FDA Approves Halflytely® for Colonoscopy Prep

Braintree Laboratories, Inc. announced that the U.S. Food and Drug Administration has approved the HalfLytely® and Bisacodyl Tablets Bowel Prep Kit (PEG-3350, sodium chloride, sodium bicarbonate, potassium chloride for oral solution and bisacodyl delayed release tablets) as a prescription preparation for bowel cleansing prior to colonoscopy.

HalfLytely® enables patients to ingest half the volume of solution traditionally required with a significant reduction in bowel-prep related discomfort, according to clinical trial results.

"The arrival of a more tolerable bowel prep is crucial because the cramping, nausea and fullness associated with traditional prep is a major reason that people avoid having a colonoscopy," said Jack A. DiPalma, MD, Medical Director for Braintree. "Almost 90 percent of nearly 60,000 colon cancer deaths in the United States this year could have been prevented if diagnosed in the early stages through colonoscopy," said Dr. DiPalma, who is also vice president of the American College of Gastroenterology and Director, Division of Gastroenterology, University of South Alabama College of Medicine. "Screening rates remain far below where they would need to be to significantly reduce the number of cancer deaths."

Beyond cancer, accurate, tolerable colonoscopy is needed to diagnose Crohn's disease and ulcerative colitis, collectively known as inflammatory bowel disease (IBD), that affect an estimated one million Americans. Early diagnosis and treatment of these conditions may prevent a worsening of symptoms (e.g. diarrhea, abdominal pain and fever) and complications (e.g. abscesses, malnutrition, and anemia).

Transnasal Esophagoscopy Reduces Major Complications in Diagnosing Swallowing and Reflux-Related Disorders

A new method of diagnosing swallowing disorders and problems caused by gastroesophageal reflux can significantly reduce the major complications associated with traditional esophagoscopy, a physician from Wake Forest Baptist Medical Center reported at their conference, "Laryngopharyngeal Reflux, Dysphagia, and Laryngology."

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The new method is called transnasal esophagoscopy (TNE), "and it's a huge advance," said Greg Postma, M.D., associate professor of otolaryngology at Wake Forest Baptist and one of the course directors.

TNE employs an endoscope that is only about 5 millimeters in diameter and is threaded through the nose, down the throat and esophagus and into the stomach, with no sedation and only a topical anesthetic in the nose and throat.

Traditional esophagoscopy, Postma explained, requires heavy sedation by intravenous injection, while a larger endoscope is deployed down the esophagus through the mouth. "More than half the complications of esophagoscopy are due to sedation. So we eliminate more than half the complications just by the nature of how we do it."

Postma said that Wake Forest Baptist had done more than 700 TNE procedures without a single major complication and only eight minor complications."The key is that it's easier and safer," he said.

"When we use that (smaller) scope we can biopsy things just about anywhere," Postma said. TNE can be used to detect and biopsy precancerous lesions in the esophagus, as well as fungal infections, strictures (narrowings), pouches and other abnormalities.

A major advantage of TNE is convenience for the patient, Postma said. "When you have this done, you walk out of the clinic and drive yourself home," in contrast to the traditional method, in which the patient spends an additional two hours in the recovery room, with restricted activity for at least the remainder of the day."

PREVACID® I.V. (Lansoprazole) for Injection Approved by the FDA for the Treatment of Erosive Esophagitis in Hospitalized Patients

New Intravenous Administration Option for Leading Proton Pump Inhibitor

TAP Pharmaceutical Products Inc. has received U.S. Food and Drug Administration (FDA) approval to market an intravenous (I.V.) formulation of Prevacid (lansoprazole). When patients are unable to take oral formulations, Prevacid I.V. for Injection is indicated as an alternative for the short-term (up to seven days) treatment of all grades of erosive esophagitis. Once the patient is able to take medications orally, therapy can be switched to an oral formulation of Prevacid for a total of six to eight weeks. The safety and efficacy of Prevacid I.V. for Injection as an initial treatment of erosive esophagitis have not been demonstrated.

"I.V. treatment can provide an important treatment bridge for managing severe to mild erosive esophagitis in patients who are unable to take medication by mouth," said Xavier Frapaise, M.D., vice president of research and development at TAP. "After treatment with Prevacid I.V., patients may be switched to oral Prevacid to help them continue to manage their erosive esophagitis for up to eight weeks."

GlaxoSmithKline Releases Multi-Language Hepatitis B Educational Materials

New Video and Brochures Designed as Educational Tools for Healthcare Providers and Consumers

GlaxoSmithKline (GSK) has released new educational materials that address the causes, symptoms and risks associated with chronic hepatitis B. The video, Hepatitis B: Facing the Challenge, is now available to healthcare professionals and consumers at www.hepatitisb-help.com, GSK' hepatitis B Web site. The video is available in English as well as Cantonese, Korean, Mandarin, Spanish and Vietnamese. In addition to the video, a 12-page, full-color, hepatitis B disease awareness brochure is available for download on the Web site in the same languages.

Konsyl® Pharmaceuticals Introduces SennaPrompt™

Konsyl Pharmaceuticals has introduced SennaPrompt™, an important innovation in the Laxative Category. It is a natural fiber therapy that also provides gentle overnight relief.

Each capsule of SennaPrompt contains 500mg of psyllium and 9mg of Senna. It provides a rich source of natural fiber with no sugar or sugar substitutes and comes in a convenient EZ Caps form—no mixing required.

Biohit Quick Test Innovation for Diagnosis of Lactose Intolerance

Biohit has developed and launched a new Lactose Intolerance Quick Test for biopsy specimens. This Point of Care test enables a rapid diagnosis of hypolactasia on the basis of the biopsy specimens taken in connection with gastroscopy. In case of normolactasia, the color develops as the lactase enzyme of the biopsy specimen breaks down the lactose added to the test buffer. If there is no or only a slight color development it can be concluded that the patient suffers from the deficiency of lactase enzyme in the mucosa of the small intestine, i.e., lactose intolerance. The Biohit test is a simple and reliable procedure with ready for use reagents, and enables easy visual interpretation of the results, i.e., the color development in 20 minutes.

Molecular Defect Found for the First Time in IBS Patients

New Research Demonstrates that IBS Is Not "All in Your Head"

New research published in a recent issue of *Gastroenterology* identifies for the first time a molecular defect in the gastrointestinal (GI) tracts of patients with irritable bowel syndrome (IBS) that does not appear in those without the condition.

The findings reinforce the critical role normal serotonin (5-HT) signaling plays in regulating GI function, pinpointing a difference in the way serotonin functions in certain cells lining the GI tract of IBS patients. This defect may underlie the clinical manifestations of IBS—abdominal pain or discomfort, bloating, constipation and/or diarrhea—that affect more than 40 million Americans.

Although serotonin generally is recognized as a chemical in the brain, only five percent of this naturally occurring neurotransmitter is found in the brain and central nervous system. The remaining 95 percent of serotonin resides in the cells lining the GI tract. In the gut, serotonin binds to 5-HT receptors on nerve cells, initiating intestinal movement. SERT (serotonin transporter), also found in cells lining the GI tract, initiate the uptake of serotonin by deactivating it when appropriate. Without this natural regulation, the mechanisms of digestion cannot function properly. In this study, patients with IBS were found to have decreased expression of SERT, which could lead to either overstimulation of the gut (IBS with diarrhea) or receptor desensitization (IBS with constipation or IBS-C).

The research findings represent a major step forward into understanding the cause of chronic disorders of the gut, including IBS, according to the scientists.

Study Findings

In patients with both IBS and ulcerative colitis, the study found a significant decrease in serotonin content while the release of serotonin from endocrine (EC) cells was not significantly different compared to controls. In terms of the way the body inactivates serotonin signaling, or the serotonin re-uptake system, SERT mRNA and SERT immunoreactivity were markedly reduced in both patient populations compared to controls. This reduction is expected to decrease the capacity of epithelial cells to remove serotonin from intercellular space once it is released, thus increasing serotonin availability and ultimately causing abnormal bowel function.

From Digestive Disease Week, New Orleans 2004

New Era of Colon Screening Emerging

New technologies are becoming available to perform colonic tests in alternative fashions. In a study funded by the National Cancer Institute and conducted at Duke Clinical Institute, researchers found that colonoscopy fairs better than other imaging tests in the overall comparison of accuracy, cost and patient acceptance

Colonoscopy (C) is generally considered to be the optimal method for colon evaluation, but in practice other imaging tests, including the air/barium enema (ACBE) and computed tomographic colonography (CTC), are also used. In this study, fourteen sites recruited patients with an increased need for colon examination to undergo each of the three procedures due to fecal occult blood, hematochezia, iron deficiency anemia, or a family history of colon cancer. ACBE was performed seven to fourteen days prior to C and CTC (performed on the same day), with a primary outcome of sensitivity compared to a consensus colon examination for the detection of colon cancers and polypoid lesions greater than or equal to one centimeter in diameter. The prevalence of colon cancer or the specified lesions in this patient population was 10.3 percent (63/614 patients).

The sensitivity point estimates for the three imaging tests for lesions greater than or equal to 10 millimeters were 0.48 (ACBE), 0.59 (CTC) and 0.98 (C): the differences between ACBE and CTC were statistically significant. The specificity point estimates were 0.90 (ACBE), 0.96 (CTC), and 1.00 (C).

"As patients undergo these screening procedures, it is important to be confident in the accuracy of the test, as colon cancer is a significant cause of death that may, in some cases be preventable," said Don Rockey, M.D., lead author of the study. "Based on these findings, colonoscopy is significantly more accurate than either the ACBE or CTC procedures. But it is important to note that technologies are rapidly evolving and CTC is likely to improve."

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Colon screening can be challenging for some patients and barriers to a complete exam can lead to inaccuracies and misdiagnosis. To quell these barriers, scientists from St. Mary's Hospital in London used capsule endoscopy as an adjunct to conventional colonoscopy and yielded significant results. Barriers to accurate screenings often include cleanliness, slow transit times, intermittent rapid movements, larger diameter lumen and capsule transmission time.

Researchers viewed colonic images in 38 patients with obscure gastroentestinal bleeding obtained without preparation using Given Imaging M2A capsules with a seven-hour life. An additional 34 patients took colonic preparation and were studied with the capsule. In 13 of these patients, long-play (LP) capsules with a potential transmission time of 10 hours were used and in 21, short-play (SP) capsules with a two-hour delay were tested. Fourteen patients were tested with seven LP and seven SP capsules.

In 38 clinical studies performed without colonic preparation, 35 had interpretable colonic images. Both the LP and SP capsules used with colonic preparation increased the number of interpretable colonic images compared with M2A.

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The introduction of the colonoscopy procedure was a major advance in the diagnosis and prevention of colorectal cancer and other colonic diseases. However the technology has progressed very little over the last few years and has several disadvantages, including the need for disinfection of the equipment between procedures, high costs for equipment repair and the need to push the instrument from outside the patient to advance to the colon. This can cause significant discomfort for the patient, stretches the colon and increases the risk of perforation.

An FDA-approved novel device, the ColonoSight, addresses these issues. The device was developed and tested by researchers from Memorial Sloan-Kettering Cancer Center, centers in Italy and the Sightline Corporation from Israel. The ColonSight uses air-pressure-assisted pull technology that incorporates a disposable system. The pneumatic mechanism generates a for-ward force just below the tip of the scope, which pulls the scope while the operator navigates with the handles, drastically reducing the need to push the

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instrument. Simultaneously, the equipment deploys a protective disposable sheath as the scope advances to the colon, which incorporates disposable work channels, eliminating the need for disinfection between procedures while at the same time reducing the instrument downtime and possibly the risk of infection. The equipment uses also uses integrated LED (light emitting diode) as a light source in the tip of the scope, eliminating the need for fiber-optics and reducing repair costs.

A complete screening or therapeutic colonoscopy was attempted in 72 patients with the ColonSight. The success rate in reaching the cecum was 88 percent, at an average rate of 12.3 ± 7 minutes, though in nine patients it was reached in less than five minutes. There were no complications during the procedures or for the following two-week period.

Bacteriological cultures obtained post-procedure from various areas of the equipment protected by the sheath showed that the barrier was effective in protecting the non-disposable components.

"According to our findings, the three unique functions of the ColonSight—disposability, power-assisted advancement and integrated LED illumination—function well and safely," said Moshe Shike, M.D., lead author of the study. "We believe this could be an important breakthrough to improving the costs, function and operation of the endoscopic examination of the colon.

Studies Identify Risk Factors for Colon Cancer

In two new studies, scientists report that women's preferences for a female physician may delay or prevent proper colorectal screenings due to a lack of females in the field and diabetes may be a significant risk factor for development of colon cancer.

Female patients tend to prefer seeing female physicians in most specialities of medicine. A study presented by researchers at the University if Michigan found that for colorectal screenings in particular, women's preference for female health care professionals is strong enough to delay the procedure and incur additional expenses, as there is a lack of available female endoscopists.

A second study by researchers at the Overton Brooks VA Medical Center in Louisiana have found a strong association between diabetes and the risk of developing colon cancer, according to a conclusive study of more than 50,000 U.S. veterans.

In the retrospective, cross-sectional, case-control study, researchers evaluated the medical records of 60,697 patients between October 1998 and June 2003 using regression analysis and adjusting for obesity, smoking, use of aspirin and alcohol. The 17.7 percent of patients in the study who had diabetes (8,974 patients) were 32 percent more likely to develop colon cancer than patients without diabetes.

"Given the increasing prevalence of diabetes and the serious mortality associated with colon cancer, we cannot ignore the strong possibility that the two diseases are related in some way and hope to confirm this theory with further study," said Rambabu Chalasani, M.D. lead author of the study. "However, our results should be viewed with caution due to the limitations of a case-control study and the population in the database.

Data Show Investigational Antibiotic Safe and Effective in Preventative Treatment of Travelers' Diarrhea

New data suggest the investigational drug rifaximin, a non-absorbed (<.5%) antibiotic with few side effects and low potential for resistance, is effective in preventing travelers' diarrhea, an illness that affects up to 60 percent of international travelers. Until now, antimicrobial prophylaxis, while effective, has been discouraged because of side effects and the encouragement of resistance. The study results, presented at the 2004 Digestive Disease Week (DDW) annual meeting by lead investigator, Herbert L. DuPont, M.D., Chief of the Internal Medicine Service at St. Luke's Episcopal Hospital in Houston, showed that, over two weeks, 85 percent of the rifaximin-treated subjects remained free of diarrhea, compared with 49 percent of the placebo-treated subjects.

Dr. DuPont is also Director, Center for Infectious Diseases, University of Texas, Houston School of Public Health and Vice-Chairman, Department of Medicine at Baylor College of Medicine.

The antibiotic, rifaximin, with the projected brand name of Xifaxan, is currently under review by the U.S. Food and Drug Administration. It has previously been shown by researchers to be a safe and effective form of therapy for treatment of travelers' diarrhea in clinical studies conducted in Mexico, Peru, India and Kenya and has been prescribed internationally since 1987 and is currently approved in 17 countries worldwide.

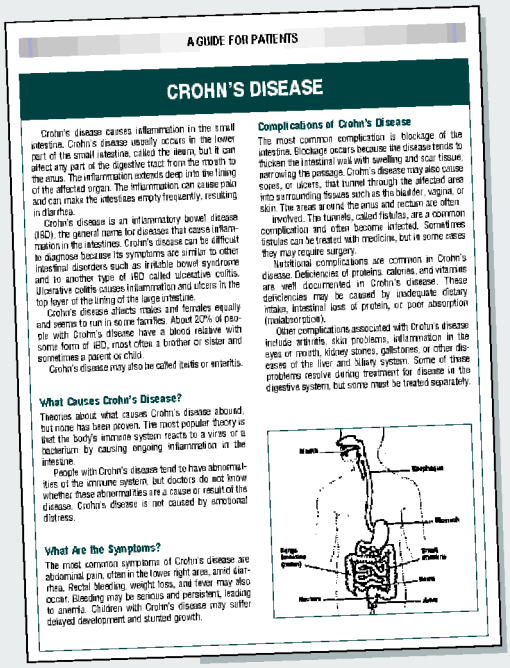
"This is potentially one of the most important advances over the past 50 years toward reducing the occurrence of illness of travelers to the high-risk areas," said Dr. DuPont. "The characteristics of rifaximin—it is non systemic since it stays in the intestine after taking it by mouth and has been shown to be "gut-selective" in clinical trials—make it an ideal drug for prevention of diarrhea in international travelers. It particularly practical in that it was effective in preventing illness with as little as one dose a day."

The randomized double-blind, placebo-controlled study evaluated the tolerability and efficacy of rifaximin as prophylaxis for travelers' diarrhea. Two hundred and twenty U.S. college students were enrolled in the trial within 72 hours of their arrival in Guadalajara, Mexico. Study participants received 200 milligrams of rifaximin once daily, twice daily, three times daily or placebo for two weeks. Eleven students dropped out of the study, leaving 209 participants to be evaluated daily for three weeks for the occurrence of diarrhea, mild diarrhea or severe diarrhea, and for five weeks for drug related side effects.

Rifaximin protected the young adults from the U.S. against all forms of diarrhea and intestinal symptoms in all drug doses tested (one dose, two doses, or three doses per day). Over the two-weeks in Mexico, 85 percent of the rifaximin-treated subjects compared with 49 percent of the placebo-treated subjects remained free of diarrhea. In the groups not developing diarrhea, rifaximin also prevented the occurrence of milder forms of diarrhea and prevented the occurrence of moderate and severe abdominal pain and cramps and excessive gas-related symptoms. The drug was safe, having in incidence of adverse events comparable to placebo.

A GUIDE FOR PATIENTS

The more that a patient knows about his or her problem, the easier it is for the patient to cooperate with you and the more effective can be the prescribed treatment. Each "Guide" is on a different subject among the digestive diseases. You may cut out the "Guide" and photocopy as many reprints as you wish for distribution to your patients. You may want to include your name and address. The information in "A Guide for Patients" has been prepared by the National Digestive Diseases Information Clearing House, a service of the National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, U.S. Public Health Service. The material it contains has been carefully reviewed by NDDIC for scientific accuracy and content.


A GUIDE FOR PATIENTS

CROHN'S DISEASE

Crohn's disease causes inflammation in the small intestine. Crohn's disease usually occurs in the lower part of the small intestine, called the ileum, but it can affect any part of the digestive tract from the mouth to the anus. The inflammation extends deep into the lining of the affected organ. The inflammation can cause pain and can make the intestines empty frequently, resulting in diarrhea.

Crohn's disease is an inflammatory bowel disease (IBD), the general name for diseases that cause inflammation in the intestines. Crohn's disease can be difficult to diagnose because its symptoms are similar to other intestinal disorders such as irritable bowel syndrome and to another type of IBD called ulcerative colitis. Ulcerative colitis causes inflammation and ulcers in the top layer of the lining of the large intestine.

Crohn's disease affects males and females equally and seems to run in some families. About 20% of people with Crohn's disease have a blood relative with some form of IBD, most often a brother or sister and sometimes a parent or child.

Crohn's disease may also be called ileitis or enteritis.

What Causes Crohn's Disease?

Theories about what causes Crohn's disease abound, but none has been proven. The most popular theory is that the body's immune system reacts to a virus or a bacterium by causing ongoing inflammation in the intestine.

People with Crohn's disease tend to have abnormalities of the immune system, but doctors do not know whether these abnormalities are a cause or result of the disease. Crohn's disease is not caused by emotional distress.

What Are the Symptoms?

The most common symptoms of Crohn's disease are abdominal pain, often in the lower right area, and diarrhea. Rectal bleeding, weight loss, and fever may also occur. Bleeding may be serious and persistent, leading to anemia. Children with Crohn's disease may suffer delayed development and stunted growth.

Complications of Crohn's Disease

The most common complication is blockage of the intestine. Blockage occurs because the disease tends to thicken the intestinal wall with swelling and scar tissue, narrowing the passage. Crohn's disease may also cause sores, or ulcers, that tunnel through the affected area into surrounding tissues such as the bladder, vagina, or skin. The tissue around the anus and rectum are often involved. The tunnels, called fistulas, are a common complication and often become infected. Sometimes fistulas can be treated with medicine, but in some cases they may require surgery.

Nutritional complications are common in Crohn's disease. Deficiencies of proteins, calories, and vitamins are well documented in Crohn's disease. These deficiencies may be caused by inadequate dietary intake, intestinal loss of protein, or poor absorption (malabsorption).

Other complications associated with Crohn's disease include arthritis, skin problems, inflammation in the eyes or mouth, kidney stones, gallstones, or other diseases of the liver and biliary system. Some of these problems resolve during treatment for disease in the digestive system, but some must be treated separately.

This month's "A Guide for Patients" appears on pages 73–74.

The Requisites in Gastroenterology, Volume 3

Reddy KR and Long WB, eds;
(Editor in chief: Anil K. Rustgi), Mosby 2004
ISBN: 0-323-01837-8; $95.00

This slim volume is the third in the "Requisites in Gastroenterology" and is dedicated to the study of the liver, gallbladder, biliary tract and pancreas. The "home base" for this book is the University of Pennsylvania where the majority of contributors are based; however, other distinguished experts in their respective fields from elsewhere have also participated in the writing of this book. The inclusion of gastroenterologists, hepatologists, pathologists, radiologists, and transplant surgeons has enabled a broad based and comprehensive review of these organ systems.

The hallmark of this book is the organ based approach to the review, with an emphasis on clinical practice. Ample review of the physiology and pathology of the liver and pancreas is provided, useful for the medical student as well as a refresher course for the more experienced clinician. This is also a good foundation for the clinical discussion that comes later. A major part of the book is dedicated to liver disease—about 256 pages—with a smaller 75 page section on pancreatic disorders. The concise nature of this book does not hamper its ability to provide a pertinent and comprehensive review in any way. The incorporation of current developments and newer data into this book while still focusing on essential knowledge is quite impressive. Each chapter has boxed areas of text that tabulate such information as differential diagnosis or proposed algorithms for management, to name a few. Ample illustrations are also appended to each chapter, in addition to color plates at the beginning of the book.

In summary, this is an easily readable, focused, comprehensive yet concise, clinical review with incorporation of newer developments in the field. It goes beyond its target audience of physicians needing a rapid review for recertification exams. This is an excellent review that may be as applicable to the medical student or resident on the GI service, as it is to a practicing gastroenterologist who needs a quick refresher on the latest in the field.

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The Requisites in Gastroenterology, Volume 4: Endoscopy and GI Radiology

Ginsberg GG, Kochman ML, eds., Mosby 2004
ISBN: 0-323-01885-8; $95.00

This book is the final volume in a series of four clinically oriented gastroenterology texts. While the first three volumes cover gastroenterology by way of an organ system approach, this volume describes the various diagnostic techniques spanning the entire field of gastroenterology.

The first few chapters focus primarily on endoscopy—including upper endoscopy, colonoscopy, enteroscopy, and capsule endoscopy. Topics include indications and contraindications, endocarditis prophylaxis, anticoagulation management, and conscious sedation. The focus is on common disease processes for which endoscopy is employed, both from a diagnostic as well as a therapeutic standpoint. Representative pictures of selected, relatively common endoscopic findings are demonstrated, but not to the extent of a comprehensive endoscopic atlas.

Advanced endoscopic techniques, endoscopic ultrasonography (EUS) and endoscopic retrograde cholangiopancreatograpy (ERCP) are discussed next. The use of EUS in staging of luminal gastrointestinal malignancy, clarifying submucosal lesions, and diagnosing pancreaticobiliary disease is outlined. Similarly, common indications for ERCP including choledocholithiasis, biliary strictures, and pancreaticobiliary malignancy are touched upon. As the focus is on a general review of EUS and ERCP, the technical aspects of both procedures are only briefly covered.

The final several chapters provide an overview of gastrointestinal radiology, particularly contrast radiology, percutaneous transhepatic cholangiography (PTC), magnetic resonance imaging (MRI), abdominal ultrasound, and computed tomography (CT). The chapter on contrast radiology, while at times sounding like an advertisement, provides perhaps the broadest review of gastrointestinal disease, employing the best illustrations of the entire text. It serves as an appropriate reminder of the complementary nature of contrast studies and endoscopy. The section covering PTC focuses on management of commonly encountered bil-

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iary problems, clearly outlining the pros and cons of PTC in comparison to ERCP. In the chapters discussing MRI, CT, and ultrasound specific organ pathologies are discussed and corresponding radiologic findings are demonstrated, enabling nonradiologists to recognize classic findings associated with common gastrointestinal diseases.

Endoscopy and Gastrointestinal Radiology serves as an excellent overview of the diagnostic modalities utilized in the field of gastroenterology. The book is enjoyable to read, and contains information which will benefit practitioners of all levels of experience, from medical students to practicing gastroenterologists. While lacking the detail of a reference text, it serves as a superb introduction or a well-balanced review of common gastrointestinal diseases and the diagnostic modalities employed in their diagnosis.

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George W. Meyer, M.D., Book Editor, is on the Editorial Board of *Practical Gastroenterology*

Twenty-Four Hour Simultaneous Ambulatory Impedance and pH Monitoring in GERD

A total of thirty-one 24 hour simultaneous ambulatory pharyngeo-esophageal impedance and pH recordings are reported in 11 GERD patients and in l0 patients who had reflux-attributed laryngitis and additionally in 10 healthy controls.

On average, the total number of reflux events of all kinds in the pharynx was less than half of that in the proximal esophagus. Most of the pharyngeal reflux events were gas events and were observed in all three study groups. Prevalence of, these gas reflux events ranged between 0 and 74, and were accompanied by a minor pH drop in laryngitis patients. This finding was significantly higher than those in GERD and control patients. There was no significant difference in the number of nonacid gas reflux events a month in the three groups. Impedance recording identified a total number of 566 events in the pharynx. Of these, a total of 563 events were comparable with gas reflux events, 101 events were accompanied by minor drops in intrapharyngeal pH, where as 460 events were not accompanied by any pharyngeal pH change.

It was concluded that concurrent impedance and pH recordings detect significantly more events qualifying as reflux in the pharynx than pH recordings alone. A substantial majority of these events are gaseous reflux, both with and without minor pH drops. Gas reflux events with weak acidity appear to be more common among patients with reflux-attributed laryngeal lesions, compared to GERD patients and controls. (Kawamura O, Aslam M, Rittmann T, Hofmann C, Shaker R. "Physical and pH properties of Gastroesophageal Refluxate: A 24-Hour Simultaneous Ambulatory Impedance and pH Monitoring Study." *Amer J Gastroenterol,* 2004; Vol 99, 1000-1010.)

MII-EM to Clarify Esophageal Function Abnormalities

From July 2002 through March 2003, prospectively performed combined multichannel intraluminal impedance and manometry (MII-EM) on all patients referred for esophageal function testing. Each patient received ten liquid and ten viscous swallows. Manometric findings were reported, as were MII findings as having normal bolus transit if 80 percent or more of liquid and 70 percent or more of viscous swallows had complete bolus transit.

Three hundred fifty studies were evaluated from patients with a variety of symptoms, including those with normal manometry, achalasia, scleroderma, ineffective esophageal motility, diffuse esophageal spasm, nutcracker esophagus, hypertensive lower esophageal sphincter, hypotensive lower esophageal sphincter and poorly relaxing lower esophageal sphincter. None of the patients with achalasia and scleroderma had normal bolus transit. Fifty-one percent of the patients with ineffective esophageal motility and 55 percent of the patients with diffuse esophageal spasm had normal bolus transit, while almost all patients with normal esophageal manometry, nutcracker esophagus, poorly relaxing lower esophageal sphincter, hypertensive lower esophageal sphincter and hypotensive lower esophageal sphincter had normal bolus transit. Dysphagia occurred most often in patients with incomplete bolus transit on MII testing.

It was interpreted that esophageal body pressures primarily determine bolus transit, with isolated LES abnormalities appearing to have little effect on esophageal function. MII clarifies functional abnormalcies in patients with abnormal manometric studies. (Tutuian R, Castell DO. "Combined Multi-Channel, Intraluminal Impedance and Manometry Clarifies Esophageal Function Abnormalities: A Study in 350 Patients." *Amer J Gastroenterol,* 2004; Vol 99,1011-1020.)

Azathioprine With or Without Olsalazine in UC

Patients with steroid-dependent UC in remission were randomized to receive Azathioprine (AZA), alone or in combination with Olsalazine (0.5 grams t.i.d.). Remission was defined as steroid withdrawal, and ulcerative colitis clinical activity index (UCDAI) score of less than 2, an ulcerative colitis disease activity index (UCDAI) score of 0, and a negative colonoscopy and histology. The patients were followed for two years with monthly clinical examinations and assessment of the above studies, as well as compliance with treatment, with sigmoidoscopy and completion of inflammatory bowel disease quality of life questionnaire (IBD-Q), and UCDAI every three months, and total colonoscopy with biopsies at the end of the first and second year of the trial.

Seventy patients were randomized to receive AZA alone, or with Olsalazine. Three patients in each group developed side effects, or could not comply with treatment and were withdrawn from the study. Three patients receiving AZA relapsed after the first year of the study and three after the second year of the study. In the combination therapy, four patients relapsed after the first year of the study, and two after the second year of the study. There were no significant differences between groups in time to relapse or discontinuation of therapy. However, the number of adverse events and the cost of treatment were significantly higher in the combination therapy, whereas compliance with treatment was poor.

It was concluded that patients with steroid- dependent UC, successfully maintained in remission on AZA are not in need of 5-Aminosalicylic acid compounds. (Mantzaris GJ, Sfakianakis M, Archablis E, et al. "A Prospective, Randomized, Observer-Blind Two-Year Trial of Azathioprine Monotherapy Versus Azathioprine and Olsalazine For The Maintenance of Remission of Steroid-Dependent Ulcerative Colitis." *Amer J Gastroenterol,* 2004, Vol 99, 1122-1128.)

Low-Molecular-weight Heparin to Bridge Interruption of Warfarin

Six hundred fifty consecutive patients with a mechanical heart valve, chronic atrial fibrillation or embolic stroke, who required interruption of Warfarin therapy because of an invasive procedure, were studied. Warfarin was stopped five to six days before the procedure and patients received subcutaneous Dalteparin sodium, 100 i.u./kg. b.i.d. starting three days before the procedure. The risk of post-procedural bleeding determinated post-procedure anticoagulant management. In patients undergoing a non-high-bleeding risk procedure who had adequate post-procedural hemostasis, Warfarin was resumed on the evening of the procedure and Dalteparin sodium in same dosage was resumed on the next day and continued until the international normalized ratio was 2.0 or more.

If post-procedural hemostasis was not secured, the resumption of Dalteparin was delayed. In patients undergoing a high-bleeding risk procedure, Warfarin was resumed on the evening of the procedure, but Dalteparin was not given after the procedure.

Follow-up during the pre- and post-procedural period was carried out for a mean of 13.8 days in 542 patients who underwent non-high-bleeding risk procedure. There were two thromboembolic events (0.4 percent), four major bleeding episodes (0.7 percent), and 32 episodes of increased wound-related blood loss that precluded post-procedural Dalteparin administration (5.9 percent). In 108 patients who underwent a high-bleeding risk procedure, there were two deaths (1.8 percent), possibly due to thromboembolism, and two major bleeding episodes (1.8 percent).

It was concluded that with patients with increased risk for arterial thromboembolism, who required temporary interruption of Warfarin therapy, a standardized periprocedural anticoagulant regimen with low-molecular-weight heparin is associated with a low risk of thromboembolic and major bleeding complications. (Douketis JD, Johnson JA, Turpie AG. "Low-Molecular-Weight Heparin as Bridging Anticoagulation During Interruption of Warfarin: Assessment of a Standardized, Periprocedural Anticoagulation Regimen." *Arch Int Med,* 2004; Vol 164, 1319-1326.)

GERD Symptoms and Relation to pH Findings

Fifty patients with GERD, without Barrett's esophagus were studied by dual-sensor 24 hour pH monitoring while receiving PPI therapy for complete control of GERD symptoms. Analysis of intraesophageal symptoms and intragastric pH profiles were made. Fifty percent of patients had abnormal intraesophageal pH profiles, despite adequate symptom control on therapy, which was associated with significant breakthrough of control in both the upright and supine positions. Low intragastric pH correlated highly with intraesophageal acid reflux, only in patients with persistent abnormal esophageal acid exposure.

It was concluded that 50 percent of patients with GERD without Barrett's esophagitis continue to exhibit pathological GERD and low intragastric pH, despite PPI therapy that achieves complete reflux symptom control. (Milkes D, Carson LB, Triadafilopoulos G. "Complete Elimination of Reflux Symptoms Does Not Guarantee Normalization of Intraesophageal and Intragastric pH in Patients With Gastroesophageal Reflux

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Disease (GERD). *Amer J Gastroenterol,* 2004; Vol. 99, pp. 991-996.)

Gastroesophageal Reflux Disease Poorly Responsive to Single-Dose Proton Pump Inhibitors in Patients Without Barrett's Esophagus:Acid Reflux, Bile Reflux or Both?

Sixty-five patients without Barrett's esophagus and with persistent heartburn or regurgitation during standard proton pump inhibitory therapy were studied. They were evaluated by upper GI endoscopy and simultaneous 24 hour ambulatory pH and Bilitec monitoring while proton pump inhibitor therapy was continued.

Thirty-three patients, or 51 percent, had persistent esophagitis. Seven (11 percent), had only pathological acid exposure. Twenty-five (38 percent), had only pathological duodeno-gastroesophageal reflux exposure and 17 (25 percent), had exposure to both.

Adding Bilitec increased the diagnosis of persistent reflux to 75 percent. Patients with persistent esophagitis had similar acid exposure, but significantly higher BGER exposure than those without esophagitis. The highest prevalence of esophagitis was found in patients with pathological exposure to both. Symptoms did not differ according to the type of reflux.

It was concluded that combined pH and Bilitec monitoring is superior to pH monitoring alone in demonstrating ongoing pathological reflux in patients with medically poor responsive reflux disease. (Tack J, Koek G, DeMedts I, Sifram D, Janssens J. "Gastroesophageal Reflux Disease Poorly Responsive to Single-Dose Proton Pump Inhibitors in Patients Without Barrett's Esophagus, Acid Reflux, Bile Reflux or Both?" *Amer J Gastroenterol,* 2004; Vol. 99, 981-988.)

Pneumatic Dilation in Achalasia

The potential predictors of outcome in a large group of patients with achalasia receiving graded pneumatic dilation (PD), was investigated, testing the hypothesis that this therapy may not be appropriate for all patients, evaluating patients undergoing PD from 1992 to 2002 retrospectively. Seventy-five patients with achalasia without previous therapy constituted the study's population. Three year success rates for PD, using 3 cm., 3.0 cm. followed by 3.5 cm., and 3 cm. and 3.5 cm., followed by 4 cm. Rigiflex balloons were 37 percent, 76 percent, 88 percent, respectively. Patients age and sex were important treatment outcome predictors.

3 cm. PD was significantly more likely to fail in younger men than older men. In 25 of 68 patients initially treated with a 3 cm. balloon, PD failed within 3 months. Twenty-two of 25 patients with early failure were men.

It was concluded that young men have a greater failure rate with 3 cm. PD than older men or women in general, and graded PD in this group, starting initially with the 3 cm. balloon, is more likely to fail. (Frahoomand K, Connor JT, Richter JE, Achkar E, Vaezi MF. "Predictors of Outcome of Pneumatic Dilation in Achalasia." *Clin Gastroenterol and Hepatol,* 2004; Vol. 2, 389-394.)

Chronic Abdominal Wall Pain

The records of all outpatients referred to a gastroenterologist in five years recorded referral indications and identified patients initially diagnosed with chronic abdominal wall pain (CAWP) for irritable bowel syndrome. Of 2,709 patients, CAWP was diagnosed by physical examination in 137 patients; the diagnosis remained unchanged after 47.3 ± 17.7 months in 133 patients. Women predominated over men 4:1. Pain was usually upper abdominal, and lasted 25.3 ± 46.3 months. Obesity and painful comorbidities and depression were common.

CAWP and IBS comprised 7.8 percent and 16.3 percent of symptomatic referrals, respectively. Prereferral, physicians rarely suspected CAWP and often prescribed therapy for acid peptic disease. Post-consultation, primary care, emergency and specialist visits and radiologic visits markedly decreased and estimated cost decreased significantly. Therapy varied and 44 patients had no pain at follow-up evaluation.

It was concluded that CAWP is a common, underrecognized disorder. Comorbidities are frequent and health care use is high. The diagnosis is accurate and reduces health care costs over the long term. Pain disappearance and persistence occurs in approximately equal proportion to patients. (Costanza CD, Longstreth GS, Liu AL. "Chronic Abdominal Wall Pain: Clinical Features, Health Care Costs and Long-Term Output." *Clin Gastroenterol and Hepatol,* 2004; Vol. 2, 395-399.)

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