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WORLD GASTROENTEROLOGY NEWS

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OMGE PRACTICE GUIDELINE ON

MANAGEMENT OF ACUTE VIRAL HEPATITIS

Views on the **Irritable Bowel Syndrome,** Treatment of **Crohn's disease,** and the Treatment of **Hepatitis C**

Brilliant Successes with the **Train-The-Trainers** Program

Endoscope Disinfection: Quality Assurance is **Key**

Official Newsletter of the World Gastroenterology Organisation (OMGE/WGO) and the World Organisation of Digestive Endoscopy (OMED)

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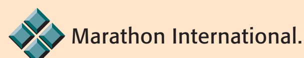

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Message from the Editor-in-Chief

Jerome D. Waye, MD

Jerome D. Waye

The World Congress of Gastroenterology will be held in Montreal less than 2 years from now. It is time for gastroenterologists from every specialty: medicine, surgery, pathology, hepatology, pediatrics, and radiology to clear our calendars for the quadrennial meeting which will bring everybody together in Montreal for great science, great education, and great fun. Let's everybody get behind this congress in Montreal, Canada to make it the best ever.

This issue brings you science, information, and updates in the field of gastroenterology. We have invited world experts who presented papers at the annual meeting of the American College of Gastroenterology in Baltimore (October 2003) to share with us their views on the Irritable Bowel Syndrome, treatment of Crohn's disease, and the treatment of Hepatitis C. We have also enlisted the aid of Dr. Henry Cohen, Secretary General of the World Congress of Gastroenterology who was the director of a course in gastroenterology in Uruguay (28 September to 2 October, 2003) who directed us to some of the speakers who were invited to present talks at the Uruguay Congress of Gastroenterology meeting. These lectures concerned NASH, cox-2 inhibitors, and biphosphonates used for bone integrity. We also have special articles on complications of colonoscopic polypectomy, and on colon cancer prevention. The ICDA has completed a survey of gastroenterologists in the management of patients with colon cancer, and there is a report on a new initiative on colon cancer screening in Germany. The cancer articles are part of the overall GI cancer initiative by the OMGE-sponsored "International Digestive Cancer Alliance". There are meaningful comments from two surgical endoscopists, and sadly, there is an obituary by Professor Vilardell concerning the death of world-renowned Professor Kunio Okuda. The combined OMGE/OMED education and training committee continues to achieve brilliant successes with the Train-The-Trainers program, and with an endoscopic outreach program spearheaded Dr. DiSario, appointed through OMED. Once again we are publishing an OMGE practice guideline. This one, on the management of Acute Hepatitis, is packed with useful information.

Lastly, we bring you an interesting article which will help every gastroenterologist interface with PubMed (a free website published by the US National Library of Medicine). This article and the one in the next issue will vastly improve the capability of finding all the articles possible by using various search strategies that are relatively straightforward, but not widely known.

It is uplifting to share with you the exciting advances that OMGE and OMED are continuing to develop in the field of gastroenterology as we explore new frontiers and take the lead in establishing standards for education and training throughout the world. ■

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Message from the Senior Editor

OMED at the Beginning of the 21st Century

Alberto Montori

Alberto Montori

The Organisation Mondiale d'Endoscopie Digestive/World Organization of Digestive Endoscopy (OMED) has been very active in the last two years under the chairmanship of its President, Professor H. Niwa. Thanks to the invaluable support provided by the technical secretariat, with their dedication to the work of our members and colleagues, and thanks to the generosity of our partners, OMED is able to continue its quest for excellence in endoscopy and is continuing to be a driving force in the field.

Recent activities included the first OMED Spring Meeting, held in Rome on 4–5 May 2003 at the same time as both the fifth International Gastric Cancer Congress and a meeting of the International Digestive Cancer Alliance (IDCA; see the OMED web site, www.omed.org). The international colorectal screening campaign has been a real challenge, and thanks to Paul Rozen, it has been possible for the Ad Hoc Committee to discuss results obtained in this field all over the world. The joint meetings with the IDCA in Rome and in Orlando were very successful, and this type of cooperation appears to be promising for the future.

OMED has been strongly involved in the following efforts:

- Further developing the internationally accepted standard terminology for endoscopy reporting.
- Issuing international guidelines for endoscopic procedures.
- Supporting research in endoscopy.
- Extending the availability of endoscopy training.
- Improving the standard of care in areas of great need throughout the world.
- Improving understanding and collaboration between gastroenterologists, endoscopists and laparoscopic surgeons.
- Expanding the OMED web site as a vehicle for exchanging information among endoscopists.

Cooperation with the Organisation Mondiale de Gastro-Entérologie/World Organization of Gastroenterology (OMGE) is excellent, and we have already merged a number of initiatives: the educational programs, the Train the Trainers Workshops, the Gastro-Pro web portal, and *World Gastroenterology News* with Jerry Waye as Editor-in-Chief.

Following this policy of development and cooperation, OMED has expanded enormously, to the benefit of everyone in the endoscopic community, and has also been fully involved in many specific events throughout the world.

The second OMED Spring Meeting will be held in Yokohama, Japan, on 4–5 May 2005 in conjunction with the sixth International Gastric Cancer Congress. While of course OMGE and OMED continue to maintain their own distinctive identities, these joint meetings show that cooperating rather than working in isolation is easier and more productive – saving time, reducing costs and effort, and achieving the best possible results. ■

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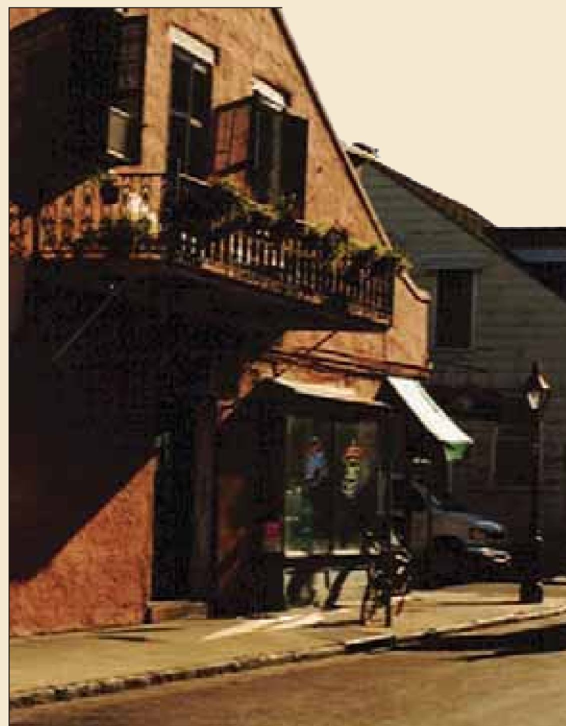
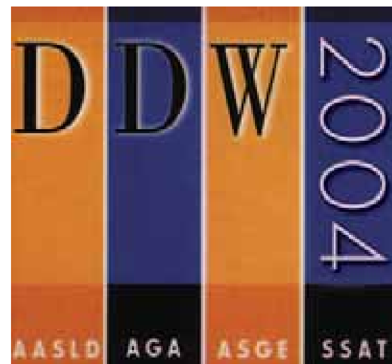


Lagniappe from the Big Easy



The 'Big Easy', otherwise better known as New Orleans, has a strange local word 'lagniappe' (pronounced lan-yap), which means 'a little something extra'. During the period of 15–20 May, that little something extra will take the form of Digestive Disease Week (DDW®). DDW is the largest gathering of gastroenterological professionals in the world and, although a long way from being little, it will bring that something extra to the city and be the place for gastroenterologists for a few days.

Sponsored by four of the world's premier medical societies, the American Association for the Study of Liver Diseases (AASLD), the American Gastroenterological Association (AGA), the American Society for Gastrointestinal Endoscopy (ASGE) and the Society for Surgery of the Alimentary Tract (SSAT), DDW continues to provide a diverse and comprehensive programme for participants from around the globe.

Educational offerings are provided in a variety of formats and settings to meet the varied objectives of attendees—from small group settings that facilitate the participation of attendees and interaction with faculty to larger, classroom style settings. With nearly 5 000 abstracts and six full days of educational programming, DDW and the DDW societies' postgraduate courses promise a wide selection of topics designed for clinicians and researchers alike. Each of the four sponsoring societies will offer programming unique to their specialties as well as collaborate on joint programming.

AASLD is hosting state-of-the-art lectures on topics such as treatment of hepatitis B, management of ascites and hepatorenal syndrome and alcoholic liver disease as well as three highly focused plenary sessions, where the best scientific papers in the areas of liver biology, clinical hepatology and viral hepatitis will be presented. Clinical symposia on a number of topics, including hepatocellular carcinoma and apoptosis will be offered, as well.

AGA's highlights at DDW 2004 in New Orleans include some new, restructured and returning program elements. New for this year are Focused Research Roundtables, where expert moderators review and preview selected basic science abstracts from the DDW program. Restructured for 2004 is the plenary session, where major developments in basic science and clinical research will be reviewed. Back by popular demand are the clinical track, Focused Clinical Updates and Problem Based Learning Luncheons, all focusing on a wide array of topics in the fields of gastroenterology and liver disease.

ASGE will offer some new and expanded educational programming, as well. The hands-on learning course on anti-reflux devices, using animal models, focusing on endocinch, NDO (full thickness plicator), stretta and enteryx techniques, will likely be popular, as should the poster tours lead by experts in the field of endoscopy. This year's "Test your Knowledge" session has been expanded to include three topic areas: luminal endoscopy, ERCP and EUS.

SSAT offers a new opening session with introduction of new members, reports on the society and foundation, recognition of foundation donors, the Presidential Address and the Presidential Plenary Session. Additional SSAT program highlights include a state-of-the-art conference on management of radiation induced intestinal injury, a video breakfast session featuring colorectal reconstruction, hepatic ablation techniques and respective procedures for rectal cancer. A public policy session, titled "Physician Competency: Teaching an Old Dog New Tricks" is also part of the SSAT programme.

As ever, you can find all of the information about DDW at **www.ddw.org.** For more on this famous host city, go to **www.neworleanscvb.com**, where you'll find out more about its cute nicknames – the Crescent City and the Big Easy – and learn that the 'neutral ground' is the local term for the median or middle of the road. Sounds more like a challenge! ■

SEPTEMBER 10-14, 2005

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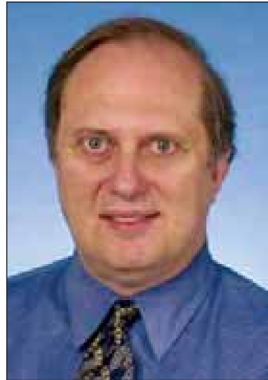
Integrated Approach To Irritable Bowel Syndrome

Douglas A. Drossman

Classification and definition


Douglas A. Drossman

The understanding of the pathophysiology of irritable bowel syndrome (IBS) has evolved from an etiological concept – that it is a disorder of abnormal motility – to a more integrated understanding consistent with a biopsychosocial framework. It is a composite of several physiological components: dysmotility, visceral hypersensitivity, and abnormalities in brain–gut regulation. IBS is defined as a functional gastrointestinal disorder of the lower bowel characterized by abdominal pain associated with disturbed defecation (diarrhea or constipation), often with feelings of bloatedness and/or distension. Psychosocial disturbances are not a part of the definition, and in fact are not present in most persons with IBS.

IBS is seen primarily in young to middle-aged women (M : F ratio 1 : 2). In the USA, it has been reported that the disorder represents 12% of family practice work and 28% of cases in gastroenterology practice. Recent studies in the USA have looked at the cost of IBS to society. This is estimated at $1.6 billion (primarily due to inpatient hospitalizations and clinic visits), with an additional $20 billion due to indirect costs (lost workdays owing to health-care visits and illness in general).

IBS patients differ from normal individuals in the degree of physiological response to various stimuli; however, there is no specific stimulus or response pattern that is characteristic of IBS.

Symptom-based criteria, known as the Rome criteria, for the diagnosis of IBS have been established by multinational consensus (Rome II). They are based on epidemiological and clinical studies, as well as factor-analytic studies (Table 1).

Recent interest has also focused on basing more invasive diagnostic studies on the presence of historical information from simple laboratory studies, "alarm signs" or "red flags" such as: weight loss, blood in stools, nocturnal symptoms, abnormal physical examination, anemia, or a family history of cancer or inflammatory bowel disease. Thus, the presence of Rome II criteria and the absence of red flags reduces the need to carry out more invasive diagnostic tests. This view was supported in one study, in which the positive predictive value for IBS was 98–100% when patients were screened in this manner.

Treatment

Treatment is directed toward ameliorating symptoms, modifying factors that aggravate the disorder, and helping the patient adapt to the condition.

General approach. Continuity of care is needed to minimize unneeded diagnostic procedures, to offer symptomatic treatment, and to educate, counsel, and provide psychological support. An effective physician–patient relationship is at least as important as any specific treatment.

Addressing the predominant symptom. For example, after excluding other medical disorders, a patient with *predominant diarrhea* might receive antidiarrheal agents (such as loperamide or cholestyramine), while a patient with *predominant constipation* would be treated with fiber or osmotic cathartics (such as sorbitol or lactulose). However, because many patients with constipation-predominant IBS may also have visceral hypersensitivity, they may develop more bloating or discomfort with fiber. In these cases, it might be better to use a nonosmotic agent, such as polyethylene glycol (PEG) solutions or the new 5-hydroxytryptamine4 (5-HT_4) agonists (eg. tegaserod) that increase colonic transit rate and reduce pain.

The treatment of *predominant pain or discomfort* varies with the severity of the symptoms. If the pain/discomfort is mild or infrequent and is clearly meal-related (i.e., occurring about 20 min after a meal), an anticholinergic or antispasmodic agent can be considered and should be taken about 20–

Table 1. *Rome II diagnostic criteria for irritable bowel syndrome*

At least 12 weeks (need not be consecutive) of abdominal discomfort or pain in the preceding 12 months, with two of the following three features:
1. Relieved with defecation; and/or
2. Onset associated with a change in frequency of stool; and/or
3. Onset associated with a change in form (appearance) of stool

30 min before the meal. If the pain is associated with diarrhea, a 5-HT_3 antagonist (alosetron) may be considered. If the pain is more constant and severe (see below), an antidepressant – tricyclic antidepressant (TCA) or selective serotonin reuptake inhibitor (SSRI) – can be prescribed for central analgesic effect and for treatment of psychiatric comorbidity (e.g., depression, panic), if present.

The majority of patients with IBS most often seen in primary care have mild or infrequent symptoms and no significant functional impairment or psychological difficulties. The physician should offer education and reassurance. Patients should eliminate offending food items and increase dietary fiber if constipation is present.

A smaller proportion of patients have moderate symptoms that occur intermittently and occasionally result in functional impairment (such as missing work or school, etc.). These patients often identify a close relationship between symptoms and inciting events (e.g., dietary indiscretion, distressing experiences). It is helpful to have the patient *keep a symptom diary* in which the time, severity, and presence of associated factors are recorded over several weeks. *Pharmacotherapy directed at the gut* should also be considered when symptoms flare (see above). In addition to the *supportive psychotherapy* inherent in listening and providing explanation and reassurance, these patients may benefit from *stress management advice*. Recent evidence favors the use of cognitive-behavioral treatment for moderate to severe IBS.

A very small subset of IBS patients (less than 5%) have severe, refractory symptoms. The pain does not always correlate with meals, activity, or other physiological changes. Because symptoms are severe, patients may be convinced that a serious disease is being overlooked. There is usually concomitant psychological distress (anxiety, depression) and impaired daily functioning. The patients may request more diagnostic studies or even narcotics, in the hope of finding an "answer" or obtaining relief. Here the physician also must help the patient find ways to understand the disorder and to learn ways of adapting to and coping with the symptoms. For this group of patients, ordering tests to provide reassurance is counter-therapeutic. It is best to state clearly that the focus of care is on management rather than diagnosis. Usually, pharmacotherapy directed at the gut alone is not sufficient. Treatment must also include: a) setting realistic goals; b) not reinforcing illness-related behaviors; c) when needed, withdrawing the patient from narcotics; d) developing behavioral techniques for pain control (e.g., stress management, biofeedback, exercise); and e) the use of centrally acting psychopharmacological agents for mood disturbance and pain control. In the most severe cases, referral to a pain treatment center may be needed. Continuing care needs to be provided through brief, regular appointments with the primary care physician, and less frequently with the consultant.

- Consider a 5-HT_4 agonist (e.g., tegaserod) for constipation-predominant symptoms and a 5-HT_3 antagonist (e.g., alosetron) for diarrhea-predominant symptoms.

Management of Crohn's Disease

William J. Sandborn

Treatment agents

A number of different medications that are currently available for clinical use in the United States have been studied in randomized controlled trials for the treatment of Crohn's disease. The efficacy of these agents will be reviewed here.

Sulfasalazine. Sulfasalazine was show to be effective at a dosage of 1 g/15 kg body weight (4.7 g for a 70-kg patient), compared to placebo, for active Crohn's disease. However, a subgroup analysis suggested that only patients with colonic involvement benefited from sulfasalazine therapy.

Mesalamine. Three large trials compared mesalamine (Pentasa) 4 g/day to placebo for active Crohn's disease. Pentasa was somewhat better than the placebo, but the small absolute difference is of dubious clinical significance. A meta-analysis of 10 studies showed that oral mesalamine is not consistently effective for maintenance of medically induced remission, and that the overall benefit is minimal.

Metronidazole. Significant toxicity from metronidazole has been recorded. Studies demonstrate that metronidazole is not effective in inducing remission in patients with active Crohn's disease, and that it did not maintain clinical remission after 1 year when administered for postoperative remission maintenance.

Prednisone. Studies demonstrate that although high-dose conventional corticosteroids are very effective in inducing remission,

- Centrally acting analgesics (antidepressants) are recommended, using low-dose tricyclic antidepressants, particularly for symptoms of pain and diarrhea and serotonin reuptake inhibitors if there is a high level of anxiety, obsessional behaviors, or other psychiatric comorbidities.

Prognosis

With an adequate (and usually minimal) diagnostic evaluation, the likelihood of overlooking a serious medical disorder is very small (0–3%). Outcome studies of patients followed for a mean of 6 years indicate a missed diagnosis rate of 3–5% Yet, when followed over this period of time, the majority will still have symptoms. The physician's effort is to help the patient manage a chronic or recurrent disorder with a minimum of diagnostic studies and a cost-effective plan of care. ■

Note: This paper was presented at the American College of Gastroenterology annual meeting held in Baltimore, Maryland, USA on October 10–15, 2003. The full-length version of this article and an accompanying reference list are available in the online version of World Gastroenterology News (www.worldgastroenterology.org).

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low-dose corticosteroids are not effective for maintaining medically induced remission, and that many patients treated with conventional corticosteroids will become steroid-dependent.

Budesonide. Budesonide is a corticosteroid that is administered topically to the terminal ileum and right colon. Because budesonide undergoes high first-pass hepatic metabolism, it has fewer systemic effects than conventional corticosteroids. Budesonide is more effective than mesalamine 4 g/day for inducing remission in patients with active Crohn's disease. Budesonide prolongs the time to relapse in patients with medically induced remission, but does not meet the conventional criteria for maintenance of remission at 1 year.

William J. Sandborn

Azathioprine and 6-mercaptopurine. Azathioprine and 6-mercaptopurine are immunosuppressive drugs with a relatively slow onset of action, requiring 4–12 weeks to achieve a therapeutic effect. They are clearly effective in maintaining steroid-induced remission. Uncontrolled studies have also suggested possible efficacy for fistula closure.

Methotrexate. Methotrexate, an immunosuppressive drug administered intramuscularly or subcutaneously at a dosage of 25 mg/week, is effective in inducing remission in patients with steroid-dependent and steroid-refractory Crohn's disease. It is also effective for maintaining remission in patients with steroid-dependent Crohn's disease who have previously responded to methotrexate.

Infliximab. Infliximab is a chimeric monoclonal antibody to tumor necrosis factor (TNF). It is effective for inducing remission in patients with active Crohn's disease and for closing fistulas in patients with fistulizing Crohn's disease. Infliximab administered every 8 weeks is effective for maintaining remission and for maintaining fistula closure in patients with inflammatory Crohn's disease who have previously responded to infliximab.

Treatment indications

Induction of remission. Sulfasalazine is modestly effective for inducing remission in patients with active Crohn's disease, with the benefit confined largely to patients with Crohn's colitis. Mesalamine and metronidazole are not consistently effective for inducing remission. Budesonide is more effective than mesalamine and as effective as, but safer than, prednisone. Budesonide is therefore the first-line treatment of choice for inducing remission in patients with mild to moderately active Crohn's disease involving the terminal ileum or right colon, whereas sulfasalazine is the optimal first-line therapy in patients with Crohn's colitis. Figure 1 shows an evidence-based treatment algorithm for first-line therapy of Crohn's disease.

For patients who have disease that is moderate to severe, and in patients in whom budesonide or sulfasalazine treatment has failed, the next step is second-line therapy

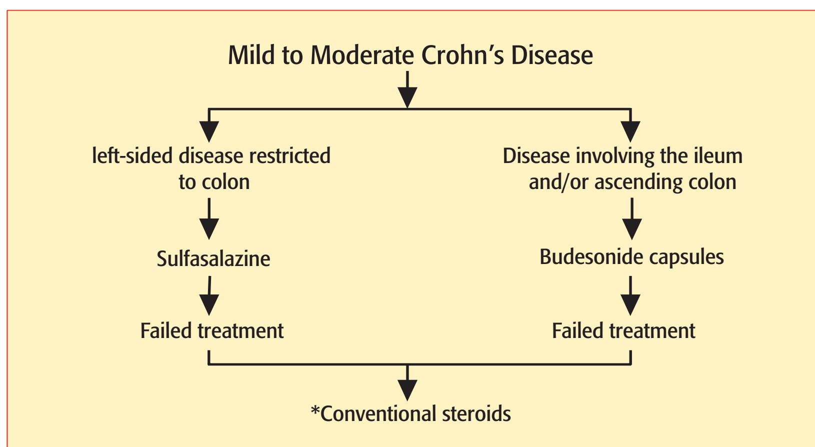

Fig. 1. *First-line treatment for Crohn's disease. * Indicates that if there is no improvement, there is a need to reclassify the patient as having moderate to severe disease and evaluate for treatment with infliximab, immunomodulators, or surgery.*

with prednisone. Azathioprine, 6-mercaptopurine, and methotrexate are of limited value as induction agents in patients with significantly active Crohn's.

Maintenance of medically induced remission. Sulfasalazine is not effective for maintenance of medically induced remission, and mesalamine is not consistently effective. Low-dose prednisone is not effective for maintenance of remission; patients treated with steroids for active Crohn's disease often become steroid-dependent. Azathioprine, 6-mercaptopurine, and methotrexate are all effective for maintenance of remission, particularly steroid-induced remission. Infliximab is effective for maintenance of remission in patients refractory to other therapies. Concomitant immunosuppression is required.

Conclusions

The conclusions regarding therapy for different treatment indications in patients with Crohn's disease are summarized in Table 1. ■

Note: This paper was presented at the American College of Gastroenterology annual meeting held in Baltimore, Maryland, USA on October 10–15, 2003. The full-length version of this article and an accompanying reference list are available in the online version of *World Gastroenterology News* (www.worldgastroenterology.org).

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Table 1. *Indications for treatment in patients with Crohn's disease.*

Drug	Mildly to moderately active	Refractory	Fistulizing	Severely active	Remission maintenance
Sulfasalazine	Yes	? Yes[2]	No	No[3]	? Yes[1]
Oral mesalamine	? Yes[1]	? Yes[2]	No	No[3]	? Yes[1]
Antibiotics	? Yes[1]	? Yes[2]	? Yes[1]	No	? Yes[1]
Oral corticosteroids	Yes	Yes[2]	No	No	No
Intravenous corticosteroids	No	Yes[4]	No	Yes	No
Azathioprine/6-mercaptopurine	No	Yes	Yes	No	Yes
Methotrexate	No	Yes	No	No	Yes
Ciclosporin	No	No	? Yes[5]	? Yes[5]	No
Infliximab	No	Yes	Yes	? Yes	? Yes
Surgical resection	No	Yes	Yes	Yes	No

1. Controlled trials do not consistently show benefit, but the treatment is commonly used in clinical practice.
2. Typically continued as a carry-over of treatment for mildly to moderately active disease when additional agents are added.
3. Typically discontinued because of the possibility of intolerance to sulfasalazine or mesalamine.
4. Some patients in whom oral corticosteroid treatment fails will respond to hospitalization with intravenous administration of corticosteroids.
5. No controlled trials conducted; uncontrolled studies suggest benefit.0

Current Status of HCV Therapy

K. Rajender Reddy

Major advances have been made in the treatment of chronic hepatitis C during the last 10 years, but major challenges remain, since treatment with pegylated interferons and ribavirin is effective in only around 55% of patients. Newer therapies are needed for the increasing numbers of patients who do not respond to or relapse after current treatments with pegylated interferons and ribavirin.

Polyethylene glycol (PEG) is a nontoxic polymer that can be attached to interferons, a process termed "pegylation". Modification of proteins by pegylation can lead to prolonged absorption, delayed clearance, and reduced immunogenicity. Their delayed clearance and their longer half-life allow once-weekly rather than three times weekly dosages with standard interferon (IFN).

Two PEG-IFN formulations have been developed. Pegylated interferon alfa-2b uses a 12-kDa polyethylene glycol, and pegylated interferon alfa-2a has a branched-chain PEG. Both are given with ribavirin in the treatment of chronic hepatitis C (HCV) infection. Pegylated interferon alfa-2b is administered as a weight-based regimen, whereas pegylated interferon alfa-2a is a fixed-dose regimen.

In several clinical trials, the response rates with pegylated interferon monotherapy have been twice as high as those with unmodified interferon. Combinations of PEG-IFNs and ribavirin are the current standard of care for the treatment of hepatitis C, as this regimen has been shown to be more effective and equally well tolerated as unmodified IFN/ribavirin.

The variables that have been associated with improved response rates include genotypes other than 1, lower pretreatment viral loads, lower body weight of 75 kg or less, younger age, and to a lesser extent the absence of cirrhosis. A post-hoc analysis of the virological data from the two large pivotal trials has led to the concept of evaluating an early virological response (EVR) in predicting the subsequent response to ongoing therapy. The absence of an EVR (defined either as a drop of 2 log or more in HCV RNA or negative HCV RNA findings at week 12 of therapy) has been associated with a very low probability of achieving a sustained virological response with continuing therapy. Overall, approximately 80% of patients receiving therapy achieve an EVR. More importantly, less than 2% of patients who do not achieve an EVR go on to have a sustained viral response (SVR) with ongoing therapy. Thus, it is reasonable to apply a "stop therapy" rule at week 12 in patients who do not achieve an EVR.

A multicenter global trial focusing on several important issues relevant to genotype, viral load, duration of therapy, and dose of ribavirin has validated the post-hoc analysis of PEG-IFN alfa-2b and ribavirin therapy and supports the use of a higher dosage of ribavirin in genotype 1 patients, particularly those with a high viral load, as opposed to the lower dose of 800 mg used in the clinical trial.

Increasing numbers of patients receiving the combination therapy with pegylated interferon and ribavirin do not respond, or relapse after treatment. Recognizing that there is a potential histological benefit from interferon therapy, the issue of maintenance therapy arises in virological nonresponders – particularly those with advanced fibrosis. The hypothesis that fibrosis can be reversed – particularly with a favorable impact on certain end points of cirrhosis, such as liver failure and liver cancer – is currently being tested in a large multicenter trial (the HALT-C trial). Preliminary data have shown that treatment with pegylated interferon alfa-2a (180 µg/week) and ribavirin (1000–1200 mg/day) in previous nonresponders to interferon treatment or interferon and ribavirin treatment led to an overall sustained virological response rate of 18%.

Ribavirin-like drugs

The mode of action of ribavirin is not well understood, but it is an effective drug in the treatment of chronic hepatitis C when used in combination with interferon. A combination of actions of the drug may exist – inhibiting viral replication and also enhancing the host's immune response. The use of ribavirin is limited by the development of anemia, which not infrequently leads to dose reduction or discontinuation of the drug. Levovirin, a second-generation L-isomer of ribavirin, is associated with less anemia, presumably due to a lack of conversion of the agent in the erythrocytes to monophosphate, diphosphate, and triphosphate intermediates. Clinical trials with this compound are awaited. Viramidine, a prodrug of ribavirin, has a longer residence time in the liver and produces less hemolysis owing to a comparatively lower uptake by the erythrocytes. Phase II trials are

currently under way with viramidine in combination with pegylated interferon.

Clinical trials of several therapies for HCV are currently in progress, including molecular-based therapies. Direct inhibitors of HCV enzymes (protease, helicase, and polymerase) intuitively offer the best chance of clearing HCV infection. Several compounds are being evaluated in the replicon systems that have targeted inhibition against HCV polymerase, NS3 helicase, and NS2-3 and NS3-4A proteinases. These compounds have not entered clinical trials, although it is expected that these drug groups will provide the next line of treatment for chronic hepatitis C, particularly with the goal of eradicating hepatitis C infection.

Summary

Treatment with pegylated interferon (either alfa-2b or alfa-2a) and ribavirin is the current standard of care for patients with chronic hepatitis C. To achieve the best response, genotype 1 patients need a longer period of therapy, at 48 weeks, with a higher dose of ribavirin of 1000/1200 mg. Genotype 2 and 3 patients respond as well to a combination of pegylated interferon alfa-2a 180 µg/week and ribavirin 800 mg/day orally for 24 weeks as compared to 48 weeks of such combination therapy, even at a higher dose of ribavirin of 1000–1200 mg; 24 weeks of therapy are therefore adequate in these patients. Current therapies are effective in approximately 55% of the overall population of patients with chronic hepatitis C. There are a number of special population groups in whom the role of treatment is less well established. In addition, there is a significant number of nonresponders to current therapy for whom improved treatments need to be developed. A lack of an early virological response (defined either as a drop of 2 log or more in HCV RNA or negative HCV RNA findings at week 12 of therapy) is an important negative predictor of a sustained virological response to continued therapy.

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NASH and NAFL in 2004

Keith D. Lindor

Introduction

Nonalcoholic steatohepatitis (NASH) is characterized by elevated serum aminotransferases with hepatic steatosis, inflammation, and occasionally fibrosis that may progress to cirrhosis. This condition is part of a spectrum of nonalcoholic fatty liver disease (NAFL). No established treatment exists for this potentially serious disorder. Small, uncontrolled studies have shown biochemical and histological improvement in patients with NASH who are treated with pioglitazone or rosiglitazone.

Keith D. Lindor

Background

Nonalcoholic steatohepatitis (NASH) refers to the development of histological changes in the liver that are comparable to those induced by excessive alcohol intake, but in the absence of alcohol abuse. Macrovesicular and/or microvesicular steatosis, lobular and portal inflammation, and sometimes Mallory bodies with fibrosis and occasionally cirrhosis characterize NASH. NASH is commonly associated with hyperlipidemia, obesity, and type II diabetes mellitus, but this is not always the case. Other clinical conditions characterized by hepatic steatosis and inflammation include excessive fasting, jejunoileal bypass, total parental nutrition, chronic hepatitis C, Wilson's disease, and adverse drug effects such

as those from corticosteroids, calcium-channel blockers, high-dose synthetic estrogens, methotrexate, and amiodarone. The term "nonalcoholic steatohepatitis" is used to describe patients with the previously described biopsy findings and a lack of significant alcohol consumption, previous surgery for weight loss, a history of drugs associated with steatohepatitis, and evidence of genetic liver disease or chronic hepatitis C infection.

Pathogenesis of nonalcoholic steatohepatitis

The pathogenesis of NASH is unknown. A correlation seems to exist between the degree of steatosis and the degree of fibrosis. Steatotic livers secondary to alcohol abuse and type II diabetes mellitus contain predominantly triglycerides, and to a lesser extent cholesterol esters. Elevated free fatty acids have been identified in liver specimens from patients with fatty liver of pregnancy, alcoholic hepatitis, and morbid obesity.

The metabolism of triglycerides in adipose tissue leads to the release of free fatty acids into the circulation with uptake by hepatocytes. Insulin inhibits the metabolism of triglycerides in adipose tissue, increases the hepatic synthesis of free fatty acids and triglycerides, and inhibits the beta-oxidation of free fatty acids in hepatocytes. Obesity and type II diabetes mellitus are hyperinsulinemic states with decreased tissue sensitivity to insulin. This resistance to the effects of insulin seems to be an almost universal underlying feature of NAFL. In-vitro studies have shown that free fatty acids are potentially cytotoxic. Cellular damage may result in cellular death and subsequent fibrosis. Reduction of hepatic free fatty acids could decrease hepatocellular injury. Elevated hepatocellular free fatty acids cause membrane injury with subsequent inflammation, possible cholestasis, and subcellular organelle dysfunction. Cell death and fibrosis follow persistent inflammation, and cirrhosis occurs if the injury continues.

Bacterial overgrowth may contribute to higher levels of endotoxin-inducible cytokines such as tumor necrosis factor (TNF), which have been implicated in NASH. The role of hepatic iron remains controversial. Elevated iron levels may contribute to oxidative stress. On the other hand, we and others have not found evidence of excess iron or any correlation between hepatic iron levels and the histological severity of NASH.

Natural history

The natural history of NASH is incompletely defined. There are no symptoms specific for the disease. Patients with nonalcoholic steatohepatitis frequently have evidence of fibrosis at the time of initial liver biopsy, with an incidence ranging from 14% to 100%. Cirrhosis, though less common, may be present in 0–38% of cases. Among 42 patients followed up for a median of 4.5 years, 13 patients had serial biopsies over a period of 1–9 years. Approximately 30% had evidence of disease progression – a figure similar to the numbers of patients with hepatitis C who develop progressive liver disease. Older age, obesity, diabetes mellitus, and an aspartate aminotransferase/alanine aminotransferase (AST/ALT) ratio greater than 1 were independent predictors of liver fibrosis in NASH.

Steatohepatitis is now regarded as an important cause of end-stage liver disease and may be the cause of an unknown number of cases of cryptogenic cirrhosis. Unfortunately, once cirrhosis has become established, the only therapeutic modality available for advanced disease is orthotopic liver transplantation. However, after liver transplantation for NASH, the disease may recur.

Treatment

Because the etiology is unknown, empirical approaches have been used, based primarily on findings of hyperlipidemia, the presence of diabetes, iron overload, or presence of inflammation. Weight loss is usually advocated as an initial treatment; however, the value of this has not been well substantiated. More recently, a study showed that diet and exercise led to a reduction in AST, ALT, serum lipids, and body weight in patients with NASH; however, less than 5% of obese patients seem to be able to sustain weight loss. Lipid-lowering agents have been tested. The fat in hepatocytes usually consists of triglycerides, and hypertriglyceridemia is a common coexisting condition. A pilot study of clofibrate treatment in 16 patients with hyperlipidemia did not lead to any beneficial effects in liver biochemistry or histology, and side effects were common. Gemfibrozil potentiates lipoprotein lipase in the same way as clofibrate. In a clinical study of 46 patients who received the drug for 1 month, improvements in transaminases and lipid levels were found. Orlistat, a lipase inhibitor, was administered for 6 months in eight obese patients with NASH. The drug reversed fat completely in six patients and improved inflammation and fibrosis.

Oxidant stress has also been proposed as a mechanism of liver injury in these patients. Metformin has been tested in pilot studies and led to normal liver tests after treatment in some patients, with

an improved liver biopsy at 1 year. This interesting finding was further pursued in a study with 20 patients treated for 4 months, who showed biochemical improvement. The insulin sensitizers proglitazone and rosiglitazone also appear promising in uncontrolled trials.

Cytoprotective agents have been used as well. Ursodeoxycholic acid (UDCA) is potentially cytoprotective, may prevent membrane injury, and has been useful in primary biliary cirrhosis. In a pilot study, in patients with NASH, the use of ursodiol led to improvement in alkaline phosphatase, ALT, and gamma-glutamyl transferase (GGT), as well as the grade of fat on biopsy. A long-term randomized controlled trial was recently completed, but failed to confirm the benefits of UDCA.

Another recent abstract suggested that low-dose prednisone led to improvement in transaminase levels. Most recently, homocysteine levels have been found to be higher in patients with nonalcoholic steatohepatitis. Betaine, the drug used to treat homocystinuria, was tested in 10 patients with NASH for 1 year of therapy. Seven of the 10 completed the year's treatment. Of these, three showed normalization of liver biochemistry, another three had greater than 50% improvement, and histological improvement by two or more points was seen in half of the patients – suggesting that this is a very promising new therapy.

Liver transplantation

As mentioned above, NASH is becoming an increasingly important reason for liver transplantation. NASH can recur aggressively after transplantation, which suggests that the metabolic defect underlying the development of the condition is not principally controlled by the native liver. ■

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Gastrointestinal Effects of Bisphosphonates

Frank L. Lanza

Bisphosphonates are a relatively new class of compounds that prevent osteoclast-mediated bone resorption and are therefore now used extensively in the treatment of patients with osteoporosis and Paget's disease. They are of particular interest to gastroenterologists because of their adverse effects in the gastrointestinal tract, especially esophageal injury and gastroduodenal ulceration. These side effects may significantly limit the use of these agents.

Frank L. Lanza

Alendronate and risedronate are the most commonly used orally administered drugs of this type. Shortly after the introduction of alendronate, numerous reports of erosive esophagitis and ulceration appeared. This was thought to be due to contact injury and reflux of acidified alendronate (alendronic acid) into the distal esophagus. Appropriate dosing instructions were subsequently devised that alleviated this problem, except in patients with preexisting reflux disease or motility disorders of the esophagus.

Short-term studies of 2 weeks or less in normal volunteers or patients with osteoporosis with both alendronate and risedronate also revealed acute ulceration in the stomach and duodenum in 5–15% of participants. However, studies in similar populations carried out for 30 days with both drugs revealed an ulcer incidence of only 3%. Patients with osteoporosis were subsequently evaluated for 10 weeks with the now more commonly used once-weekly 70-mg dose of alendronate, and no ulcers were seen.

Symptomatic ulcers and the complications of peptic ulcer disease, perforation, obstruction, and bleeding have not been significantly increased in numerous efficacy trials of both of these agents. The largest of these, the Fracture Intervention Trial, evaluated over 3000 women taking alendronate

for 3 years, with a similar matched number of patients receiving a placebo; no differences in the incidence of gastrointestinal side effects were seen between the two groups. A recent case-controlled cohort study of over 6000 alendronate users revealed no increase in gastrointestinal bleeding, perforation, or ulcer hospitalizations for the alendronate-exposed group in comparison with a control group having osteoporosis and osteoporotic fractures.

Conclusions

Erosive esophagitis is a significant problem with bisphosphonate drugs. It can be avoided by following the recommended dosage instructions and by not administering these agents to patients with reflux disease or motility disorders of the esophagus. The acute ulcers seen in the stomach and duodenum of patients taking these agents are self-limited in duration, and are not associated with the symptoms or complications of peptic ulcer disease. ■

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The Cox-2 Inhibitors – Are They Really Safer?

Frank L. Lanza

The cyclooxygenase-2 (Cox-2) inhibitors are a relatively new class of nonsteroidal anti-inflammatory drugs (NSAIDs) that selectively inhibit the form of cyclooxygenase that catalyzes prostaglandin production at sites of inflammation. Theoretically, these drugs offer a significant advantage over the older traditional NSAIDs, which are nonselective in that they inhibit both Cox-1 and Cox-2. Cox-1 is found in almost all tissues, including the stomach, where it facilitates the production of mucosal protective prostaglandins. Inhibition of Cox-2 leads to mucosal injury and ulceration in 20–30% of all patents using these drugs chronically. Two to four percent of these patients develop gastrointestinal bleeding or other complications of ulcer disease.

The Cox-2 inhibitors that have been evaluated most extensively are rofecoxib and celecoxib. Numerous clinical trials have evaluated these two drugs in comparison with the older nonselective NSAIDs with regard to the rates of erosive gastropathy and ulcer in both normal volunteers and arthritic patients. All of these studies have shown conclusively that the degree of injury seen with the Cox-2 agents is much less than that with the nonselective agents. Two large outcome trials have also been reported, each evaluating over 8000 patients for gastrointestinal bleeding and other complications of ulcer disease. In one trial, rofecoxib 50 mg/day was compared with naproxen 500 mg b.i.d., and in the other, celecoxib 400 mg b.i.d. was compared with either ibuprofen 800 mg t.i.d. or diclofenac 75 mg b.i.d. Both studies showed an approximately 50% reduction in the occurrence of complicated ulcers in patients receiving the Cox-2 inhibitors in comparison with patients receiving the traditional nonselective inhibitors. However, both studies left unanswered questions concerning the concurrent use of low-dose aspirin with the Cox-2 inhibitors.
In the rofecoxib study, in which patients receiving low-dose aspirin were excluded, there was a significant increase in the number of myocardial infarctions in the group receiving rofecoxib – which, unlike its comparator, naproxen, does not inhibit thromboxane.
In the celecoxib study, low-dose aspirin was allowed in 21% of the patients, and the advantage for the reduction in the rate of complicated ulcers with celecoxib versus the comparator drugs disappeared when the aspirin users were analyzed separately.

Conclusions

From the point of view of gastrointestinal safety, Cox-2 inhibitors are safer than traditional nonselective NSAIDs. The increased level of safety seen with Cox-2 inhibitors may be qualified by the concurrent use of low-dose aspirin. ■

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Complications of Polypectomy and their Treatment

J.R. Armengol-Miró

J.R. Armengol-Miró

Colonoscopic polypectomy is the most common therapeutic procedure performed in most endoscopy units. It is a safe technique when conducted by experts using a cautious technique and equipment that is in proper working order. In these conditions, complications should be uncommon. Most of the situations regarded as complications after polypectomy, especially immediate bleeding, should be termed "incidental events" rather than complications, as they can often be successfully treated at the time of polypectomy.

Complications

Bleeding. The most common complication after polypectomy is bleeding, which occurs in about 0.3–6% of cases. The risk is increased when blended current is used and when the snare is pulled through the polyp without cautery being used. Bleeding that occurs immediately after polypectomy can usually be stopped endoscopically, and transfusion is rarely needed. Delayed bleeding can occur in 2% of cases, often more than 1 week after the polypectomy procedure. Most patients in whom this complication occurs can also be managed endoscopically, and only a few require surgery.

Perforation occurs in 0.3% of polypectomies. It can appear when the whole thickness of the intestinal wall is captured within the snare. Perforations are usually seen immediately by the endoscopist, but can appear later due to the spread of thermal injury to the deeper layers of the bowel.

Postpolypectomy coagulation syndrome is seen in 0.5–1% of patients. It results from a transmural burn causing irritation of the serosa, with a localized inflammatory response in the absence of frank perforation, and occurs 6 h–5 days after polypectomy. It is important to recognize this syndrome in order to avoid unnecessary laparotomy, since it resolves with conservative treatment in most patients. The patient complains of abdominal pain and tenderness, and sometimes fever and leukocytosis. Twenty percent of patients will have an acute presentation, with guarding, rigidity, and fever. All symptoms usually disappear in 2–5 days. Computed tomography can exclude free intraperitoneal air or retroperitoneal air.

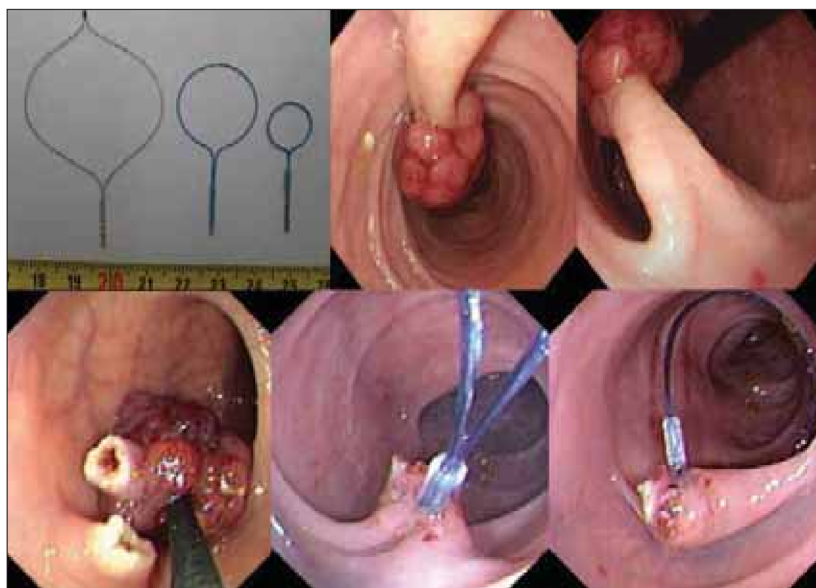
Prepolypectomy procedures

Coagulation status should be optimized in patients who are scheduled to undergo colonoscopy with possible polypectomy.

Epinephrine injection. The efficacy of this has not been demonstrated. Because of the low risk of immediate bleeding, most endoscopists do not pre-inject the stalk of pedunculated polyps with epinephrine.

Loop. A detachable nylon loop has been developed that can be placed over the stalk in the same way as a wire snare, and tightened. It may be placed over the polyp head or onto the bleeding stalk after transection. The loops spontaneously slough in 4–7 days.

Two-snare technique. One wire snare is placed on the pedicle near



Use of detachable loop placed on the residual stalk after polypectomy to ensure hemostasis.

the colon wall, and after tightening, the snare handle is cut off and the scope is removed. When the instrument is reintroduced, another snare is used to transect the polyp. The original snare, left in place, sloughs within 4 days, after which it is expelled.

Hemoclips. These can also be placed to prevent bleeding from pedunculated polyps, but they are more useful for bleeding after polypectomy.

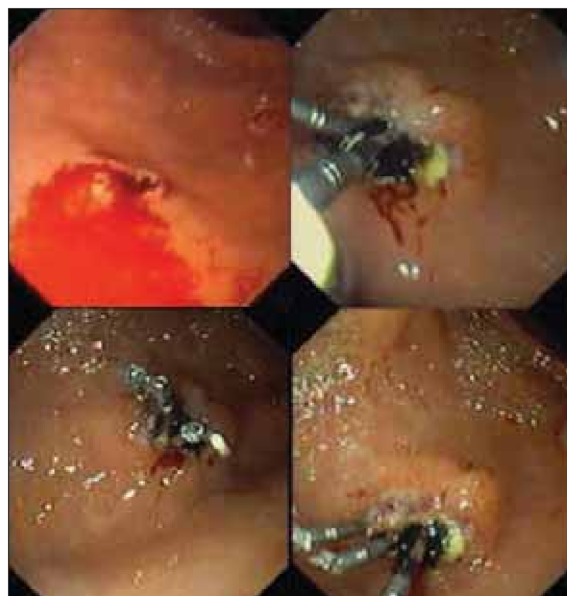
Immediate bleeding

The technique for controlling bleeding depends on the severity of the bleeding, the type of polyp, and preference of the endoscopist. A combination of techniques is frequently required.

Pedunculated polyps. Immediate bleeding after resection of a pedunculated polyp can usually be stopped by regrasping the pedicle with a snare and holding it on the pedicle for 5 min to stop the blood flow. Once active bleeding is controlled, there is usually no need for additional hemostatic measures. When bleeding cannot be stopped by regrasping the pedicle, several additional methods used alone or in combination can be effective. Epinephrine at a dilution of 1 : 10 000 can be injected. A thermal probe can be used, but the current delivery should be decreased by approximately 50%, as the colon wall is very thin. Bleeding can also be controlled by placing Hemoclips on the pedicle.

Band ligation has been used to control massive postpolypectomy bleeding, but the high suction pressure may entrap the muscularis propria and serosa within the band, leading to full-thickness necrosis and perforation.

Sessile polyps. There are several options for controlling bleeding after the excision of a sessile polyp. The bleeding site can be injected with dilute epinephrine (1 : 10 000). The hot biopsy forceps can be used as a cautery probe by direct application of monopolar current. Hemoclips can be placed directly on the bleeding site in an attempt to occlude the bleeding vessel. Spurting or oozing can be controlled using the argon plasma coagulator.



Clips placed on a bleeding polypectomy site with complete hemastasis.

Delayed bleeding

Most polypectomy bleeding can be managed endoscopically, with only unusual cases requiring surgery. Therapy is usually with epinephrine injection, often in combination with a thermal method. Swelling and induration at the polypectomy site within 1–2 days of polypectomy, resulting in increased thickness of the wall, makes it safer to use thermal modalities, so that repeated applications of current can be used to achieve hemostasis. Hemoclips can also be effective.

Perforation

If the perforation is immediately seen after polypectomy and it is small and localized, it can be managed endoscopically, as the colon is usually clean and Hemoclips can be placed. If a large perforation occurs or the perforation happens several days later, surgery is recommended.

Postpolypectomy electrocoagulation syndrome

Treatment is conservative, consisting of intravenous fluids, a nil-by-mouth regimen, bed rest, and antibiotic treatment until the symptoms improve. In one report, hospitalization was required in approximately 20% of patients, all of whom responded to the above treatment. Outpatient management with clear liquids and oral antibiotics is reasonable in patients with mild symptoms. In the presence of free intraperitoneal air, treatment is directed toward a perforation. ■

Note: The full-length version of this article and an accompanying reference list are available in the online version of *World Gastroenterology News* (www.worldgastroenterology.org).

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The Launch of the Cairo Center

OMGE and OMED have designated the development of Training Centers, in areas of need as a major component of their Education and Training platform, the core of our mission. Thus, our support of the training program in Soweto and the initiation of the program in Rabat, Morocco; the latter to serve Francophone Africa. Now the spotlight turns to Cairo and the launch of the Cairo training Center.

In the presence of the Prime Minister of Egypt and the Ministers for Health and Population, Higher Education and Scientific Research, Tourism and International Cooperation of the Government of Egypt the Center was officially launched in Cairo and an agreement, pertaining to the Center signed by Professor Eamonn Quigley, representing OMGE and the Minister for Higher Education and Scientific Research. To promulgate the launch a multidisciplinary conference in gastroenterology was held simultaneously and attended by gastroenterologists from Egypt, the Middle East and Africa. The real focus, however, was on the trainees; drawn from 15 countries throughout the Middle East and Africa, these young physicians enjoyed exclusive sessions at the conference, participation in all of the conference sessions and, most importantly, and once the other attendees had departed, several days of intensive "hands-on" and didactic training at the Theodor Bilharz Institute, in Cairo.

All of this would not have been possible without the tremendous efforts of Professor Hussein Abdel-Hamid, the Center Director, Professor Ibrahim Moustafa, the co-director, and the entire team in Cairo who worked so hard in putting this course together and in ensuring that such a diverse representation of trainees from throughout the Middle East and Africa could be present. We are all indebted to the Prime Minister and the Government of Egypt as well as to the President of the Theodor Bilharz Institute and her faculty for making all of this possible.

The focus of the first training session was on portal hypertension and its management, a most appropriate topic given the importance of this issue in the region, whether related to schistosomiasis or chronic hepatitis. The Cairo Training Center could not have enjoyed a more appropriate launch; a success which reflects the strengths of Egyptian gastroenterology and which augur well for the center as a focal point for education and training in gastroenterology throughout the region.

OMGE and OMED look forward to a long and productive partnership with our friends in Egypt and are eager to establish contact with those who practice, or who aspire to practice, gastroenterology throughout the Middle East and Africa. Our goal is the same: to promote the highest standards in the care of patients with gastrointestinal disorders. ■

Signing of the Cairo Training Center Agreement with the Minister of Higher Education, His Excellency Prof. Dr.Mofid Shehab, in the presence of the Prime Minister, His Excellency Prof. Dr. Atef Ebeid. Also present were the Minister for Health and Population, Ismail Sallam, CTC Director, Professor Abdel-Hamid, the President of the Theodor Bilharz Research Institute, Prof. Gihan El-Fandi and Professor Meinhard Classen, Past President of OMGE.

The inauguration of the OMGE-OMED Cairo Training Center.

Trainees at the first CTC course together with Prof. Eamonn Quigley, Vice-President of OMGE and Dr. Cihan Yurdayadin from the OMGE-OMED Education and Training Center.

Who Trains the Trainers Who Train the Trainers?

James Toouli

James Toouli

The above title was a question asked in jest by a colleague participating in the recent workshop held in Queenstown, New Zealand. However, it is a pertinent and quite appropriate question. Underlying it is the fundamental issue of the qualifications that the faculty members of the Train the Trainers program have for running the workshop, and in addition where and how the standard for the curriculum was developed.

The answer to the question is simple. The trainers who train the trainers have had no specific training – but indeed nor have the majority of teachers in medicine and, more specifically, in the fields of gastroenterology and gastrointestinal surgery. The workshop evolved from ideas derived from undergraduate and postgraduate teaching currently practiced at the universities in which the faculty members work. I am particularly indebted to the many curriculum conferences I have attended with my faculty colleagues for providing many of the ideas for the structure that is used in the Train the Trainers (TTT) meetings. Furthermore, ideas have been adopted from a variety of sources, including the writings of Sackett and colleagues, as well as similar programs run in the UK for the College of Surgeons and in the Netherlands for the training of gastrointestinal surgeons. However, without doubt much of the content of what is currently being offered has been developed out of faculty discussions and from interchanges between the participants and faculty members.

TTT has evolved since its beginnings to become an educationally framed workshop that is highly rated by the participants because it gives them an opportunity to share with colleagues their ideas on medical education. Over time, faculty members have acquired extensive expertise in teaching methods, and within the format of the TTT meetings they share this with the participants. It is a workshop that is relevant to all educators in gastroenterology and gastrointestinal surgery, whether they work in major tertiary referral centers in the heart of London or New York or rural outposts in Sudan or Indonesia. The issue that is common to all is education of colleagues and students and techniques are applicable to all levels of medical specialist practice.

Thus, the trainers who train the trainers have been self-trained, and the validity of their training is attested to by the enthusiastic support and acclaim received from the colleagues who have contributed to all of the past workshops. I am very grateful for their support and, more importantly, for their contribution to what I and many of my colleagues have learned from the association. Many of our colleagues have written to us after the workshop when asked to record their experience. Below is a collection of some of these responses following the TTTs in Queenstown.

These testimonials from the world's leaders in the field of gastroenterology have been very important to our association with regard to raising financial support for the Train the Trainers program. I am delighted to welcome Altana, Inc. as a partner in the future running of Train the Trainers. Altana have recently committed a substantial financial grant in support of this educational activity. ■

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Train the Trainers on the move again!

Train the Trainers 2004 in Crete, Greece, was fully subscribed. A registration list has been opened for applicants wishing to participate in Train the Trainers 2005. TTT 2005 will take place in Punte del Este, Uruguay, on 16–18 March 2005. For further information on the application process, please refer to our web site (**www.worldgastroenterology.com**) or contact the **OMGE Executive Secretariat** at:

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What the Participants Thought of Train the Trainers 2003

New Zealand

"I was not disappointed. From the start, the emphasis on a casual informal atmosphere in a convivial 'resort-style' atmosphere where learning would be amongst peers was what I had hoped for. There was the right amount of semi-formal presentation from well-recognized experts that set up the vital break-out sessions. The caliber of the faculty was first-class and had to be. With the level of seniority and experience of the workshop participants, anything less than the best would have been worthless.

Since returning to 'normal life', the Train the Trainers participants from New Zealand have embarked on establishing an 'Introduction to Flexible Gastrointestinal Endoscopy' course aimed at basic medical and surgical trainees. This course will be based on many of the principles emphasized at the Train the Trainers Workshop."

Dr. David Theobald, New Zealand

Malaysia

"One would hope that the workshop would be held more frequently, so that more trainers could benefit from the course. One should also not underestimate the value of the camaraderie engendered between trainers from all corners of the world. The Train the Trainers workshop is an outstanding contribution by the OMGE to the future of gastroenterology training. Long may it continue."

Dr. Jayaram Menon, Malaysia

New Zealand

"The most important take-home message for me would be the Pendleton Rules for assessing performance: what the person thought went well, what the observer thought went well, what the person thought could be improved and what the observer thought could be improved. This is a much more supportive and constructive way to critique performance and it can be applied to many situations."

Dr. John Wyeth, New Zealand

South Africa

"There was such good camaraderie, it was hard not to be positive about the whole experience. There was lots we can take and apply now to our teaching methods. The next step is for a couple more to go to Crete next year and then for us to organize one in South Africa. If the New Zealanders can do it, then so can we."

Dr. Sandie Thomson, South Africa

New Zealand

"We have had initial meetings from all those from our region who attended Train the Trainers, with a view to establishing an Endoscopy Skills Training Course, by starting a basic foundation course 2004. Without the Train the Trainers workshop in Queenstown, I do not think we would have had the empowerment and ideas to allow us to proceed, and we received excellent direction for future training programs."

Dr. David Morris, New Zealand

Pakistan

"The endoscopy training models were superb and the hands-on training was conducted very well. The session by Eamonn Quigley on publishing was one of the best parts of the workshop. During the workshop, I did mention that the statistical part of conducting any significant research was missing, and I was told that it itself is a big topic and needed more time."

Dr. S.M. Wasim Jafri, Pakistan

Indonesia

"It is very useful for improving the gastroenterology services in our hospital in Balikpapan, East Borneo, Indonesia. As we are far from Indonesia's capital city, we have to try to develop our skills and our instruments with more effort. We hope that this course will continue

The international faculty for the TTT workshop in New Zealand.

Participants in the TTT workshop in New Zealand.

and provide more opportunity for participants from developing countries."

Dr. Lukman Hatta Sunaryo, Balikpapan, Indonesia

New Zealand

"Such a buzz to be surrounded by keen – and often young – gastroenterologists and surgeons from all round the world. A great opportunity to meet similar people from such different ways of life with such different types of gastrointestinal practice. That has to be the highlight of the whole experience – the people. And not just the other participants, the faculty – dedicated, enthusiastic, and believers. And it's contagious. I caught whatever was going and came back enthused – not just about improving myself as a trainer, but my whole country, and enthused not just about training but about Gastro in general. Please can we have a workshop on how to stay enthused?"

Dr. Judith Collett, New Zealand

Australia

"For me the course was a huge success and met and exceeded all my expectations.

Following the course, I was more confident in providing feedback to advanced trainees in gastroenterology. The general consensus among them was that they were previously not accustomed to feedback sessions, and they were generally positive about this procedure. I therefore wondered why this course is not more widely publicized or even compulsory for any potential departmental heads, directors of endoscopy, or anyone with similar interests. I am also most interested in upcoming moves toward introducing simulators as part of training for gastroenterology trainees.

I appreciated the full 4 days of the course, and it was one of the best-organized workshops I have ever attended."

Dr. Rupert Leong, Australia

Latvia

"Train the Trainers course gave me new experience, both professional and intellectual. The good aura of the TTT is thanks to your input."

Dr. Aldis Pukistis, Latvia

Kenya

"The course was gratifying. The modules were well chosen, the faculty was excellent. There is a need to either reduce the syllabus content or reduce the module numbers. There is a need to give more time to discussion sessions after the break-away sessions. I feel that they were rushed a lot. The time allotted for the teaching skills on procedures was inadequate."

Dr. Elly Ogutu, Kenya

India

"When I first received the invitation to attend the course, I was skeptical regarding its usefulness. I always thought teaching is an art, an inborn talent – either you have it or you do not. What can this type of workshop teach us? But this turned out to be one of the best conferences I have ever attended. Minute details of organization were worked out meticulously. The venue was great, and the people were friendly. But above all, a great deal of thought had been put into selecting the discussion topics and preparing the syllabi. There was the right mixture of educational lectures and interactive sessions. The idea of group presentations was great, and it showed how people can be creative, given the chance."

Dr. Ajay Kumar, India

A hands-on endoscopy workshop module.

OMED/OMGE Outreach Program Initiated

James DiSario

James DiSario

A new OMED/OMGE Outreach Program, designed to introduce or restore endoscopic services to areas in need, was started at the Eva Perón Teaching Hospital in Rosario, Santa Fe province, Argentina, in September 2003, under the direction of Dr. James DiSario of Salt Lake City, Utah, USA. The program, administered by the Combined Education and Training Committee, is a bold humanitarian step by OMED/OMGE to help those lacking specialized medical care due to economic hardships.

The site was chosen on the basis of a request-for-proposals system and was reviewed by an international committee. The selected proposal was submitted by Dr. Diego Murature, a surgeon and endoscopist at the Eva Perón Teaching Hospital. The Olympus Corporation donated the endoscopic equipment and supplies to OMED and the site was provided by the OMED/OMGE Combined Education and Training Committee. Dr. James DiSario and Dr. Roque Saenz of Santiago, Chile, representing the Combined Education and Training Committee, and Roberto Grau and Elsa Waku of Olympus/Latin America presented the equipment to the hospital. Dr. Jose Lopez, Hospital Director, and Mr. Fernando Bondesio, Minister of Health for the Province of Santa Fe, formally received the donation in a public ceremony on 26 September 2003. An overflow crowd of local dignitaries, medical staff and trainees, and members of the public attended the opening ceremony, and a number of local broadcasting and print media covered the event.

The Eva Perón Teaching Hospital is a 120-bed public facility that services a large and economically disadvantaged population. Currently, there are five trained medical and surgical endoscopists on the staff and trainees at all levels. The hospital has a history of excellence in digestive surgery, counting Professors Juan Miguel Acosta and Carlos Pelligrini among its former distinguished faculty members. However, due to a struggling economy and a disastrous flood of the nearby Paraná River, the facility had deteriorated and basic endoscopic services were not reliably available.

An important aspect of this project was governmental, institutional, and community support, which are the key to continued success. Because of the donation, a wing of the hospital was remodeled for the new endoscopy unit and includes an intake and processing area, the endoscopy room, a recovery area, and a combined endoscope-processing space and nurses' area. Community volunteers carried out the construction work, and there is a community activities office adjacent to the endoscopy suite. In addition, because of the formal educational program associated with this project, a new auditorium was constructed that will

OMED

OLYMPUS

En beneficio de la población de Argentina, la Organización Mundial de Endoscopía Digestiva (OMED) y la Organización Mundial de Gastroenterología (OMGE) junto con la compañía Olympus Latin America, Inc. proceden de esta forma a dotar el equipamiento para la Unidad de Endoscopía Gastrointestinal del Hospital Escuela Eva Perón en Granadero Baigorria de la ciudad de Rosario en la Provincia de Santa Fé, Argentina.

Presentado el
26 de Septiembre de 2003
por

Melvin Schapiro, M.D.
OMED Chairman
Education and Training Committee

James Toouli, MBBS, FRACS, PhD
OMGE Chairman
Education and Training Committe

James A. DiSario, M.D.
OMED Chairman
Training Sub-committee

César Vásquez
Endoscope Group
Olympus Latin America, Inc

Roque Saénz, M.D.
OMGE Member
Education and Training

The official certificate of donation. Translation: "For the benefit of the people of Argentina, the Organisation Mondiale d'Endoscopie Digestive (OMED) and Organisation Mondiale de Gastro-Entérologie (OMGE), in conjunction with Olympus Latin America, Inc., hereby equip the Gastrointestinal Endoscopy Unit at the Hospital Escuela Eva Perón in Granadero Baigorria in the city of Rosario in the Province of Santa Fe, Argentina."

Formal presentation of the certificate of donation by (left to right): Mr. Roberto Grau (Olympus), Dr. Roque Saenz, Dr. James DiSario, and Ms. Elsa Waku (Olympus), with Dr. Diego Murature in attendance.

Mr. Fernando Bondesio, the Provincial Minister of Health, Dr. James DiSario, and Dr. Jose Lopez, the hospital director (left to right), at a press conference for the formal donation ceremony.

Capacity attendance in the new auditorium for the first medical congress in over 20 years at the Eva Perón Teaching Hospital.

be used for continuing medical education and future regional medical conferences. The Provincial Minister of Health pledged that an appropriate budget will be provided to maintain the endoscopy unit at its current state of function, and Dr. Lopez sent several nurses and technicians to be trained in Buenos Aires.

Dr. DiSario and Dr. Saenz provided on-site training, including practical discussions with the medical and nursing staff on topics such as unit management, safety procedures, and appropriate handling of complications. Following the ceremony, Dr. DiSario and Dr. Saenz presented talks on endoscopic approaches to gastrointestinal bleeding, endoscopic therapy for gastrointestinal cancers, and an update on Barrett's esophagus. Dr. Murature then displayed video-endoscopy demonstrations and provided commentary. The auditorium was filled to capacity with the hospital medical staff, regional physicians and surgeons, and trainees.

In the 3 months following the opening of the Endoscopy Unit, 129 upper endoscopies, 60 colonoscopies and sigmoidoscopies, and 21 ERCPs were performed for a wide variety of diagnostic and therapeutic indications. Regarding the OMED/OMGE Outreach Program, Dr. Murature commented, "You are doing great work, and your project is helping a lot of people in my country."

Dr. DiSario said, "This project was a success by all measures, and a win-win initiative for all parties involved. It will ensure endoscopic services to the community and a venue for medical and surgical education for years to come. We are grateful for the generosity of the Olympus Corporation and look forward to continuing this program in other areas in need throughout the world."

The next Outreach Program donation site is intended for Sub-Saharan Africa, and the selection will then rotate to the Asia and Pacific zone the following year (see the accompanying box for details on how to present a proposal). ■

The medical staff from the Eva Peron Teaching Hospital with Dr. James DiSario and Dr. Jose Lopez (hospital director) at the center.

Request for Proposals

Proposals are now being accepted for the new OMED/OMGE Outreach Program, designed to donate endoscopic equipment to areas in need. The next Outreach Program donation site is to be located in Sub-Saharan Africa.

To meet the program's requirements, a candidate site has to be a public facility with adequate space for the unit, with a defined need for services, with one or more trained endoscopists, with nursing and technical personnel who are or can be trained, and with an appropriate guaranteed operational budget for supplies and maintenance. Proposal details for the Sub-Saharan Africa project can be obtained online at **www.omed.org** or www.omge.org and should be submitted to Bridget Barbieri (address below) and received by 30 April 2004.

Contact: **OMGE Executive Secretariat**
Bridget Barbieri, Medconnect, Bruennsteinstrasse 10, 81541 Munich, Germany
E-mail: Bridget.Barbieri@medc.de

The camera pill for kids – more 'sci-fi endocscopy'

A further step in the acceptance of the camera pill was made recently, when the US FDA approved its use in children. The M2A® Capsule Endoscope, produced by Given Imaging, uses a disposable miniature video camera located inside a capsule, similar in size to a large vitamin. The procedure is already being used successfully in adults. The capsule is effective because it can view more of the small bowel than physicians have ever been able to see before.

The mini capsule marks just another milestone in the path being taken by the major device companies towards alternatives in endocscopic techniques. Chromoendoscopy is already starting to be clinically employed, but other newer ideas are the subject of 'sci-fi' in the GI world. Raman spectroscopy and fluorescence endoscopy are both techniques, similar in nature, where light is used in different forms and wavelengths.

Zorbitive gets approval after orphan status

Serono's Zorbitive (somatropin), a recombinant human growth hormone for use in the treatment of short bowel syndrome (SBS) has been given approval by the FDA. This approval came despite concerns that the positive clinical data could not be repeated in a larger population. Zorbitive, administered with specialised nutritional support significantly reduced patient dependence on parenteral nutrition in a double-blind, controlled study. Serono already markets the drug as Serostim for treating severe AIDS-related weight loss and the rapid decision came as a surprise to many.

Erbitux finally gets its US nod

The troubled years of Imclone's history with Erbitux now appear to be behind them. After years of failed starts with the regulatory authorities and internal financial scandals, FDA approval has now been given to the drug which is indicated for the treatment of advanced colorectal cancer. It is the first in a series of expected approvals of similar drugs, to be marketed by Bristol-Myers Squibb in the US and Merck KgA in Europe. Erbitux will shortly be followed by launches from Genentech and Roche (Avastin) and from Sanofi-Synthalabo (Eloxatin).

Roche rebound helped by Hepatitis drugs

Roche, one of the two big pharmaceutical companies based in Basel, Switzerland, has rebounded in 2003 with promising growth from its hepatitis drug unit, seeing a 13% increase in sales of Pegasys. Pegasys has been stealing market share from Schering-Plough's competing product Pegintron. All of this adds to the improving fortunes of Roche, who is also a major shareholder in Genentech and the marketing partner for Avastin (see above) awaiting and expecting approval in 2004. Avastin is expected to be a multi-billion dollar earner for the company.

Double dosing; PPI's and Cox-2's

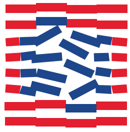
A study published late last year found that drugs such as TAP's Prevacid or AstraZeneca's Nexium are often prescribed along with Cox-2 inhibitors such as Pfizer's Clebrex and Merck's Vioxx. This is somewhat unexpected, since this class of pain relievers is often touted as not being the cause of gastrointestinal problems compared to other pain treatments. The double prescribing is likely to help fuel sales of all of these drugs.

Long-term study to test role of aspirin and Nexium

A news source is reporting that British scientists are embarking on a 10-year study of 5000 men to see whether a combination of aspirin and AstraZeneca's Nexium (esomeprazole) can prevent cancer of the oesophagus. Scientists are keen to examine the possible role of aspirin's anti-inflammatory properties in cancer prevention.

Zelnorm (Zelmac) shows overall symptom relief for IBS

A study published in the Scandanavian Journal of Gastroenterology and released by Novartis, showed that Zelnorm significantly improved overall symptoms and showed efficacy in providing relief from irritable bowel syndrome. The study included 600 participants from Nordic countries and patients using the drug "were 78 percent more likely to experience satisfactory relief of their symptoms over a period of 12 weeks than patients taking placebo".



Prevention of Colorectal Cancer

Robert Sandler

Colorectal cancer is a preventable disease. When people migrate from low-incidence countries, such as Japan or Africa, to a high-incidence country such as the United States, the rates of disease among their offspring increase to those of their adopted country. This indicates that there is something in the environment that is responsible. If we could identify and modify these environmental factors, we could prevent colorectal cancer.

Diet

There have been a large number of studies of diet and colon cancer. Unfortunately, it has been difficult to draw firm conclusions about the association between diet and colorectal cancer.

Red meat. The majority of studies have shown an increased risk of colorectal cancer with high intakes of red meat. Heterocyclic amines and polyaromatic hydrocarbons are produced when red meat is cooked at high temperature. These compounds may be carcinogenic.

Fiber. Burkett advanced the hypothesis that fiber prevents colorectal cancer almost 40 years ago. Although the hypothesis is appealing, recent studies indicate that it may not be correct. A large, carefully conducted cohort study found no protective effect of fiber from any source – cereals, fruits, or vegetables. Two randomized trials of fiber in post-polypectomy patients did not show that fiber prevented new adenomas during the 3-year study period.

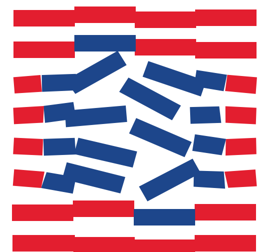
Fruits and vegetables. There are a large number of studies of fruits and vegetables in connection with colorectal cancer, and virtually all of them demonstrate a moderate protective effect. One exception is a report from the Nurses' Health Study, which did not find a protective effect against colon or rectal cancer. While the mechanism for protection by vegetables is not known, there are a large number of chemicals from the plant kingdom that have been found to be anticarcinogenic or antimutagenic in test systems. These chemicals operate at a number of different sites in the carcinogenic pathway.

Robert Sandler

Calcium. A large randomized controlled trial has shown that 1200 mg per day of calcium, in the form of calcium carbonate, resulted in a 19% reduction in the development of new adenomas and a 24% reduction in the number of new adenomas in comparison with a placebo. The end point in the study was adenomas, rather than cancer, but because virtually all cancers are thought to arise from adenomas, the protective effect is thought to extend to cancer. The mechanism for protection by calcium is not known.

Selenium. Trace metals such as selenium, zinc, iron, and fluoride may be capable of influencing the risk of colorectal cancer. A large randomized trial of selenium administration to prevent skin cancer found that colorectal cancer deaths were 60% less frequent in individuals who were assigned to the selenium group. These results are quite surprising and need to be confirmed.

Micronutrients. Because fruits and vegetables are associated with a lower risk of colorectal cancer, one might speculate that the protective effect might be due to vitamins, particularly the antioxidant vitamins A, C, and E. Antioxidants can inhibit free-radical reactions and thereby prevent oxidative damage to DNA. Unexpectedly, clinical trials of antioxidant vitamins have not shown an effect against colonic neoplasms. In the large Nurses' Cohort, women who took multivitamins that contained folic acid for at least



15 years were about 75% less likely to develop colon cancer than women who never took multivitamins. Protection required vitamin use for 15 years or more; a shorter duration of use conferred no protection. The protective effect seen in the Nurses' study was primarily due to the folic acid component of the multivitamins, rather than the antioxidant vitamins.

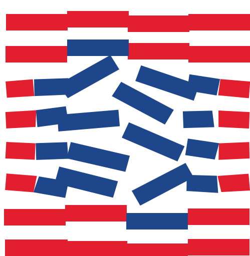
Smoking and alcohol. The majority of studies demonstrate an increased risk of colorectal cancer and adenomas with cigarette smoking.

Alcohol has been linked with an increased risk for both adenomas and cancer. The data are more consistent for adenomas, but the majority of studies also support an association between alcohol and cancer. The effect of alcohol may relate to its antagonism of methyl group metabolism, and the effects appear to be increased by low levels of the folic acid, a methyl donor.

Physical activity. Physical activity has consistently been shown to protect against colorectal cancer. Both leisure-time and occupational activities appear to be important.

Obesity. The amount of food, rather than the type, may be important. Obesity has been linked to colon cancer in both men and women. Recent cohort studies have shown that obese women were 50% more likely to develop colon cancer, and obese men 80% more likely.

Constipation. There has long been speculation that constipation might be responsible for large-bowel cancer, due to more prolonged contact with the mucosa by carcinogenic substances in feces. However, neither constipation nor the use of laxatives appears to be an important risk factor for colorectal cancer.



NSAIDs. Aspirin and nonsteroidal anti-inflammatory drugs appear to be protective against colorectal neoplasia, based on evidence from a variety of different types of studies. In a randomized trial of polyposis patients, sulindac has been shown to result in polyp regression. The mechanism is not known, but it could be related to increased apoptosis in transformed mucosa. There has been speculation that the effect could be due to inhibition of the cyclooxygenase-2 pathway to prostaglandin production, since Cox-2 is up-regulated in colon tumors. Celecoxib has been shown to decrease the numbers of polyps in polyposis patients. Three recent randomized controlled trials have shown that daily aspirin can decrease the risk of recurrent colorectal adenomas. Taken together, the three studies, along with extensive observational studies, show that aspirin is an effective chemopreventive agent.

Despite the compelling evidence of a protective effect of aspirin and conventional NSAIDs, these drugs have well-known adverse effects. Drugs in this class can increase the risk of hemorrhagic strokes and gastrointestinal bleeding. Because of an unfavorable cost–benefit ratio, these drugs should not be recommended for routine prevention in low-risk individuals.

Hormone use. Postmenopausal hormones have been shown to be associated with a decreased risk of colorectal cancer. A meta-analysis has shown that postmenopausal women who had taken hormone replacement were 20% less likely to develop colon cancer. A recent study showed that hormone replacement reduces the overall risk of colon cancer.

Practical recommendations

Sensible modifications in diet and lifestyle could have a favorable impact on the development of colorectal cancer. At the same time, it is important to recognize that the benefits of screening for colorectal cancer completely overshadow the effects of primary prevention. In discussing strategies for cancer prevention with our patients, it is very important to make it clear that the most important strategy is screening.

Practical, evidence-based recommendations for primary prevention might include the following:

- Eat a sensible diet, high in vegetables and fruits; limit red meat (less than two servings per week).
- Avoid obesity (body mass index < 26 kg/m^2).
- Take regular exercise – 30 min/day, moderate or vigorous.
- Consider supplements with calcium (1200 mg/day) and folic acid (1 mg).
- Limit alcohol consumption; don't smoke.
- Participate in regular screening.
- Avoid health claims and fads based on weak data. ■

Note: This paper was presented at Digestive Disease Week, Orlando, Florida, 2003.

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Letter in Support of IDCA from His Holiness John Paul II

SECRETARIAT OF STATE

FIRST SECTION . GENERAL AFFAIRS

Prot. No. 552172 — From the Vatican, 17 January 2004

The Holy Father is pleased to have been informed of the International Colorectal Cancer awareness month being promoted for March this year. He sends prayerful best wishes and heartfelt encouragement to all those participating his initiative.

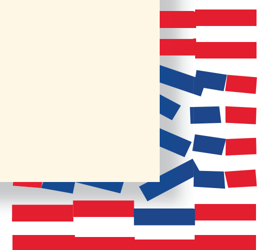
His Holiness is appreciative of the work of the International Digestive Cancer Alliance, which steadfastly seeks to promote screening for the early detection and primary prevention of digestive cancers throughout the world. The Church is always open to genuine scientific and technological progress, and she values the efforts and sacrifices of those who, with dedication and professionalism, help to improve quality of service rendered to the sick, and who seek to reduce factors which adversely affect human life and health (cf. No. 4 *Message for the World Day of the Sick, 2003*). The Holy Father reminds the members of the international medical community of the increasingly urgent need to close the unacceptable gap that separates the developing world from the developed in terms of preventive health care education and treatment. In this regard he is confident that they will address the question of access to the health care programmes and structures, lacking in many parts of our world.

Entrusting the activities of the International Colorectal Cancer awareness month to the guidance of Mary, Seat of Wisdom, His Holiness invokes God´s abundant blessings upon all those involved and he cordially imparts his Apostolic Blessing.

With every good wish, I am

Yours sincerely,

Leonardo Sandri
Substitute



Results of an OMGE International Survey

The Role of the Gastroenterologist in the Management of Patients with Digestive Cancers

Position Paper from an OMGE Working Party*, chaired by Sidney J. Winawer

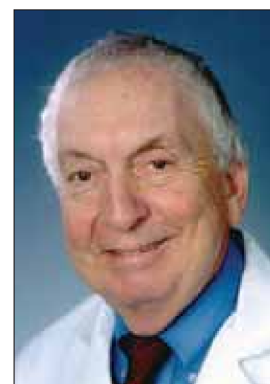
Digestive cancers as a group have the highest incidence of all cancers worldwide. More than 3 million new cases occur each year, with 2.2 million deaths. A Working Party was organized by OMGE to evaluate the role of the gastroenterologist in the overall management of patients with digestive cancers and to make recommendations for improving the management and continuity of care of these patients.

A survey was developed and sent to OMGE's member organizations. The survey asked questions in four main areas: practice directly related to these patients, including prevention, treatment, follow-up, and administration of chemotherapy; training of fellows in gastrointestinal programs in the area of digestive cancer; postgraduate education in digestive cancer; and society interactions in digestive cancer. Ninety surveys were distributed to leaders of member societies of OMGE worldwide.

Results

Of the 90 surveys, 47 responses were received from 47 countries. Collated responses to the survey are listed below.

- Gastroenterologists administer chemotherapy often/occasionally (30%) or rarely/never (69%).
- Gastrointestinal cancer treatment is *administered* by a multidisciplinary team of medical oncologists, gastroenterologists, radiation oncologists, and surgeons often/occasionally (57%) or rarely/never (40%).
- Gastrointestinal cancer treatment is *planned* by a multidisciplinary team of medical oncologists, gastroenterologists, radiation oncologists and surgeons often/occasionally (71%) or rarely/never (27%).
- Gastrointestinal cancer prevention programs are organized by gastroenterologists occasionally/often (68%) or rarely/never (30%).
- The top two components of cancer prevention programs are educational lectures for a medical audience and cancer screening guidelines, regardless of whether gastroenterologists or other individuals organize the programs.
- Among respondents with a gastrointestinal training program, fellows are trained most often in screening (94%), pathology of gastrointestinal cancer (94%), and follow-up of gastrointestinal cancer patients (91%), and least often trained in surgical oncology (51%), radiation oncology (20%), and alternative medicine (14%).


Sidney J. Winawer

- The top five topics that respondents believe should be presented at postgraduate courses and clinical symposia are: new therapeutic approaches (97%), chemoprevention (90%), screening (88%), palliative care (85%), and the biology of gastrointestinal cancer (84%). Low scores were given for alternative medicine (48%) and lifestyle and cancer (75%).
- Ninety-one percent of respondents believed there should be more interactions between gastrointestinal and oncology societies.

Discussion

The management of patients with cancer has become exceedingly complex. Patients with digestive cancers are faced with an enormous increase in the range of options available for diagnosis and treatment. This usually works to the patient's advantage, providing a benefit that has strikingly reduced the likelihood of deaths from cancer. However, patients may become lost in the maze of specialty medicine without a doctor who provides continuity of care throughout their illness. This can be disconcerting to the patient and family, and counterproductive for the specialists involved in the case. It was this perception that led OMGE to organize a working party to evaluate the role of the gastroenterologist in the management of patients with digestive cancers. The gastroenterologist is often the first physician to see the patient and make the diagnosis, and refer the patient for treatment. Often, however, the gastroenterologist does not remain involved during a long course of treatment, but may be called back to help in diagnosis or palliation at a later stage.

The purpose of the international survey reported in this paper is to evaluate the gastroenterologists' role, and serve as a basis for making recommendations to

OMGE. The recommendations that this working party has made to OMGE are listed below. Others have also addressed this issue. A dialogue with other interested societies regarding this issue would be a good beginning, with a matrix provided by the newly formed International Digestive Cancer Alliance, whose mission is to raise awareness of digestive cancers worldwide.

OMGE Working Party Recommendations

- More interaction among physicians in the management of patients
- Gastroenterologists should be part of a digestive cancer team
- Gastroenterologists should be involved with patients throughout their management
- Fellowship training should include the full range of cancer management
- Postgraduate meetings should include multidisciplinary sessions on digestive cancers ■

***OMGE Working Party**:
S. Winawer, Chair (USA); J.R. Armengol-Miró (Spain); D.K. Bhargava (India); M. Bushey (USA); M. Classen (Germany); M. Crespi (Italy); E.V. Cutsem (Belgium); W. Fleig (Germany); R. Fujita (Japan); J. Geenen (USA); S.J. Konturek (Poland); A. Kulakowski (Poland); S. Labib (Egypt); B. Levin (USA); P. Rougier (France); P. Rozen (Israel); W. Schmiegel (Germany); B. Wong (China); S.-D. Xiao (China); G. Young (Australia); A. Zauber (USA)

Note: The full-length version of this working party report is available at **www.worldgastroenterology.org**. Readers are encouraged to refer to this full publication, which also contains suggested reading.

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First National Working Party Conference on Colorectal Cancer Screening (Berlin, Germany)

Meinhard Classen

Germany is the first country to offer its population an early detection program for colorectal cancer that includes colonoscopy (available since 1 October 2002). Although the number of screening colonoscopies increased by 500% over the past year, the compliance rate remains low. The first National Working Party on Colorectal Cancer (meeting on 25 and 26 February 2004) brought together 120 representatives from 100 professional fields for one and a half days' intensive discussion and consensus searching. Politicians, doctors from various disciplines, epidemiologists, naturopathic and homeopathic doctors, corporations, union representatives, press and media – and, last but by no means least, colorectal cancer patients – took part in this interactive meeting.

The following topics were dealt with simultaneously by five subcommittees:

- Information and motivation in the healing professions
- The informed patient
- Colorectal cancer screening in large corporations
- Model projects in neighboring countries
- Identification of relatives in high-risk groups

The conference was hosted and organized by German Cancer Aid (*Deutsche Krebshilfe*) and the Network against Colorectal Cancer (*Netzwerk gegen Darmkrebs*). The conference's patrons were the President of the Cancer Research and Prevention Foundation (CRPF), Ms. Carolyn Aldigé from the USA, and the International Digestive Cancer Alliance (IDCA) represented by Prof. S. Winawer. The CRPF's Dialogue for Action program provided the inspiration for this national conference.

The working party is now busy compiling the results of this conference, which will be published as a position paper to be presented to authorities, government bodies, and organizations concerned with colorectal cancer, as well as any other interested parties. The workshop participants are expected to commit themselves to the implementation of the decisions taken at this conference, and these will be reported on in more detail in the next issue of *World Gastroenterology News*. We are convinced that all of these measures will lead to increased participation in colorectal cancer screening programs. ■

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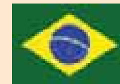
Brazilian Federation of Gastroenterology



Fernando Cordeiro (President, Brazilian Federation of Gastroenterology)

The Brazilian Confederation of Gastroenterology (CBG) was founded on December 12, 2003. It comprises the following associations:

- Brazilian Federation of Gastroenterology (Federação Brasileira de Gastroenterologia, FBG)
  President: Fernando Cordeiro, M.D.
- Brazilian College of Digestive Surgery (CBCD)
  President: Paulo Roberto Savassi Rocha, M.D.
- Brazilian Society of Gastrointestinal Endoscopy (SOBED)
  President: Flávio Antonio Quilici, M.D.
- Brazilian Society of Hepatology (SBH)
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- Brazilian Society of Coloproctology (SBCP)
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- Brazilian Society of Digestive Motility (SBMD)
  President: Ary Nasi, M.D.

The main aims of the new confederation are to promote and organize the Brazilian Digestive Disease Week and to devote itself to enhancing the understanding and prestige of the speciality of gastroenterology in all its aspects. It will not interfere with the internal organization of its constituent bodies or undermine their autonomy in any way.

The President of the Brazilian Federation of Gastroenterology, Dr. Fernando Cordeiro, was elected coordinator of the Confederation. ■

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Inaugural meeting of the Brazilian Confederation of Gastroenterology (CBG)

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OMED

A View from Hong Kong

Endoscopy: Surgical or Medical?

Sydney Chung

Surgery and internal medicine, by their very nature, attract different types of personality. Extrovert types who enjoy the manual satisfaction and immediate gratification of an operation well done will be attracted to surgery, whereas the more intellectually inclined, who derive more pleasure out of solving a difficult diagnostic puzzle, may gravitate toward internal medicine. The stereotypes of the blood-and-guts, knife-happy Sir Lancelot and the cerebral, pipe-smoking Sherlock Holmes may be archaic, but we are all influenced by the traditions of our chosen specialty, ingrained into us during long years of training by our mentors and icons. Add the turf battles, issues of resource allocation and reimbursement for competing procedures, is it really surprising that surgeons and gastroenterologists never really see eye to eye?

Nonetheless, important advances in endoscopy are more often than not made in units that are the exceptions to the rule, in which gastroenterologists and surgeons enjoy a congenial working relationship. Indeed, to practice current state-of-the-art medicine, gastroenterologists and surgeons must work as a team. The advent of laparoscopic surgery has increased our reliance on accurate preoperative diagnosis, as there is no longer the luxury of an "exploratory laparotomy" in which the surgeon palpates all the abdominal organs as a first step after opening the abdomen. Localization of colonic tumors prior to laparoscopic colectomy is a cogent example. The advent of mucosectomy for early cancer, on the one hand, and upfront adjuvant chemotherapy for advanced tumors on the other, underlined the importance of accurate staging by endoscopic ultrasonography. As therapeutic endoscopy advances into territories that are traditionally surgical, the boundaries between the two specialties are becoming increasingly blurred. Such advanced procedures also carry significant risks of complications such as bleeding and perforations; close cooperation between endoscopists and surgeons are necessary for peace of mind of the pioneers of these new techniques and for the safety of patients.

Sydney Chung

The flexible endoscope, the laparoscope, or indeed the scalpel are but tools we use for the benefit of our patients. They should not be viewed as competing technologies. The patient should be managed by a multidisciplinary team, with the most suitable techniques according to the patient's clinical condition. Ideally, the training of a digestive disease specialist should encompass molecular biology, clinical gastroenterology, endoscopy, laparoscopy, gastrointestinal surgery, and interventional radiology, with specialization in one of these areas.

In the meantime, how do we engender a closer working relationship under the present system? As a first step, the "us" and "them" attitude must be dispelled, and this needs to come from the top. Senior staff must be careful about making disparaging remarks about colleagues from a different background, as juniors tend to emulate our worst behavior. Joint meetings and clinics in which management decisions are made in consultation may evolve into joint care by a multidisciplinary team according to common protocols. Combined gastroenterology and gastrointestinal surgery wards mean that patients do not need to be transferred to a different part of the hospital when referrals are made. It is also easier for the referring team to follow the progress of their patients and to appreciate at first hand how safe and effective modern surgery can be. Evolution into a dream team – working together under one administrative roof – would, however, require radical revamping of our system of training and credentialing for gastroenterologists and surgeons, as well as a major restructuring of hospital departments based on organ systems rather than traditional specialties. ■

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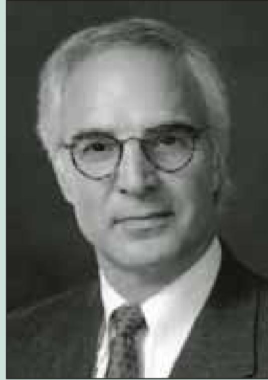
Gastrointestinal Endoscopists and Minimally Invasive Surgeons: a Relationship in Evolution

Jeffrey L. Ponsky


Jeffrey L. Ponsky

Surgeons were critically involved in the development of early flexible endoscopic procedures such as colonoscopy, ERCP, control of hemorrhage, and gastrostomy. Yet, despite its leadership in these areas, the American surgical community has not enthusiastically embraced endoscopic practice in the past few decades. The reasons for this are multifactorial and involve economic competition with gastroenterologists, who discovered that these methods were invaluable in the diagnosis and treatment of the maladies they encountered in their daily practice. Frequently, they would discourage surgical practice of endoscopy by withholding referrals from surgeons who chose to undertake these procedures. Equally, few surgeons embraced the techniques as a primary part of their practice, but rather regarded them as being ancillary to the major interventional procedures of traditional surgery. With few exceptions, gastroenterologists became the leaders in gastrointestinal endoscopy, both diagnostic and therapeutic, calling on surgeons to assist with complications or to manage therapy outside the boundaries of endoscopic practice. In a few institutions, gastrointestinal surgeons and gastroenterologists work side by side in combined endoscopy units, complementing each other with their individual skills. These situations, however, are the exception rather than the rule.

With the emergence of laparoscopic cholecystectomy and the field of minimally invasive surgery in the past decade, it seemed initially that surgeons would pursue intracavitary endoscopic procedures such as thoracoscopy and laparoscopy, while gastroenterologists would maintain their dominance in endoluminal endoscopic practice. The two disciplines occasionally combined to share in complex "laparo-endoscopic" procedures such as excision of large colonic polyps, drainage of pancreatic pseudocysts, and excision of gastric stromal tumors. More recently, recognizing the tremendous potential to extend the capabilities of their traditional techniques, a number of surgeons have once again involved themselves in endoluminal methods in order to facilitate minimally invasive approaches to gastrointestinal disease. Such endeavors have been noted in the areas of colorectal surgery, pancreatic, esophageal, biliary, and bariatric surgery.

At the same time, aggressive, imaginative, and thoughtful gastroenterologists have been extending the boundaries of traditional endoluminal endoscopy. Mucosal resection of premalignant and early malignant disease has become commonplace, and full-thickness resection with subsequent suture closure will soon follow. Endoscopic methods of controlling reflux esophagitis and morbid obesity are rapidly emerging. New techniques that will allow transluminal intra-abdominal surgery are also being developed. Soon, the world of minimally invasive surgery will no longer belong exclusively to the traditional surgeon. Yet gastroenterologists will need to have surgeons' skills and background in order to address the challenges associated with tissue dissection, resection, and anastomosis. Surgeons and gastroenterologists must, and will, come together in order to develop and practice these emerging methods. The old paradigms of surgical and gastroenterological practice will dissolve as new minimally invasive therapies evolve. In the end, both patients and physicians will benefit. ■

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Kunio Okuda, 1921–2003

Francisco Vilardell (Honorary President, OMGE)

I first met Kunio Okuda in 1953, when we were both taking an introductory course on American culture at Columbia University in New York, as part of our Fulbright scholarships. It was the beginning of a long friendship. After the 2-month course, Okuda went to Johns Hopkins University, where he worked for several years doing research on vitamin B_{12} and was awarded a Ph.D. After publishing several important papers on his thesis topic, he returned to Japan, where he was soon appointed professor at Kurume University, and a few years later at Chiba University, where he remained for the rest of his career. At Chiba University Hospital, he established a center for the study of hepatic disease that earned him wide international recognition. He was a tremendous worker and left an outstanding legacy both in the fields of hepatology and hematology – as shown by his 553 published papers in English and 14 books on a variety of subjects such as idiopathic portal hypertension, hepatocellular carcinoma, intrahepatic lithiasis, and imaging techniques in hepatobiliary disease.

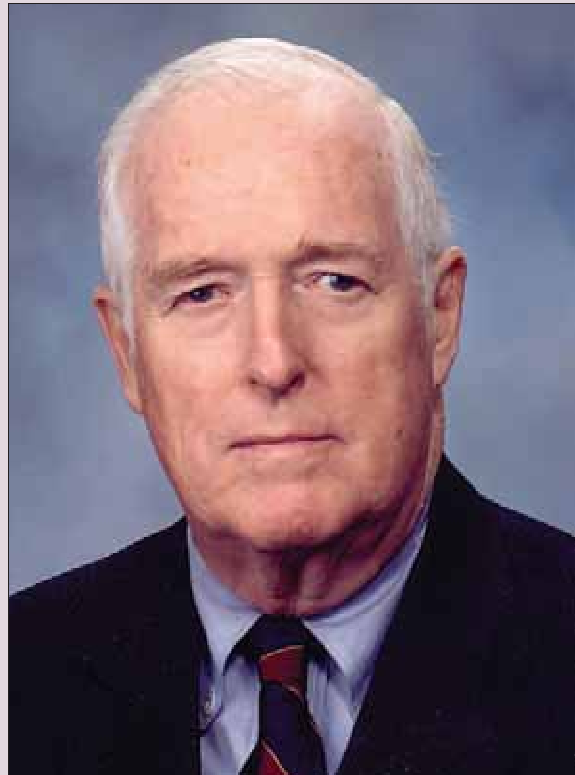
Among his scientific achievements, particular mention should be given to his research on vitamin B12; his original technique for isolating intestinal loops in the rabbit to study intestinal absorption; and his investigations on liver cancer and other hepatic diseases. He was particularly interested in techniques of imaging diagnosis, and among other instruments, he designed the "Chiba needle" for percutaneous transhepatic cholangiography.

Kunio Okuda played an important role in the International Association for the Study of the Liver (IASL), of which he was president from 1978 to 1980. He received the IASL's Distinguished Service Award in 1990. He was also very active in the Asian–Pacific Association for the Study of the Liver (APASL), of which he was President in 1980–1982. From 1996 to 2002, he served as Editor-in-Chief of the Journal of Gastroenterology and Hepatology. He also contributed substantially to OMGE, of which he was Vice-President in 1982–1986. In 1998, he was awarded the Bockus Medal by the OMGE's Governing Council, and he gave the Bockus Lecture at the World Congress of Gastroenterology held in Vienna in 1998. He also received honors in his own country; the Emperor of Japan nominated him a Commander of the prestigious Order of the Rising Sun.

Kunio had an excellent command of English, which enabled him to edit several manuals and audio devices on medical English for Japanese physicians. He traveled a great deal, and visited 83 different countries, while himself welcoming many distinguished leaders in the fields of hepatology and gastroenterology to Chiba. He was a man with wide cultural interests, an expert fisherman, an able wildlife photographer, and an accomplished violinist who was capable of giving concerts of Mozart violin sonatas (when we were in New York together, he used to play the violin for me in the evenings).

He leaves an important scientific as well as human legacy. His son Hiroaki and daughter Keiko are both physicians. During the last months of his life, when he was bearing with fortitude the severe pain caused by his terminal condition, he was able to finish his autobiography, which has just been published by his son Hiroaki. He was an example to all of us, and he will not be easily forgotten by his many friends and students. ■

Douglas B. McGill, 1929–2004



Douglas McGill, President of the American Gastroenterological Association (AGA) in 1986 died in Rochester MN on February 21, 2004 from viral pneumonia. Dr. McGill was a distinguished gastroenterologist who had worked at the Mayo Clinic since 1961 and was Professor of Medicine and the Director of the Division of Gastroenterology from 1974 to 1982. His unexpected death came as a great loss to his many friends and colleagues throughout the world who appreciated his charm, his wisdom, his liberal views, and his many talents as a physician, as a researcher, and as a statesman.

Dr. McGill had served the AGA and the discipline of gastroenterology in many ways including Chairman of the Scientific Committee of the World Congress of Gastroenterology that was held in Los Angeles in 1994

Dr. McGill was born in New York City, and educated at Phillips Andover Academy, Yale University, and the Tufts School of Medicine. He interned at the Boston City Hospital and pursued his subsequent residency and subspecialty training at the Mayo Clinic.

Dr. McGill had a variety of research interests and made substantial contributions in each. His earliest research work was concerned with bilirubin and hepatic secretory function. With Al Newcomer, he characterized lactase deficiency biochemically, analyzed its clinical significance, and validated new diagnostic procedures He worked with David Ahlquist to define the most sensitive method for detecting fecal occult blood. With Juergen Ludwig, the pathologist, and his colleague Keith Lindor, he described non-alcoholic steatohepatitis, a condition that is rapidly becoming one of the most common liver diseases in America, given the increasing prevalence of obesity. He took an interest in percutanous liver biopsy, summarized the vast Mayo Clinic experience, and became a national expert on its indications and utility.

Dr. McGill was known as a man of catholic tastes, and an articulate defender of liberal values. His hospitality was legendary. He had lived in France as a child, spoke fluent French and served on the Editorial board of Gastroenterologie Clinique et Biologique. He was a citizen of the world and for the World Congress of Gastroenterology, he worked effectively with Melvin Schapiro to develop the Young Scholars Program that brought promising young gastroenterologists from underdeveloped countries to the congress and had them interact personally with the luminaries in world gastroenterology. He also had a deep interest in medical economics and was the first AGA president to have an economist speak at its plenary session. ■

This obituary was edited and excerpted from one written by Dr. Alan Hofmann, a friend and colleague.

The Power of Protection

- Clinically proven to **heal more** reflux esophagitis **patients** compared to omeprazole[1,2], lansoprazole[3] and pantoprazole[4].
- Faster and sustained **freedom from GERD symptoms** in more patients than omeprazole[1,2], lansoprazole[3] and pantoprazole[4].
- **More effective acid control** compared to all other PPIs[5].

ABBREVIATED PRESCRIBING INFORMATION: Nexium® (esomeprazole magnesium). See local prescribing information for full details. **PHARMACODYNAMIC PROPERTIES:** Nexium® reduces gastric acid secretion through a highly targeted mechanism of action by being a specific inhibitor of the acid pump in the parietal cell. **INDICATIONS AND DOSAGE: Treatment of erosive reflux esophagitis:** Nexium® 40 mg once daily for 4–8 weeks. **Long-term management of patients with healed esophagitis to prevent relapse:** Nexium® 20 mg once daily. **Symptomatic treatment of gastro-esophageal reflux disease:** Nexium® 20 mg once daily in patients without esophagitis. Once symptoms have resolved, an on demand regimen of 20 mg once daily can be used when needed, to control subsequent symptoms. ***Helicobacter pylori*-associated peptic ulcer disease:** Healing of *H pylori*-associated duodenal ulcer, prevention of relapse of peptic ulcers in patients with *H pylori*-associated ulcers: Nexium® 20 mg, amoxicillin 1 g and clarithromycin 500 mg, all bid for 1 week. USA – Nexium® 40 mg once daily, amoxicillin 1 g and clarithromycin 500 mg twice daily, all for 10 days **CONTRAINDICATIONS:** Known hypersensitivity to esomeprazole, substituted benzimidazoles or any other constituents of the formulation. **WARNINGS AND PRECAUTIONS:** In the presence of any alarm symptoms (e.g. significant unintentional weight loss, recurrent vomiting, dysphagia, haematemesis or melena) and when gastric ulcer is suspected or present, the possibility of gastric malignancy should be excluded before treatment is initiated. **INTERACTIONS:** Due to the decreased intragastric acidity, the absorption of ketoconazole and itraconazole can decrease during esomeprazole treatment. Concomitant administration of esomeprazole resulted in a 45% decrease in clearance of diazepam. Concomitant administration of esomeprazole resulted in a 13% increase in trough plasma levels of phenytoin in epileptic patients; but dose adjustments were not required in this study. In healthy volunteers, combined therapy with esomeprazole and cisapride resulted in a 32% increase in AUC and a 31% prolongation of elimination half-life but no significant increase in peak plasma levels of cisapride. Concomitant administration of 40 mg esomeprazole to warfarin-treated patients showed that, despite a slight elevation in the trough plasma concentration of the less potent R-isomer of warfarin, the coagulation times were within the accepted range. However, as with all patients receiving warfarin, monitoring is recommended during concomitant treatment with esomeprazole. **PREGNANCY AND LACTATION:** Caution should be exercised when prescribing Nexium® to pregnant women. Nexium® should not be used during breast-feeding. **UNDESIRABLE EFFECTS:** The following adverse drug reactions have been identified or suspected in the clinical trials programme. None was found to be dose related. Common: Nausea/vomiting, diarrhoea, constipation, abdominal pain, flatulence and headache. Uncommon: Dermatitis, pruritus, urticaria, dizziness and dry mouth. From marketed use, there have been rare reports of increased liver enzymes and of hypersensitivity reactions e.g. angioedema, anaphylactic reaction. For further information please contact AstraZeneca, SE-431 83 Mölndal or the local AstraZeneca subsidiary.

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References: 1. Richter JE et al. Am J Gastroenterol 2001;96:656–65. **2.** Kahrilas PJ et al. Aliment Pharmacol Ther 2000;14:1249–58. **3.** Castell DO et al. Am J Gastroenterol 2002;97:575-83 **4.** Labenz J et al. Can J Gastroenterol 2004; vol 18 Suppl A **5.** Miner P et al. Am J Gastroenterol 2003;98:2616-20.

A Guiding Star in Gastroenterology

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Endoscope Disinfection: Quality Assurance is Key and MeSH is a Must

Justus Krabshuis

All the evidence suggests that cleaning and disinfection procedures and protocols are perfect – well, almost. There are few real differences between guidelines. To be sure, there are some problem areas – for example, the inability of 2% glutaraldehyde to cope with *Helicobacter pylori* (*Endoscopy,* 2003; 35: 295–299; PMID: 12664384) or with prion diseases such as new-variant Creutzfeldt–Jakob disease (CJD). However, the overwhelming evidence in the very few cases that have been published points to what the United States "multi-society" endoscopy disinfection guideline and the Centers for Disease Control describe as a "breach in adhering to guidelines", to what Douglas B. Nelson referred to as a "compliance" problem – and what the British Society of Gastroenterology (less diplomatically) terms "malpractice"!

So quality assurance is key!

Endoscope disinfection web sites

To familiarize ourselves with the issues, let's look up a key expert in the field and consult the introduction and clinical update by Douglas Nelson for the American Association of Gastroenterological Endoscopy (ASGE) – available at:

http://www.asge.org/gui/clinical_info/updates/cu_trans_infect_endo.asp

Now you know the issues – let's look at the top four guidelines available.

***ESGE* (http://www.esge.com)**. This very recent guideline (summer 2003) from the European Society of Gastrointestinal Endoscopy (ESGE) and European Society of Gastroenterology and Endoscopy Nurses and Associates (ESGENA), entitled "Technical Note on Cleaning and Disinfection" is easy to read and offered as a PDF file to all those interested in endoscopy – this is true "open-access" publishing. The ESGE/ESGENA author team was headed by Dr. Rey and Dr. Kruse, leading experts in this field. The guideline (**http://www.esge.com/index.php?page=guidelines**) compares the advantages and disadvantages (but not the availability globally or price) of the principal disinfection products used. It also lists who is using what in Europe; 22 European countries replied to a questionnaire on cleaning and disinfection practices, with almost every country using glutaraldehydes.

The following disinfectants are reviewed:

- 2% glutaraldehyde (GA)
- Orthophtalaldehyde (OPA)
- Peracetic acid (PAA)
- Peroxygen compounds
- Electrolyzed water (EAW)
- Chlorine dioxide
- Quaternary ammonium compounds
- Amine compounds/glucoprotamine

In their introduction to the list of "Available Products", they write: "GA is the most widely used chemical germicide in endoscopic reprocessing. The standard method is a 20 minute soak in GA. Major players such as Olympus, Pentax and Fujinon list GA as compatible with their endoscopes."

The ESGE/ESGENA guideline makes a major effort to publish options for different products and procedures, but they are not as strictly "evidence-based" as the American guideline below.

The United States "multi-society" guideline – an idea worth pursuing. In a splendid spirit of cooperation (science knows no borders!), the American Society for Gastrointestinal Endoscopy (ASGE) and the Society for Healthcare Epidemiology of America (SHEA) convened a consensus conference on endoscope disinfection. The resulting paper was published at around the same time (July 2003) as the ESGE one (science does know some borders!). The "Multi-Society Guideline for Reprocessing Flexible Gastrointestinal Endoscopes" is

GASTROENTEROLOGY ON THE INTERNET

available at:

http://www.asge.org/gui/resources/manual/gea_inf_cont.asp

The 34 recommendations, all categorized according to "strength of supporting evidence", were endorsed by key players such as the American College of Gastroenterology, American Gastroenterological Association, ASGE, SHEA, American Society of Colon and Rectal Surgeons, Society of American Gastrointestinal Endoscopic Surgeons, Society of Gastroenterology Nurses and Associates, Association for Professionals in Infection Control, and Federated Ambulatory Surgery Association.

***BSG* (http://www.bsg.org.uk).** In October 2003, The British Society of Gastroenterology (BSG) published "Guidelines for Decontamination of Equipment for Gastrointestinal Endoscopy":

http://www.bsg.org.uk/clinical_prac/guidelines/disinfection.htm

Like the ASGE/SHEA multi-society paper, these recommendations are categorized according to "strength of evidence" grades (the ESGE guideline does not do this). There are no major differences from the American "multi-society" guideline (according to the BSG), other than the recommendation for the use of single-use accessories to reduce the transmission risks for new-variant CJD – "a pathogen more relevant to gastrointestinal practice in the UK". But will that change, since late in 2003 the first cases of bovine spongiform encephalopathy (BSE) were discovered in the United States?

***SGNA* (http://www.sgna.org/resources/s&g.cfm).** The Society of Gastroenterology Nurses and Associates (SGNA) has a freely available text entitled "Guidelines for the Use of High-Level Disinfectants and Sterilants for Reprocessing of Flexible Gastrointestinal Endoscopes" (2003). It is very thorough and written particularly from the nursing point of view.

***OMGE/OMED* (http://www.omge.org).** At the Madrid United European Gastroenterology Week (UEGW) meeting in November 2003, it was decided to establish a joint OMED/OMGE team to produce worldwide guidelines on endoscope disinfection. The document is to be sensitive to Third World issues such as disinfection in difficult conditions and low-resourced settings – possibly the conditions readers are working in. If you have special problems you would like to see discussed, why not write to the joint OMED/OMGE guideline review team, chaired by Dr. Bjorkman, at omge@omge.org. The guideline is scheduled for publication in summer 2004. In line with the global focus, there will be French, English, Spanish, Russian, Arabic and Chinese versions of the OMGE guidelines in order to reach a world audience.

Endoscope disinfection in PubMed – "MeSH" is a must

The research that provides the basis for guidelines of this type is usually a few years old, due to the long and complex process involved in developing guidelines. The 79 references cited in the American multi-society guideline mostly date from before 2001, while the 39 references in the ESGE document are mostly from before 2002.

If you want to stay well-informed and really up-to-date, therefore, you need to bridge the gap and find the latest published research on endoscope disinfection on MedLine – for free, of course (**www.pubmed.org**)

Medical Subject Headings (MeSH) is the controlled vocabulary (or thesaurus) used by the National Library of Medicine (NLM) to index articles in MedLine. The MeSH terminology provides a consistent way of retrieving information from sources that may use different terminology for the same concepts. The MeSH database can be used to find MeSH terms and build a search strategy.

Anybody searching MedLine – on whatever topic – should use MeSH. Each of the 15 million or so articles listed in Medline is indexed using this controlled vocabulary. The problem in this case is that the MeSH thesaurus does not have a single term representing "endoscope disinfection".

Every article that has anything to do with endoscope disinfection – whatever the terms used by the authors in the article – is likely to be indexed using the MeSH terms “disinfection” and “endoscopes”. Using the MeSH vocabulary ensures that the searcher will find every article in MedLine dealing with this topic – assuming, of course, that you want to find all relevant articles and not just a few reviews.

If you want your search to be “evidence-based”, then MeSH is a must! Click on “MeSH Database” in the left-hand bar under “PubMed Services”. Let’s type in the term “endoscopes”. The results screen below gives you two options. Click on “Endoscopes” to review all of the MeSH terms associated with the word.

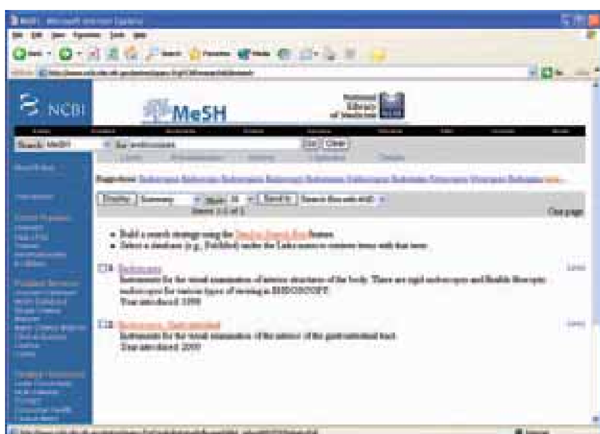


Table 1 shows the list of terms that will be searched if you search for “Endoscopes” as a MeSH term (“endoscopes [MH]”).

To illustrate how you can miss a substantial amount of research if you do not use MeSH, let’s search for endoscope disinfection research published since 1 January 2002 (20020101; click on limits and fill in the publication date 20020101).

Set 1: endoscope* disinfection (the * is the wildcard character).

Set 2: endoscopes [MH] AND disinfection [MH] (always use CAPITALS for the Boolean operators AND, OR and NOT. Putting [MH] means you are searching the term as a MeSH heading.

Set 3: #1 OR #2 (click on “history” and use the search “history” screen to combine sets).

Set 4: #3 NOT #1 (click on “history” and use the search “history” screen to combine sets).

Are you still with me ? All right then …

Set 1. This is the “free text” search. It will pick up any records including the words (endoscope or endoscopes or endoscopic) AND disinfection, anywhere in the article. You could click on “limits” and specify that these words should only occur in the “title” field. That would make your search very precise, if not sensitive.

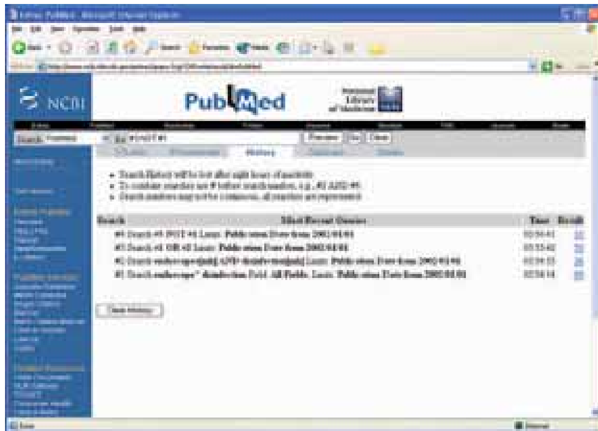
Set 2. This is the MeSH search. We are using the MeSH terms “endoscopes” and “disinfection”. Put them in square brackets [ ] to tell PubMed you want these terms searched as MeSH terms and not as free text.

Set 3. This set combines the unique records of set 1 and set 2 with the Boolean operator OR. Now you have found all records in PubMed/Medline combining free text (set 1) and indexing (set 2).

Set 4. By asking for all records in set 3 that were not found in set 1 (#3 NOT #1), we can see what we would have missed if we had only searched using the free-text terms in set 1. Fortunately, we used indexing (set 2), and all of the unique records in set 2 are present in set 3.

Table 1*. MeSH browser postings for “endoscopes”*

- All MeSH Categories
- Analytical, Diagnostic and Therapeutic Techniques and Equipment Category
- Equipment and Supplies
- Surgical Equipment
  - **Endoscopes**
    - Angioscopes
    - Arthroscopes
    - Bronchoscopes
    - Colposcopes
    - Culdoscopes
    - Cystoscopes
      - Endoscopes, Gastrointestinal
        - Colonoscopes +
        - Duodenoscopes
        - Esophagoscopes
        - Gastroscopes
        - Proctoscopes
    - Fetoscopes
    - Hysteroscopes
    - Laparoscopes
    - Laryngoscopes
    - Mediastinoscopes
    - Neuroendoscopes
    - Thoracoscopes
    - Ureteroscopes



If you had only used free-text terms, you would have missed 10 articles included in set 4, because the articles did not include the words "endoscopes" or "endoscope" or "endoscopic" (free-text terms).

But they did discuss disinfection of colonoscopes and laryngoscope disinfection, so that the indexing system picked them up.

I have a list here of the 10 (and the 50) results (in case you still have trouble doing this) – e-mail me at omge@omge.org and I will send you the results.

Happy searching, and remember … MeSH is a must! ■

Note: All of the hyperlinks given above are clickable in the electronic version of this article (**www.omge.org**).

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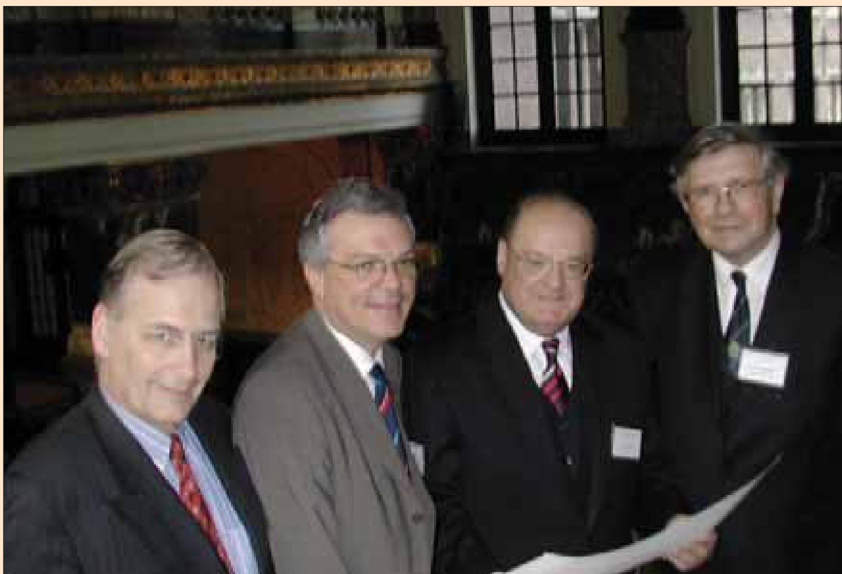
Major private-sector prize for OMGE



World Gastroenterology Organization President , Guido Tytgat (second from right) and Vice President, Eamonn Quigley (second from left) collected an $85,000 dollar prize in The Netherlands on March 17, 2004, on behalf of the entire organization. The prize, one of the Dutch private sector's most prestigious, was handed to Prof. Tytgat and Prof. Quigley by Prof. Lammert Leertouwer (far right), board chairman of the Helffer-Kootkar Prize Foundation, which has regularly awarded socially significant achievements of individuals and organizations since 1981. OMGE was recognized for its "pioneering work and concrete achievements over several decades in the organization of public-private sector medical training services in emerging nations", said Prof. Leertouwer at a ceremony hosted at Amsterdam's Royal Tropical Institute by Institute President Jan Donner (left). "This is terrific recognition for the work of OMGE's leadership, the national associations and the individuals who did the hard work over the years", OMGE Vice-President Eamonn Quigley told participants at the event. "It's also greatly encouraging for the OMGE education and training programme still ahead."

NEWS FROM THE INDUSTRY

AstraZeneca

New Frontiers in Managing Gastroesophageal Reflux Disease (GERD) – Revealing the Facts

Are patients with GERD controlled effectively? There is still an unmet need in the treatment of GERD patients. According to a multinational survey, the level of dissatisfaction is reflected by the number of patients who supplement their therapy with additional prescription medication or over-the-counter drugs – 22% and 21%, respectively [1].

How should patients be controlled? Keeping intraesophageal pH above 4 is crucial to reduce the amount of damage that gastric acid can do to the esophagus. Proton-pump inhibitors (PPIs) are highly effective in controlling gastric acid and gastric reflux into the esophagus. PPI treatment is therefore recommended as the first-line treatment in all patients with GERD [2].

Are all PPIs equally effective? Suppressing gastric acid secretion is vital for the clinical effectiveness of PPIs in the treatment of GERD. Many patients do not obtain adequate symptom resolution from prescribed PPI medication and may be switched to an alternative PPI in the search for a satisfactory symptomatic response.

What role can esomeprazole (Nexium) play in the management of GERD? Esomeprazole (Nexium®)is the first PPI developed as an isomer. Nexium has an advantageous metabolism compared with omeprazole. It has been shown to provide more effective acid control than all other PPIs and consequently faster and higher healing rates in GERD patients, as well as symptom resolution, than omeprazole, lansoprazole, or pantoprazole [3–8, 10] (Fig. 1).

Assessing the differences between PPIs with regard to the effectiveness of gastric acid suppression – the primary determinant of clinical efficacy – is vital to ensure rational switching of patients from one PPI therapy to another. Nexium has been shown to be more effective in reducing intragastric acidity than all other PPIs. These findings provide clear evidence that switching patients to Nexium from other PPIs that have not fully resolved their symptoms may translate into improved efficacy in relieving the symptoms of GERD.

Nexium's acid-reducing power has also been demonstrated in a single-center study comparing standard doses of Nexium, lansoprazole, pantoprazole, and rabeprazole in which GERD patients were switched between treatments to establish the most effective method of maintaining gastric pH above 4 for the longest period of time. Nexium achieved highly significant acid-reducing effects in more patients than all of the other PPIs. Nexium also provided more effective acid control after

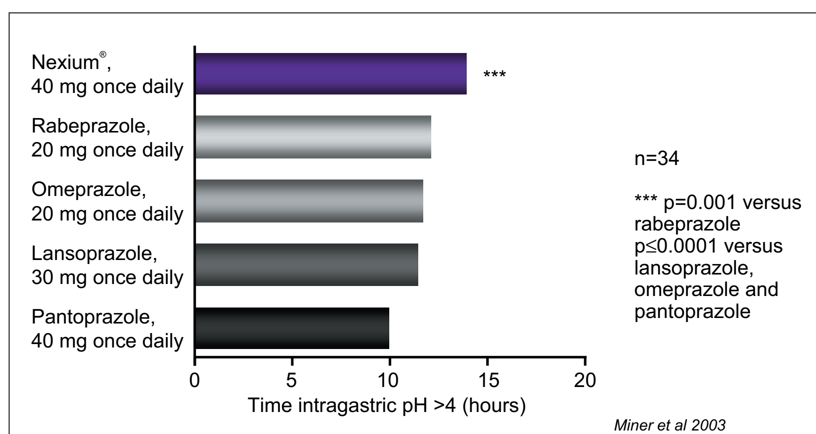


Fig. 1. *Nexium keeps the pH above 4 for significantly longer on day 5 than all of the other proton-pump inhibitors (PPIs). In this five-way cross-over study, H. pylori–negative GERD patients received each PPI for 5 days, with appropriate washout periods between treatments [3].*

GERD patients had been switched between PPIs [9].

Is Nexium the most effective PPI? In a multicenter trial including more than 5000 patients, Nexium was shown to achieve significantly higher rates of healing of esophagitis than a competitor PPI, lansoprazole. Nexium produced significantly higher healing rates for all patients with esophagitis, regardless of severity (patients with mild as well as severe esophagitis) [10].

Nexium is also associated with significantly higher remission rates after healing than lansoprazole during 6 months of maintenance therapy in patients with initially healed esophagitis, verified by endoscopy [11]. It is therefore able to provide a considerable improvement in patients' quality of life (Fig. 2).

In a head-to-head study in patients with reflux esophagitis, Nexium 40 mg achieved significantly higher healing rates and sustained resolution of heartburn throughout the 4 weeks of treatment in comparison with pantoprazole 40 mg. Patients in the Nexium treatment group also achieved sustained resolution of heartburn significantly faster than those treated with pantoprazole [8]. The more effective acid control provided by Nexium offers patients faster and more sustained relief from GERD symptoms such as heartburn, as well as offering a significantly better response with regard to acid regurgitation, epigastric pain, and upper abdominal bloating.

What is GERD?

Gastroesophageal reflux disease (GERD) is characterized by the reflux of gastric acid from the stomach into the esophagus.

What are the symptoms? Heartburn – a burning pain arising in the stomach or lower chest – is the predominant symptom of GERD [12]. Other symptoms include acid regurgitation and epigastric pain. Untreated, acid reflux can cause great discomfort, inflammation of the esophagus, and serious complications such as ulceration, sometimes followed by bleeding, Barrett's esophagus (which may be associated with cancer of the esophagus), and also stricture of the esophagus.

How common is it? The true prevalence of GERD is thought to be underestimated, and the disease is often misdiagnosed. In Western countries, an estimated 20–40% of the adult population (50 million people in Europe) experience heartburn, the predominant symptom of GERD [13].

Why do people suffer from GERD? It develops because the normal antireflux mechanisms in the esophagus are not effective.

What effect does GERD have on quality of life? According to a multinational survey in which 261 primary-care physicians and 927 patients suffering from GERD were interviewed, the condition has a substantial negative impact on everyday activities including sleep, social activities, work productivity, and sexual life [1].

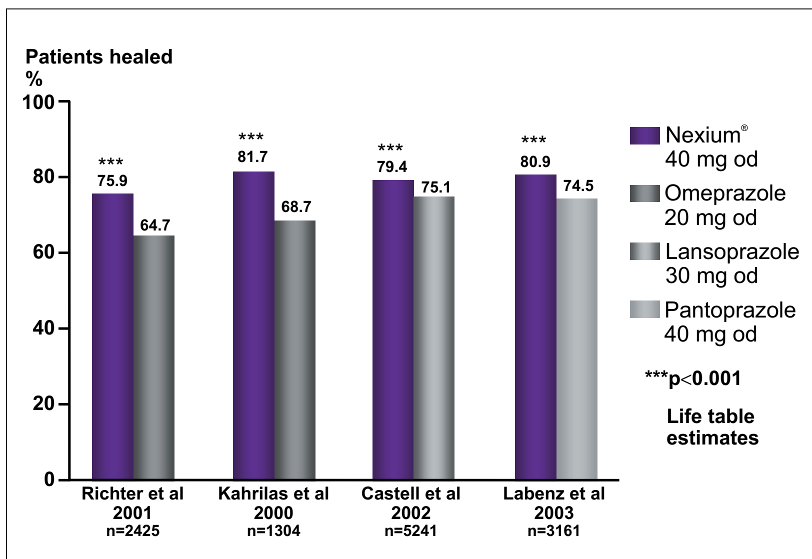


Fig. 2. *Nexium offers a consistent and significant benefit in healing reflux esophagitis at 4 weeks in comparison with three other PPIs, and this benefit is maintained at 8 weeks [6–8, 10].*

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Gastro-Pro, the gastroenterology learning website, to launch special DDW 2004 edition

Fresh for DDW

World Gastroenterology News talks to production coordinator Timothy Nater about the line-up.

WGN: *What's happened since you launched Gastro-Pro at WCOG 2002?*
Nater: We've been busy building the web platform, getting our editorial bearings and raising money. We're developing a curriculum of seven content sections and cross-disciplinary areas. Five of these are already up: endoscopy, GERD, GI cancer, functional bowel disease/IBS and IBD. We're refining interactive e-tests. We're running an CME-accredited learning series with the AGA. We've also launched conference news coverage to help keep our home-page fresh. As before, all of it is edited, peer-reviewed and presented by hands-on GE professors and practitioners.

WGN: *What is 'learning', for you?*
Nater: In our case, it's medical learning on the internet, which has to be easy to find, quick to absorb and practically useful, or users won't use it. It's still early days, but the demand and technical means are there. Almost 50 million new users of broadband went online in the last half of 2003 in the USA alone. Going online for CME credit is a real option for hundreds of thousands of US physicians, and medical practice and law are moving the same way in Europe, as well. In medicine as in many other sciences, this means faster dissemination and use of best practice. The OMGE-OMED Education Committee, which is a great source of editorial guidance and content for us, is following this closely.

WGN: *So what's on the Gastro-Pro menu for DDW?*
Nater: High-magnification video for the Barrett's module in the GERD section, interactive knowledge testing on colonic obstruction, fresh chunks of up-to-date, practice-oriented information about PPIs from an AGA forum, new endoscopic images of ileitis plus an exclusive newswatch in IBD. ■

Gastro-Pro: www.gastro-pro.org

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