with BE have been evaluated. The pilot feasibility study had only 17 patients with suspected esophageal disorders. The multicenter international trial with 136 patients included only 13 with BE. This pooled analysis included published abstracts. Analysis of the latter shows that the sensitivity of capsule techniques is much lower than has been reported in the past.

The frequency of BE in screening populations is typically much lower (5%) than this study population (42%) and the general population is where the capsule technique is ultimately going to be applied, thus yielding a much lower positive predictive value. The “acceptable test characteristic” that the authors describe is based on a much higher negative predictive value. All of these statistics raise the issue of how sensitive a test needs to be in a screening setting. Is 85% good enough? If the screening involves a premalignant disease with an associated cancer risk, does the test require better sensitivity? These are theoretical questions without an absolute answer.

### **Abstract 485** Objective Quality Control for Colonoscopy: Automated Extraction of Endoscopic Metrics From Video Files

In order to explain how significant numbers of large polyps and cancers are not detected, de Groen and colleagues developed software to digitally capture and analyze video files created during colonoscopy. The software derived 5 distinct metrics: insertion time (exact measure of length of the insertion phase), withdrawal time (exact measure of the withdrawal phase), clear withdrawal phase (measure of time during withdrawal phase where images were in focus), back and forth movements (number of events of back-and-forth movement, presumably to inspect behind folds), and fractions of clear withdrawal phase spent on inspections of the colon wall versus global inspection. Approximately 250 video files were created and algorithms were shown to detect out-of-focus frames and back-and-forth movement with sensitivity and specificity both above 95%. The authors hope that this software can be utilized to provide large-scale, continuous quality control for colonoscopy in the day-to-day medical practice setting.

**RS** This is an exceptional example of what can be done to objectively measure the quality of a colonoscopic screening procedure. The authors developed a software model that creates an automated accumulation of digital images, which can be analyzed based on a software program. In practice, it would provide an excellent method of continuous quality control for colonoscopy. Doctors are increasingly alert to this issue with the beginning of the era of pay-for-performance. The next step will be to examine the results in a real patient population to see if the automated analysis is valid.

The difference between this method and a database like the Clinical Outcomes Research Initiative (CORI) is that the CORI database is all self-reported and depends on the quality of the information provided by the examiner. It would be interesting to take data from some CORI centers and compare the information provided by the endoscopists to that provided by this manner of automated extraction.