TAP Pharmaceutical Products Receives FDA Approval for Pediatric Labeling Of PREVACID® (Lansoprazole)

TAP Pharmaceutical Products Inc. announced the U.S. Food and Drug Administration (FDA) has approved Prevacid® (lansoprazole) for the short-term treatment of symptomatic gastroesophageal reflux disease (GERD) and erosive esophagitis in children from the ages of 1 to 11 years old.

"Although people often think of GERD as an adult condition, many children are affected by it," said Benjamin Gold, M.D., director of pediatric gastroenterology and nutrition at Emory University School of Medicine. "It is important that there are FDA-approved treatment options for children who experience the often painful effects of GERD."

GERD is one of the most common esophageal disorders in children. When stomach contents, such as food and gastric acid, frequently reflux out of the stomach and into the esophagus, esophageal tissue damage may occur. Common symptoms in children include regurgitation (spitting up), chest pain (heartburn), abdominal pain, feeding resistance and difficulty swallowing.

"The symptoms of GERD are uncomfortable for children, and can be disruptive for both the child and his or her family," said Beth Anderson, executive director of the Pediatric/Adolescent Gastroesophageal Reflux Association. "We encourage parents who suspect their child may be suffering from GERD to approach their doctor and discuss symptoms, diagnosis and treatment options."

For children who have difficulty swallowing capsules, Prevacid is the only PPI with an oral suspension formulation. The oral suspension is strawberry- flavored. Additionally, the granules from a Prevacid capsule can be sprinkled on certain soft foods and mixed into select juices. Granules should not be chewed or crushed and the oral suspension should not be given through a feeding tube.

Prevacid has the most administration options and the most approved indications of any PPI for adults. It is the only PPI indicated for the healing and risk reduction of the recurrence of gastric ulcers associated with NSAIDs (non-steroidal anti-inflammatory drugs).

In adults, Prevacid is indicated for the treatment of heartburn and other symptoms of GERD; the treatment and maintenance of erosive esophagitis, a condition in which stomach acid injures the lining of the esophagus; treatment of active benign gastric ulcers; the treatment and maintenance of healed duodenal ulcers; treatment of pathological hypersecretory conditions, including Zollinger-Ellison Syndrome; and the healing and risk reduction of the recurrence of gastric ulcers associated with NSAIDs.

Symptomatic response to therapy does not preclude the presence of serious stomach problems. Prevacid is contraindicated in patients with known hypersensitivity to any component of the formulation. The most frequently reported adverse events in adults include diarrhea, abdominal pain, and nausea. In pediatric GERD patients between the ages of 1 to 11, the most frequently reported adverse events were constipation and headache.

FDA Approves ZELNORM, A Novel Treatment for Irritable Bowel Syndrome in Women With Constipation

Zelnorm is First and Only Prescription Therapy for the Relief of the Common Symptoms of Abdominal Pain and Discomfort, Bloating, and Constipation in Women with IBS

The Novartis drug Zelnorm(tm) (tegaserod maleate) has been approved by the U.S. Food and Drug Administration (FDA) for the short-term treatment of women with irritable bowel syndrome (IBS) whose primary bowel symptom is constipation. Until now, no prescription medication has been approved in the United States to treat the multiple symptoms of abdominal pain and discomfort, bloating, and constipation associated with IBS. The medical community has recognized that therapies traditionally used to treat these symptoms have been generally ineffective or poorly tolerated.

"Zelnorm marks a breakthrough for the millions of women who have suffered for years with IBS with constipation waiting for a safe and effective therapy to relieve their symptoms," said Daniel Vasella, MD, Chairman and CEO, Novartis AG. ". . . Zelnorm reflects our commitment to bring innovative treatments to patients with significant unmet needs. We will rapidly make Zelnorm available to patients, and plan for an early fall market introduction."

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IBS is characterized by abdominal pain and discomfort, bloating, and altered bowel function (constipation and/or diarrhea). IBS affects up to one in five Americans. Second only to the common cold as a leading cause of workplace absenteeism in the U.S., IBS costs the U.S. healthcare system up to an estimated $30 billion annually in direct and indirect costs.

"Patients suffering from abdominal pain, bloating, and constipation associated with IBS endure a great deal of distress, often preventing them from participating in such simple everyday activities as going to work or school, participating in sports, or enjoying a vacation with their family," said Nancy Norton, President and Founder of the International Foundation for Functional Gastrointestinal Disorders. "The approval of Zelnorm is very exciting news for millions of women who suffer from this condition."

Until recently, the cause of IBS has been poorly understood and under appreciated. However, in recent years, new research has yielded a better understanding of IBS and its causes. People who have abdominal pain and discomfort, bloating and constipation associated with IBS have a lower GI tract that may be more sensitive and work more slowly than it should. This may be due to the way their lower GI tract reacts to changes in a naturally occurring chemical in their body that regulates motility and the perception of pain and discomfort.

Zelnorm is the first agent in a new class of drugs called serotonin-4 receptor agonists (5HT4 agonist) developed to target the GI tract. By activating 5HT4 receptors, Zelnorm stimulates the peristaltic reflex and normalizes impaired motility in the GI tract. Zelnorm is the first agent proven to provide relief of the abdominal pain and discomfort, bloating and constipation of IBS.

"IBS with constipation is a very real medical disorder that has frustrated patients and physicians due to the obvious lack of safe and effective prescription medications to treat the painful symptoms," said Walter L. Peterson, MD, University of Texas, Southwestern School of Medicine in Dallas. "Zelnorm is an important advancement in IBS therapy. We can now provide safe and effective symptom relief to a significant number of patients for whom this was not possible before."

The FDA approval of Zelnorm is based on clinical trials that show Zelnorm provides relief of the abdominal pain and discomfort, bloating and constipation in women with IBS.

Three multicenter, double-blind, placebo-controlled studies involved 2,470 women with at least a three-month history of IBS symptoms prior to the study baseline period. Patients received either Zelnorm 6 mg/b.i.d. or placebo over a three-month period.

Each week, participants rated their responses to the "Subject's Global Assessment of Relief," a measurement tool which takes into account overall well-being, symptoms of abdominal pain and discomfort, and constipation. Based on this assessment, more patients on Zelnorm experienced relief than patients on placebo. In addition, Zelnorm was shown to provide relief of the individual symptoms of abdominal pain and discomfort, bloating, and constipation.

In clinical studies, Zelnorm was generally well tolerated. Side effects that occurred more often with Zelnorm than with placebo were headache (15% vs. 12%) and diarrhea (9% vs. 4%). The majority of the Zelnorm patients reporting diarrhea had a single episode. In most cases, diarrhea occurred within the first week of treatment. Typically, diarrhea resolved with continued therapy. Zelnorm is not indicated for patients who are currently experiencing or frequently experience diarrhea. The safety and effectiveness of Zelnorm in men have not been established.

Kidney & Urology Foundation Announces $1.4 Million in Grant Funding for Research

Twenty Research and Clinical Fellowships Awarded This Year

The Kidney & Urology Foundation of America has announced it is providing grant funding totaling $1.4 million for research and clinical fellowships as well as career development and young investigators awards. This year, the organization is providing more than 20 research and clinical fellowships in kidney and urologic research. The Foundation is also awarding a young investigator $50,000 for two years and the same amount to an investigator as a career development award. In addition, awards have been granted for research projects at a number of institutions such as University of Michigan at Ann Arbor and Johns Hopkins University in Baltimore, Maryland.

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The Kidney & Urology Foundation is the first organization to truly integrate the fields of nephrology and urology for the advancement of research and enhancement of patient care. The Foundation is also one of the largest sources of philanthropic funding in the U.S. for the study of disease mechanisms of action and new therapies for kidney and urologic disorders.

Kidney disease affects 20 million Americans and another 20 million Americans are at risk. Kidney diseases directly cause 60,000 deaths and are associated causes of death for more than 250,000 people in the U.S. annually. The number of kidney failures in the U.S. is increasing by about 6 to 8 percent a year. This is not surprising since diabetes and high blood pressure conditions that are on the rise in the U.S.—are two of the leading causes of kidney disease and eventually kidney failure. Another 50 million Americans, men and women, suffer from some type of urologic disorder, including prostate disease, erectile dysfunction, urinary incontinence, urinary tract infections and hypertension.

"There is a great need to support innovative scientific research in the fields of nephrology and urology, especially at the basic research stage of investigation," said Ira Greifer, M.D., of the Kidney & Urology Foundation and pediatric nephrologist at Montefiore Medical Center, New York City. "At the Kidney & Urology Foundation, we believe we can promote ground-breaking discoveries through our ongoing grants and fellowship programs."

For the 2002–2003 funding year, the Kidney & Urology Foundation awarded 21 research and clinical fellowships of $30,000 annually, each of which are renewable. The grants cover a wide range of disease study, from the functional genomics of diabetic nephropathy to the correlation between depression and urinary incontinence.

New Caltrate® Colon Health™ Helps Protect the Colon and Bone with Just Two Tablets Daily

New Caltrate® Colon Health™: just 2 tablets daily provide 400 IU of vitamin D and 3 grams of calcium carbonate (1200 mg of elemental calcium)—the dose shown in a *New England Journal of Medicine* study to help reduce the risk of recurrent colorectal adenomas and the dose recommended in gastroenterological practice guidelines on adenoma management.

Remicade® (infliximab) is the First Biologic Therapy Approved by the FDA to Induce and Maintain Clinical Remission in Patients with Moderate-to-Severe-Crohn's Disease

Reduction in Steroid Use, Improvement in Health-Related Quality of Life also Evaluated

The US Food and Drug Administration (FDA) granted marketing approval to Remicade® (infliximab) to provide long-term remission-level control of the debilitating symptoms of Crohn's disease (CD), a gastrointestinal disorder that affects more than a half-million Americans. Remicade is the first and only biologic approved to reduce signs and symptoms and induce and maintain clinical remission in patients with moderately to severely active Crohn's disease who have had an inadequate response to conventional therapy.

The approval was based on 54-week data from the ACCENT I trial, the largest study of a biologic therapy ever conducted in Crohn's disease, involving 545 patients with moderate to severe CD at centers in North America, Europe and Israel. The objective of the trial was to evaluate the safety and effectiveness of Remicade as a maintenance therapy for CD. The study also evaluated the effect of maintenance regimen on steroid use and health-related quality of life.

"The painful and debilitating symptoms of Crohn's disease can have a substantial impact on a patient's daily life," said Gary Lichtenstein, M.D., Associate Professor of Medicine, Director of the Center for Inflammatory Bowel Diseases, Hospital of the University of Pennsylvania. "For the first time, we have a therapy that can both induce and maintain remission-level control of disease symptoms, in many cases, while reducing or eliminating the need for steroid use. This is a significant advance."

Patients enrolled in the ACCENT I trial were given a single Remicade 5 mg/kg infusion. Those who responded at week two were randomly assigned to three treatment groups. One group received placebo at weeks two and six followed by repeat infusions of placebo every eight weeks. The second group received infusions of 5 mg/kg of Remicade at weeks two and six followed by subsequent infusions at the same dose every eight weeks. A third group received infusions of 5 mg/kg of

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Remicade at weeks two and six followed by repeat infusions of 10 mg/kg every eight weeks thereafter. Infusions continued for all treatment groups through week 46. The co-primary endpoints were the proportion of patients who responded at week two and were still in remission at week 30, and the time to loss of response through week 54 in patients who responded. Response and remission were assessed using the Crohn's disease activity index (CDAI). Response was defined as a decrease of 2 5% and 70 points in CDAI score. Remission was defined as a CDAI score of less than 150.

Researchers found that 57 percent of patients (311/545) responded to a single infusion of Remicade at two weeks of treatment. Among responders, significantly more patients receiving maintenance treatment with Remicade 5mg/kg achieved clinical remission at week 30 (39 percent) compared to placebo maintenance patients (25 percent). Additionally, patients in the Remicade maintenance groups had a longer time to loss of response than patients in the placebo maintenance group.

A significantly greater proportion of patients receiving maintenance therapy with Remicade were in clinical remission and able to reduce or eliminate steroid use compared to those treated with placebo. At week 54, more than twice as many patients in the Remicade 5 mg/kg maintenance group were in remission and had discontinued steroid use (25 percent) compared to patients treated with a single infusion of Remicade 5 mg/kg followed by placebo (11 percent).

In the ACCENT I trial, the Inflammatory Bowel Disease Questionnaire (IBDQ) and the Short-Form 36 (SF-36) were used to assess disease-specific and health-related quality of life, respectively. The IBDQ and the SF-36 are validated patient-reporting tools. The IBDQ provides relevant data on bowel function and abdominal pain, systemic symptoms, social functioning and emotional health. The SF-36 is a measurement tool used to assess the physical and mental health status of a patient. At weeks 30 and 54, a significant improvement from baseline was seen among patients in the 5 mg/kg and 10 mg/kg Remicade treated groups compared to the placebo group in the disease specific IBDQ, particularly in the bowel and systemic components, and in the physical component summary score of the SF-36.

Remicade is a monoclonal antibody that specifically targets and irreversibly binds to TNF-α. Overproduction of TNF-α is believed to play a role in CD and RA, and may also be important in a wide range of other immune-mediated inflammatory disorders.

In addition to reducing pain and stiffness and inhibiting the progression of structural damage, Remicade, in combination with methotrexate, is the first and only drug approved by the FDA to improve physical function in patients with moderately to severely active RA who have had an inadequate response to methotrexate alone. Remicade is the only drug that can address all key elements of RA treatment, as defined by the new 2002 American College of Rheumatology treatment guidelines.

When treating patients with Crohn's disease, the recommended dose of Remicade is 5 mg/kg given as an induction regimen at zero, two, and six weeks followed by a maintenance regimen at the same dose every eight weeks thereafter. Remicade is also approved for the reduction in the number of draining enterocutaneous fistulas in patients with fistulizing Crohn's disease. The safety and efficacy of therapy for fistulizing Crohn's disease continued beyond three doses have not been established.

Many people with heart failure should not take Remicade; so, prior to treatment, doctors should discuss any heart condition with their patients. Doctors should tell their patients to contact them right away if they develop new or worsening symptoms of heart failure (such as shortness of breath or swelling of their feet).

There are reports of serious infections, including tuberculosis (TB) and sepsis. Some of these infections have been fatal. Doctors should ask their patients if they have had recent or past exposure to people with TB. The doctor should evaluate the patient for TB and perform a skin test. If a patient has latent TB, the doctor should begin TB treatment before starting Remicade. If a patient is prone to or has a history of infections, currently has one, or develops one while taking Remicade, the doctor should be consulted right away. Doctors should ask the patients if they have lived in a region where histoplasmosis is common, or if they have or have had a disease that affects the nervous system, or if they experience any numbness, tingling, or visual disturbances.

There are also reports of serious infusion reactions with hives, difficulty breathing, and low blood pressure. In clinical studies, some people experienced the following common side effects: upper respiratory infections, headache, nausea, cough, sinusitis or mild reactions to the infusion such as rash or itchy skin. ■

Pathology of the Liver, Fourth Edition

Edited by MacSween RNM, Burt AD, Portman BC, Ishak KG, Scheuer PJ, Anthony PP.
Churchill Livingstone 2001.
982 pages.
Price: £205 (about $350)
ISBN: 0443061815

The fourth edition of *Pathology of the Liver* contains succinct, yet detailed, discussions of every aspect of liver disease by the world's most renowned experts. The content includes every liver disease identified so far, and it is up to date and clinically relevant. The color photographs including the histologic micrographs and electron micrographs are of excellent quality and well chosen to demonstrate important pathology throughout the entire book

The authors reprinted the forward to the first edition, written by Dr. Hans Popper in 1979. He emphasized the importance of the interaction of hepatologists, pathologists and basic scientists to further advance the understanding of liver diseases. This is even more important now and this book provides a framework for a better understanding of not only hepatic pathology, but hepatic anatomy, physiology, concepts, and terminology. Higher quality medical care can be delivered if communication between the hepatologist and pathologist is facilitated. The fully competent hepatologist must understand the hepatopathology and the pathologist must understand clinical hepatology. This book is an excellent resource for those working to achieve that level of competence. Each chapter is well organized to facilitate clinical pathological correlation for each topic discussed.

This comprehensive textbook is divided into 18 chapters and starts out with an excellent discussion of anatomy and physiology of the liver. The next 11 chapters are devoted to various broad categories of liver disease including developmental abnormalities, inherited metabolic diseases, autoimmune hepatitis, alcoholic liver disease, and acute and chronic viral hepatitis. Then there are chapters devoted to cirrhosis, tumors of the liver, and transplantation pathology. Included in the chapter on viral hepatitis is a good clinical discussion of acute and chronic hepatitis B and C including a discussion of the various systems of grading and staging chronic viral hepatitis. There is an excellent state of the art discussion of the mechanisms of fibrosis and the role of the stellate cell in the chapter on cirrhosis. The chapter devoted to hepatic injury due to drugs and toxins, co-authored by Dr. Hyman Zimmerman, is comprehensive and superb. Chapter 16 which covers liver pathology associated with diseases of other systems, includes a good discussion of non-alcoholic steatohepatitis. This is also discussed in conjunction with alcoholic liver disease. The chapter on Autoimmune Hepatitis is excellent and contains a state of the art summary of autoimmune hepatitis and overlap syndromes, complete with clinical and pathologic criteria for diagnosis. Each chapter contains excellent illustrations and is followed by an extensive list of key references to facilitate additional study in each area.

The two diseases that hepatologists see most in clinical practice are hepatitis C and non-alcoholic fatty liver disease (NAFLD). These diseases are discussed but I would have liked to see more on each topic, including some more illustrations and examples of histology of the various grades and stages of each.

This is a comprehensive reference text that can be used by hepatologists and pathologists in daily practice. It should be in every pathology department and readily available to hepatologists and hepatology fellows. This is a hardcover book containing just under

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1000 pages and it is not portable. That may be its only drawback. This book may be easier to use on CD-ROM and perhaps we may look forward to that in the next edition.

M.P. Pauly, M.D.
Sacramento, CA

Schuster Atlas of Gastrointestinal Motility in Health and Disease

Schuster MM, Crowell MD and Koch KL, eds
2002 BC Decker Inc, Ontario, Canada
ISBN: 1-55009-104-2
Price: $149.00

Advances in the understanding of gastrointestinal motility disorders have inspired the second edition of this definitive text on the subject. First published in 1993 as the *Atlas of Gastrointestinal Motility in Health and Disease,* this new edition has been renamed the *"Schuster Atlas of Gastrointestinal Motility in Health and Disease* in honor of the original editor. Two additional editors participate in this new edition as well as an impressive list of contributing authors. The second edition, which has been expanded from 323 to 472 pages, is organized in a more reader friendly fashion than the first. It begins with a brief introduction into the physiology of motility, with the subsequent chapters organized by organ system, describing normal function and clinical disorders of each. Other motility-related topics are discussed including post-operative motility disorders, pharmacology, therapeutic modalities, issues specific to pediatrics, and surgical therapies. This text includes a complete CD-ROM version which, although easier to slip into one's shirt pocket than the text, it is merely an exact PDF format version of the text and does not offer any special features.

Those with a strong interest in the details of myoelectrical activity, calcium channels, and brain-gut interaction will find the first fifty-five pages an elegant and detailed review. Other readers may walk away with a headache after trying to digest the complicated information and detailed figures. The inclusion of this information is, however, important to the completeness of the text and serves as a useful reference.

The sections devoted to each organ system are well organized and written. Disorders of the esophagus, stomach, small bowel, and colon are discussed separately. Much like the first edition a large amount of the information is in the form of sample tracings and figures. Visually oriented readers will appreciate the multitude of figures, charts, and graphs, but others may find this distracting. Readers who would prefer to sift through paragraphs of written text may have a difficult time looking at pages containing only figures with occasionally very long captions. Although awkward at first, the reader tends to become familiar with this format. A majority of the figures appear to be transferred from the first edition.

Physicians familiar with the frustration of treating motility disorders will find the sections on biofeedback and pharmacologic therapies fairly satisfying. These sections are quite up to date and include information on newer drugs such as tegaserod and alosetron. The chapter on surgical therapies provides important information for the most difficult to treat cases. In general the text is quite up to date but some topics are left out. Examples are the emerging technologies of wireless pH monitoring and gastric pacing.

In summary, this is the definitive text on gastrointestinal motility and a must for the bookshelves (or hard-drives) of physicians and surgeons who are involved in the diagnosis and treatment of motility disorders. Every gastroenterologist will find parts of this text useful and interesting, although some sections are fairly detailed and technical. Gastroenterology and surgical training programs should have this important text available in their libraries.

Brennan A. Scott, MD
Sacramento, California

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

ORDER PRACTICAL GASTROENTEROLOGY REPRINTS

HCV and HIV

A prospective cohort study that was university-based in an urban clinic in the United States reviewed 1955 patients enrolled between January, 1995 and January, 2001, and who were free of acquired immunodeficiency syndrome at enrollment. Follow-up was an average of 2.19 years for HCV-infected and 2 years for HIV uninfected patients. No difference was detected in the risk of acquiring an AIDS-defining illness, with HCV infected patients having 26.4 percent with the events and HCV uninfected patients 24.4 percent, or in the risk of death (HCV-infected patients 17.5 percent and HCV uninfected patients 15.5 percent), although an increased risk of death was detected in 429 HCV-infected patients with a baseline CD4 cell count of 50 per microliters through 200 per microliters, after adjustment for exposure to HAART and its effectiveness in a multivariate cox regression analysis, death was not independently associated with HCV infection in this subgroup. Similarly, in those receiving effective HAART, there was no difference in the increase in CD4 cell count or CD4 percentage during HAART in HCV-infected, compared with HCV uninfected patients.

It was concluded that among patients in this urban US cohort, they did not detect evidence that HCV infection substantially alters the risk of dying, AIDS or responding immunologically to HAART, especially after accounting for differences in its administration and effectiveness. (Sulkowski MS, Moore RD, Mehta FH, Chaisson RF, Thomas DL. "Hepatitis C and Progression of HIV Disease." *JAMA,* 2002; Vol. 288, pp. 199–206.)

Budesonide Capsules in Active Crohn's Disease

A multi-centered, double-blind, randomized trial, including 200 patients in the United States with mild to moderate Crohn's disease with a Crohn s disease activity index (CDAI) between 200 and 450, involving the distal ileum and/or ascending colon was carried out, administering 9mg of Budesonide CIR (controlled ileal release) once daily, 4.5mg b.i.d. or placebo for an 8 week period.

The primary outcome was evaluated, to include remission, defined as a CDAI of 150 or less.

In this study, remission was achieved in 48 percent, 53 percent and 33 percent, with 9 mg once daily, 4.5mg b.i.d. and placebos respectively after a week of treatment. The difference between the groups was not significant statistically, but there was a difference in the CDAI. There was no difference in adverse effects between treatment groups, though a modest decrease in plasma cortisol levels was observed, compared with placebo.

It was concluded that in treatment of symptomatic Crohn's disease with Budesonide, CIR capsules 9mg daily was safe and remission rates were similar to those achieved in previous trials, with a change in the CDAI from baseline, but no difference in remission, compared with placebo. (Tremaine WJ, Hanauer SB, Katz S, et al. "Budesonide CIR Capsules (Once or Twice Daily Divided-Dose) in Active Crohn's Disease: A Randomized Placebo-Controlled Study in the United States." *American Journal of Gastroenterology,* 2002; Vol. 97, pp. 1748–1754.)

Botox in Non-Cardiac Chest Pain

Twenty-nine non-cardiac chest pain patients with non-achalasia, non-reflux, non-related spastic esophageal motility disorders were enrolled in an open label trial of Botulinum toxin injection at the gastroesophageal junction. Chest pain was a major complaint in all patients. Symptoms were scored before and one month after injection. A response was defined as at least a 50 percent reduction in symptom score, with a possible total chest pain score of 4.

72 percent of the patients responded with at least a 50 percent reduction in chest pain. In those responding, there was a 79 percent reduction in the mean chest pain score. The mean duration response was 7.3, ± four months, with a range of 1 to 18 months. There was a significant reduction in the mean regurgitation score, dysphagia score and total symptom score.

It was concluded that Botulinum toxin injection at the gastroesophageal junction leads to significant symptomatic improvement in patients with spastic esophageal motility disorders, whose major complaint is chest pain. (Miller LS, Pullela SV, Parkman HP, et al. "Treatment of Chest Pain in Patients with Noncar-

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diac, Non-Reflux, Non-Achalasia, Spastic Esophageal Motor Disorders using Botulinum Toxin Injection into the Gastroesophageal Junction." *American Journal of Gastroenterology,* 2002; Vol. 97, pp. 1640-1646.)

One Dose Polyethylene Glycol Laxation

Twenty-four adult study subjects who met Rome II criteria for constipation were randomized in a double-blind parallel pilot study to receive a single dose of placebo or PEG laxative in doses of 51, 68 or 85 grams in 500mL of flavored water. Over a 72-hour period, subjects rated bowel movements, completeness of evacuation and satisfaction.

A 68 gram dose seemed to be the most satisfactory. Five of six subjects had a bowel movement within 24 hours. The time to first bowel movement was l4.8 hours for 68 grams versus 27 hours for placebo. The time to second bowel movement was 19 hours, versus 47 for 68 grams and placebo, respectively.

The average number of bowel movements in a 24-hour period ranged from one to two for placebo to 4.2, with 84 grams. There were no adverse reactions, no incontinence, cramps or diarrhea at any dose. There were no changes in biochemical studies or osmolality.

It was concluded that a 68 gram dose of PEG laxative seems to produce safe and effective relief in constipated adults within a 24-hour period. (DiPalma JA, Smith JR, Cleveland NB. "Overnight Efficacy of Polyethylene Glycol Laxative." *American Journal of Gas - troenterology,* 2002; Vol. 97, pp. 1776-1779.)

Cholecystectomy vs. Endoscopic Sphincterotomy in Gallstone Pancreatitis

Eighty-three patients (group A) underwent cholecystectomy after initial ERCP in 43 and ERCP with sphincterotomy in 38. The remaining 34 underwent successful ERCP with sphincterotomy alone. Mean follow-up was 33 to 34 months. Recurrent gallstone pancreatitis was noted in two patients in group A and one patient in group B. Ten patients in group B had follow-up ultrasound with disappearance of stones in three. During follow-up, there was no significant difference in the rate of biliary complications. 3.6 percent versus 11.6 percent were serious complications (pancreatitis, cholecystitis, cholangitis). There was no significant difference in procedure-related complications.

It was concluded that recurrence of pancreatitis after ERCP with sphincterotomy alone for gallstone pancreatitis is rare. In those patients who have undergone endoscopic sphincterotomy alone, cholecystectomy should be considered only if there are overt manifestations of gallbladder disease (biliary pain, cholecystitis, cystic duct obstruction), and not for the prevention of recurrent gallstone pancreatitis. However, because treatment by sphincterotomy alone may be associated with a higher risk of biliary complications during follow-up compared with cholecystectomy, these patients may require close surveillance. (Clark AWM., Al-Antably Y, Clark AWP, "Management of Gallstone Pancreatitis: Cholecystectomy or ERCP and Endoscopic Sphincterotomy." *Gastrointestinal Endoscopy,* 2002; Vol. 56, pp. 61-65.)

Botox in Idiopathic Gastroparesis

Ten patients with idiopathic gastroparesis, nonresponsive to prokinetic therapy underwent Botulinum toxin injection into the pyloric sphincter. Gastric emptying scintigraphy was performed before and four weeks after treatment. Total symptom scores were obtained from the sum of eight upper GI symptoms, graded on a scale from 0 to 4. Solid gastric retention and symptoms score decreased remarkably and improvement in symptoms tended to correlate with improved gastric emptying of solids.

This initial pilot study suggested that Botulinum toxin injection into the pylorus in patients with idiopathic gastroparesis improves both gastric emptying and symptoms. (Miller LS, Szych GA, Kantor SB, et al. "Treatment of Idiopathic Gastroparesis With Injection of Botulinum Toxin Into The Pyloric Sphincter Muscle." *American Journal of Gastroenterology,* 2002; Vol. 97, pp. 1653–1660.)

Treatment of Recurrent C. Difficile Disease

One hundred and sixty-three cases with recurrent *Clostridium Difficile* disease were prescribed either Vancomycin or metronidazole and randomized to

either the investigational biological or a placebo. All patients were observed for at least 2 months for subsequent episode. A tapering course of Vancomycin resulted in significantly fewer recurrences, as did post-dosing of Vancomycin.

A trend for a lower recurrence frequency was observed, with high dose Vancomycin (2 grams or more per day). Vancomycin was significantly more effective in clearing *C. difficile* culture and/or toxin by the end of therapy than metronidazole was.

The persistence of *C. difficile* spores suggest that additional strategies to restore the normal colonic micro flora may also be beneficial. (McFarland LV, Elmer GW, Surwicz CM. "Breaking the Cycle; Treatment Strategies for 163 Cases of Recurrent Clostridium Difficile Disease." *American Journal of Gastroenterology,* 2002; Vol. 97, pp. 1169-1775.)

Recombinant Factor VIIa in Patients With Liver Disease

Activated Recombinant Factor VII (rFVIIa) has been shown to be effective in correcting prothrombin time in cirrhotic patients. Seventy-one patients with advanced liver disease, platelet count greater or equal to 60,000 and of prothrombin time in a range of 3 to 5 seconds above normal were included in the study. End points were a normalization of PT and time to hemostasis.

PT was corrected to normal levels in the majority of patients. The duration of normalization of PT was longer in patients treated with higher doses of rFVIIa. Forty-eight (74 percent) of 65 patients achieved hemostasis within 10 minutes in the larger dose group. No correlation between the time to hemostasis and the duration of correction of PT was observed. None of the patients required operative intervention. Laparoscopic liver biopsy was performed to control bleeding. One thrombotic event and one case of disseminated intravascular coagulation were reported, but both events were considered by the investigator as unlikely the be related to treatment.

It was concluded that treatment with rFVIIa may offer benefit for patients with liver disease undergoing laparoscopic biopsy.(Jeffers L, Chalasani N, Balart L, et al. "Safety and Efficacy of Recombinant Factor VIIa in Patients with Liver Disease Undergoing Laparoscopic Liver Biopsy." *Gastroenterology,* 2002; Vol. 123, pp. 118-126.)

Botox and Chronic Anal Fissure

Fifty-seven patients with idiopathic chronic anal fissure who had completely healed six months after injection of Botulinum toxin were reassessed every six months. Follow-up was 42 months in all patients. Clinical and manometric differences between the permanently healed and the relapsed group were statistically analyzed. Four patients were lost to follow-up. A fissure recurrence was shown in 22 patients (41.5 percent). Statistical differences between the permanently healed and the relapsed group were detected when analyzing the anterior location of the fissure (6 percent versus 45 percent), at longer duration of the disease, (38 percent versus 68 percent), the need for reinjection (26 percent versus 69 percent), a higher dosage injected to achieve definitive healing (13 percent versus 45 percent), and the percentage decrease of maximum squeeze pressure after injection (28 percent versus 13 percent).

It was concluded that the late recurrence rate of chronic anal fissure is high when the effect of Botulinum toxin disappears. The highest risk of recurrence is associated with anterior location of the anal fissure, prolonged illness, the need for reinjection and for high doses to achieve healing, and the lower decrease of maximum squeeze pressure after treatment. (Minguez M, Herreros B, Espi A, et al. "Long-Term Follow-Up (42 Months) of Chronic Anal Fissure After Healing with Botulinum Toxin." *Gastroenterology*, 2002 Vol. 123, pp. 112-117.)

Budesonide and Antibiotics in Crohn's Disease

A double-blind, multicenter study of patients with active Crohn's disease of the ileum, right colon or both was carried out, randomized to receive oral ciprofloxacin and metronidazole, both 500 mg b.i.d. or a placebo for 8 weeks, establishing efficacy, depending on the proportion of patients in remission at week eight. 134 patients were randomized, 130 were evaluated for efficacy, 66 received placebo and 64 received

antibiotics. 21 patients (33 percent) were assigned to antibiotics and were in remission as compared to 25 patients (38 percent) in the placebo group. Among patients with disease of the colon, 53 percent were in remission after treatment with antibiotics, compared with four of those who received placebo.

Discontinuance of therapy because of adverse events occurred in 13 of 66 (20 percent) treated with antibiotics, compared with none in the placebo group.

In this group of patients with active Crohn's disease of the ileum being treated with Budesonide, further improvement was produced only when there was involvement of the colon. (Steinhart AH, Fleagan BG, Wong CJ, et al. "Combined Budesonide and Antibiotic Therapy for Active Crohn's Disease: A Randomized, Controlled Trial." *Gastroenterology,* 2002; Vol. 123, pp. 33-40.)

Preoperative Staging in Rectal Cancer

Eighty consecutive patients with newly diagnosed rectal cancer were prospectively evaluated. Therapy decisions were recorded after sequential disclosure of staging information to the patient and surgeon. In 31 percent of the patients, EUS staging information changed the surgeon s treatment plan that was originally based on CT scans alone. The further addition of FNA changed therapy in one patient. TT staging accuracy was 71 percent by CT and 91 percent by EUS. End staging accuracy was 78 percent by CT, 82 percent by EUS and 78 percent by combined EUS and FNA.

It was concluded that preoperative staging with EUS results in more frequent use of preoperative neoadjuvant therapy than if staging were performed with CT alone. The addition of FNA only changed the management in one patient, but did not significantly improve end staging accuracy over EUS alone. FNA seems to offer the most potential for impacting management in those patients with early T-stage disease and its use should be confined to this subgroup of patients. EUS is more accurate than CT for determining T-stage of rectal carcinoma. (Herewood GC, Wiersema MJ, Nelson H, et al. "A Prospective Blinded Assessment of the Impact of Preoperative Staging on the Management of Rectal Cancer." *Gastroenterology,* 2002 Vol. 123, pp. 24-32.)

Erythromycin For Pre-Endoscopic Use in UGI Bleeding

Fifty-one patients were evaluated administering intravenous bolus infusion of Erythromycin 250mg, compared with placebo twenty minutes before endoscopy, evaluating endoscopic yield as assessed by objective and subjective scoring systems and endoscopic duration. Those end points included the need for a second look, endoscopic-related complications, blood units transfused and length of hospital stay. Fifty-four patients received the placebo. A clear stomach was found more often in the Erythromycin group (82 percent versus 33 percent), and shortened the endoscopic duration and reduced the need for second-look endoscopy. Length of hospital stay and blood units transfused did not significantly differ between the two groups. No complications were noted.

It was concluded that Erythromycin infusion before endoscopy in patients with recent hematemesis makes endoscopy shorter and easier, therefore reducing the need for a repeat procedure. (Frossard JL, Spahr L, Edouard P, et al. "Erythromycin Intravenous Bolus Infusion in Acute Upper Gastrointestinal Bleeding; A Randomized, Controlled Double-Blind Trial." *Gastroenterology,* 2002 Vol. 123, pp. 17-23.)

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