Official newsletter of the World Gastroenterology Organisation

WGN
WORLD GASTROENTEROLOGY NEWS

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THIS ISSUE

MESSAGE FROM THE WGO PRESIDENT

WGO: the next 50 years!

A few acorns—many oak trees

Despite this attention-grabbing title, I have no intention of predicting the future of the World Gastroenterology Organisation (WGO)—it is certain that all that I augur will not come to pass. Rather, I wish to ponder a little on where WGO is and on the direction in which we have set our course.

Our distinguished past-presidents, Professors Villardell and Bouchier, elegantly described the origins, growth, and development of WGO in the 50th anniversary edition of *WGN*. As they describe it, WGO in its early days was primarily preoccupied with the quadrennial World Congress, with choosing the location for the conference and ensuring its timely and appropriate delivery. Later, WGO progressively expanded its spheres of activity and influence, with increasing emphasis being placed on the year-round activities of its committees on education, research, and ethics.

Training and education

More recently, the WGO has taken the strategic decision to focus its resources and efforts on one primary area: training and education. Accordingly, special emphasis has been placed on training centers, with our other flagship programs, Train-the-Trainers (TTT) and Global Guidelines supporting and enhancing the training centers' educational and training activities. This shows how today's WGO is seeking to streamline its activities to ensure delivery of a primary goal. The Train-the-Trainers (TTT) and Global Guidelines programs have both enjoyed unprecedented success and have attracted considerable attention in recent years. This year, TTT will be traveling to Croatia, the USA, and India and has attracted record numbers of applications from educators across the globe. Three important new guidelines have also arrived—on colorectal cancer screening, probiotics, and hepatitis B, incorporating our unique cascade approach that ensures guidance that can be applied in any part of the world, regardless of resources. Each of these projects started as a tentative idea (two more acorns!), and they have now grown to global prominence as unique and much-sought-after tools in the modern gastroenterologist's armamentarium.

This has been a banner year: in keeping with the focus on training mentioned above, three further WGO-affiliated training centers have been inaugurated in recent months—in Mexico City (Fig. 1), Bogota, and Ribeirão Prêto (Brazil), with a fourth in Suva (Fiji)

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Editorials

Scientific News

International Digestive Cancer Alliance News

Gastroenterology on the frontiers

Tempora mutantur, et nos in illis mutamur. *Latin*

(Times change, and we are changing with them.)

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John Owen (*c.* 1564–1622), the famed Welsh epigram writer, is credited with inventing this saying; the great Austrian composer, Joseph Haydn (1732–1809), a close friend of Mozart (1756–1791), liked it so much he made it the title of his Symphony No. 64. Starting with this edition, *World Gastroenterology News* is moving to an Internet-based format. Much of the medical world now looks to the Internet for its information. Medical journals are costly to produce and distribute. Internet-based publishing is fast and accessible. Advertising revenue, which drives the medical journal industry, is increasingly scarce. Recognizing that the future lies in electronic publishing, *WGN* is therefore moving to an all-electronic format. The publishing times have changed, and we are changing with them.

A lot of work by many people has gone into producing this web-based issue of *WGN*. Great care has been taken to maintain the variety and depth of articles that our readers have come to expect. As Editor, I admit to being biased, but I really think this may be the most diverse and interesting issue so far:

- The WGO President, Professor Eamonn Quigley, has written a provocative leading article on the importance of nutrition to the future of gastroenterology worldwide. From the fate of millions suffering from malnutrition to his own research interest in probiotics in health and disease, Dr. Quigley provides a "30,000-feet view" of the global nutrition landscape and challenges us to get involved.
- Two of *WGN*'s staunch supporters, Dr. Robert Enns and Dr. Klaus Mergener, review some of the best abstracts on capsule endoscopy and Barrett's esophagus, respectively, from the 2008 Digestive Disease Week meeting held in San Diego, California.
- Professor René Lambert and Dr. Silvia Franceschi continue an outstanding series of reviews on gastrointestinal malignancies with a fascinating look at gallbladder cancer, a disease with widely varying prevalence around the world.
- Dr. El Hassan of Sudan reports his experience of Burkitt's lymphoma, including his work with Dr. Denis Burkitt as they unraveled the mysteries of this unusual and possibly transmissible malignancy.
- The most recent addition to WGO's very successful Training Center program is being run by our Australian colleagues in Suva, Fiji. Despite the obvious distractions of a tropical paradise, it appears that training opportunities are needed and appreciated even in this remote location.
- *WGN*'s resident librarian, Justus Krabshuis, continues his series on how to navigate the bewildering maze of information resources available to physicians, this time using the Cochrane Library and the topic of esophageal varices as examples.

These articles, WGO news, meeting announcements, and much more await the readers of this inaugural electronic (e-)issue of *WGN*. We hope you will enjoy this offering and share it with your colleagues, trainees, support staff, and anyone interested in global health issues in gastroenterology.

It has been claimed that the printed word is dead, but most of us still enjoy the feel of a glossy journal and the pleasure of perusing its pages. However, we at *WGN* hope that the benefits of electronic publishing will outweigh any drawbacks. Going electronic will save an estimated 12 tons of trees needed annually to make paper for the print version of *WGN*. How "green" is that? Most journals end up incinerated in landfills, so going electronic will also reduce *WGN*'s carbon footprint. *WGN* is helping to save the planet! So, welcome again to the new *WGN*. As always, we appreciate feedback from readers, including suggestions for future articles and offers to write for us. Watch this space for new series coming up and opportunities for readers to provide comment. As Julius Caesar said as he crossed the Rubicon in 49 BC, "*Iacta alea est*" (the die is cast): we have rolled the dice at *WGN*, and we hope you will enjoy the result.

WGO: the next 50 years!
A few acorns—many oak trees

Continued from cover

due to be inaugurated at the time of the Gastroenterology Society of Australia meeting in Brisbane in October. WGO is now associated with a total of six centers in Latin America, providing the potential for a real network of interlinked centers to develop in order to serve the entire region.

Here lies the acorn that we hope will become the WGO oak of the future—a network of interlinked and mutually supportive training centers that benefit from sharing experience, educational resources, and personnel and provide a broad menu of training options at basic and advanced levels. Above all, these training centers will provide opportunities for those who currently have limited access to high-quality training in their home region. A primary goal of these centers is to provide relevant, high-quality training in regions of the world where such training is most lacking. This is achieved through partnerships with regional centers of excellence, local universities and hospitals, sponsors, and national gastroenterology societies. An exciting development has been the enthusiasm among many "first world" gastroenterology societies and gastroenterologists to participate in training and educational activities at these centers, as exemplified by the involvement of the American Society for Gastrointestinal Endoscopy (ASGE), the Canadian Association of Gastroenterology (CAG), and the Spanish Society (*Asociación Española de Gastroenterologia*, AEG) in La Paz, and of the *Association des Sociétés Nationales Européennes et Mediterranéennes de Gastroentérologie* (ASNEMGE) and the French and Belgian societies in Rabat. To encourage further collaborations of this nature, the Education and Training Committee Coordinator, Jim Toouli, and the Vice-President, Michael Farthing, have developed a template for such interactions; any physician or society that would like to get involved should contact us. Here lies another sprouting acorn—the ever-developing synergies between WGO and its member national societies.

Fig. 1
The Mexican journal, Reforma, highlights the opening of the Training Center in Mexico City on 28 July 2008.

World Digestive Health Day

WGO does not restrict its educational mission to physicians and gastroenterologists, but endeavors to promote public education as well. With campaigns spearheaded initially by our oncology division, the International Digestive Cancer Alliance (IDCA), through its highly successful public awareness campaigns on digestive cancers and especially colorectal cancer, the WGO has now expanded its public awareness and education initiatives into other areas. This is now enshrined in the concept of World Digestive Health Day (WDHD), which annually highlights a key global issue in digestive health (Fig. 2). Beginning with *Helicobacter pylori* in 2006 and moving to hepatitis in 2007, WDHD this year addressed the issue of nutrition and digestive health. Although it focuses on 29 May, the WGO's anniversary, the concept this year expanded to include activities spread throughout the year.

WDHD offers a tremendous opportunity for collaboration with national member societies through the development of local and national public awareness campaigns and events and the provision of a variety of educational resources. Generously supported by the Danone Group,

A

B

Fig. 2
Public awareness events on World Digestive Health Day (29 May 2008) in Montevideo (A) and Las Piedras (B), Uruguay. Left to right in a: Zenia Toribio (Danone, Uruguay), Carolina Olano (Secretary-General, Uruguayan Society of Gastroenterology), Elena Trucco (President), and María Laura Roberts (Danone).

WDHD has been an outstanding success this year, generating thousands of media items in several countries across the world and generating interest in nutrition, digestive health, and WGO and its activities. This is one acorn that has already broken through and is already sending leaves up to the sunlight and roots deep into the earth.

The next 50 years

WGO has come a long way by focusing its work, through judicious use of its resources, a great deal of effort, and above all through collaboration with and support from its member societies and their representatives on our committees, council, and executive. These collaborations are central to our current success and the key to our future. Our major challenge will be to find the resources to fund these activities: meaningful collaborations with the pharmaceutical industry, instrument manufacturers, and the diagnostics, accessory, and nutrition industries, as well as the philanthropic community, must be pursued in an ever-changing economic and business climate.

To streamline and bolster its fund-raising efforts, the WGO has launched the WGO Foundation (WGOF), which seeks support from individuals, institutions, corporations, and foundations to ensure that the WGO's goals will continue to be realized. I encourage readers to visit its web page (*www.wgofoundation.org*) and think about ways of helping to secure our financial future.

As our 50th anniversary year draws to a close, I would like to take this opportunity to thank all of those who have served this wonderful organization over the past 50 years—let's look forward together to the next 50! I wish to say a special word of thanks to all those who have hosted events and activities to mark the 50th anniversary and to acknowledge the support of our regional partners—*the Asociación Interamericana de Gastroenterologia* (AIGE), the African and Middle East Association of Gastroenterology (AMAGE), the Asian-Pacific Association of Gastroenterology (APAGE), and through ASNEMGE, the United European Gastroenterology Federation (UEGF).

Gastro 2009, a joint United European Gastroenterology Week (UEGW)–WGO presentation, will represent not only the gastroenterology event of the decade, but a perfect example of collaboration at the very highest level. The future of the WGO lies in collaboration, whether it be with regional or national societies or with individual gastroenterologists. Together, we can see that each of the acorns that we have sown will grow and prosper and provide this world with the mature and sustainable trees that it so sorely needs.

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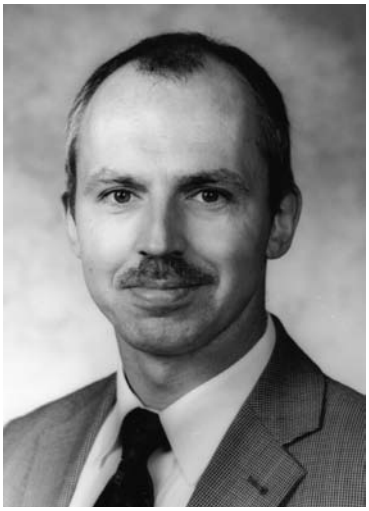
Barrett's esophagus



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Barrett's esophagus is an acquired premalignant condition that is associated with a 30–50-fold greater risk than in the general population of developing into esophageal adenocarcinoma. Some of the major studies on Barrett's esophagus presented at this year's Digestive Disease Week (held at the San Diego Convention Center, 17–22 May), are highlighted here, with a focus on their clinical implications.

Epidemiology and pathophysiology

It has been suggested that in Barrett's esophagus, lesions progress from low-grade dysplasia (LGD) to high-grade dysplasia (HGD) before esophageal adenocarcinoma develops. However, it is not known whether there are any specific clinical, demographic, or endoscopic features that are associated with the development of LGD and HGD.

Sharma and colleagues (M1295) prospectively compared the clinical and endoscopic characteristics of 127 Barrett's esophagus patients with LGD and HGD who were enrolled in a large multicenter randomized trial of radiofrequency ablation. Demographic and clinical features such as age, gender, ethnicity, and weight were assessed, and endoscopic landmarks and histopathological findings recorded. While this study essentially confirmed the well-known fact that the majority of Barrett's esophagus patients are white males, it failed to show significant differences between patients with LGD and HGD in relation to age, duration of the Barrett's esophagus diagnosis, or the endoscopic extent of Barrett's esophagus.

Gill and colleagues (M1397) used endoscopic ultrasound (EUS) to assess the thickness of the esophageal wall in 68 Barrett's esophagus patients and 53 control individuals, and correlated these measurements with the histological findings. Although a trend was observed towards increasing thickness of the distal esophageal wall with greater degrees of dysplasia, this did not reach statistical significance. The authors concluded that while the thickness of the distal esophageal wall is greater in Barrett's esophagus patients in comparison with normal controls, wall thickness does not predict the histological findings in Barrett's esophagus patients.

Siersema and colleagues (231) conducted a large, prospective, multicenter trial investigating the incidence of neoplastic progression in Barrett's esophagus patients. In a group of 783 patients in the Netherlands, they evaluated the annual risk of progression from no dysplasia (ND) to LGD and from ND or LGD to HGD or intramucosal cancer (IMC). Surveillance was carried out in accordance with the 2002 American College of Gastroenterology (ACG) guidelines. Over a mean follow-up period of 2 years, 32 of 604 ND patients developed LGD, equivalent to one LGD case per 37 patient-years. HGD developed in 11 of 703 Barrett's esophagus patients and IMC in a further 11 patients, corresponding to one case per 125 patient-years for both HGD and IMC. The authors conclude that in Barrett's esophagus patients with a columnar Barrett's esophagus segment of 2 cm or more and ND or LGD at baseline, the annual risk of progression towards HGD or IMC is 1.6%, and that the annual risk of progression from ND to LGD is 2.7%.

Endoscopic treatment

Esophagectomy has traditionally been the standard treatment for Barrett's esophagus patients with HGD and IMC, but it is associated with a

high morbidity rate (20-50%) and mortality rate (3-5%) even when performed in high-volume centers of excellence. Endoscopic ablative treatments such as photodynamic therapy (PDT) can eliminate HGD in approximately 75% of treated patients. Two emerging techniques in this area are radiofrequency ablation and cryotherapy.

In an interim analysis of an ongoing randomized sham-controlled trial, Shaheen and colleagues (213) assessed the efficacy of radiofrequency ablation for the treatment of 127 Barrett's patients at 19 centers in the USA. Patients were randomly assigned to receive circumferential or focal radiofrequency ablation therapy using the HALO™ system, in comparison with sham therapy. Biopsies were obtained every 3 months (HGD) or 6 months (LGD) after randomization. The authors found complete histological clearance of dysplasia in 83% of patients, in comparison with 0% in the sham treatment group. There was one stricture in the treatment group, which resolved with dilation. The authors conclude that if these interim results are confirmed, radiofrequency ablation may prove to be superior to other ablative therapies for the clearance of dysplasia in Barrett's esophagus.

In an ongoing study, Hernandez and colleagues (M1321) also used radiofrequency ablation in a community-based setting, treating patients with short-segment or long-segment Barrett's esophagus who had either LGD, HGD, or nondysplastic epithelium. In the first 38 of 50 patients, 44% showed a complete response (defined as an absence of Barrett's esophagus on follow-up biopsies) after 3 months of follow-up. At the time of the report, 10 patients had completed the 12-month follow-up period, and 70% of them showed no evidence of residual disease. One case of buried Barrett's metaplasia was found in a total of 828 post-ablation biopsies, and the metaplasia was successfully eradicated with repeat ablation. No serious complications were reported. The authors conclude that their preliminary data on radiofrequency ablation in a community setting are comparable to those in previously published reports.

Pouw et al. from Amsterdam (M1323) studied the safety and efficacy of combination therapy—i.e., focal endoscopic mucosal resection (EMR) followed by radiofrequency ablation in patients with HGD/IMC. The cap or multiple-band mucosectomy technique was used for EMR, followed 6 weeks later by radiofrequency ablation, which was then performed every 2 months until complete eradication of Barrett's esophagus was achieved. Using this combination therapy, the authors were able to achieve a 97% rate of complete eradication (30 of 31 patients) after an average of one EMR and two or three radiofrequency ablation sessions. In three patients, a superficial laceration was observed at the level of the prior EMR, which the authors attributed to overstretching with the radiofrequency ablation balloon. Four patients developed postprocedure dysphagia, which resolved with dilation. The authors conclude that for patients with HGD or intramucosal cancer, focal EMR of visible lesions followed by stepwise radiofrequency ablation is safe and effective.

Dr Miriam ("Mimi") Canto and the Johns Hopkins group (M1318) studied the safety and efficacy of CO2 cryotherapy for the treatment of Barrett's esophagus with HGD or IMC. Patients considered to be at high risk for esophagectomy were treated with a cryogen administered through a forward-spraying catheter. Treatments consisted of four to six applications of 5–15 s of ice effect to each area. Thirty-three patients were studied, and the median follow-up period was 4 months (range 1–8 months). Complete eradication of Barrett's esophagus was achieved in 21% of the patients, with a partial response (reduction in Barrett's esophagus and/or dysplasia) being observed in 79%. No significant complications occurred. The authors conclude that CO2 cryotherapy for Barrett's esophagus is safe and feasible. The Cleveland Clinic group (Dumot et al., M1304) used the same technique in patients with either Barrett's esophagus or squamous cell–associated HGD or IMC. Patients were treated every 6 weeks until endoscopic resolution, and the outcome was assessed using four-quadrant biopsies every 1 cm. The overall response in eliminating or downgrading dysplasia was 89% for HGD and 66% for IMC. Responses were better in patients with a shorter Barrett's esophagus segment. Minor strictures occurred in three of 32 patients, requiring one dilation each. One gastric perforation occurred in a patient with Marfan syndrome. The authors concluded that endoscopic cryotherapy ablation with a low-pressure liquid nitrogen spray is effective in HGD and IMC.

Capsule endoscopy

The best form of patient preparation needs to be taken into account when capsule endoscopy (CE) is performed. In a poster session, Maeda et al. (T1653) presented a retrospective study comparing capsule transit times in patients with diabetes mellitus or renal failure with transit times in control individuals. The authors found that in diabetes mellitus and renal failure, the cecum was visualized in only 54% and 44% of patients, respectively, a result that was significantly poorer than in controls. They concluded that in these patients, promotility agents and bowel preparation may be beneficial. Others (including Nguyen at al., W1430) have also suggested that patients with significant comorbidities may benefit from interventions to improve visualization and bowel transit.

In the same poster session, Barkun and colleagues from Montreal presented a prospective, randomized trial of CE versus push enteroscopy (T1517). This study sought to assess outcomes after 1 year in patients randomly assigned to capsule endoscopy or push enteroscopy in the setting of obscure gastrointestinal bleeding. Preliminary data demonstrate that there is less recurrent bleeding in the capsule group (21%) than in the push enteroscopy group (41%). Using the "hard" end point of recurrent bleeding, CE appears to improve the outcome, with a reduced need for repeat interventions. This adds support to previous studies that have described improved diagnostic accuracy with CE, but which did not address the long-term outcomes.

It is always challenging to select patients for CE. Although it is rarely difficult to justify CE for patients with obscure gastrointestinal bleeding, the yield of the test varies considerably between institutions. In our own institution, we have found the yield of CE to be high, probably because we select patients carefully and do not offer "on-demand" (direct access) procedures. However, when all of our referrals for CE are reviewed, small-bowel disease is found to account for the problem in only 19% of the patients. Garcia et al. (T1623) evaluated factors associated with positive outcomes of CE and determined that overt bleeding was a good indication for the procedure. In contrast, in patients with occult bleeding and a hemoglobin level over 10 g/dL, the yield was very low; in fact, the authors felt it was useless.

Bellutti et al. (T1652) found that many patients (29%) who had been referred for double balloon enteroscopy (DBE) had lesions that were actually within the reach of a standard endoscope. The authors therefore advocate repeating standard tests (i.e., EGD and colonoscopy) *before* DBE, which is costly and time-consuming.

Mehendiratta et al. (T1624) looked at the ease with which lesions can be reached using DBE. They compared the positive findings from 34 CE studies, and the location of the associated pathology, with the subsequent DBEs. When CE demonstrated a lesion in the small bowel, the closer the lesion was to the pylorus the more likely it was to be reached with DBE for confirmation. Lesions that were more than 50% of the way down the small intestine (as estimated by the CE transit time) were rarely identified on DBE, suggesting that usually only the first half of the small bowel can be routinely visualized with the technique.

CE is known to be limited in its ability to inspect the duodenum. It rarely "sees" the main duodenal papilla. This was confirmed by Ioquinto et al. (M1108) when screening patients with familial adenomatous polyposis (FAP) for small-bowel polyps. CE was useful for screening the jejunum and ileum. However, in a group of 23 patients, more duodenal polyps were recognized with EGD than with CE.

A recent new application of CE has been for identifying esophageal varices. There have been conflicting results in the literature, which may reflect differences in technique, grading systems, and prevalence of disease, as well as the type of capsule used (e.g., the standard capsule versus the Eso-2™ model). A well-conducted meta-analysis by Raina et al. (M1123) has demonstrated acceptable levels of utility (with a diagnostic odds ratio of 44) and safety for CE in ruling out esophageal varices in patients with cirrhosis.

CE is also being used to evaluate the colon. A study by Delveaux et al. (W1590) was designed to assess the positive and negative predictive values (PPV and NPV) of CE in comparison with optical (standard) colonoscopy in 77 patients. For CE, the PPV was 75% and the NPV 62% (with a kappa value for any lesion of 0.68). In the multicenter study by Devière et al. (282), the PPV was 72% and NPV 77% in 320 patients, 134 of whom had significant findings. These two studies lay a solid foundation for further work in this area. Aggressive colon preparation and a lack of prokinetic agents to accelerate the capsule through the colon when necessary continue to hamper progress in this area.

Future prospects in CE were outlined by Morita et al. (S1417), using a simulated stomach environment. They modified a standard capsule endoscope by adding a fin that can be used to steer it. An externally applied magnetic field creates a current that causes the capsule to vibrate. With the aid of the fin, the capsule can then be steered to a site of interest. The idea of a capsule endoscope that can be controlled in real time to investigate lesions seen in passing has been a dream since the inception of the method—and the realization of this dream may be closer than we think.

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Nutrition:
a wake-up call to gastroenterologists

Eamonn M.M. Quigley, MD

The World Gastroenterology Organisation designated nutrition as the theme for World Digestive Health Day (WDHD) in 2008 and participated in a host of awareness and educational events throughout the world. As this year draws to a close, let us take a few minutes to contemplate the importance of this topic in the management of digestive disorders and in sustaining digestive health.

For decades, nutrition had a somewhat peripheral role in everyday practice for gastroenterologists treating adults. The gastroenterologist's interest in nutritional issues extended little beyond administering total parenteral nutrition (TPN) for the occasional very ill patient with inflammatory bowel disease or placing percutaneous endoscopic gastrostomy (PEG) tubes when requested by fellow internists, neurologists, or geriatricians. Several factors have now converged to make nutrition a primary concern for physicians treating patients suffering from a host of gastrointestinal ills. Regrettably, unlike their pediatric colleagues, who—mindful of the critical issues of growth and development in the care of the infant or child with digestive disorders—have been ever vigilant regarding nutritional issues, modern gastroenterologists treating adults are largely ill-equipped to cope with the diversity and complexity of current nutritional issues. Gastroenterologists of a certain (quite recent) generation were quite simply not trained in the fundamentals of nutritional science or in the most basic concepts of nutritional therapy and are sorely in need of high-quality education in these areas.

Why make a fuss about nutrition today?

There are several factors that make it imperative for gastroenterologists treating adults to learn to imitate their pediatric counterparts and become comfortable with nutritional assessment and management, over and above the basics of recognizing and dealing with the consequences of malnutrition. The following are but a few of the "modern" issues that we must all learn to deal with.

Malnutrition. The fact that as many as 3 million children die each year from malnutrition in the developing world is a sad indictment of our collective failure to solve this most basic and tragic nutritional issue. To address this, we must understand the scope of the problem and its causes and consequences and must work assiduously and creatively to develop optimal and sustainable approaches to resolving it.[1]

The "obesity epidemic." As alarm concerning the ever-expanding weight and girth of the populations we serve increases, and as more and more effort is expended on pharmacological, endoscopic, and surgical approaches to obesity management, the likelihood increases that the gastroenterologist will be called on to participate at various stages in the care of the obese patient. The modern gastroenterologist must be conversant with the gastroenterological and hepatological consequences of obesity and of the likely response to weight loss. It is critical to understand that this is a global issue—obesity and its complications are endemic both in developed and in developing countries. The endoscopist may be called on to evaluate the patient before surgery or to evaluate any number of upper gastrointestinal complications that may arise in the postoperative period. It stands to reason that a thorough understanding of the anatomical and physiological derangements that result from the various surgical approaches commonly employed is imperative before one embarks on such interventions.[2] Some believe that the

gastroenterologist of the future should play a pivotal role in all stages of the management of the obese patient. Most recently, it has been suggested on the basis of considerable laboratory evidence and some clinical evidence,[3,4] that the gut flora, or microbiota, may be a key player in the pathogenesis of obesity; we may not be what we eat, but rather what our bugs eat!

The metabolic consequences of chronic inflammation. With the recognition that the development of osteopenia in patients with inflammatory bowel disease (IBD) is not limited to patients who are taking corticosteroids on a chronic basis, but is a direct consequence of the chronic inflammatory process per se, it has become obligatory for every gastroenterologist to understand the metabolic consequences of chronic inflammation and instigate therapeutic measures that may reduce the risk of bone loss.[5]

Understanding the gut responses to food and dietary constituents. Many patients with any number of gastrointestinal symptoms attribute their symptoms to certain foodstuffs, self-diagnose themselves as suffering from a food "allergy," and institute draconian restrictions that may have serious nutritional consequences. Regrettably, they are all too often assisted in this unwise course by those who offer a variety of "allergy tests," the basis for which owes little to science but much to opportunism. If we are to help such patients, we must understand the true nature and range of the gut's reactions to food ingestion. This may range from simply physiological effects (the primary purpose of the gut is, after all, to digest food and facilitate the absorption into the body of essential nutrients) to full-blown anaphylactic IgE-mediated food allergy. Recent evidence suggests that the prevalence of true food allergy is on the increase. All the more reason, therefore, to be equipped to accurately recognize and diagnose this potentially fatal condition. There has also been a suggestion that IgG-mediated antibody responses may play a role in the pathogenesis of symptoms among some who are labeled as having irritable bowel syndrome (IBS). Thanks to the advent of widely available and highly sensitive and specific antibody tests, the true prevalence and real clinical spectrum of celiac disease—a cell-mediated immune response to another dietary component, gliadin—is now beginning to be appreciated and cases of what was previously thought to be a rare disorder are being diagnosed more often. For many patients, however, our role is to reassure and, armed with our understanding of food–gut interactions, to direct the patient toward a practical and nutritionally sound dietary regimen. At the same time, it must be admitted that our understanding of the role of dietary components in some of the most common gastrointestinal disorders, such as IBS, is a long way from being clarified; some surprises may await us.

Understanding the role of food and particular nutrients in disease pathogenesis or prevention. The literature is replete with data on the role of various dietary components or their deficiency in the pathogenesis of a host of gastrointestinal ills, ranging from gastroesophageal reflux disease (GERD) to constipation and to colon or pancreatic cancer. While this is a highly complex and, in part, incompletely understood area that has its fair share of unresolved controversies, clinicians must be sufficiently knowledgeable concerning the role of diet and dietary interventions in these diseases to be able to provide reasonable and reasoned advice to their patients.

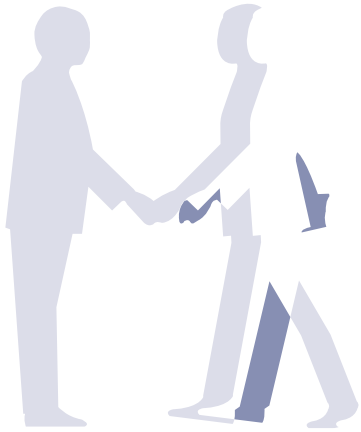
Appreciating the key role of interactions between the enteric flora, luminal contents, and the host in homeostasis and disease. At long last, the enteric flora is beginning to achieve the recognition and attract the scientific attention that it truly deserves.[6] As the flora is now recognized as playing a pivotal role in many aspects of homeostasis and as being relevant to the pathogenesis of disorders as varied as obesity and arthropathies, it has become incumbent on the modern gastroenterologist to understand how what we eat or drink affects the flora. In parallel, but not always in synchrony, with this increase in research into human microbiota, we have witnessed an explosion in interest in the therapeutic potential of this area—most commonly expressed in the form of exhortations to consume a variety of prebiotic or probiotic products. While evidence continues to accumulate to indicate a real and clinically meaningful role for probiotics in gastrointestinal infections, some manifestations of IBD and IBS,[7] and other conditions, consumers and physicians are bombarded with many products whose quality and clinical efficacy is often unknown. Here again, the patient will turn to the physician for advice and recommendations, neither of which can be imparted without a knowledge of the issues. So-called "functional foods," which include but are not limited to prebiotics and probiotics, have tremendous therapeutic potential, and their advent presents the gastroenterologist with the opportunity to be at the forefront in guiding the optimal introduction of such products into the clinical arena. We are rapidly moving into an era in which food will come to be regarded as medicine.

A call to arms!

From the issues summarized above —as well as many others, such as the role of nutrition in the care of the patient with liver or pancreatic disease—it is abundantly clear that there is a gaping void in the diagnostic and therapeutic armamentarium of the modern practicing and aspiring gastroenterologist. This is a void that must and can be filled through carefully developed and attractively delivered educational programs; gastroenterologists must learn to embrace nutrition as a fundamental component of their daily practice and become at ease with addressing patient concerns on such issues, as well as in instituting appropriate dietary regimens and nutritional therapies for an individual patient. Clearly, the primacy of various issues will vary tremendously across the globe, given the diversity of diets and the common occurrence of malnutrition in too many areas. Education must be tailored to local needs.

(see page 28 for references)

GASTRO 2009
YOUNG CLINICIANS PROGRAMME
19–25, November 2009



A fantastic opportunity to meet and learn with colleagues from around the world

It is with pleasure that we announce the Call for Nominations for young active GI trainees from around the world to participate in the Gastro 2009 Young Clinicians Programme (YCP). This unique opportunity is being developed as a joint organisational venture between the host societies of Gastro 2009 (UEGF, WGO, OMED and BSG) as well as the Association of National European and Mediterranean Societies of Gastroenterology (ASNEMGE).

In the first part of the YCP, a dedicated two-day course immediately prior to the Gastro 2009 meeting, young clinicians from different cultures and geographic regions will be exposed to important GI topics and issues relevant to their current training and their future academic and practical work. Successful candidates will also be hosted during the Gastro 2009 meeting in London where the themes of the YCP programme will continue in the framework of the core meeting.

OMED
ASNEMGE
WGO
UNITED EUROPEAN GASTROENTEROLOGY FEDERATION
British Society of Gastroenterology

GASTRO 2009
UEGW/WCOG, London

CALL FOR NOMINATIONS TO
WGO/OMED/ASNEMGE/UEGF Member Societies

- Dates: 19–25 November 2009 including sessions during GASTRO 2009
- Venue: Pre-course at a hotel situated in close vicinity to London; participants will move to London for the core Gastro 2009 programme

YCP PROGRAMME

Case-based interactive sessions, training in practical methods

Core themes:
- Dyspepsia/Barrett's oesophagus
- Liver
- IBD
- Colorectal Cancer

Parallel skills training sessions on the following topics will be offered:
- Endoscopy – basic training using simulation/advanced imaging
- Capsule endoscopy
- Ultrasound
- LFT interpretation
- Motility testing
- Research
- Presentation skills

APPLICATION DEADLINE:

30 November 2008

SUCCESSFUL CANDIDATES TO BE NOTIFIED BY:

31 January 2009

Application Information and Forms available at

www.gastro2009.org

ELIGIBILITY CRITERIA

- The candidate should normally be under the age of 35 years at the time of the meeting
- The candidate must be a junior member of the gastroenterological community, still in or having recently completed their specialty training in gastroenterology within the past 4 years.
- The candidate must have demonstrated some level of academic performance and intellectual curiosity as reflected by scholarly activity in teaching or research thereby indicating his/her potential role in the future as a leader in their respective country
- A good command of the English language is required
- Indication of the intent to submit an abstract to Gastro 2009 will be a favourable attribute

YCP OFFER

A total of 90 trainees will be selected from the submitted names. These successful candidates will receive the following support:
- Travel grant (only for non UK participants) for economy class travel only, to be paid to participants after the event. Participants are responsible for their own travel bookings.
- 7 nights accommodation shared with another same sex Young Clinician participant, assigned by the congress organisers (single accommodation can be arranged at additional personal cost)
- GI Postgraduate Course registration Gastro 2009
- Congress registration to Gastro 2009
- Transport from the YCP venue to the Gastro 2009 venue in London
- Transport to social events
- All meals during the initial two-day programme

TASTER VISITS TO UK TRAINING CENTERS

Successful candidates will be offered the opportunity to spend a few days either prior to the YCP or after Gastro 2009 at a host training center in the United Kingdom. A selection of leading centers around the country has offered to host YCP participants and to provide accommodation. This is an optional feature and further detail will be provided after the initial selection process has been completed.

APPLICATION PROCESS

Applications to YCP will only be accepted through official national member societies of WGO/OMED/ASNEMGE/UEGF. Societies wishing to submit candidates for the YCP must have paid up their annual dues to their respective organisation. Each national society is entitled to submit the names of a maximum of TWO candidates only.
Please visit the WGO/OMED/ASNEMGE/UEGF websites for application forms and requirements.

SELECTION PROCESS

Applications will be reviewed by the YCP Organising Committee and acceptance will be based on criteria of academic excellence, intellectual curiosity, leadership, initiative. The need for balanced regional and gender representation in the YCP will be taken into account.
All selected participants will be required to attend the YCP and Gastro 2009 programmes in full (November 19 – 25, 2009 inclusive) and attendance at all scheduled events is mandatory, including scientific and social activities that will span over the 7 days. Selected participants may also be required to present a review of a poster or oral presentation on a pre-assigned topic.

Denis Burkitt and the first cases of Burkitt lymphoma

During his clinical practice as a general surgeon in Uganda in 1957, Dr. Denis Burkitt was asked to see a pediatric patient who had an unusual tumor involving the jaw. Soon after, another child with the same condition was referred to him. The tumor was a rapidly growing one, and the children died within a few weeks. Burkitt recognized that this unusual condition was possibly a previously undescribed malignant tumor. He contacted a large number of hospitals and institutions in Africa, including my own, and asked us to look for this tumor in Sudan. Burkitt undertook a geographical survey of the incidence of the disease and found that it correlated with the same temperature and rainfall zones as malaria. This suggested that the tumor might be caused by an infective agent that was linked to the distribution of certain insect carriers. In 1958, he published his first paper on the tumor. Burkitt's lymphoma survey is regarded as one of the pioneering studies in geographical pathology.

At first, the tumor was described as "multicentric sarcoma of the jaw." It was later found to be a lymphoma and was named Burkitt's lymphoma. There was a strong suspicion that it was caused by Epstein–Barr virus (EBV). The type described in Uganda and other African countries is the endemic form. Sporadic cases, mainly involving parts of the body other than the jaws, are reported in Europe, North America and Japan. A form associated with HIV/AIDS infection has also been described.

Lynch and El Hassan described the first two cases of Burkitt's lymphoma in the Sudan. A Sudanese surgeon, I. Nabri, described more cases in Equatoria province in southern Sudan, on the border with Uganda. Mr. Nabri sent me biopsies from his patients, and the condition proved to be Burkitt's lymphoma. Thanks to Professor Burkitt, I received funds to establish a National Cancer Registry in Khartoum, and more cases of Burkitt's lymphoma were entered in the registry. The tumor occurred mainly in the southern and western parts of the Sudan, where malaria is hyperendemic. It was mainly of the endemic type.

My colleagues and I recently realized that the pattern of Burkitt's lymphoma was changing. In the last 7 years in my laboratory, patients with this lymphoma have been having more of the sporadic type, with involvement of the gastrointestinal tract and retroperitoneum, rather than the jaws. We are at present trying to figure out what the possible cause for this change might be.

There is now more evidence that arboviruses may be involved as cofactors in the etiology of some Burkitt's or Burkitt-like lymphomas. ("Arbovirus" is a nontaxonomic term used for an epidemiologic class of viruses that replicate in blood-feeding arthropods and are transmitted by bite to the host; they are found in various viral families, including the Bunyaviridae and Flaviviridae). Several outbreaks of dengue fever (caused by a Flavivirus) and Rift Valley fever (caused by one of the Bunyaviridae) have been documented in central Sudan. The latest outbreak of Rift Valley fever occurred toward the end of 2007. The distribution of a plant, *Euphorbia tirucalli*, has been found to correlate with that of Burkitt's lymphoma in some African countries. Extracts of the plant induce a t(8;14) translocation of EBV-infected B cells in vitro, which is the same translocation found in Burkitt's lymphoma. The plant is distributed in the dry savannah parts of Sudan, where we are seeing cases of gastrointestinal lymphoma.

Although Burkitt's lymphoma is a highly malignant tumor, it can be cured with modern therapy. Over the years since Burkitt first described the tumor, a great deal of information has been revealed about its epidemiology, pathogenesis, possible etiology, and treatment.

Ahmed El Hassan, MD

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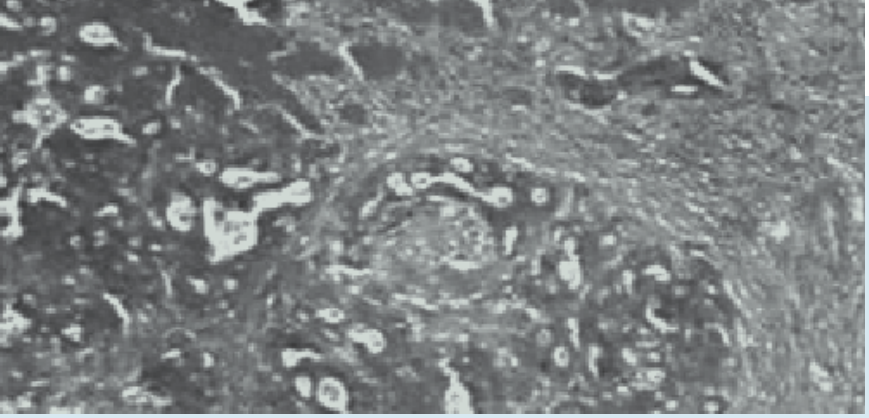
Further reading:

Ahmed MA, Omer A, El Hassan AM. Malignant lymphomas at the Pathology Department, University of Khartoum, Sudan. East Afr Med J 1984;61:627–31 (PMID: 6336041).
Burkitt D. A sarcoma involving the jaws in African children. Br J Surg 1958;46:218–23 (PMID: 13628987).
El Hassan AM. Malignant disease in Sudanese children. Sudan Med J 1967;5:69–75.
Lynch JB, El Hassan AM. Multicentric sarcoma of the jaw. Sudan Med J 1962;1:168–72.
Veress B, Malik MO, Satir AA, EL Hassan AM. Burkitt's lymphoma in the Sudan. Afr J Med Sci 1976;5:115–9 (PMID: 829716).



Carcinoma of the gallbladder

René Lambert and Silvia Franceschi

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The burden

Biliary cancer occurs at three distinct sites: the gallbladder, the extrahepatic bile ducts, and the ampulla of Vater. Cancer of the gallbladder, a cholangiocarcinoma, is the most common malignant tumor in the biliary tract (Table 1); its proportion in biliary tract cancer varies from 35.8% in women and 18.9% in men in Denmark (National Cancer Registry) to 91.6% in women and 74.5% in men in Chile (Valdivia Registry), or 93.6% in women and 80.4% in men in India (New Delhi). Symptoms appear late in the course of the disease, and early and silent cancer is detected incidentally by pathologists on specimens from cholecystectomy carried out due to gallstone disease. The epidemiology of gallbladder cancer was recently reviewed by Randi et al.[1]

Incidence, mortality and survival in gallbladder cancer

Incidence

Cancer of the gallbladder is more frequent in women (70% of cases) than in men, and it shows marked geographic variation. The age-standardized rate (ASR) varies from 1.5 to 12.3 per 100,000 in men and from 1.6 to 27.3 per 100,000 in women (Table 2). Countries with a high incidence are in the Far East (Korea, Japan), northern India, Pakistan, South America (Chile, Ecuador Colombia), and eastern Europe (Slovakia, Poland, Czech Republic). Ethnic variations in the incidence also occur, with high rates among the Mapuche (Araucanians) in Chile and native Americans in the USA. Hispanic white women have a 3–5-fold higher incidence than non-Hispanic women in the USA.

Saika and Matsuda[3] analyzed ethnicity and temporal variations in the ASR of gallbladder cancer during the period 1978–1997 in 18 cancer registries (included *in Cancer Incidence in Five Continents*) vols. IV–VIII. In East Asia, the ASR was higher in Japan (Miyagi, Nagasaki, and Osaka) than in China (Shanghai and Hong Kong). In Europe, the highest figure was in an Italian registry (Varese) and the lowest in two registries in England (South Thames and West Midlands). In the USA, Koreans had the highest ASR in the Los Angeles registry, while the black and Caucasian populations showed the lowest rates.

With regard to time trends, the ASR declined during the period 1978–97 in Denmark, France (Bas-Rhin registry), and Sweden. In the USA, there was a slow decrease among the white population between 1973–77 and 1993–97, while the level in the black population remained stable.

Mortality

The age-standardized mortality rate from gallbladder cancer is particularly high in Chile. In a study conducted in 1985–2003 by Andia et al.,[4] the figure ranges from 8.2 to 12.4 per 100,000 (both sexes) depending on the region, with the highest value in the inland region in the south. In a previous

	Gallbladder	EHBD	Ampulla of Vater
Americas			
Chile: Valdivia registry	74.5%	4.5%	11.8%
USA: SEER, 14 registries	41.3%	34.9%	20.6%
Asia			
China: Hong Kong registry	46.4%	35.7%	17.9%
Japan: Osaka registry	36.5%	52.0%	10.7%
Europe			
Denmark: national registry	18.9%	46.7%	28.4%
France: Calvados registry	32.7%	23.6%	29.1%
Italy: Venetia registry	33.3%	26.7%	21.8%

Source: Curado et al.[2]

Table 1
Relative proportions of biliary cancer in three anatomical sectors—the gallbladder, extrahepatic bile ducts (EHBD), and ampulla of Vater, both sexes included. Cases not specified in the tumor registry and other tumors are not reported in this table. Gallbladder cancer accounts for three-quarters of all biliary tumors in Chile. The proportion is much lower in all other countries.

study in Chile, the mortality ASR was estimated at 15.6 per 100,000 in women and 7.0 per 100,000 in men.[5] In Europe, the figures are much lower. Zatonski et al.[6] conducted a study of official death certifications in the WHO database during the period 1985–89 in 25 countries. The ASR for mortality varied from 1.5 to 3.9 per 100,000 in men and from 2 to 7.4 per 100,000 in women. High-mortality areas were in Germany and central European countries. Intermediate levels were found in Scandinavian countries and in Switzerland, and low levels in Belgium, France, England, and Mediterranean countries. In the mortality statistics for the year 2000 in the USA, the ASRs for mortality due to gallbladder cancer in men and women were 0.49 and 0.85 per 100,000, respectively. The time trend for mortality in 1975–2005 shows an annual decrease of 2.2% in men and 2.7% in women.

Survival

Gallbladder cancer is often detected at a late stage, and the survival is poor.[7] In Europe, data from the Eurocare study[8,9] showed a 5-year relative survival rate of 14.1% for patients with gallbladder cancer diagnosed in the period 1995–99 for the two sexes combined. In the Surveillance Epidemiology, and End Results (SEER) registry in the USA (all races, all ages), the 5-year relative survival for patients with gallbladder cancer (both sexes) improved from 5.4% to 16.6% during the period 1975–2005[10]. The overall 5-year relative survival was less than 5% in the study conducted by Donohue et al.[11] in 5488 cases collected in hospital cancer registries in the USA during two periods: 1989–90 and 1994–95 (Table 3). The respective figures analyzed by the TNM stage of the tumor at detection were: 60% for stage 0 (5% of all cases); 39% for stage I (13% of cases); 15% for stage II (13% of cases); 5% for stage III (20% of cases); and 1% for stage IV (46% of cases). In Japan, Kayahara et al.[12] analyzed the 5-year relative survival from gallbladder cancer by TNM stage in 4774 cases collected in the period 1988–97. The figures were 77% in stage I, 60% in stage II, 29% in stage III, and 11% and 3% in two categories of stage IV.

Precursors and carcinogenesis sequence in the gallbladder

Adenocarcinomas (Fig. 1) originate from the glandular epithelium, and most arise in the fundus of the gallbladder. Premalignant neoplastic lesions in the gallbladder have been described in surgical specimens after cholecystectomy for gallstones. Small polypoid adenomas rarely show malignant transformation, but polyps larger than 1.5 cm are associated with a 50% risk of malignancy. The focus is on flat areas of the epithelium with low-grade or high-grade intraepithelial neoplasia. These epithelial lesions were analyzed by Duarte et al.[13] in 162 gallbladders after cholecystectomy for lithiasis in Chile, where there is a high incidence. Antral-type metaplasia was found in 95.1% of the cases, intestinal metaplasia in 58.1%, hyperplasia in 46.9%, dysplasia in 16%, and carcinoma in situ in 2.5%. Hyperplasia was more extensive when it was associated with dysplasia and carcinoma in situ. As described by Wistuba and Gazdar,[14] the most common molecular alterations in the multistage sequence that links flat areas of dysplasia, carcinoma in situ, and invasive carcinoma of the gallbladder are mutation of the *TP53* gene with loss of heterozygosity at 17p, and mutation of the *KRAS* gene on 12p, codon 12.[15]

Causal factors

Role of gallstones and resultant cholecystitis

Gallbladder cancer is frequently associated with gallstones, and the presence of one or more large gallstones is the best-recognized factor for gallbladder cancer. The percentage of patients found to have gallbladder cancer after cholecystectomy for gallstones is 0.5–1.5%. The role of gallstones as a causal factor for cancer has been evaluated in many studies, including a large cohort studied by Chow et al.[16] in Denmark, consisting of 60,176 patients discharged from hospital after treatment for gallstones. The summary relative risk for gallbladder cancer is estimated at 4.9 in patients with a history of gallstones. A case–control study of gallbladder cancer was conducted by Zatonski et al.[17] in five centers in Australia, Canada, the Netherlands, and Poland in the period 1983–88. In this study, control individuals without previous cholecystectomy were compared

	Men	Women
Americas		
USA: SEER, 14 registries	1.5	1.6
Chile: Valdivia registry	12.3	27.3
Asia		
China: Hong Kong registry	2.9	2.8
China: Shanghai registry	3.5	5.1
Japan: Osaka registry	5.7	4.7
Korea: Seoul registry	8.0	6.3
Europe		
Denmark: national registry	1.4	1.5
France: Calvados registry	2.0	1.6
Italy: Venetia registry	3.0	3.0

Source: Curado et al.[2]

Table 2 Age-standardized incidence of gallbladder cancer in registries from various countries in men and women for the period 1998–2002

T0 or Tis (carcinoma in situ), intramucosal carcinoma	5%
T1, localized cancer T1a, invasion of the lamina propria under the mucosa T1b, superficial invasion of the muscularis propria	13%
T2, localized cancer with invasion through the full thickness of the muscularis propria	13%
T3, nonlocalized cancer superficial invasion into the liver	20%
T4, nonlocalized cancer with invasion over 2 cm into the liver or pancreas, stomach, or intestine	46%

Source: Curado et al.[11]

Table 3 Proportion of each TNM stage of cancer in the gallbladder at detection in the USA. Radical surgery is possible in Tis, T1, and T2 tumors, but not in T3 and T4 tumors.

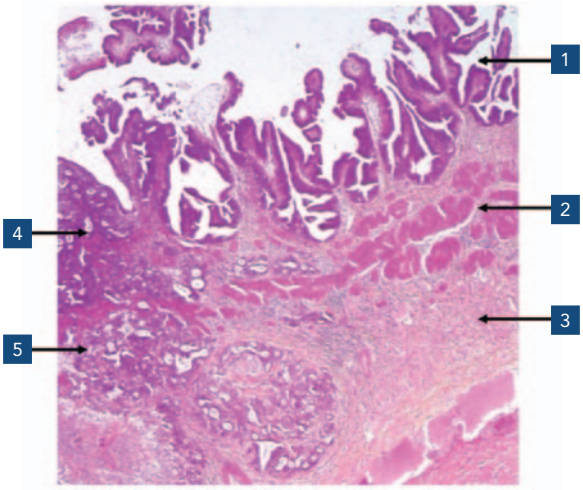

Fig. 1
Small adenocarcinoma in the gallbladder. Transverse histopathological section of the tumor.

1 Epithelium in the gallbladder wall.
2 Muscular layer in the gallbladder wall.
3 Peritoneum outside the gallbladder wall.
4 Adenocarcinoma in the epithelium and muscular layer.
5 Invasion outside the gallbladder wall, staged T3.

with patients in whom gallbladder cancer had been confirmed by either biopsy, cholecystectomy, or autopsy. The cases differed from the matched controls in having gallstone disease and presenting a dietary pattern characterized by a high rate of consumption of red chili pepper and a low intake of fresh fruit; they also had a lower socioeconomic level.

Role of an abnormal pancreaticobiliary duct junction

A premature junction between the common bile duct and the pancreatic duct results in regurgitation of pancreatic juice into the gallbladder and chronic inflammation. An abnormal pancreaticobiliary junction is related to less invasive papillary carcinoma of the gallbladder, which has a good prognosis. This anomaly of the junction is more frequent in Japan, Korea, and possibly China than elsewhere in the world. In Japan, gallbladder patients are younger and have a lower incidence of gallstones when the pancreaticobiliary junction is abnormal.[18]

Role of infectious agents

Infectious agents in the biliary tract may play a role due to chronic inflammation of the gallbladder, and it has been suggested that they may also be causal factors for gallbladder cancer. A significant relationship between carrier status for *Salmonella typhi* and *S. paratyphi* and gallbladder cancer has been demonstrated in case–control studies, with a summary relative risk for gallbladder cancer of 5.2 (personal communication). The role of *Helicobacter* species deserves special mention; it is plausible that it may be involved in biliary tract cancer.[19–22] Since the discovery of *H. pylori*, 30 species of *Helicobacter* have been isolated from the stomach, intestinal tract, and liver of mammals and birds. *Helicobacter bilis, H. pullorum, H. hepaticus*, and even *H. pylori* have been identified in bile and biopsies of biliary tissue. Methods of bacterial detection and analysis include amplification by polymerase chain reaction, histology, immunohistopathology, and culture. *Helicobacter* is often detected in benign biliary diseases such as gallstones and cholecystitis. The prevalence of *Helicobacter* in bile is lower in Western countries with a low incidence of gallbladder cancer and higher in countries like Japan. In studies of bile or tissue biopsies that have included a control group, the summary for the pooled odds ratio for an association between *Helicobacter* species and biliary cancer was approximately 5. However, the currently available tests for *Helicobacter* species are far from perfect, and notably are often unable to distinguish *H. pylori* from other *Helicobacter* species (personal communication).

Early detection and prevention

Abdominal ultrasonography is the traditional method of examination in gallbladder diseases. The procedure is potentially suitable for screening of the gallbladder in countries with a high incidence of gallbladder cancer. More efficient and noninvasive diagnostic procedures can be used as a second step after the abdominal ultrasound examination. These include computed tomography and magnetic resonance cholangiopancreatography. Invasive procedures include endoscopic retrograde cholangiography (ERCP), which is the gold standard procedure for detecting an abnormal pancreaticobiliary junction. Samples for cytology can be obtained with guided brushing during ERCP and fine-needle aspiration during endoscopic ultrasonography.

Silent gallstones have often been detected since the use of abdominal ultrasonography became widespread. Preventive measures might therefore rely on an opportunistic diagnosis of silent gallstones, leading to a dilemma over whether cholecystectomy should be recommended. Wood et al.[23] have shown that an increased tendency for cholecystectomies to be carried out in Scotland during the period 1968–98 was accompanied by a reduction in the mortality from gallbladder cancer.

Cholecystectomy is an effective treatment for stage Tis tumors when cancer is an incidental finding. However, the best form of management for T1 cancer is still a matter of debate. Stage T1a can be treated by laparoscopic or open cholecystectomy, while T1b tumors require cholecystectomy and hepatoduodenal lymph-node resection. The role of surgery for advanced disease remains controversial, but it should be recommended when a potentially curative R0 resection is possible.
(see page 28 for references)

For a further perspective on gallbladder cancer, see Dr. Kapoor's article in this issue on page 24

IDCA colorectal cancer screening symposium at UEGW

Date: Saturday 18 October 2008
Location: Austria Center, Vienna, Hall K/Level U2
Time: 09:30–17:00

A workshop on “Future Directions in Colorectal Cancer Screening in Europe” is to be held at the United European Gastroenterology Week (UEGW) in Vienna. The IDCA took the initiative to hold the workshop, and the Public Affairs Committee of the United European Gastroenterology Federation (UEGF) endorsed it. The International Agency for Research on Cancer (IARC) also wanted to take this opportunity to present the new European guideline that is being prepared. All the representatives of the 40 European gastroenterology societies that took part in earlier surveys conducted by the IDCA are being invited not only to attend, but also to offer a poster if possible, in which the results of scientific and feasibility studies conducted to date can be presented.

With its eight sessions, the scientific program will cover a broad spectrum that will be of interest to “clients, patients, professionals, and scientists” and will place special emphasis on quality assurance in the treatment of colorectal cancer. International societies will for the first time be working jointly in the field of colorectal cancer screening, in order to assist the representatives of the individual national societies in developing quality-assured cancer screening in their own countries.

The UEGF has generously offered to meet traveling costs and conference fees for the national representatives of the European gastroenterology societies for the day of this meeting.

IDCA

The International Digestive Cancer Alliance

PROGRAM OUTLINE

- **Introduction: principles of primary prevention.** Speaker: Colm O'Morain
- **Overview of colorectal cancer screening in Europe.** Chairs: J. Patnick, N. Segnan; speakers: L. von Karsa, M. Classen
- **Rationale of screening and selection of tests.** Chairs: S. Winawer, C. Senore; speakers: M. von Ballegooijen, N. Segnan
- **Range of colorectal cancer screening programs in Europe.** Chairs: M. Classen, L. von Karsa; speakers: J. Faivre (France), W. Schmiegel (Germany), N. Malila (Finland), M. Zavoral (Czech Republic), J. Regula (Poland), J. Patnick (UK), W. Atkin (UK), M. Zappa (Italy), J. Zakotnik (Slovenia)
- **Developing guidelines for colorectal cancer screening.** Chairs: W. Atkin, W. Schmiegel
  – WGO guidelines. Speaker: S. Winawer
  – European guidelines. Speakers: J. Patnick, N. Segnan, L. von Karsa
- **Therapy of lesions detected by screening.** Chair: R. Lambert
  – Endoscopy. Speaker: R. Valori
  – Surgery. Speaker: M. Keighley
  – Digestive oncology. Speaker: E. Van Cutsem
- **Quality assurance issues in colorectal cancer screening.** Open discussion; moderators: J. Patnick, J.-F. Rey, N. Segnan, S. Winawer
- **Advocacy for colorectal cancer screening of appropriate quality.** Chairpersons and speakers: C. Maar, H. Sundseth
- **The high-risk patient—environmental and genetic factors.** Chair: R. Lambert; speaker: H. Vasen; discussion panel members: J. Faivre, J. Regula, W. Schmiegel, N. Segnan

ORGANIZING COMMITTEE

C. O'Morain,[1] M. Classen,[2] J. Patnick,[3] N. Segnan,[4] L. Faulds Wood,[5] L. von Karsa[6]

1. UEGF Publication Committee
2. International Digestive Cancer Alliance
3. National Health Service Cancer Screening Programmes Coordination Office and University of Oxford, United Kingdom
4. CPO and S. Giovanni Battista University Hospital, Turin, Italy
5. European Cancer Patient Coalition, Brussels
6. European Cancer Network, International Agency for Research on Cancer, Lyons, France

IDCA EXECUTIVE SECRETARIAT

Medconnect GmbH, Bruennsteinstrasse 10,
81541 Munich, Germany
Tel.: +49-89-4141-9240, fax +49-89-4141-9245

Future directions in colorectal cancer screening in Europe: a workshop for clients, patients, professionals, and scientists
Workshop participants who are interested in advocacy are encouraged to visit the European Cancer Patient Coalition (ECPC) web site for further information:

www.ECPC-online.org or **www.darmkrebs.de** (in German)

Pakistan

Interview with Dr. Muhammad Umar

In April 2007, Prof. Muhammad Umar, President of Pakistan Society of Gastroenterology, attended WGO's seventh Train-the-Trainers (TTT) workshop in Portugal—accompanied by his wife, Prof. Hamama-tul-Bushra, a practicing gastroenterologist who was also a participant. Dr. Umar talked with WGN about how the workshop has affected their clinical practice and about health care in Pakistan.

WGN: Prof. Umar, what are the biggest health-care challenges facing Pakistan today?

MU: In the field of gastroenterology, the most important issues are shortages of training institutes and trained faculty. Clinically, the top health issues in gastroenterology are acute and chronic gastrointestinal infections due to poor sanitation, and gastrointestinal bleeding as a complication of portal hypertension caused by hepatitis B and C. Nutritional deficiencies are also a major concern.

WGN: What provisions does the government make for public health care?

MU: The government spends less than 1% of GDP on the health sector. A public health-care system has been in place since 1947. It covers about 70% of the population and offers free health care, including medication. A private health-care system has also developed during the last 10 years, although only 20–30% of the population can afford to visit a private hospital. Government medical schools provide medical education at much lower cost than private medical schools.

WGN: Why is there such a lack of trained faculty and training institutes in Pakistan?

MU: As Pakistan is a developing country, there is a major lack of institutes that offer specialized training. Additionally, fewer doctors are returning home to practice after studying abroad, due to low salaries and few job opportunities. Recently, however, we have seen some very positive developments, and in terms of specialty training we are beginning to catch up with international standards.

WGN: As head of the gastroenterology and hepatology department at Rawalpindi Medical College, you train junior doctors on a daily basis and develop the curriculum—so you have a great deal of experience in medical education. Why did you attend the TTT workshop?

MU: Attending TTT was part of my continuous professional development, and I strongly believe that interaction with international colleagues deeply improves our understanding of teaching and training methodology and research. I also wanted to make connections with international faculty to improve my awareness of international standards. I found the TTT workshop fulfilled all of these goals.

WGN: What did you "take home" from TTT and how did you put this into practice?

MU: The TTT adult education and "hands-on" modules were particularly interesting for me, as I noted a need in my college to improve the teaching of procedural skills, and the methods we learned in the TTT workshop were ideal. The TTT workshops are ideally suited to improving training in the developing world, where medical training is in need of support. When I returned to Rawalpindi, Dr. Hamama-tul-Bushra and I organized the first course in "Basic Skills in GI Endoscopy," based on material from the TTT workshop. Twenty-five medical professionals from all over Pakistan attended the course, as well as several professors from other teaching hospitals, who returned to their home institutions to teach the same skills to their medical students and junior doctors. More information about activities at the Rawalpindi Research Center is available on its web site (*www.rawalianresearch.org*).

Editor's note: The WGO Foundation is in the process of raising funds to enable more educators from developing, low-resource countries to attend the WGO's Train-the-Trainers workshops. Readers wishing to get involved or to find out more should contact info@wgofoundation.org.

A

B

(A) Rawalpindi Hospital, (B) Dr. M. Umar (center) and staff at the Endoscopy Center, Holy Family Hospital Rawalpindi

History of the Pakistan Society of Gastroenterology

The Pakistan Society of Gastroenterology and Gastrointestinal Endoscopy (PSG) was established in 1985–86 by a group of gastroenterologists, gastrointestinal surgeons, and pathologists. The Society has five provincial chapters, each of which held 3-day meetings every 5 years until 2006, when a Pakistan Society of Gastroenterology Week (PSGW) replaced the provincial meetings. The one-week meeting includes a formal core program and symposia, as well as postgraduate courses and specialized workshops. Gastroenterologists, hepatologists, gastroenterology fellows, and general practitioners from all over Pakistan attend PSGW. The Society's official journal, the Pakistan Journal of Gastroenterology, is published twice a year and is accredited and indexed by the Pakistan Medical and Dental Council.

Training in gastroenterology in Pakistan

There are two types of training program in gastroenterology in Pakistan. The first is the Fellowship in Gastroenterology run by the College of Physicians and Surgeons of Pakistan, which is a 5-year program. The other course is a master's degree in gastroenterology, which is a university program involving 5 years' training in gastroenterology. Both programs are well structured and standardized.

There are also two types of gastroenterology training center in Pakistan—public and private. In both sectors, the facilities are well equipped and the curriculum is standardized, but the courses do not currently meet the country's needs and require improvement and international assistance. The PSG is currently lobbying the government to establish new training and research centers for gastroenterology and liver disease. This is especially important now, with the increasing numbers of cases of acute and chronic infections, gastrointestinal malignancies, and complications of hepatitis B and C.

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President Pakistan Society of Gastroenterology

World Digestive Health Day 2008

Optimal Health and Nutrition

Thank you WGO Members and Danone!

WGO is honored by the tremendous work of its members to celebrate World Digestive Health Day. Medical professionals around the world joined together to draw attention to the importance of good nutrition to patient health.

Members in 31 countries planned educational symposia and events and developed patient material to raise nutritional awareness. WGO would like to acknowledge the generous support of Danone: with this support at international and local level, WDHD reached over 263 million people via 2832 pieces of media coverage ranging from newspaper articles to educational toolkits and television spots featuring celebrities such as actress Jamie Lee Curtis. Extracts from this extensive media campaign are highlighted here. Unfortunately, space limits do not permit us to include all events and items.

Map showing the extent of WDHD activities which reached most continents and corners of the world.

WDHD Activities around the World

WGO Training Centers
Suva, Fiji

The Gastroenterological Society of Australia has partnered with the World Gastroenterology Organisation (WGO) to develop the latest WGO Training Center at the Fiji School of Medicine (FSM). In close consultation with the FSM, a program has been developed for integration into the School's postgraduate medical training course.

FSM is one of only three institutions in Fiji and the Pacific Island nations to offer local medical training in the region. With such limited training available, and with a regional population totalling approximately 1.7 million people, the ratio of doctors per 1000 population is at a mere 0.1–0.4. The shortage of doctors in nearby countries such as Australia and New Zealand has also contributed to this "brain drain," as local doctors seek employment abroad. From 1987 to 2002, 510 doctors left the government health service in Fiji, while during the same period only 284 graduated from the Fiji School of Medicine.

Until recently, specialist training in the South Pacific was unavailable and has often been undertaken abroad, making it difficult for doctors who have become accustomed to life in their new environment to return home again once their training has been completed. The lack of local specialist training has thus also contributed to the brain drain in the region. However, it has been shown that local postgraduate programs can help combat this trend, with trainee physicians working for most of the time in their home country while learning to diagnose and treat disease with the resources locally available—thereby making them less likely to leave their home country once specialist qualifications have been achieved.

The new program has been created to meet this need. Members of the Gastroenterological Society of Australia's Fiji Training Team (GESAFiTT) will contribute to training in endoscopy, hepatology, and luminal gastroenterology. To further address the need for specialist training in the region, programs in gastrointestinal surgery and pediatric gastroenterology are also being developed.

GESAFiTT members visited the Fiji School of Medicine and the Colonial War Memorial Hospital in Suva for the first time for 4 weeks during August and September 2008. Team members included Dr. Andrew Taylor, Dr. Don Ormonde, Dr. Peter Katelaris (Associate Professor) and Dr. Tony Clarke. The training course was organized by Prof. Finlay Macrae (Royal Melbourne Hospital) and Thein Htut from Australia, in close consultation with Dr. Joji Malani (Fig. 1) and Prof. Robert Moulds at the Fiji School of Medicine.

The official inauguration of the WGO Training Center in Suva, Fiji will take place on 26 October 2008. Please join us in welcoming this latest WGO Training Center!

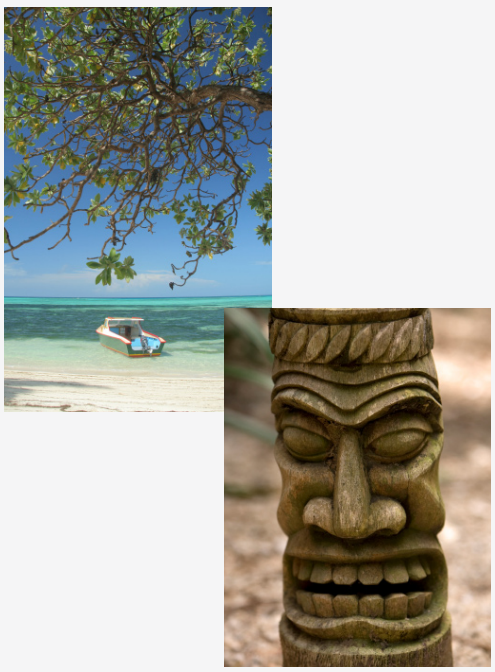

Fig. 1
Left to right: Thein Htut, Finlay Macrae, and Joji Malani at the WGO Training Center in Suva.

Gallbladder cancer—
a challenge in India too

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Although it is the commonest cancer of the biliary tract worldwide, gallbladder cancer is not a common condition in the West (North America, western Europe, Australia, and New Zealand). Gallbladder cancer has a peculiar geographical distribution and is common in Central and South America, central and eastern Europe, and Japan. Xabier de Aretxabala and Ivan Roa recently highlighted the very high prevalence of gallbladder cancer in Chile and the challenges faced by Chilean physicians and surgeons in tackling the disease (*WGN* 2007;12(1):41).

Gallbladder cancer is also common in northern India. The National Cancer Registry Program of the Indian Council of Medical Research has documented a very high incidence (over nine per 100,000 per year) of gallbladder cancer in women in Delhi, in whom it is the commonest gastrointestinal cancer. Having worked in Delhi as well as in Lucknow (500 km to the east of Delhi in northern India), I have observed that gallbladder cancer is even more common in Lucknow than it is in Delhi. The commonest cause of malignant obstructive jaundice requiring surgery in Lucknow is gallbladder cancer, which is more common than pancreatic and periampullary cancers and cholangiocarcinoma. Between 1989 and 2006, we operated on more than 650 patients with gallbladder cancer, 275 of whom underwent resection. Gallbladder cancer is an "Indian disease," and Lucknow is a strong contender for the title of "gallbladder cancer capital" of India.

Most patients with gallbladder cancer are diagnosed when the disease is advanced, as early gallbladder cancer mimics gallstone disease; ultrasonography is not very helpful in detecting early gallbladder cancer. Contrast-enhanced computed tomography is a useful investigation for staging the disease and assessing resectability. We have documented the important role of staging laparoscopy for picking up metastatic deposits on the surface of the liver, omentum, and peritoneum, which are frequently seen in gallbladder cancer, avoiding unnecessary laparotomy. Upper gastrointestinal endoscopy can detect duodenal involvement, which again indicates unresectability unless pancreaticoduodenectomy is contemplated.

Most Indian surgeons are not as aggressive toward gallbladder cancer as their Japanese colleagues and do not routinely perform ultraradical or supraradical procedures such as extended right hepatectomy, hepatopancreaticoduodenectomy, hepatic artery and portal vein resection, or extensive retroperitoneal lymphadenectomy in patients with advanced gallbladder cancer. The commonest resectional procedure performed is extended cholecystectomy, including a 2-cm, nonanatomical wedge resection of liver in the gallbladder bed and lymphadenectomy at the hepatoduodenal ligament (behind the head of pancreas and to the right of the celiac trunk). This procedure is curative (with R0 resection) in patients with disease confined to the gallbladder wall and lymph nodes limited to the hepatoduodenal ligament (i.e., early gallbladder cancer).

The majority of early gallbladder cancers are identified incidentally on histopathological examination of gallbladders removed when there is a presumed diagnosis of gallstone disease. We advocate repeat surgery to complete an extended cholecystectomy in such cases, except when the disease is confined to the mucosa. It is not uncommon to see a patient who has recently undergone an uneventful cholecystectomy (during the previous 3–12 months) present with surgical obstructive jaundice and/or gastric outlet obstruction due to local growth of a gallbladder cancer. This is due to the surgeon failing to send the resected gallbladder for histopathologic examination because it looked grossly normal. Unfortunately, this is not an uncommon practice amongst surgeons, but it is precisely the way in which an incidental (inapparent) gallbladder cancer, which is usually early and potentially curable, is missed.

The Chilean government should be complimented for developing and supporting a program to promote cholecystectomy in the high-risk population to reduce the prevalence of gallbladder cancer in Chile. I hope the Indian government and surgical societies will take a cue from this and make it mandatory for all surgeons to send the removed gallbladder for histopathological examination in order to detect incidental gallbladder cancer.

Further reading

Kapoor VK. Incidental gallbladder cancer. Am J Gastroenterol 2001; 96:627–9 [PMID: 11280526].
Kapoor VK. Gallbladder cancer: a global perspective. J Surg Oncol 2006; 93:607–9 [PMID: 16724344].
Kapoor VK. Advanced gallbladder cancer: Indian "middle path". J Hepatobiliary Pancreat Surg 2007;14:366–73 [PMID: 17653634].
Kapoor VK, Benjamin IS. Resectional surgery for gallbladder cancer. Br J Surg 1998;85: 145–6 [PMID: 9501805].
Kapoor VK, McMichael AJ. Gallbladder cancer: an "Indian" disease. Nat Med J India 2003;16:209–13 [PMID: 14606770].

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Managing esophageal varices:

Should the search go beyond the Cochrane Library?

Your practice is evidence-based. It is, isn't it? So you need to find the evidence. Appraisal will come later. And later still, the even more difficult "integration with clinical experience and your patients' norms and values." The latter is the really difficult part, which is often forgotten or glossed over, even though all definitions of "evidence-based medicine" emphasize its importance. Why might that be?[1]

All right, let's go and find the evidence. We can start at different levels. Clinicians may want to be higher up the pyramid (Fig. 1), while teachers and researchers usually start lower down.

You can start at the bottom of this famous triangle and gather all the published randomized controlled trials (RCTs) on your topic—management of esophageal varices—and appraise and analyze them. But why reinvent the wheel? Could you not simply gather existing systematic reviews, or higher up, still use evidence-based synopses or guidelines? They have done the work for you already.

I will focus mostly here on level 2, finding systematic reviews. The Cochrane Library (*http://www.cochrane.org/*) is the only source of "full-text" systematic reviews (Table 1). And here—immediately—some of us are in trouble. Let's say you are in Syria or in Pakistan and you don't have free access to the Cochrane Library (see here whether you qualify: *http://www.who.int/hinari/eligibility/en/*). Pakistan does not qualify for free or low-cost access, but Syria qualifies for low-cost (not free!) access (1000 per year). Assuming you have no budget, what then? Before we answer that, let's have a look at what is in the Cochrane Library. Once we know that, we may be able to find other ways to collect evidence.

The Cochrane Library, produced by the Cochrane Collaboration, is the world's premier source of evidence-based systematic reviews and controlled clinical trials.

The powerhouse behind this total of nearly 5000 systematic reviews is the Cochrane Review Group. Each discipline or major topic is likely to have a Cochrane Review Group, and there are over 50 groups in all (see *http://www.cochrane.org/contact/entities.htm#CCSG*). In the field of gastroenterology and hepatology, there are four Cochrane Review Groups in the following areas:

- Colorectal Cancer Group (Copenhagen, Denmark), *www.cccg.dk*
- Hepatobiliary Group (Copenhagen, Denmark), *www.ctu.rh.dk/chbg*
- Inflammatory bowel disease and functional bowel disorders (London, Ontario, Canada), *www.cochrane.uottowa.ca/ibd*
- Upper Gastrointestinal and Pancreatic Diseases Group (Leeds, UK), *www.cochrane.leeds.ac.uk*

Let's imagine you are a gastroenterologist who is putting together a presentation on "evidence for the management of esophageal varices," and let's assume you have access to the Cochrane Library. You decide to go for level 2—after all, there's no point in reinventing the wheel and anyway, searching for RCTs in Embase and Medline to top up the results from the Cochrane Library itself does not look like an attractive option. It takes more time than you have, and it is not as easy as it looks.

So you search the Cochrane Library for systematic reviews. Four relevant results come up when you search with the MeSH term "Esophageal and Gastric Varices."

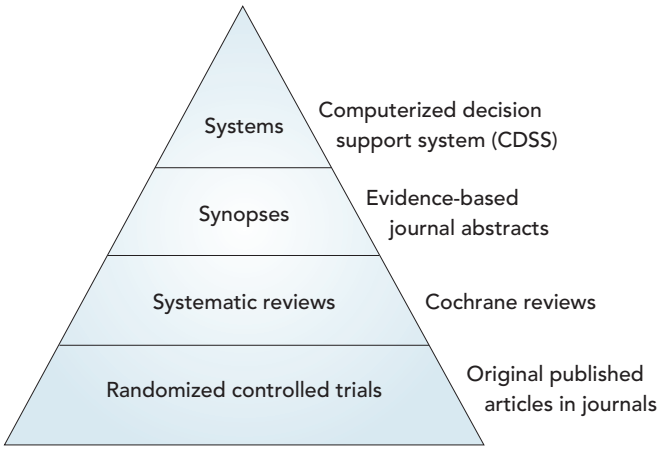

Fig. 1
The evidence pyramid.[2]

Database	Number of records	Limitations
Systematic reviews	4941	• Not all systematic reviews are included • Treatment bias • Currency/updating? • Not always free
Controlled trials	503826	• Top up with last 2 years' RCTs in Embase and Medline • No reindexing of Embase records with MeSH? • Search interface not so good (e.g., no "explosion" of MeSH terms)

Table 1
Size and some limitations of the two key Cochrane databases

Search term	PubMed limited to systematic reviews	PubMed limited to meta-analyses	Cochrane Library systematic reviews
Esophageal varices (free text)	127	48	10 (includes four protocols and one irrelevant systematic review)
Esophageal and gastric varices (MeSH term)	115	47	4

Table 2
Searching PubMed and the Cochrane Library for systematic reviews on the management of esophageal varices

- Portosystemic shunts versus endoscopic therapy for variceal rebleeding in patients with cirrhosis
  S Khan, C Tudur Smith, P Williamson, R Sutton
  Year: 2006
- Somatostatin analogues for acute bleeding oesophageal varices
  PC Gøtzsche, A Hróbjartsson
  Year: 2005
- Terlipressin for acute esophageal variceal hemorrhage
  G Ioannou, J Doust, DC Rockey
  Year: 2003
- Emergency sclerotherapy versus medical interventions for bleeding oesophageal varices in cirrhotic patients
  G D'Amico, LLP Pagliaro, GGPI Pietrosi, IITA Tarantino
  Year: 2002

All of these "hits" are relevant, and the precision of the search is therefore 100%—but have we found everything that is in the database? Is the search sensitive enough?

Let's search for "esophageal varices" in the "title, abstracts or keywords" fields as well. Now we have ten hits. Four of these are protocols. Of the other two systematic reviews, one is a new one (it is unclear why this was not found using the MeSH indexing term, possibly an indexing error) and the other systematic review is not relevant to the query. So the search has now found a total of five relevant systematic reviews. Now you are very pleased with yourself—you sit down, but then you wonder "Do I truly have all the evidence now?"

Bad news at level 2

If you search PubMed/Medline with the MesH indexing term "Esophageal and Gastric Varices" and limit this search to "systematic reviews," you get 115 hits (Table 2).

If you also search PubMed/Medline with the MesH indexing term "Esophageal and Gastric Varices" and limit this search to "meta-analyses," you get 47 hits.

Now go to the "History" tab and do #1 OR #2 to de-duplicate and create a unique set of records. This produces 120 hits.

For the moment, let's assume your Cochrane Library search strategy was fine, and let's assume also that all the correct indexing terms were assigned to each record. What now?

Well, you have just found 120 systematic reviews and meta-analyses in PubMed dealing with esophageal varices which you did not find in the Cochrane Library. Here is a general rule: "Many published systematic reviews are not available through the Cochrane Library." I am not making any statement about the quality of Cochrane or non-Cochrane reviews—all I am saying is that, from an evidence-based point of view, you will need to go beyond the Cochrane Library if you want to find all systematic reviews on esophageal varices.

The key place to go is PubMed/Medline. This includes citations and abstracts of all systematic reviews available in the Cochrane Library, and very often many more. The only thing you cannot get in PubMed is the full text of the Cochrane review—all you get is a summary of the review.

Bad news at level 1

Suppose you are putting together a systematic review on the management of esophageal varices. In this case, you need to drop down a level and find all randomized controlled trials. Now you need to search the Cochrane Database of Randomized Controlled Trials (called "Central" by insiders). The bad news has to do with the "currency" of the information (whether it is up to date), as well as with problems with the search interface.

A Cochrane review is a magnificent piece of research, often undertaken as voluntary work. It is a major publication, with many people giving their time freely to compile it. But then what? Medical research does not stand still—looking at PubMed/Medline, I see that every year there are at least 250 publications dealing with esophageal varices. Now we are in deeper trouble. Updating Cochrane reviews is the

responsibility of the original team. But teams change, the science changes, and the world moves on.

The Cochrane Library search experts recommend searching Medline and Embase for all RCTs published in the last 2 years. You also would need to search for trials published in non-Western regions (see Appendix 1 for a list of non-Western sources).

The best handbook on evidence-based searching for evidence is Chapter 6 of the Cochrane handbook for systematic reviews of interventions (version 5.0, updated February 2008), available for free from: *www.cochrane-handbook.org/*, written by Carol Lefebvre, Eric Manheimer, and Julie Glanville.[3] This is the gold standard for "evidence-based" searchers.

So is it possible to find enough in the Cochrane Library when searching for RCTs on how to manage esophageal varices? No! Can we add to it from Embase and Medline and in this way get evidence that is more "complete"? Yes, almost certainly—but it is not always easy.

Bad news at level 3

Finally, let's suppose you are a clinician with only minutes to spare. You want to find out about "management options for esophageal varices." Then you go up one level more—forget about trials, forget about systematic reviews, we go directly to evidence-based synopses or evidence-based guidelines. A recent Canadian study[4] looked at the most frequently used evidence-based bedside information tools and found that the following (in alphabetical order) were the top five (Table 3). The bad news is that all of them are fee-based, although Bandolier is free after 6 months.

The top one is probably UpToDate, but it costs money. Gastroenterologists in low-income countries should lobby the HINARI management in Geneva to include such tools in their HINARI package.

The best free resources for level 3 bedside information tools are listed in Table 4.

And then, of course, there is Wikipedia. Type "esophageal varices" in the search box, and you'll be surprised. It is free—the main drawback is that it is not evidence-based (*http://en.wikipedia.org/wiki/Esophageal_varices*).

And guidelines, I hear you ask? As long as there is no central repository for guidelines on gastroenterology and hepatology, you will need to check the National Guidelines Clearinghouse at *www.ngc.org*, and of course the sites of the large gastroenterology and hepatology societies. Some real treasures are available here—the best and most recent evidence-based guideline on esophageal varices was published in September 2007 in the journal Hepatology, the top journal in the field, with the highest impact factor of all hepatology journals (10.446) (see Appendix 2). Like the Cochrane Library, it is published by the oldest science publisher in the USA, John Wiley. It was written by an eminent team with members from both the American Association for the Study of Liver Diseases and the American College of Gastroenterology.[5]

That is the state of the art—but then, what if you are in Syria or in Pakistan? the guideline is 'resource-blind', like most others. Only the World Gastroenterology Organization is trying to take account of resources in its cascade-based guidelines. The WGO's brand-new, cascade-based esophageal varices guideline is available at *http://www.worldgastroenterology.org/*treatment-of-esophageal-varices.html.

Whatever your search strategy in the Cochrane Library, you are not going to find these guidelines—not because they are too recent, but because of the way the Cochrane Library is designed. To find them, you have to go beyond the Cochrane Library—reluctantly, perhaps.

Acknowledgment

The author is grateful to the publishers John Wiley for providing temporary free access to the Cochrane Library.

(see page 28, 29 for references and appendixes)

UpToDate	*www.uptodate.com*
BMJ Clinical Evidence	*clinicalevidence.bmj.com*
ACP Pier	*pier.acponline.org*
Bandolier	*www.jr2.ox.ac.uk/bandolier* (free after 6 months)
First Consult/MD Consult	*www.mdconsult.com*

Table 3
The top five evidence-based bedside information tools

Bandolier	*www.jr2.ox.ac.uk/bandolier* (free after 6 months)
Emedicine	*www.emedicine.com*
BestBets	*www.bestbets.org*

Table 4
Free evidence-based bedside information tools

Nutrition: a wake-up call to gastroenterologists

Page 10

1. Prentice AM, Gershwin ME, Schaible UE, Keusch GT, Victora CG, Gordon JI. New challenges in studying nutrition–disease interactions in the developing world. J Clin Invest 2008;118:1322–9 (PMID: 18382744).
2. Hussain Z, Quigley EMM. Gastrointestinal issues in the assessment and management of the obese patient. Gastroenterol Hepatol 2007;3:559–69.
3. Turnbaugh PJ, Ley RE, Mahowald MA, Magrini V, Mardis ER, Gordon JI. An obesity-associated gut microbiome with increased capacity for energy harvest. Nature 2006;444:1027–31 (PMID: 17183312).
4. Ley RE, Turnbaugh PJ, Klein S, Gordon JI. Microbial ecology: human gut microbes associated with obesity. Nature 2006;444:1022–3 (PMID: 17183309).
5. Bernstein CN. Osteoporosis and other complications of inflammatory bowel disease. Curr Opin Gastroenterol 2002;18:428–34 (PMID: 17033317).
6. O'Hara AM, Shanahan F. The gut flora as a forgotten organ. EMBO Rep 2006;7:688–93 (PMID: 16819463).
7. Quigley EM, Flourie B. Probiotics and irritable bowel syndrome: a rationale for their use and an assessment of the evidence to date. Neurogastroenterol Motil 2007;19:166–72 (PMID: 17300285).

Carcinoma of the gallbladder

Page 15

1. Randi G, Franceschi S, La Vecchia C. Gallbladder cancer worldwide: geographical distribution and risk factors. Int J Cancer 2006;118:1591–602.
2. Curado MP, Edwards B, Shin HR, et al., eds. *Cancer Incidence in Five Continents*, vol. IX. Lyons: IARC, 2007 (IARC Scientific Publications no. 160).
3. Saika K, Matsuda T. Comparison of time trends in gallbladder cancer incidence (1973–1997) in East Asia, Europe and the USA, from *Cancer Incidence in Five Continents*, vols. IV–VIII. Jpn J Clin Oncol 2007;37:974–6.
4. Andia ME, Hsing AW, Andreotti G, Ferreccio C. Geographic variation of gallbladder cancer mortality and risk factors in Chile: a population-based ecologic study. Int J Cancer 2008;123:1411–6.
5. Andia KM, Gederlini GA, Ferreccio RC. [Gallbladder cancer: trend and risk distribution in Chile; in Spanish.] Rev Med Chil 2006;134:565–74.
6. Zatonskí W, La Vecchia C, Levi F, Negri E, Lucchini F. Descriptive epidemiology of gall-bladder cancer in Europe. J Cancer Res Clin Oncol. 1993;119:165–71.
7. Lai CH, Lau WY. Gallbladder cancer—a comprehensive review. Surgeon 2008;6:101–10.
8. Coleman MP, Gatta G, Verdecchia A, et al. EUROCARE-3 summary: cancer survival in Europe at the end of the 20th century. Ann Oncol 2003;14 Suppl 5: v128–49.
9. Berrino F, De Angelis R, Sant M, et al. Survival for eight major cancers and all cancers combined for European adults diagnosed in 1995-99: results of the EUROCARE-4 study. Lancet Oncol 2007;8:773–83.
10. SEER Cancer Incidence Public Use Database, 1973–1995. Bethesda, MD: National Cancer Institute/National Institutes of Health, 1998.
11. Donohue JH, Stewart AK, Menck HR. The National Cancer Data Base report on carcinoma of the gallbladder, 1989–1995. Cancer 1998;83:2618–28.
12. Kayahara M, Nagakawa T. Recent trends of gallbladder cancer in Japan: an analysis of 4,770 patients. Cancer 2007;110:572–80.
13. Duarte I, Llanos O, Domke H, Harz C, Valdivieso V. Metaplasia and precursor lesions of gallbladder carcinoma. Frequency, distribution, and probability of detection in routine histologic samples. Cancer 1993;72:1878–84.
14. Wistuba II, Gazdar AF. Gallbladder cancer: lessons from a rare tumour. Nat Rev Cancer 2004;4:695–706.
15. Moreno M, Pimentel F, Gazdar AF, Wistuba II, Miquel JF. *TP53* abnormalities are frequent and early events in the sequential pathogenesis of gallbladder carcinoma. Ann Hepatol 2005;4:192–9.
16. Chow WH, Johansen C, Gridley G, Mellemkjaer L, Olsen JH, Fraumeni JF Jr. Gallstones, cholecystectomy and risk of cancers of the liver, biliary tract and pancreas. Br J Cancer 1999;79:640–4.
17. Zatonski WA, Lowenfels AB, Boyle P, et al. Epidemiologic aspects of gallbladder cancer: a case–control study of the SEARCH Program of the International Agency for Research on Cancer. J Natl Cancer Inst 1997;89:1132–8.
18. Nuzzo G, Clemente G, Cadeddu F, Ardito F, Ricci R, Vecchio FM. Papillary carcinoma of the gallbladder and anomalous pancreatico-biliary junction. Report of three cases and review of the literature. Hepatogastroenterology 2005;52:1034–8.
19. Fukuda K, Kuroki T, Tajima Y, et al. Comparative analysis of *Helicobacter* DNAs and biliary pathology in patients with and without hepatobiliary cancer. Carcinogenesis 2002;23:1927–31.
20. Kobayashi T, Harada K, Miwa K, Nakanuma Y. *Helicobacter* genus DNA fragments are commonly detectable in bile from patients with extrahepatic biliary diseases and associated with their pathogenesis. Dig Dis Sci 2005;50:862–7.
21. Murata H, Tsuji S, Tsujii M, et al. *Helicobacter bilis* infection in biliary tract cancer. Aliment Pharmacol Ther 2004;20(Suppl 1):90–4.
22. Tiwari SK, Khan AA, Ibrahim M, Habeeb MA, Habibullah CM. *Helicobacter pylori* and other *Helicobacter* species DNA in human bile samples from patients with various hepato-biliary diseases. World J Gastroenterol 2006;12:2181–6.
23. Wood R, Fraser LA, Brewster DH, Garden OJ. Epidemiology of gallbladder cancer and trends in cholecystectomy rates in Scotland, 1968–1998. Eur J Cancer 2003;39:2080–6.

Managing esophageal varices: should the search go beyond the Cochrane Library?

Page 25

1. Krahn M, Naglie G. The next step in guideline development: incorporating patient preferences. JAMA 2008;300:436–8 [PMID: 18647988]. Full text online (payment required).
2. Strauss SE, Richardson WS, Glasziou P, Haynes RB. Evidence-based medicine: how to teach and practice EBM, 3rd ed. Edinburgh: Churchill Livingstone, 2005. ISBN 0-443-07444-5. (Available at: Centre for Evidence-Based Medicine, www.cebm.utoronto.ca.)
3. Lefebvre C, Manheimer E, Glanville J. Chapter 6: Searching for studies. In: Higgins JPT, Green S, eds. Cochrane handbook for systematic reviews of interventions, version 5.0.0 (updated February 2008). The Cochrane Collaboration, 2008. (Available at: www.cochrane-handbook.org.)
4. Farrell A. An evaluation of the five most used evidence based bedside information tools in Canadian health libraries. Evid Based Library Inf Pract 2008;3:2(http://ejournals.library.ualberta.ca/index.php/EBLIP/article/view/1515/1240).
5. Garcia-Tsao G, Sanyal AJ, Grace ND, Carey W. Prevention and management of gastroesophageal varices and variceal hemorrhage in cirrhosis. Hepatology 2007;46:922–38 [PMID: 17879356].

Managing esophageal varices: should the search go beyond the Cochrane Library?

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APPENDIX 1

Examples of regional electronic bibliographic databases (adapted from the Cochrane Handbook, Chapter 6)

Region	Bibliographic database
African Index Medicus	*indexmedicus.afro.who.int*
Australasian Medical Index (fee-based)	*www.nla.gov.au/ami*
China	*www.imicams.ac.cn/cbm/index.asp*
Eastern Mediterranean Index	*www.emro.who.int/HIS/VHSL/Imemr.htm*
India (Indian Medlars Center)	*www.indmed.nic.in*
Korea	*www.koreamed.org/SearchBasic.php*
Latin America and the Caribbean (Literatura Latino-Americana e do Caribe em Ciências da Saúde, LILACS)	*LILACS*
Index Medicus for South-East Asia Region (IMSEAR)	*IMSEAR*
Russian Federation and Ukraine	*www.panteleimon.org/maine.php3*
Western Pacific Region Index Medicus (WPRIM)	*WPRIM*

APPENDIX 2

The five highest-ranking journals in hepatology

Journal	PubMed/*Index Medicus* title abbreviation	Impact factor	Publisher
Hepatology		10.446	Wiley
Journal of Hepatology	J Hepatol	6.073	Elsevier
Seminars in Liver Disease	Semin Liver Dis	5.302	Thieme
Liver Transplantation	Liver Transpl	4.629	Elsevier
Journal of Viral Hepatitis	J Viral Hepat	3.290	Blackwell

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Digestive disorders – from diarrhea to obesity to cancer – are pre-eminent among healthcare issues, a significant burden on national healthcare budgets and the single greatest cause of cancer deaths.

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The WGO delivers Training & Education, Communication and Awareness Programs with a goal to establish a **Global Network of Gastroenterology Training Centers** with a special emphasis on those developing countries in greatest need.

As the global representative for gastroenterology, the role of the WGO is:

To make a significant and sustainable difference to the prevention and treatment of digestive disorders across the world through educational programs directed at the general public and healthcare professionals alike whose aim is to promote equal access to high quality patient care.

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Zip code, Town/City, Country

_____

Contact Telephone Number

_____

Contact E-Mail Address (please print clearly)

_____

My/Our Donation

A single donation of:

☐ $/€ 100 ☐ $/€ 250 ☐ $/€ 500 ☐ $/€ 1000 Other amount: _____ (please specify currency)

An annual donation of:

☐ $/€ 500 ☐ $/€ 750 ☐ $/€ 1000 ☐ $/€ 2000 Other amount: _____ (please specify currency)

for _____ years beginning 2008

My/Our Payment Options

☐ I/we enclose a cheque for _____ in favour of the WGO Foundation. (please specify currency)

☐ Please debit my credit card with a single donation of _____ (please specify currency)

☐ Please debit my credit card annually with _____ for _____ years beginning 2008 (please specify currency)

My credit card details are:

Type of card ☐ Visa ☐ MasterCard ☐ American Express

Card Number _____

Expiry Date _____

_____ _____

Date Signature

Tax Receipt • Together with a letter of acknowledgement donors will receive a tax receipt upon payment.

Please return to WGO Foundation Executive by fax or email: info@wgofoundation.org
c/o Medconnect GmbH • Bruennsteinstr. 10 • 81541 Munich, Germany
Tel: +49 89 4141 9240 • Fax: +49 89 4141 9245