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World Digestive Health Day 2013: LIVER CANCER Act Today. Save Your Life Tomorrow.

Awareness. Prevention. Detection. Treatment.



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Professor, Internal Medicine
University of Iowa Healthcare
Chairman, WDHD 2013 Steering Committee

The World Gastroenterology Organisation (WGO) established World Digestive Health Day (WDHD) in 2004. Although still celebrated on May 29th each year, the date on which WGO was incorporated in 1958, WDHD has become a year long, global, public health, advocacy and awareness campaign. WDHD annually focuses on a specific digestive or liver disorder with the goal of increasing awareness by the public, medical practitioners, government health policy makers, and philanthropic groups of the need for prevention, diagnosis and management of a specific global health problem. The theme in 2013 is: LIVER CANCER: Act Today. Save Your Life Tomorrow. Awareness. Prevention. Detection. Treatment.

Why liver cancer? Hepatocellular carcinoma (HCC, also known as primary liver cancer) is variably estimated to be the fifth to seventh most common cancer in the world^{1,2} and it continues to be the third most common cause of death from cancer (second most common in men)^{1,2}. In some countries, it is either the number one (Mongolia) or number two malignant neoplasm (China). In the United States of America, it is the fastest rising cancer by incidence and death rate³. Every 30 seconds, one person in the world dies from liver cancer, which is almost entirely preventable. The annual global death rate from HCC of just under 700,000 approximates the annual incidence, reflecting the limited therapeutic options as well as the late diagnosis in most cases^{4,5}.

Significant advances in diagnosis and therapy now produce a 50-70% five year survival in those diagnosed with early, minimal disease who receive the best current therapies. But such therapies are almost exclusively available in high resource countries, and even there not to all of the affected patients. Low resource countries tend to lack the broad public



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awareness and medical infrastructure, as well as generally available state of the art technology (ultrasound, CT, MRI) for early diagnosis. The current best surgical and medical therapies are of very limited availability, if available at all, due to high costs, lack of adequately trained medical personnel, and limited to no coverage by government health plans.

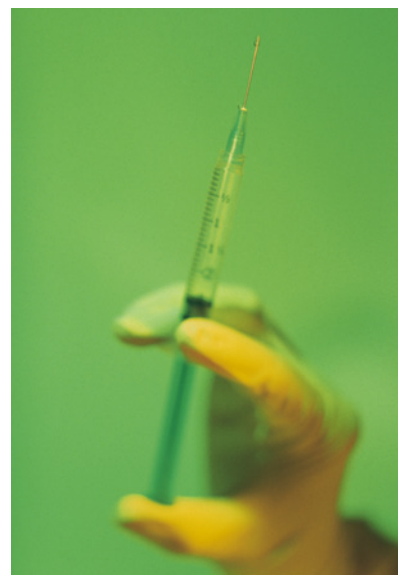
Unfortunately, low resource countries are disproportionately affected by HCC. More than eight out of ten (84%) of the almost 700,000 deaths reported by WHO in 2008 occurred in low resource countries. Over 80% of HCC occur in sub-Saharan Africa, southeast Asia and East Asia (including Mongolia)^{1,5}. At least 80% of all HCC are associated with chronic viral infection with the hepatitis B virus (HBV) or hepatitis C virus (HCV). HBV infections alone account for 75% to 80% of these cases. HCV is responsible for 10% to 20% of cases⁶. Additional risk factors, which may cause HCC or act as co-factors in producing cirrhosis and HCC, include consumption of foodstuffs contaminated by the fungal toxin aflatoxin B1 (AFB1), which contaminates groundnuts, maize and tree nuts in warm, humid environments in sub-Saharan Africa, SE Asia and China. Aflatoxin produces a specific DNA mutation in a hotspot region of the p53 cancer suppressor gene and is synergistic with HBV in the production of HCC. Some studies suggest a possible synergistic role with HCV as well. Other risk factors include excess alcohol intake, diabetes/obesity/non-alcoholic steatohepatitis (NASH) and rare metabolic disorders, including tyrosinemia, hemochromatosis, alpha-1 anti-trypsin deficiency, and several prophyrias^{6,7}.

The above facts are well known. The two primary causes, HBV and HCV infection, are both preventable and treatable and 1 in 12 of the world's population is currently living with chronic hepatitis B or C.

HEPATITIS B

Hepatitis B is one of the most neglected epidemics in the world. One in 3 people worldwide have been infected with HBV and 400,000,000 have chronic hepatitis B. It is second only to tobacco in causing the most cancer deaths worldwide. The hepatitis B vaccine, the FIRST true anti-cancer vaccine, has been available since 1982 and is more than 95% effective. Global efforts at HBV vaccination of infants began in 1990, when the WHO estimated that only 1% of infants received the recommended three doses of hepatitis B vaccine. Although 93% of countries had introduced the hepatitis B vaccine into their routine vaccination schedules by 2011 the number actually vaccinated had risen to only 75%⁸, which still leaves a full quarter of the world's infants uncovered and they live in areas of the world with chronic carrier rates for hepatitis B of up to 20% and more. Coverage in the SE Asia Region languishes at only 56%⁸. Seven percent of countries still have not introduced hepatitis B vaccine into their routine childhood vaccination schedules and only 52% recommended that the initial dose be given within the first 24 hours to prevent perinatal transmission of the hepatitis B virus as per international standards⁹. Thirty to forty percent of those infected with chronic hepatitis B can be expected to die from liver failure or HCC. The benefits of national vaccination campaigns have been well documented in areas as diverse as Taiwan, The Gambia and Amazonia, Brazil, where dramatic drops in hepatitis B carrier rates from 10% to 1.1%, 10% to 0.6%, and 15.3% to 3.7%, respectively, with subsequent drops in the occurrence of HCC, have been demonstrated.

While the benefits of true universal infant immunization against hepatitis B are obvious as a preventive measure, they will also not be realized for



many decades. In the meantime, over 400 million individuals with chronic hepatitis B remain at risk from the dire complications of this devastating infection. Excellent therapies are now available which significantly reduce the risk of progression to cirrhosis, liver failure and HCC. However, these drugs remain generally unavailable in major parts of the world where identical drugs are now routinely available for the treatment of HIV infection. This obvious inequity must be addressed and resolved quickly before additional large numbers of individuals die unnecessarily. Programs to prevent aflatoxin contamination of foodstuffs have also been demonstrated to be highly successful, but remain difficult to implement broadly due to lack of education and cost.

HEPATITIS C

Prevention of hepatitis C infection presents a somewhat more difficult problem because there is no effective vaccine to prevent hepatitis C infection and there is unlikely to be one in the foreseeable future. Prevention must rely on education of patients concerning the risks of acquiring HCV infection from exposure to blood and bodily fluids and strict

adherence to the principles of infection control. The WHO estimated in 2006 that 16 thousand million injections were administered annually in developing and transitional countries alone¹⁰ and that the habitual reuse of needles and syringes accounted for 2 million new HCV infections each year (42% of new infections), 21 million new HBV infections per year (33% of new HBV infections) and 260,000 new HIV infections (2% of new infections)^{11,12,13}. Fewer than 10% of injections were for vaccines and a large percentage of injections were actually unnecessary. Misconceptions concerning the belief that a syringe could be safely reused if the needle was changed, a multi-dose vial or infusion bag could be re-entered with a used needle or syringe and a bag or bottle of iv solution can be safely used multiple times have also led to multiple outbreaks of infections, including in high resource western countries. A major educational effort must be mounted to stop such practices. This must include patient education, since in many countries, especially in SE Asia, the Middle East and sub-Saharan Africa, patients believe that injections are “stronger” and “more effective” than pills and demand them of their health care workers^{14,15,16}. Additionally, not every country's blood supply is entirely safe due to irregular screening, especially for the hepatitis C virus. Finally, highly effec-



tive therapies for hepatitis C are now available which will cure 70% or more of patients and even better treatments are on the near horizon. However, as with earlier HIV therapies, they are extremely costly. A major campaign, similar to that carried out for treatment of HIV, must be mounted to make such curative therapies generally available for those in low resource countries.

FIRST STEPS

This editorial has intentionally focused on preventive measures. While introduction of broad based screening and regular ultrasound and alpha-fetal protein (AFP) surveillance would increase the early diagnosis of HCC, and such approaches must be implemented for those currently at risk, early diagnosis will not benefit these patients unless effective therapies are available. The costs of such therapies and the medical facilities and practitioners necessary to provide them will be prohibitive for many nations unless a major global effort is mounted to underwrite such an effort, e.g. has been done for HIV and polio eradication. In the meantime, universal hepatitis B vaccination, reduction of exposure to aflatoxin¹⁷, strict infection control measures, eliminating the reuse of needles, syringes, etc., and programs to make effective therapies for hepatitis B and C widely available should be achievable. Regional campaigns must be organized in a practical way, based on available resources, and accurate epidemiological data must be collected in order to design such programs. WDHD 2013 will attempt to collect such data through our 100+ national organizations and discussions held at nine regional meetings scheduled throughout the year during 2013.

CONCLUSIONS

The effects of HCC, along with hepatitis B and hepatitis C, are global

tragedies whose burden of disease has been neglected for far too long. Without swift preventive action, the death toll due to these diseases will continue to rise. Tens of billions of dollars have been invested effectively in the global attack on HIV/AIDS by the Bill and Melinda Gates Foundation, the U.S. President's Emergency Plan for AIDS Relief, UNAIDS, and The Global Fund, among others. The same groups plus Rotary International, the American Centers for Disease Control (CDC), UNICEF, WHO and the Islamic Development Bank have contributed additional billions to the global eradication of Polio since 1988. These remarkable and laudable efforts have had dramatic results in the fight against HIV/AIDS in the 34 million individuals chronically infected with HIV globally; and only 222 new cases of polio occurred in only 3 countries in 2012. A similar effort to eliminate HCC, with a full bore attack on hepatitis B and hepatitis C and their 600 million chronically infected patients (20 times more patients than those with HIV), is long overdue. The lessons learned and infrastructure developed to eliminate HIV and polio must be applied to HCC, HBV, and HCV.

The WGO and its foundation (WGOE) will attempt to put the spotlight on this long neglected epidemic in hopes of sparking greater recognition of the human tragedy caused by these inter-related diseases. In this battle it is critical to recognize that these diseases can be prevented and these diseases can be treated. But it will require a major global effort and investment by all affected parties.

To see what is happening around the globe in support of this year's campaign, read the World Digestive Health Day section in each issue of *e-WGN*, and visit <http://www.wgofoundation.org/wdhd-2013.html>.

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An Introduction to Two Perspectives on Colorectal Cancer Prevention

This issue of *e-WGN* includes two articles about the future of colorectal cancer prevention. Professor Dennis Ahnen (University of Colorado, USA) delivers the perspective from a high resource country and Professor Rene Lambert (International Agency for Research against Cancer, France) discusses colorectal cancer prevention in less resourceful countries. The two articles highlight important differences in disease dynamics and resource availability that may influence decision-making regarding screening and diagnosis of colorectal cancer. Emphasis is placed on westernization of lifestyles and age being most important determinants affecting prevalence of colorectal cancer. We think the two articles enhance our understanding of colorectal cancer as a global problem. They also illustrate the problems involved in selecting an optimal strategy for prevention of colorectal cancer in many parts of the world. We would like to take the opportunity to recommend readers to WGO's global [Practice Guideline on Colorectal Cancer Screening](#) that can be downloaded from the [WGO website](#).



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The Future of Colorectal Cancer Prevention in Developing Countries



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The burden of colorectal cancer in the world

Over the world, colorectal cancer is the third most common cancer in men, and the fourth in women. In the IARC GLOBOCAN database¹ incident cases of colorectal cancer in 2008 were estimated, for both genders, at 1,234,000, out of which 727,000 are in developed countries and 506,000 are in developing countries. Colon cancer is located either in the proximal segment (ascending colon and right angle), the transverse segment and left angle, or the distal segment (descending colon and sigmoid). Rectal cancer is located distally between the recto-sigmoid junction and the anal margin.

In each region of the world the burden of colorectal cancer is estimated in population based cancer registries. Observed data in cancer registries display precise information in the fraction of population concerned. For the global population of a country estimated figures are found in the 2008 edition of the IARC database GLOBOCAN¹. Incidence, or the annual number of cases occurring in a corresponding population of 100,000 persons is expressed as an age standardized rate of Incidence (ASR)/100,000 persons which refers to a standard of distribution of age classes in the world population in 1960. This standard, adopted in the IARC monographs

(Cancer Incidence in V continents² and GLOBOCAN¹), allows comparisons of the risk between countries having a different distribution in the age classes of the population. Mortality is the yearly number of deaths in the corresponding population of 100,000 persons. The mortality rate is also expressed as an ASR mortality/100,000 persons, in reference to the standard of the world population in 1960. Survival is estimated from registries having a regular follow-up of the cases included. The 5-year Relative Survival (5y-RS) takes in account the life expectancy of persons of the same sex and age, not suffering from this cancer. In addition the index of Disability Adjusted Life Years (DALY), based on incidence and mortality, includes successive steps from cancer detection to death, with the years of disability. DALY is expressed as the number of years lost/100,000 persons of the target population.

Colorectal cancer in developing countries

In geographical regions of the world, countries are also classified in reference to their development: more developed countries predominate in all regions of Europe and in North America, Australia/New Zealand and Japan. Less developed countries are found in all regions of Africa, Asia (excluding Japan), Latin America and

the Caribbean, Melanesia, Micronesia and Polynesia. Some countries like Brazil, Russia, India, China, not yet classified in the more developed group, are called “emerging” because of the fast development of their resources. Country resources have been classified in four categories by the World Bank³, according to the annual Gross National Income (G.N.I.) “per capita”, expressed in US Dollars. In 2011 the G.N.I. per capita was \$1,000, or less, in the Low Income group of countries, \$1,000 to \$4,000, in the Lower Middle Income group \$4,000 to \$12,000 in the Upper Middle Income group, and more than \$12,000, in the High Income group. A more precise classification is the Human Development Index (H.D.I.), based on multiple parameters including G.N.I, education and years of school, health education and living standard.

1) **Incidence:** Considerable variations in the incidence, of colorectal cancer between regions, and countries of the world depend on causal factors in relation to development. In the GLOBOCAN, in 2008¹ the average ASR incidence of colorectal cancer for 100,000 is much higher in More Developed (30.1/100,000) than in Less Developed countries (7.1/100,000). As an example, in the more developed countries, the respective figures (both sexes) are 29.4/100,000 in France and 38.0/100,000 in Norway in Europe and 29.2/100,000 in the USA in North America, and 31.5/100,000 in Japan in Asia. Lower figures occur in the less developed countries as 14.2/100,000 in China in Asia, 6.5/100,000 in Mexico in Central America, 9.8/100,000 in Algeria, 5.9/100,000 in Uganda, and 5.4/100,000 in Zimbabwe in Africa.

2) **Mortality:** In 2008, the average figure of the ASR mortality from colorectal cancer was 12.0/100,000 in the More Developed countries and 6.0/100,000 in the Less Developed countries. Mortality is related to survival of colorectal cancer, which depends on the proportion of early detection and curative treatment. The ratio of Mortality to Incidence rates is much lower in More Developed countries (39%) than in Less Developed countries (84%). The respective rates of Incidence and of Mortality in different large regions of the world are displayed in Table 1, with the ratio of Mortality to Incidence. The lowest ratio is for North America region, and the highest ratio is for Africa.

3) **Survival:** In cancer registries with a regular follow-up, the five year survival of the cases included can be determined. Survival depends on the early diagnosis and proportion of cases detected at a curable stage. At the country level, survival from colorectal cancer is analyzed in period 1990-94 in the CONCORD study⁴. The respective 5y-RS for men and women is high in 1990-94 in the USA at 51.9% and 60.2%, and in Japan, at 61.1% and 77.3%. Screening is developed in both countries. In contrast, the 5y-RS is low, in the range 10% - 20%

in Less Developed countries of Africa where early detection is not frequent.

Causal factors of colorectal cancer

In a large majority of cases, cancer is a sporadic disease and the risk is influenced by exposure to environmental carcinogenic factors, classified as toxic, infectious and linked to diet and nutrition. This justifies a primary prevention of cancer through control of these factors connected to lifestyle and environment. Diet and nutrition play a determinant role in the risk for colorectal cancer, in relation to an excess of calories ingested with a high proportion of red and processed meat and fat. The altered diet is associated to overweight, resistance to insulin and production of insulin-like growth factors, like the IGF-1 which stimulates the proliferation of intestinal cells^{5,6,7}. A sedentary lifestyle with decreased physical activity is a frequent associated causal factor. In more developed countries, these factors that closely relate to the development of resources and urbanized life likely explain the higher incidence of colorectal cancer. In the UK, a European country classified in this group, the proportion of colorectal cancer attributable to lifestyle and environmental factors, is estimated at 54% in

2010⁸. In Japan, an Asiatic country classified in the same group, the ASR incidence/100,000 of colon cancer increased from 8.3 in 1973-1977 to 36.0 in 1998-2002 for men, and from 7.3 to 21.5 for women. This variation correlates with ascending resources and development of a Westernized style of life.

In Less Developed countries of Africa often classified in the Low Income Group, the incidence of colorectal cancer remains low in 2008, as shown in Table 1. On the other hand, in “emerging” countries, like Brazil and China, the incidence of colorectal cancer correlates to the progression of the country income and a rapid increase is expected in relation to the progression of their resources and the urbanized style of life. However, a different situation occurs in India⁹ where a spontaneous prevention is afforded by the generalized practice of a vegetarian diet, with enough physical activity; in 1998-2002, the respective figures of the ASR incidence/100,000 of colorectal cancer in men and women in the IARC database “Cancer Incidence in V Continents” were still low at 5.9 and 4.4 in the urban registry of Mumbai, and 4.1 and 3.6 in the rural registry of Karuganappally². The incidence of colon cancer remained stable and low in the Urban Mumbai registry, during the period 1973 to 2002 in spite of the development of the city.

Perspective on evolution of the burden of colorectal cancer

The worldwide burden of colorectal cancer will increase in the next few decades in relation to the increase in the world population and in the proportion of older age groups. An estimation of the variation expected in 2030 is given in GLOBOCAN¹: - the annual number of incident cases worldwide, in 2008 for both sexes is estimated at 1,235,198 with 59% of cases over 65 years. In 2030 the

Region of the World	Incidence	Mortality	Ratio of Mortality/Incidence
Northern America	30.1	9.1	30.2%
Europe	28.1	12.8	45%
Eastern Asia	18.0	8.0	44%
Western Pacific Asia	17.9	7.9	44%
Latin America and Caribbean	11.4	6.6	57%
South East Asia	6.9	4.8	69%
Africa	5.9	4.8	78%

Table 1: Estimated Age Standardized rate of incidence and mortality for colorectal cancer, in 2008 in a population of 100,000 persons, for both sexes, in different regions of the world. In addition is given the ratio of the mortality to incidence rates.

From IARC GLOBOCAN database in 2008.

Country	N° incident cases in 2008	N° expected in 2030
Algeria	2,619	5,364 (+106%)
Brazil	21,768	42,447 (+ 95%)
India	36,476	66,801 (+ 83%)
China	221,313	400,086 (+ 81%)
USA	155,881	247,442 (+ 61%)
France	38,394	55,344 (+ 42%)
Japan	101,656	129,974 (+ 28%)

Table 2: Estimated number of incident cases occurring in 2008, in both sexes and projected number of cases in 2030, based on population growth and ageing in some countries of the world. From IARC GLOBOCAN database.

expected number of incident cases should be 2,179,771, with 65% in the age classes from 65 years. At the level of a single country the variation depends of multiple factors: 1) The structure of its population in age classes in 2008, and the birth rate; 2) The perspective in development and increased resources of the country; and 3) The strategy adopted for screening and treatment of precursors. Considerable differences occur between countries, as shown in Table 2. As a More Developed country, Japan already has an aged population, stable resources, and an established policy of screening; as a consequence, incident cases of colorectal cancer during the period 2008-2030 are expected to increase only by 28%.

In developing countries, a major increase in the incidence of colorectal cancer is expected if they have a young population and increasing resources. In these countries a policy of prevention of colorectal cancer is justified. This applies particularly to emerging countries like Brazil, India, and China; however, in India, spontaneous primary prevention is provided by the generalized practice of a vegetarian diet with enough physical activity. In the group of emerging countries, Brazil has a relatively young population and a fast increase

in resources: in 2030, incident cases are expected to increase by 95%. In conclusion, in developing countries increased income will correlate with increased risk of colorectal cancer with modifications based on variations in the nutrition and physical activity of the populace.

Perspective on screening and early detection of colorectal cancer

Primary prevention of colorectal cancer is based on a reduction of ingested calories and increase in physical activity. This prescription has an impact on weight and obesity. In perspective the control of nutrition and diet is necessary in developing or in “emerging” countries as well as in the more developed countries.

To complement primary prevention, secondary prevention aims to reduce the number of incident cases by the destruction of premalignant adenomatous precursors and early detection of cancer at a curable stage. Screening modalities for the selection of asymptomatic persons susceptible to harbor neoplastic colorectal lesions include two distinct steps: 1) A simple preliminary filter test like the detection of fecal occult blood, with an acceptable compliance and a negative or positive response; and 2) A more complex endoscopic exploration,

requiring material and experience, to be performed only in persons positive to the first test. Endoscopic procedures, either with flexible sigmoidoscopy or complete colonoscopy, will confirm the presence of the lesion and eventually proceed to the resection of a superficial cancer or a premalignant adenoma.

Repeated screening trials for colorectal cancer are often offered in Developed Countries in Europe, North America and in Japan, to persons in the age range 40 to 70 years. The policy of secondary prevention deserves to be generalized in the Developing Countries. The incidence of colorectal cancer is still low in the less developed countries of the world, but the impact of delayed diagnosis and poorly adapted treatment increases the global burden of cancer, with impact on survival and mortality.

1) The Role of Health

Authorities: As a rule, in each country, the prevention of cancer is under control of a National Health Service, like in the UK, or of a Ministry of Health and Family Welfare; like in India. For prevention of colorectal cancer, the National Authorities should actively encourage the control of environmental carcinogenic factors, linked to diet with excess in calories and lack of vegetables and the development of physical activity. The organization of a screening policy of secondary prevention also depends on the National Authorities. Developing Countries with low resources have not yet structured their National Health Care System. “Emerging” countries with higher resources, have already built Health Care structures and cancer control in urban areas; but heterogeneity persists with a lower impact in rural than in urban areas. In developing countries with low resources, any progress in the prevention of colorectal cancer will also require the establishment of a National Policy of Health Care.

2) **The Fecal Occult Blood Test:** The Fecal Occult Blood Test (FOBT), is a filter test, repeated at 2-year intervals¹⁰. Colonoscopy is proposed to persons positive to this filter test. The global sensitivity of FOBT is around 50% for colorectal cancer and much lower, around 20%, for adenomas, with a significant proportion of false positive reactions. In spite of some debate about efficacy, the capacity of the FOBT protocol to reduce colorectal cancer mortality, has been confirmed in the period 1990-2000, by three randomized trials in the USA, UK and Denmark, with a reduction of 15% in colorectal cancer mortality, but no impact on incidence. Overall screening with the FOBT test ensures a reduction in colorectal cancer mortality of 15%, reaching 23% when adjusted for individual attendance. The Guaiac FOBT is progressively replaced by a more specific immunochemical test (I-FOBT) based on human hemoglobin. Molecular markers of colorectal cancer, now developed through proteomics and genetics, should replace FOBT in the near future in organized screening protocols. DNA tests with a high sensitivity, based on molecular markers of the k-ras gene, are now available as stool tests¹¹. Circulating micro-RNAs also offer a large opening on easy screening with a simple blood sample¹². These tests, not yet cost-effective, are expected in the near future to replace in Mass Screening protocols the stool samples of FOBT by a simple blood sample.

Organized Mass Screening protocols with the FOBT test are proposed to the population of asymptomatic persons of both sexes in the age 50 to 70 years, by the Health Authorities, in the majority of Developed Countries in North America, Europe and Japan. As yet, the risk of colorectal cancer is lower in Developing Countries and Mass Screening protocols are consid-

ered as not justified; however, when the incidence increases in relation to development of the country the screening protocol should be developed. However, filter tests with molecular markers of cancer are still very costly, and it is unlikely that they will be deployed in Developing Countries.

3) **Flexible Sigmoidoscopy:** Flexible sigmoidoscopy explores distal large bowel with rectum and sigmoid. The procedure can also be performed by trained nurses. Guidelines on screening recommend that flexible sigmoidoscopy be repeated 5 years after an initial negative procedure. A cohort study conducted in 24,744 health professionals in the USA has shown that screening flexible sigmoidoscopy reduces mortality from colorectal cancer by 50%, and incidence by 44%.

In perspective, flexible sigmoidoscopy could offer a valuable protocol for colorectal cancer screening in Developing Countries classified by their G.N.I. in the Low Income group or in the Lower Middle Income group because of a better acceptance than colonoscopy and a lower cost.

4) **Colonoscopy:** is the gold standard procedure for the early detection of colorectal cancer and premalignant adenomatous polyps, which can be resected, preventing the later development of a cancer. The endoscopic destruction of premalignant precursors achieves a reduction of cancer incidence, as shown in the SEER registries of the USA¹³: the ASR incidence/100 000, both sexes, decreased from 64.2 in 1985, to 60.6 in 1990 to 49.5 in 2003. Colonoscopy can be proposed in two situations:

a) As a primary procedure, without a filter test, in non organized, or "opportunistic screening". In a group of average risk persons, aged 50 years or more, the yield of colonoscopy is under 1% for cancer, under 10% for advanced adenomas, and in the range 25 to

30% for all adenomas.

b) As a second procedure, performed after a positive filter FOBT in organized Mass Screening protocols. In the National Polyp study conducted in the USA the reduction of the risk of colorectal cancer in persons submitted to a colonoscopy was estimated at 75%.

Numerous screening trials have confirmed the reduction in mortality from colorectal cancer after colonoscopy, in spite of false negative procedures, resulting two or three years later in a so-called "interval" cancer^{14,15}. The endoscopic resection of adenomas has also an impact on the incidence of colorectal cancer. In the USA SEER Registries¹³, during the period 1975/2003, the ASR incidence of colorectal cancer decreased by 19.4%, presumably as a consequence of the increased utilization of endoscopic treatment of their precursors.

Colonoscopy is currently performed in the More Developed countries in organized Mass Screening protocols in persons with a positive response to a filter FOBT. However compliance is limited, cost is high and there is a small toll of severe complications. In perspective, colonoscopy tends to be performed more often as a primary test in opportunistic non-organized screening for asymptomatic persons asking for prevention. In the USA colonoscopy every 10 years, from age 50 years is proposed without filter test as an alternative to Mass Screening. In addition Virtual colography with a 3D-multidetector scanner is an alternative to primary colonoscopy in non organized screening; however colonoscopy has to be performed when there is an abnormal finding.

In Developing Countries, the risk of colorectal cancer may increase, contrasting with a persistent weakness in organized Mass Screening, under control of Health Authorities. The discrep-

ancy should encourage the growth of opportunistic indications for primary colonoscopy in spite of its high cost. However this is not a population-based strategy of prevention.

Conclusion on screening strategies

Implementation of screening measures in a country depends on Health Authorities, reimbursement facilities, and compliance of the population. In the Developed Countries of Europe and in Japan mass screening with the FOBT is proposed to the population and reimbursed, Germany and Italy also have organized screening protocols based on primary colonoscopy. Screening with primary sigmoidoscopy is encouraged in Scandinavian countries and in the UK with nurse endoscopists. In the USA the Medicare policy recommends annual FOBT or sigmoidoscopy every five years or colonoscopy every 10 years. In studies of the cost/effectiveness ratio, the screening of colorectal cancer is placed in the USA well under the financial benchmark adopted in screening (\$40,000 per year of life gained). Developing countries with increasing resources should develop a policy of prevention of colorectal cancer based on population-based screening interventions with the less costly FOBT, and over time to primary endoscopy, with flexible sigmoidoscopy being the priority.

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The Future of Colorectal Cancer Prevention in the United States

A perspective from a high burden, sufficient resource country



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Colorectal cancer (CRC) is one of the most common cancers with over 1.2 million new cases of colorectal cancer and more than 600,000 deaths worldwide per year. CRC is the fourth most common cause of cancer death and the second most common cancer in the world and the best estimates are that the rate will continue to increase substantially over the next decade¹. There is substantial variability in CRC incidence (10 fold) and mortality (5-6 fold) among countries with rates continuing to increase in many developing countries while they are stable or decreasing in some developed countries¹, particularly those that have substantial CRC screening programs. Winawer et al² have presented the concept of Cascade CRC Screening Guidelines among countries that are evidence based and resource driven². The guidelines suggest that countries like the US that have a high CRC burden and have sufficient (at least for now) resources might opt for colonoscopy as a major screening option whereas countries with substantial CRC burden but severely limited resources might opt for fecal occult blood testing as the only affordable screening approach.

CRC time-trend data in the US illustrate one of the great cancer

prevention success stories of the last 30 years. Both CRC incidence and mortality have been steadily decreasing and CRC deaths have been cut in half since 1975. It is tempting to attribute these decreases to CRC screening but the decreases started well before screening for CRC was widely used. The best estimates are that about half of the decreases have been due to screening and the rest due to changes in risk factors along with some improvement in treatment.

Some future trends seem certain. The demand for CRC prevention efforts will continue to rise as the 50-75 year old population is projected to slowly grow in the US over the next 35 years. It also seems likely that whatever screening/prevention choices are made, the recent favorable trends in CRC incidence and mortality will continue; the uncertainty is what the magnitude of the future decreases will be. CRC screening rates have been steadily increasing in the US for the last 25 years; currently almost 70% of the population is being screened and colonoscopy is by far the dominant screening strategy. We will, no doubt, continue to see the benefit of this high and increasing screening rate over the next decade or longer. In contrast, trends in some CRC risk factors are

not encouraging, the decline in smoking rates has stabilized, there is little evidence that we are eating a healthier diet and rates of obesity and physical inactivity are still increasing. Efforts that successfully address these risk factors could substantially decrease CRC risk but there is little doubt that screening will continue to be the major CRC-specific preventive strategy for the foreseeable future. In a similar way, chemoprevention, particularly with aspirin and other NSAIDs, has great promise as an adjunct to screening but chemoprevention will not replace screening in the foreseeable future.

In the US, thinking about CRC screening has been evolving from the concept of early detection of cancer toward CRC prevention by identification and removal of colonic polyps. As this trend continues it will benefit screening tests that can identify advanced adenomas with relatively high sensitivity such as endoscopic or radiologic imaging tests and the higher sensitivity fecal occult blood tests.

Colonoscopy will likely continue to be the dominant method of colon cancer screening in the US, at least in the near future. Colonoscopic screening for CRC has great appeal; it is the only currently available colon screening test that can both identify and remove colonic polyps in the entire colon in a single procedure. Currently clinical and financial incentives in the US strongly favor colonoscopic screening. Primary care physicians in the US overwhelmingly view colonoscopy as the "best" colon cancer screening option and are concerned

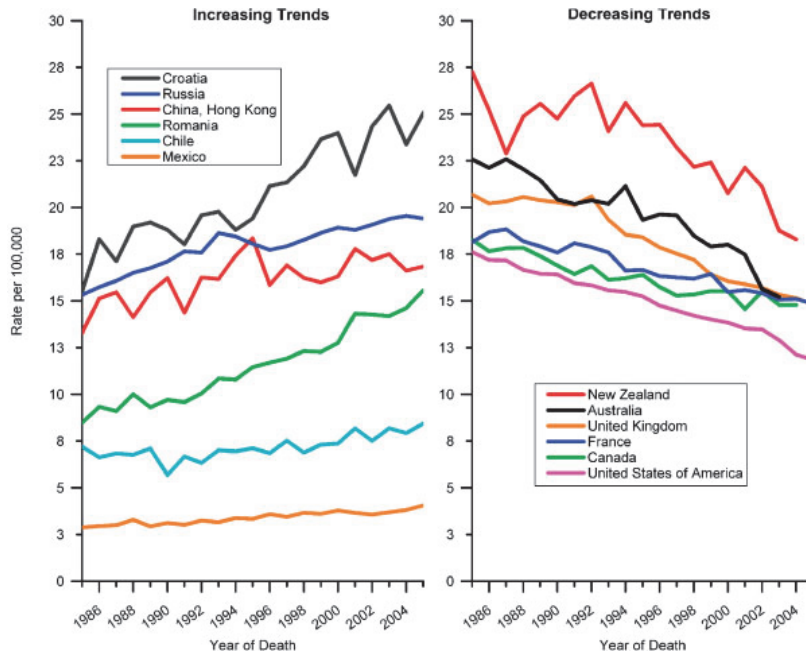


Fig 1. Trends in Colorectal Cancer Mortality Rates for Select Countries in Males, 1985 Through 2005. Source: World Health Organization Mortality Database. Available at: <http://www-dep.iarc.fr/>. Accessed December 15, 2008. Reprinted from Reference 1 with permission.

that doing anything less would leave them legally liable for failure to properly screen for CRC. Colonoscopic screening has the added advantage of satisfying the CRC screening requirement for up to 10 years and shifting some of the responsibility for screening from the primary care provider to the endoscopist. For endoscopists, colonoscopy is satisfying both clinically and financially and until recently payers have largely passed the higher cost of colonoscopy to employers, taxpayers or the individual purchaser.

In the longer term, colonoscopic screening is at serious risk of being replaced for two major reasons; variability in colonoscopy quality and cost. There is substantial evidence that colonoscopy quality is variable. Adenoma detection rates, an accepted measure of colonoscopy quality, vary substantially among endoscopists³. There is particular concern about the quality of colonoscopy in the right colon with some earlier studies report-

ing that colonoscopy did not have any protective effect for right sided colorectal cancers^{4,5}. Fortunately, colonoscopy quality appears to be improving. Reported adenoma detection rates are increasing and it is reassuring that recent studies have shown that colonoscopy was associated with a decreased right sided CRC risk albeit less than that for left sided cancers^{6,7}.

The apparent increase in adenoma detection rates is an indicator of improving colonoscopy quality but it also raises a clinical paradox. Improved colonoscopy quality should lead to a lower future CRC risk for the screened group but it will also lead to substantially increased surveillance intensity of the now lower-risk group. As more adenomas are found, more patients will move from screening to surveillance and more will move from 5-10 year to 3 year surveillance intervals leading to a substantial increase in costs unless surveillance recommendations are adjusted.

The more serious threats to colonoscopic screening/surveillance are the cost increases that are not associated with improved outcomes. Colonoscopy screening and surveillance intervals recommended by endoscopists are often shorter than those recommended by the current guidelines⁸, and there has been a marked increase in the use of anesthesiology services to provide sedation for endoscopy⁹ and some groups have incorporated anesthesiology and pathology services as part of the revenue streams of their endoscopy units. These practice patterns can all lead to substantially increased costs of colonoscopy without evidence of patient benefit.

If colonoscopy is going to be replaced, the change will likely be driven by Accountable Care Organizations or similar groups who will have responsibility for costs of overall health care of a population. The strongest initial challenge will likely come from fecal immunochemical testing. Modeling studies suggest that FIT, if done annually, would be as effective as colonoscopy¹⁰ and the cost of the test itself is about 1% that of colonoscopy. There will, however, be substantial costs associated with trying to assure annual adherence to FIT. Controlled trials comparing colonoscopy to annual FIT have been initiated but results won't be final for at least a decade.

Gastroenterologists can and should lead the CRC prevention effort providing the best risk stratification and modification and by using the best prevention and screening tools available, including providing high quality colonoscopy without excessive costs. Such an approach will be good for our patients and what is good for our patients will ultimately be good for Gastroenterology.

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Letter to the Editors: Gallstone Disease – a Heavier Burden in India!



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I have read with interest the article ‘The Growing Global Burden of Gallstone Disease’ by Monica Acalovschi and Frank Lammert in *World Gastroenterology News* December 2012: 6-9.

The Authors have unfortunately missed India, the second most populous country on the globe, with a population of more than 1.2 billion and huge ethnic diversity. Gallstone disease (GSD) is common in India and also shows differences between North and South. In a retrospective survey of railroad workers (between the ages of 18 and 55 years), Malhotra (1968) found that GSD (diagnosed by oral cholecystography OCG and at operation) was as many as seven times more common in north India than in south. In an ultrasonographic (US) survey of 1,104 subjects more than 15 years of age in Srinagar, the capital of Jammu and Kashmir state in north India, Khuroo et al (1989), found the prevalence of GSD to be 6.1% (3.1% in men and 9.6% in women). In another US survey of 1,104 subjects in Delhi, again in north India but with more cosmopolitan population, Tandon et al (1989) found the prevalence of GSD to be 4.3%. The prevalence

was higher in some ethnic groups (Punjabis 7.4% and Gujaratis 7.4%) than other (Bengalis 4.4% and South Indians 1.8%). Not only the difference in prevalence of GSD, the type of GS also differs between north and south India. While most (80-90%) GS in north India were cholesterol (75% of dry weight as cholesterol), GS in south India were predominantly (60-70%) pigment stones (<20% of dry weight as cholesterol) (Tandon 1994). GSD starts at a much younger age in India than in the west. In the survey by Khuroo et al (1989), the prevalence of GSD in women was 4.9% in the age group of 21-30 years, 15.0% in 31-40, 16.5% in 41-50 and 29.1% in 51-60 years.

The prevalence rates of GSD parallel the incidence rates of gall bladder cancer (GBC). In India too, while GBC is very common (incidence rate of about 10 per 100,000 per year in women) in the north, it is uncommon (incidence rate of less than 1 per 100,000 per year in women) in the south.

GSD is a *heavier burden* in north India because of its association with GBC.

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tions close to the Congress Venue or in the City Center at special rates for Gastro 2013 participants. To view a listing of recommended hotels for your visit to Shanghai please visit the official Congress website at www.gastro2013.org.

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evening, at the Bund, a picturesque riverfront promenade, and expand your journey outward through the city. You will find that Shanghai has an eclectic mix of modern culture, such as the shops along Nanjing Road, and deep-rooted tradition found within the many venerated sites such as, the Temple of Jade Buddha, Yuyuan Garden, and the Longhua Temple. You will soon see that Shanghai is a city alive with excitement!

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World Digestive Health Day 2013

LIVER CANCER: ACT TODAY. SAVE YOUR LIFE TOMORROW.
AWARENESS. PREVENTION. DETECTION. TREATMENT.

Another successful World Digestive Health Day (WDHD) is well underway. Events have been taking place since 2012 in support of the 2013 theme, **LIVER CANCER: Act Today. Save Your Life Tomorrow. Awareness. Prevention. Detection. Treatment.** with many more to come. The 2013 WDHD seeks to raise awareness of this growing health crisis and reduce the number of individuals affected by supporting the worldwide fight to bring recognition through education and training concerning this disease. Prevention, early detection, treatment, and curability, supported by relevant epidemiological and clinical data, will be the main focus of the 2013 campaign. Through a multi-faceted approach, to include local and regional campaigns and conferences, the WDHD 2013 campaign will endeavor to inform healthcare providers and the community at large of the prevalence, risk factors, and causes of liver cancer and to present an evidence-based and patient-centered



Professor Dr. Sadik Memon delivers a talk on the management of HBV and HCV.

approach to the prevention, detection and treatment of hepatocellular carcinoma (HCC) and its underlying causes.

2013 WDHD Highlighted Event PAKISTAN Hepatitis Awareness Program Awareness screening and vaccination camp @ Khyber, Hyderabad

On the morning of February 2, 2013, an awareness, screening and vaccination camp was arranged jointly by AIMS Hospital and AGA KHAN HEALTH Services. The Chief Minister of the program for the prevention and treatment of hepatitis B and C management team screened 1,000 people and the first vaccine was inoculated to an HBSAg negative subject.

Professor Sadik Memon from (ISRA) AIMS Hospital delivered a comprehensive talk regarding the HBV and HCV management. The majority of people who came were HBV or HCV positive. The session became interactive once the audience started asking interesting questions.

Professor Memon answered the questions in detail and added that the only way to get rid of Viral Hepatitis is awareness in regard to the spread and risk factors for the diseases. Those that were positive planned to have a sonogram of their abdomen, routine blood tests, liver function tests and PCR testing (in the case of treatment seeking individuals). Dr. Tahir, Dr. Saghar and Dr. Sikandar worked day and night for the arrangement of this camp.



Participants attend the awareness, screening and vaccination camp in Khyber, Hyderabad.

Mr. Adeel Khan, marketing manager of AIMS hospital, distributed the awareness materials regarding chronic hepatitis B and C both in Urdu and Sindhi. The participants and attendees appreciated the efforts taken by the program manager for the prevention and management of hepatitis B and C in Sindh and for his team for HBV and HCV vaccines - three doses for each individual.

During the last part of the day, Professor Memon agreed to do free consultations for those individuals that tested positive and AIMS research laboratory offered, at very reasonable prices, PCR (HCV & HBV viral load) testing.

WDHD 2013 Calendar of Events: Past, Present, and Future

Egypt

Multiple presentations on HCC have taken place including two during the 5th Hepatology and Gastroenterology Post Graduate Course on December 8, 2012 in Cairo titled "Medical

Management of Advanced Hepatocellular Carcinoma” and “Hepatitis C and Cryoglobulinemia; An Update”, and another in February 2013 during the 16th International Congress of the Egyptian Hepato-Pancreato-Biliary Society in Hurghada.

Kazakhstan

A WDHD 2013 conference will be held June 6 in the city of Almaty, through the National Gastroenterology Association of Kazakhstan, under the direction of Professor Roza Bektayeva.

Portugal

A conference on “HCC: Global Warning, Global Answers” will take place May 31.

United Arab Emirates

The Emirates Gastroenterology & Hepatology Conference (EGHC) 2013 will devote two hours of the EGHC 2013 scientific program to cover HCC, during their annual meeting March 22-24 in Dubai.

USA

1. A presentation was given by WDHD Chairman Dr. Douglas LaBrecque on February 5 in California titled “World Digestive Health Day 2013-Liver Cancer.” Goals of the program included making those aware of the burden of liver disease in the United States and the steady and rapid rise in incidence of HCC, including the fact that most cases are diagnosed only at an advanced stage; recognizing the critical role of the primary care health provider in addressing this national public health problem; and becoming aware of the global health crisis due to liver disease, especially viral hepatitis and HCC, and place the severity of this health problem in perspective with other global health problems.

2. During the 2012 annual American Association for the Study of Liver Diseases’s meeting November 9-13 in Boston, a two hour symposium on *HCC: Geographical Challenges*, took place.

Venezuela

1. Various activities will be taking place at the Hospital Universitario from February through May, 2013. A meeting with the community “How to Prevent Liver Cancer” took place in February, an exhibition by medical students for the community will take place in April, and a Walk For Health will take place on May 19. Educational materials are also being developed in support of the campaign.

2. A symposium on “How to Get to Hepatocarcinoma”, coordinated by Dr. Maribel Lizarzabel, will be held on May 23. It will include lectures on: “From Hepatitis B and C to HCC. Involved Mechanisms”, “Alcoholism and Its Relationship with Cirrhosis and Liver Cancer”, “Metabolic Syndrome – Hepatic Steatosis – Insulin Resistance - Obesity may be attached to Cirrhosis and HCC?”, “Impact of the Images for Screening – Diagnosis and Treatment of HCC”, and “Utility of HCC Screening and Therapeutic Alternatives.”

For a full listing of events taking place, visit <http://www.wgofoundation.org/wdhd-2013-events-calendar>.



5th Egyptian Hepatology and Gastroenterology Post Graduate Course; 14th Egyptian International Workshop on Therapeutic Endoscopy

Hope Work Success



Ibrahim Mostafa, MD

Professor of Gastroenterology and Hepatology
Theodor Bilharz Research Institute
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The Egyptian International Workshop on Therapeutic Endoscopy was started in 1999 and is a three day live endoscopy workshop, endorsed by the European Society of Gastrointestinal Endoscopy (ESGE) and the American Society for Gastrointestinal Endoscopy (ASGE). This program has become one of the largest GI Endoscopy course gatherings in the Middle East and Africa. The International Educational Post Graduate Course is endorsed by the American College of Gastroenterology (ACG) and is in collaboration with the World Gastroenterology Organisation (WGO).



Professors Cihan Yurdaydin, Turkey, WGO Secretary General, Douglas LaBrecque, USA, WGO Foundation Member and WDHD 2013 Chairman, and Ibrahim Mostafa, Egypt, Course Director.

For the 10th Anniversary of the workshop, the organizing committee decided to be more specialized and to organize two back-to-back events: a two-day Hepatology and Gastroenterology Post Graduate Course and a two-day Live Endoscopy Workshop. These events are now attracting more than 1,000 physicians, not only from the region but worldwide.

The meeting promotes and supports clinical and scientific activity of young physicians, through the emerging stars award, and offers help and support to African physicians in the field of GI and Endoscopy. The meeting delivers high standard education and scientific programming and is an excellent place to learn about the latest advances in the fields of Gastroenterology, Hepatology and Therapeutic Endoscopy.

It has been held annually for the past 12 successive years in December. It is considered the main window to Africa and the Middle East as we have around 1,000 attendees (increasing every year), from more than 50 different countries, including all Arab and African Countries, in addition to the Bahamas, Belgium, Canada, Croatia, Cyprus, Czech Republic, France, Germany, Greece, India, Indonesia,

Japan, Lithuania, Nepal, Netherlands, Pakistan, Philippines, Romania, Russian Federation, Switzerland, Turkey, United Kingdom, and the USA, as well as Egyptian experts.

The main theme of the **Post Graduate Course** is improvement of the educational level in the fields of Hepatology and Gastroenterology for physicians in the Middle East and Africa. The hot topics were GIT, liver diseases and GIT endoscopy. The course consisted of four sessions including 24 state of the art lectures.

The 2012 event was accredited by the European Accreditation Council for Continuous Medical Education (EACCME) and was granted nine European CME credits.

Success of the **Workshop on Ther-**



Meeting attendees participate in hands-on training stations during the Workshop on Therapeutic Endoscopy.

apeutic Endoscopy was generated from supporting partners, outstanding organizing companies, 670 enthusiastic doctors from 32 countries, 12 international experts, and 30 Egyptian and Arabic experts.

There were 200 keen trainees at 10 hands-on training stations including Diagnostic Colonoscopy, Gastroscopy, Endoscopic Hemostasis, Endoscopic Mucosal Resection, Endoscopic Polypectomy, GIT Stenting and ERCP, and 40 sessions (60 hours) were performed in two days.

Five state of the art lectures with 24 selected video cases were held, in addition to the 500 cases done in the previous workshops over the last 12 years. This 2012 event was also accredited by the EACCME and was granted 10 European CME credits.

I would like to convey that success would never have been possible without very hard work and team spirit.



A lecture during the December 2012 meeting in Cairo.

We faced very hard times organizing such an event in all surrounding circumstances. However, the success that I have seen this year would never be possible without support. I would like again to thank all for what you have done for us to reach that success.





WGO Membership Update

WGO National Member Society Information and Update Forms

Each year, WGO national member societies and regional affiliates are asked to submit a current WGO National Member Society Information and Update Form. Each society has received a form via email, which may be updated and returned to membership@worldgastroenterology.org. If you need another copy of the form or have any questions about the information requested, please contact the WGO Executive Secretariat at membership@worldgastroenterology.org. Invoices are created based on the information received on these forms, and you will receive your 2013 invoice promptly upon receipt of the completed form. Your expedient response ensures important WGO news and information will be received promptly by the appropriate contacts within your national member society, and your cooperation is greatly appreciated!



Visit us at the Orange County Convention Center during DDW 2013 in Orlando, Florida, USA!

WGO National Member Societies – Dues are Payable at DDW 2013!

Did you know you can pay your WGO national member society's membership dues during Digestive Disease Week (DDW)? Just visit WGO at booth 710 in Foundation Row at the Orange County Convention Center in Orlando, Florida, USA, during DDW 2013! The WGO booth will be open during the hours of 10:00 and 16:00, Sunday through Tuesday, 19-21 May. If you wish to pay your dues at DDW, prior receipt of your society's National Member Society Information and Update Form by WGO will allow us to have a current and correct invoice ready and waiting for you when you visit the booth!

Dues Payment Methods

Membership dues may be paid by cash (in US dollars) or check, made payable to the World Gastroenterology Organisation. Please note, if you elect to pay dues at the WGO booth, a receipt will be emailed to you as promptly as possible following payment.

The dues that WGO national member societies contribute each year are channeled into training, education and advocacy in the developing world, while also strengthening these aspects in developed regions. WGO looks forward to receiving your society's 2013 dues and to keeping you, our national member societies, apprised of all the current WGO and WGO Foundation news and events. Please watch the monthly *e-Alert* and the quarterly *e-WGN* for the latest news!



The 2013 General Assembly will convene at Gastro 2013 APDW/WCOG Shanghai in Shanghai, China.

Participation in the 2013 General Assembly

As 2013 is a quadrennial World Congress year, with Gastro 2013 APDW/WCOG Shanghai taking place from 21-24 September 2013 in Shanghai, China, WGO national member societies are respectfully reminded that, in order to participate and vote in the General Assembly meeting to be convened in Shanghai in September, payment of membership dues must be up-to-date. If you are unsure of your society's membership status, please contact the WGO Executive Secretariat at membership@worldgastroenterology.org.

Prospective Members

Are you interested in becoming a WGO national member society? Interested national societies are encouraged to apply. Please visit the membership application section of the WGO website to learn more about the application process and required materials.

WGO representatives in the WGO booth during DDW 2013 will be more than happy to share with you the benefits of WGO membership.

We invite you to stop by the booth, speak with us, and read a wide variety of materials on the various WGO programs and initiatives which you may take with you. If you have any questions about the membership application process, please contact membership@worldgastroenterology.org and the Executive Secretariat will answer any queries you may have!

Promote your Society's Event with WGO!

National member societies are encouraged to keep WGO informed of their meetings and events. To submit the details for your society's upcoming meetings and/or events for promotion on the WGO Online Conference Calendar, please submit these via the WGO website at <http://www.worldgastroenterology.org/submit-event.html>.

Questions About Membership?

To inquire on the status of your membership, or if you have any questions regarding the information update or dues payment processes, please contact the WGO Executive Secretariat at membership@worldgastroenterology.org.



WGO Training Centers in Africa – A New Partnership in Training

As the global population steadily increases, so too does the need for access to healthcare close to home. To provide training for local and visiting physicians from across the globe, the World Gastroenterology Organisation (WGO) has established 15 Training Centers located throughout the world, the most recent addition being the Porto Alegre Hepatology Training Center located in Porto Alegre, Brazil. WGO Centers have served over 2,200 trainees and medical professionals since their inception. They offer locally relevant comprehensive training in the fields of gastroenterology, hepatology, endoscopy, oncology and GI surgery to further develop trainees' skills and education.

WGO Training Center Mission

The mission of the WGO Training Centers is to establish and nurture core training centers for general and focused GI training in locations of need, thereby, improving the standard of training at a grassroots level while ensuring a focus on regionally-relevant diseases. With this in mind, WGO is embarking on a collaboration with Karl Storz GmbH & Co. KG who has committed to support the establishment of Training Centers in sub-Saharan Africa, where the need for such education and training is increasing.

Training Center Locations

Of the 15 WGO Training Centers eight are in Latin America: Mexico City, Mexico; Bogotá, Colombia; San Jose, Costa Rica; La Paz, Bolivia; Santiago, Chile; La Plata, Argentina;

Ribeirão Preto and Porto Alegre, Brazil; in other parts of the world, WGO Training Centers are sited in Rome, Italy; Karachi, Pakistan; Bangkok, Thailand; and Suva, Fiji thus serving the needs of communities in and surrounding Europe, Asia, and the South Pacific. The Training Centers in Soweto, South Africa; Rabat, Morocco; and Cairo, Egypt provide research and training opportunities for gastrointestinal-focused training and education of nurses, medical practitioners and healthcare professionals within Africa and neighboring regions. Through Training Center programming, WGO aims to optimize the standards of patient care while ensuring a focus on regionally-relevant digestive disorders; and reduce the "brain drain" of highly skilled practitioners from developing countries by providing training and opportunities close to home.

The Need for African Training Centers

Whilst WGO Training Centers are geographically dispersed, a growing need has been identified in sub-Saharan Africa. WGO seeks to expand its efforts in promoting and advancing the practice of gastroenterology through the development of additional training initiatives within Africa. These programmatic endeavors have been made possible through a five-year partnership with Karl Storz, who has generously agreed to provide an educational grant for the establishment of three additional training centers. These new centers, once established, will provide a series of short and long-term courses, currently in development. These training initiatives will expose trainees and healthcare professionals with opportunities to enhance their skills and education



not deemed possible due to lack of resources in their current environment.

About Karl Storz

KARL STORZ GMBH & CO. KG is one of the world's leading suppliers of endoscopes, endoscopic instruments and devices for more than 15 surgical disciplines in human medicine. The company designs, engineers, manufactures and markets all its products with an emphasis on visionary design, precision craftsmanship and clinical effectiveness. The family-owned company was founded in 1945 by Dr. med. h. c. Karl Storz in Tuttlingen, Germany and in 1996, the daughter of the family founder, Dr. h. c. mult. Sybill Storz, took over the manage-

ment of the KARL STORZ group. In 2013, KARL STORZ has about 2,000 employees in its headquarters, and throughout the world 5,800 employees are engaged.

On a world-wide level KARL STORZ is very involved and dedicated to support medical training institutions with equipment so that young physicians can receive endoscopic training in order that more patients can benefit from the great advantages of this surgical technique. In this respect KARL STORZ strongly believes that medical education should remain in the hands of physicians. Therefore, KARL STORZ focuses on supporting training institutions by providing logistics and high quality

equipment. WGO is grateful for the generous support of Karl Storz and looks forward to a continued partnership between the organizations to grow the presence of WGO Training Centers in sub-Saharan Africa to address the growing need of training and education close to home.

Looking to the Future

As this endeavor progresses, we look forward to bringing you more information and updates as they become available. For more information on WGO Training Centers, please visit <http://www.worldgastroenterology.org/training-centers.html>.



WGO's New Graded Evidence System

AN INTERVIEW WITH DRS. JUSTUS KRABSHUIS, PUBLISHING EDITOR, WGO GRADED EVIDENCE SYSTEM



Justus Krabshuis

Highland Data
Tourtoirac, France



Anton Le Mair, MD

WGO Guidelines Project
Amsterdam, Netherlands

Introduction

WGO's 'Graded Evidence' System (GES) is built to help members of National Societies of Gastroenterology and all those interested in the practice and research of gastroenterology and hepatology keep track of the literature in topics covered by WGO Guidelines.



WGO's GES and WGO Guidelines work together closely. The guidelines are regularly reviewed and updated and built when new information becomes available. However, new evidence appears constantly, and the 'lag time' for a guideline to be updated may be

as much as 2-3 years. WGO's Graded Evidence system bridges these gaps.

The basis for GES is 'raw data' generated by very precise journal searches in Pubmed Medline for meta-analyses, systematic reviews, randomized controlled trials and practice guidelines covering the topics of all WGO Guidelines.

WGO is honored to have been able to enlist the expertise and assistance of Professor Andre Elewaut from Gent and Professor Johan Fevery from Leuven in the grading of evidence to support our WGO practice guidelines. They have an impeccable science background – for example, together they are past co-chairs of the UEGW Scientific Committee. They are a formidable pair of Editors who, together,

published more than 400 papers in gastroenterology and hepatology.

Evidence Grading means assessing relevant studies in terms of quality as well as its relevance for the guideline topic in question. Articles are then scored by assigning one, two or three stars:

★ ★ ★	key development
★ ★	very important
★	important
–	special mention

For more than 15 years, publishing responsibility for GES has been in the capable hands of Justus Krabshuis/Highland Data. We asked Justus to tell us something about the old and the new Graded Evidence System.

Adding value from Belgium



Professor Andre Elewaut



Professor Johan Fevery

What's new?**Q: Drs. Krabshuis, can you tell us about the GES improvements and why it has now changed?**

A: The time has come to put the service on a more professional footing. Management of GES will be done by WGO in-house – by EDI – the U.S.-based Association Management Company that manages all WGO interests. I will, however, remain responsible for the quarterly literature searches. A significant improvement in the new GES is that the editors now have a separate ‘field’ for ‘comments’. So the value they add is not only ‘selection of articles’ and assignment of a quality code, but they will also provide comments (if they wish); i.e. they can argue why a paper is important, not just say it is important.

Q: Which journals are now covered by GES and why?

A: It is easy to tell you which journals are covered. They are the top 10 Gastroenterology and Hepatology journals plus the top 10 general medical journals – based on the journal impact factor. It is not easy at all to justify this. We all know that evidence is not really influenced by ‘where’ we find it. Or is it? Is good research more likely to be published in high impact factor journals? We would need to consider prestige and journal quality. To be realistic – the graded evidence service will keep you up to date with key developments. It will not give you a Cochrane-like comprehensive overview of everything published in the area covered by our WGO Guidelines – it may come close though!

See <http://www.worldgastroenterology.org/graded-evidence.html> for the new list of journals.

**Q: What is the difference between GES and other information services, such as online search alerts, journal subscriptions, and practice guidelines?**

A: I think the key difference is that GES is edited by two eminent gastroenterologists. They scan and read and evaluate top research published in top journals and decide whether a new study is really ‘key’ and important. Both editors have eminent scientific backgrounds. Most other alerting services – like our own WGO Virtual Room of Gastroenterology – see <http://www.labovirtual.com.ar/vrg.htm> – are based on bibliometric and/or search parameters without ever passing the eye of a clinical expert.

Evidence & currency**Q: You only search for level-1 evidence? Why is that?**

A: We want to help everyone be aware early of new evidence. We only track Systematic Reviews, Meta-analyses and Randomized Controlled trials. Other Controlled Clinical trials, cohort studies and case studies may generate lower level evidence but we do not track this. WGO provides a free ‘Ask a Librarian service’ which can provide ‘on-demand’ high and or lower level evidence. We normally follow the CEBM levels – Oxford Centre for Evidence Based Medicine – see <http://www.cebm.net/index.aspx?o=1025>.

Q: Why do you not search the Cochrane Library and other sources of high quality level-1 evidence?

A: We search level-1 evidence in the top 10 GI journals. The databases of the Cochrane Library provide high quality information – however, the CENTRAL database with its comprehensive selection of RCTs and the Systematic Reviews Database are not available everywhere in the world – although it is getting better.

Pubmed on the other hand is ‘Open Access’ and all 20 journals are covered by Medline. Through our WGO Ask a Librarian service we can provide more comprehensive evidence and that would also involve searching the Cochrane library.

Q: So, is GES really evidence-based? How can the user be sure to trust the assigned GES levels?

A: GES is most certainly evidence-based. The update strategies are precise rather than comprehensive. Evidence levels are guided by the CEBM. The assignment of a quality score, however, involves expert opinion. Evidence is a very difficult attribute if you start to think about it. Evidence is a continuum and at the more principled end (some would say fundamentally) no effort or cost is spared to track down even the most elusive RCT – perhaps never published. But when is there enough evidence? And could it be said that for the substantial resources required to do a very comprehensive Systematic Review – taking perhaps a few years to do and major investment – instead we could do even as many as 100 rapid scoping reviews? By doing 10 Systematic Reviews you maybe condemned to worse outcomes (on average) for zillions of patients. There are opportunity costs to expending further effort, and (especially as diminishing return of evidence found per effort sets in) at some point the increased precision will not be worth the extra cost. Some of these ideas were suggested earlier this year by Jon Brassey (of TRIP database fame) on what is probably one of the best and free listservers for EBM methodology - evidence-based-health@jiscmail.ac.uk.

Q: How current is your system – when an article appears in Pubmed, how long does it take before it is available on the GES?

A: It varies. Our update searches are done quarterly so at worst the evidence is never more than three months old – on average six weeks. However, Pubmed does not evaluate – everything is published without a score for quality. By contrast, our editors carefully select and evaluate and so GES may well be the first to recognize the importance of a particular study.



Q: The source of the evidence is important - can we easily have access to the full text of selected articles?

A: This is a problem area. The Editors have long asked me to provide access to the full text of articles they consider evidence and of key importance. However, none of the gastroenterology and hepatology journals in the top 10 are open access. The copyright barrier prevents us from publishing the text ourselves and providing a link does not help as one hits a pay wall – often \$30 or even more per individual article. Sometimes the WGO ‘Ask a Librarian service’ can help to provide a copy of a key paper as published in the GES – we have wide networks and authors are always willing to share a copy of their research.

GES and WGO

Q: Why is WGO providing GES and how was it started?

A: We want to help colleagues – especially in low and middle-income countries. Professors Elewaut and Fevery have very kindly agreed to work pro-bono and this has made it possible for us to start. The Guidelines project by the way was started by another famous Belgian – Professor Guido Tytgat and not very long after that we were lucky enough to ‘find’ his fellow ‘Vlaming’ from Flanders. And so you could say this is all Evidence from Belgium.

Q: What are the main benefits of GES to the user?

A: GES helps gastroenterologists, endoscopists and hepatologists keep up to date with key developments in their subject areas. At the same time it provides an update service for all those who consult our online WGO Guidelines at <http://www.worldgastroenterology.org/global-guidelines.html>.

Q: WGO is very aware of their ‘global’ purpose, how does GES help healthcare workers in low resource regions?

A: It helps to have access to the latest high quality information – more and more CME (continuing medical information) is important to improve patient care, also in developing countries. GES is produced by Gastroenterologists for Gastroenterologists, with special attention for global issues. It provides the latest evidence, which forms an essential element of CME. And by linking it to WGO’s Ask a Librarian service, colleagues in low resource regions can sometimes by-pass the pay walls of other services.



Q: Are there more GES services available by other information providers?

A: Almost all evidence-based alerting services – and there are quite a few – are commercial ventures. There are few that are free – one excellent free service is the TRIP database at <http://www.tripdatabase.com/>. This is a free evidence-based high quality clinical information service with a special interest in Global health care – not just Western views. Of course, there are excellent commercial services like MD Consult and UpToDate as well as others, but the pay walls are often substantial.

Q: What is the future of GES in view of technical developments such as Google search and mobile access to information?

A: I am not sure. Is there a future role for ‘Expert Assessment’? Can ‘experience’ ever be ‘captured’ in evidenced based medicine? It certainly is the orphan child in all definitions of evidence-based medicine – going right back to David Sackett (and Gordon Guyatt) at McMaster in Canada. This was Sackett’s Evidence Based Practice (EBP) definition that most people know by now – but it is worth repeating I think:

Evidence Based Practice is “the conscientious, explicit and judicious use of current best evidence in making decisions about the care of the individual patient. It means integrating individual clinical expertise with the best available external clinical evidence from systematic research.” (Sackett D, 1996)

As you can see, for current evidence to be meaningful we need individual clinical expertise. This is what Andre Elewaut and Johan Fevery give us – it’s as valid today as it was when Sackett said it in 1996.

Concluding Note

Thank you very much Drs. Krabshuis for explaining what the new Graded Evidence System is and what it can provide to our WGO members and Guideline users. I am very grateful for giving us a view in the GES ‘kitchen’ and to hear more about your vision on the expert literature searches and evidence finding process behind the GES. A warm ‘thank you’ especially to the two expert editors from Belgium: Professors Elewaut and Fevery for putting in their time to make GES such a valuable information source for all interested in the GI field.



WGO Calendar of Events

The 48th International Liver Congress™

When: April 24-28, 2013

Location: Amsterdam RAI Convention Center, Amsterdam

Address: Europaplein, NL 1078 GZ, Amsterdam

PO Box 77777, NL 1070 MS Amsterdam

Organizer: European Association for the Study of the Liver (EASL)

Email: easloffice@easloffice.eu

Website: http://www.easl.eu/_the-international-liver-congress/general-information

Digestive Disease Week (DDW) 2013

When: May 18-21, 2013

Location: Orlando, Florida, USA

Organizers: American Association for the Study of Liver Diseases (AASLD), American Gastroenterology Association (AGA), American Society for Gastrointestinal Endoscopy (ASGE), and The Society for Surgery of the Alimentary Tract (SSAT)

Email: ddwadmin@gastro.org

Website: <http://www.ddw.org>

23rd Conference of the Asian Pacific Association for the Study of the Liver (APASL)

When: June 6-9, 2013

Location: Singapore

Organizer: The Asian Pacific Association for the Study of the Liver (APASL)

E-mail: apaslconference@kenes.com

Website: <http://www.apaslconference.org>

OESO 12th World Congress

When: August 27-30, 2013

Location: Paris, France

Address: UNESCO, 125 Avenue de Suffren, 75005 Paris

Organizer: World Organization for Specialized Studies on Diseases of the Esophagus (OESO)

E-mail: michele.liegeon@oeso.org

Website: <http://www.oeso.org>

ILCA 2013 Annual Conference

When: September 13-15, 2013

Location: Washington, D.C., USA

Organizer: The International Liver Cancer Association (ILCA)

E-mail: info@ilca-online.org

Website: <http://www.ilca2013.org>

Gastro 2013 APDW/WCOG Shanghai

When: September 21-24, 2013

Location: Shanghai, China

Address: Shanghai Expo Center, 1500 Shibo Avenue, Shanghai, China

Organizers: Asian Pacific Digestive Week Federation (APDWF), Chinese Societies of Digestive Diseases (CSDD), World Endoscopy Organization (WEO), World Gastroenterology Organisation (WGO)

E-mail: congress_international@gastro2013.org

Website: <http://www.gastro2013.org>

Australian Gastroenterology Week 2013 Incorporating the Federation of Gastrointestinal Societies

When: October 7-9, 2013

Address: Melbourne Convention & Exhibition Centre

Location: Melbourne, Australia

Organizer: Gastroenterological Society of Australia (GESA)

E-mail: gesa@gesa.org.au

Website: www.agw.org.au

ACG 2013 Annual Scientific Meeting and Postgraduate Course

When: October 11-16, 2013

Location: San Diego, California, USA

Address: San Diego Convention Center, 111 West Harbor Drive, San Diego, California, USA

Organizer: American College of Gastroenterology (ACG)

E-mail: info@acg.gi.org

Website: <http://www.gi.org>

United European Gastroenterology Week

When: October 12-16, 2013

Location: Berlin, Germany

Address: Messedamm 22 14055, Berlin

Organizer: United European Gastroenterology (UEG)

E-mail: office@ueg.eu

Website: <http://www.ueg.eu/week/>

Canadian Digestive Diseases Week (CDDW)

When: February 7-10, 2014

Location: Toronto, Ontario, Canada

Address: 100 Front Street W Toronto ON M5J 1E3

Organizer: Canadian Association of Gastroenterology

E-mail: CDDW@cag-acg.org

Website: <http://www.cag-acg.org>

The 32nd World Congress of Internal Medicine (WCIM 2014)

When: October 26-30, 2014

Location: COEX, World Trade Center Samseong-dong, Gangnam-gu, Seoul, Korea

Organizer: The International Society of Internal Medicine (ISIM)

E-mail: wcim2014@intercom.co.kr

Website: <http://www.wcim2014.org>

Highlighted events represent WGO member events. For a full listing of events, please visit <http://www.worldgastroenterology.org/major-meetings.html>