

# e-WGN

## WORLD GASTROENTEROLOGY NEWS

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### In this issue

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#### Enteric Infections Research Review

Expert: Eduardo Salazar-Lindo, MD

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#### The Global Village of Celiac Disease and Its Evolution Over Time

Alessio Fasano, M.D.  
Carlo Atassi, MD

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#### Revolution by Epigenetics Expected in Digestive Oncology

René Lambert, MD

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## Message from the Editors of e-WGN



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Acute diarrhea is a major public health problem in both resource-limited countries and developed countries of the world. In the former acute diarrhea is the second highest cause of death (after pneumonia) in children under five, and it is likely that repeated enteric infections may be responsible for both growth and mental retardation in a sizeable number of children. The primary factor responsible for acute diarrhea is the lack of clean water with the existing water supplies frequently contaminated with fecal wastes. Acute diarrhea also affects individuals in more economically advanced countries in several distinct ways including: a) epidemically when the food-supply chain is broken (which often becomes newsworthy and is the subject of much 'headline' news) and becomes contaminated by one or more bacteria; and b) sporadically

during travel to underdeveloped countries which is often referred to as 'Traveler's diarrhea'.

World Digestive Health Day (WDHD) - which has been held since its inauguration in 2004 on 29 May, the anniversary of the founding of the World Gastroenterology Organisation (WGO) - was established to emphasize to both the public and professionals the importance of a major digestive tract illness. The theme for this year's WDHD is the Prevention & Management of Enteric infections: the important role of clean water, clean food, clean environment. This year's WDHD will emphasize both the public health aspects of acute infectious diarrheal diseases as well as the scientific issues regarding interaction between multiple infectious agents and the small and large intestine.

▼  
Contents

### Editorials

---

- Message from the Editors of e-WGN 01  
Greger Lindberg, MD  
Henry J. Binder, MD
- 

### World Digestive Health Day 2011: Special Scientific Highlight

---

- Enteric Infections Research Review 04  
Expert: Eduardo Salazar-Lindo, MD
- 

### Scientific News

---

- The Global Village of Celiac Disease and Its Evolution Over Time 05  
Alessio Fasano, M.D.  
Carlo Catassi, MD
- 

- Revolution by Epigenetics Expected in Digestive Oncology 08  
René Lambert, MD
- 

### World Digestive Health Day 2011 News

---

- Enteric Infections: Prevention & Management, May 29, 2011 11  
Robert Steffen, MD, Hon. FFTM/ACTM
- 

### WGO & WGOF News

---

- The Importance of YOUR Membership in WGO 13  
Training Center News 15  
GASTRO-ANTALYA 2011: Joint WGO-Turkish Society of Gastroenterology Meeting Announced 17
- 

### WGO Global Guidelines

---

- The Latest News in WGO Global Guidelines 18

### VOL. 16, ISSUE 1

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## → Message from the Editors of e-WGN

*Continued from page 1*

The gastrointestinal tract has the largest surface interface to the environment and as a result has the potential for exposure to viruses, bacteria, parasites and a large variety of toxins. Equally important is that the intestine (especially the colon) has an extremely large endemic population of bacterial organisms that are associated with health and can be altered in several disease situations. Molecular methodology has opened a new world for the study of the endogenous fecal flora. When challenged by pathogens, the defense mechanisms of our innate and adaptive immune systems may respond by induction of fluid secretion and propulsive muscular activity resulting in diarrhea (and hopefully expulsion of the pathogen that initiated the process). The resulting diarrhea especially in very young children often leads to dehydration and metabolic acidosis, and primary treatment of acute diarrhea is the use of oral rehydration solution (ORS) [View the WGO Global Guideline on Acute Diarrhea Now](#). ORS leads to

enhanced fluid absorption primarily as a result of stimulation of glucose-stimulated Na and water absorption (via SGLT1) in the small intestine. Unfortunately, ORS usage world-wide is quite low (~30-35%) for many reasons, and concerted action is required to increase its use with the expectation that enhanced use of ORS will lead to improved child health.

Over the past three decades there have been several efforts to alter the formulation of ORS to reduce diarrhea and accelerate improvement. The present ORS formulation is hypo-osmolar with the administration of zinc for 10 days. An alternative approach that shows considerable progress is the incorporation of so-called amylase-resistant starch (starch that is relatively resistant to amylase digestion) that will result in both liberation of glucose in the small intestine and the production of short-chain fatty acids in the colon – a dual-action ORS.

Many diarrheal diseases find their way to the human gut via contaminated water supplies and access to clean water or means for cleaning water are crucial for preventing spread of disease. Likewise, clean food, how to avoid contamination of food, and clean environments are key issues in large parts of the world. The causative agent in many cases of acute diarrhea has eluded identification. Advances in molecular biology are now providing new knowledge and new tools for identifying virus and bacteria and one such tool, a rapid test for the most common bacterial causes for acute diarrhea in the West, is highlighted by Dr. Eduardo Salazar-Lindo in the Research Review of this issue. It is anticipated that significant improvement in the diagnosis and treatment of acute infectious diarrhea will occur during the coming decade. ■

## Enteric Infections Research Review

As part of the WGO's campaign to raise awareness about Enteric Infections throughout 2011, an expert will be recommending and highlighting a "gold standard" article, with a direct link to the original source, in each issue of e-WGN this year.



### ARTICLE

Cunningham SA et al. Three-hour molecular detection of *Campylobacter*, *Salmonella*, *Yersinia*, and *Shigella* species in feces with accuracy as high as that of culture. *J Clin Microbiol* 2010;48:2929-33



### EXPERT: EDUARDO SALAZAR-LINDO, MD

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*Dr. Salazar-Lindo's comment on the article:* This is my favorite recently published research paper on enteric infections. This work is a leap forward in developing accurate, rapid tests to identify the microorganism causing an intestinal infection. Such tests are currently available to most clinical laboratories either on ELISA or immunochromatography format only. A real-time PCR test designed to simultaneously search for several bacterial enteropathogens with a high sensitivity and specificity is more than welcome. Once these tests are widely available to clinical laboratories, the impact on improving specific therapies and decreasing unnecessary use of antimicrobials will be great.

### *Introduction to Dr. Salazar-Lindo:*

The World Gastroenterology Organization is currently updating its Global Cascade Based Guideline on Acute Diarrhea. Professor Salazar Lindo is one of our eminent Review Team Members and we are very pleased to have his selection from Peru. Dr Salazar Lindo is an important thinker in the field - you can view some of his research by [clicking here](#).



## The Global Village of Celiac Disease and Its Evolution Over Time



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Celiac disease (CD) is an autoimmune disorder characterized by damage of the small intestine mucosa occurring in genetically predisposed individuals, and triggered by the ingestion of dietary gluten (1). Gluten is the major protein component of wheat and other cereals (barley and rye). The genetic predisposition to CD is related to some HLA-related haplotypes, i.e. the DQ2 and the DQ8 heterodimers. HLA-DQ2 or -DQ8 are needed for CD development, but are not a sufficient cause, as they may be found in many not-CD healthy subjects (approximately 30% of the general population) (1). The development of the CD enteropathy is paralleled by the appearance of serum autoantibodies, e.g. IgA class anti-transglutaminase (TTG) and anti-endomysial (EMA) antibodies, which are a highly specific marker of the disease. CD presents with a wide spectrum of clinical manifestations at any age. Typical CD manifests with intestinal complaints such as chronic diarrhea, weight loss, malnutrition and abdominal distension. Atypical CD is characterized by lack of malabsorption and either intestinal (recurrent abdominal pain, irritable bowel-like

symptoms, recurrent aphthous stomatitis) or extra-intestinal manifestations (e.g. isolated increase of serum aminotransferase level, iron deficiency anemia, short stature, delayed puberty or chronic fatigue) (1). Since the introduction of serological tests, "silent" (apparently symptomless) CD has been increasingly recognized because of occasional screening. This is often the case in subjects with a family history of CD, patients with associated autoimmune (e.g. type 1 diabetes) or genetic (Down, Turner or Williams syndromes) disorders (1). Finally, potential CD is characterized by positivity for anti-tTG and EMA antibodies in subjects with a normal intestinal mucosa or subtle histological abnormalities, such as an increased number of intraepithelial lymphocytes (IEL) (so called type 1 lesion). Patients with potential CD can either be free of symptoms or have intestinal symptoms which may respond to a gluten-free diet (GFD). Over time, they may develop a flat mucosa. Treatment of CD is based on the lifelong exclusion of gluten-containing cereals from the diet (1). In many areas of the world,

including North America and Europe, gluten-rich products, such as bread and pasta, are part of the staple diet. Gluten-containing food therefore makes a substantial contribution to daily energy intake and is enjoyable to eat. The changes needed to begin and maintain a GFD are substantial and have a major impact on daily life.

CD is one of the most common life-long disorders in countries populated by individuals of European origin, affecting approximately 1% of the general population. In the early 90's researchers in Italy launched the new "era" of CD epidemiology (2). Using blood samples from 17,201 healthy Italian students in 1996, it was shown that CD is much more common than previously thought, and that most atypical cases remain undiagnosed unless actively searched for by blood tests. The prevalence of active CD in screened subjects was 4.77 per 1,000 or 1 in 210 subjects (2). The overall prevalence of CD, including diagnosed individuals, was 5.44 per 1,000 or 1 in 184 subjects. The ratio of previously diagnosed to undiagnosed CD cases was as high as 1 to 7 (2). Quite surprisingly at that time, most newly diagnosed patients with CD showed only modest complaints such as anemia or chronic fatigue or no symptoms at all (2).

A recently published large international, multicenter study investigated a wide population sample of more than 28,000 children and adults in four different European countries by screening with the serum IgA anti-TTG test (3). On average, the overall prevalence of CD was 1%, with large variations between countries (2.0 % in Finland, 1.2 % in Italy, 0.9 % in Northern Ireland, and 0.3 % in Germany) (3). This study

confirmed that many CD cases would remain undetected without active serological screening.

In the past, CD was generally perceived to be less common in North America than in Europe. This misconception was corrected in 2003 by a U.S. prevalence study conducted by the University of Maryland Center for Celiac Research that included 4,126 subjects sampled from the general population (4). The overall prevalence of CD in this U.S. population sample was 1 in 133, actually overlapping the European figures (4).

Similar disease frequencies have been reported from developed countries populated mainly by individuals of European origin, e.g. from Canada, Australia, New Zealand, Brazil and Argentina (5-8). The frequency of CD in other parts of the world is still largely unknown. However recent reports indicate that CD is a common disorder wherever gluten-containing cereals are a staple food, e.g. in Northern Africa, Middle East and part of the Indian continent (9-12).

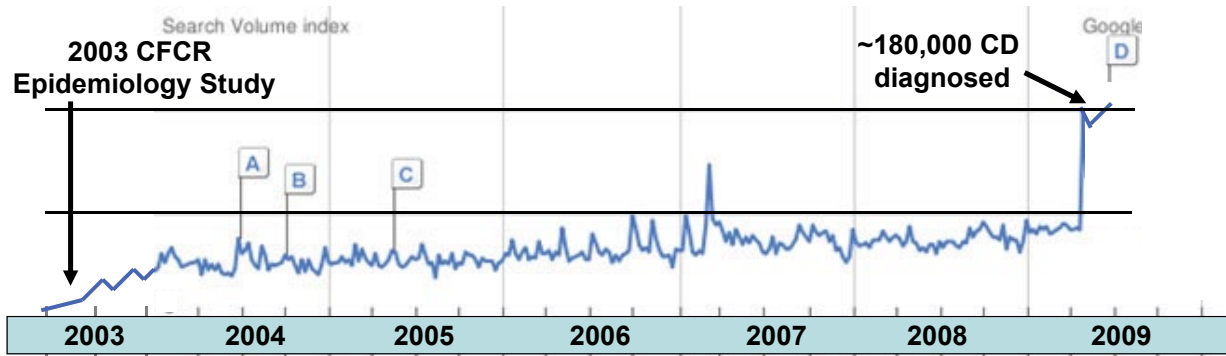
The epidemiology of CD is efficiently conceptualized by the iceberg model. The overall number of CD cases is the size of the iceberg, which is not only influenced by the frequency of the predisposing genotypes in the popula-

tion, but also by the pattern of gluten consumption. Typical CD cases are usually diagnosed because of suggestive complaints. They make up the visible part of the celiac iceberg, in quantitative terms expressed by the incidence of the disease. In developed countries, however, for each diagnosed case of celiac disease, an average of 5 cases remain undiagnosed (the submerged part of the iceberg), usually because of atypical, minimal or even absent complaints. These undiagnosed cases remain untreated, leaving individuals exposed to the risk of long-term complications, such as infertility, osteoporosis or cancer. Currently the best approach to improving the CD diagnostic rate is a process of case-finding focused on at-risk groups, a procedure that minimizes costs and is ethically appropriate (13). Increased awareness of the many clinical faces of CD, coupled with a higher inclination for using blood tests, could efficiently uncover a large portion of the submerged celiac disease iceberg. The primary care physician's office would provide the most natural setting for selective screening to first identify individuals at risk for CD who need referral for definitive diagnosis.

In a recent and rather puzzling development, the prevalence of CD

seems to be on the rise in developed countries (Figure 1). The total prevalence of CD has doubled in Finland during the last two decades (1.05% in 1978-80 and 1.99% in 2000-01) (14), and the increase cannot simply be attributed to a better rate of detection.

To learn more about the natural history of CD and to further investigate the changes in CD prevalence over time, we recently tested blood samples from an American cohort of 3,511 residents from Washington County, Maryland (15). The group has been followed since 1974 for CD autoimmunity. Blood samples were first tested for IgA anti-tTG antibodies. Samples with borderline or elevated anti-tTG antibodies were subsequently tested for the more specific serum IgA class endomysial antibody to improve the diagnostic process. We found CD autoimmunity in 7 subjects in 1974 and in an additional 9 subjects (total 16 cases) in 1989 (15). Our study indicated that celiac disease autoimmunity within an American population doubled between 1974 (1 every 501 subjects) and 1989 (1 every 219 subjects). This trend apparently continued in the following years. In a different sample of the adult American population in 2001, we reported a CD prevalence of 1 in 105 (4). During the last 30 years



**Figure 1.** Trend of Celiac Disease diagnosis in USA since the CFR 2003 epidemiology study. So far ~180,000 patients out of the 3,000,000 projected cases have been diagnosed. This increase is the combination of increased awareness and, therefore, increased diagnostic rate, and true increase in celiac disease prevalence over time.

the prevalence of CD among adults in the U.S. increased by 5-fold, doubling approximately every 15 years. Remarkably, this study showed that loss of gluten tolerance may occur at any time in life, for reasons that are currently unclear. The implications of this discovery could have a wide-ranging effect on the diagnosis and treatment of CD in elderly patients.

A steady rise in the incidence of autoimmune disorders as well as allergic disorders has been registered in industrialized countries during the last few decades. Both in Europe and the U.S., Type 1 diabetes (T1D) showed a stable and relatively low incidence during the first half of the 20th century, followed by a sharp increase that began some time after the middle of the century. According to the "hygiene hypothesis," the cleaner environment found nowadays in Western countries led to lower frequency of early childhood infections and differences in the spectrum of microorganisms populating the gut. These changes could modify the immune response and be responsible for higher risk of different autoimmune disorders. However, the rising prevalence of adult onset of CD that we observed in the U.S. study can hardly be explained by hygienic changes occurring in childhood. The amount and the quality of ingested gluten, the type and duration of wheat dough fermentation, the spectrum of intestinal microorganisms and how they change over time, intestinal infections, and stressors in general are all possible switches of the tolerance/immune response balance (16). However, more research is needed to determine if and how these factors can cause loss of gluten tolerance. Researchers could use the results of these studies to determine how to prevent not only the onset of CD but other autoimmune disorders as well. ■

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## Revolution by Epigenetics Expected in Digestive Oncology



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Considerable progress occurred in recent decades in the early diagnosis of digestive cancer or its precursors. The 3 major companies now produce electronic video-endoscopes equipped with high-resolution imaging, magnification, techniques for image processing of which Narrow Band Imaging is the more reliable. Moreover, abdominal and endoscopic ultrasonography and radiological imaging with CT-scan or MRI detect with high sensitivity tumors in biliary ducts, pancreas and liver. Nowadays, the genetic study of primary alterations in the DNA structure as well as the epigenetic study of alterations superimposed on this basic structure offers a revolutionary perspective in the diagnosis and treatment of digestive cancer. The analysis of the cancer genome (1-6) opens a wide perspective for new "filter tests" in the selection of persons at risk. The persons so selected still deserve to be explored by endoscopic or radiological imaging for the direct localization and for histopathologic confirmation. Epigenetic mechanisms also open a new field in the therapy of early or advanced cancer.

### 1 - THE GENOME OF THE NORMAL CELL

#### DNA

The human genome is stored on 23 chromosomes. The major part of the 3 billion base-pairs of DNA (deoxyribonucleic acid) is non coding and there are only around 23,000 genes coding for proteins and containing the genetic instructions used in the development and function of the cells. The tissue stability is ensured by the balanced rhythm of mitosis and apoptosis. Extensive sequencing of the nucleotides in the polymeric helix is now possible through hybridization when using microarray probes. The DNA stored in the nucleus of the cell is a double helix of nucleotides, with backbones made of sugars (deoxyribose) and phosphate groups, joined by ester bonds. Attached to each sugar is one of four types of bases: adenine, guanine, cytosine, and thymine. The two helices are linked together by hybridization between the 4 bases. The sequence of these four bases along the backbone encodes information for the building of proteins. The double DNA helix is stored in the nucleus of the cell and compacted with proteins, histones, in the nucleosomes. The histones, which ensure the stability of DNA, may interfere in the organization of DNA.

#### RNA and messenger-RNA

RNA or ribonucleic acid, is a long chain of nucleotide units. RNA is usually single-stranded. Each nucleotide with a backbone of sugar (ribose) and phosphate is linked to one of 4 nitrogenous bases (Adenine, Guanine, Cytosine, and Uracil instead of Thymine). RNA is transcribed in the nucleus from DNA by RNA-polymerases and then localized to the ribosomes of the cytoplasm where it receives information transferred from the DNA by way of the messenger-RNA (mRNA). The mRNA carries the genetic instructions for proteins and is a copy of a segment of the DNA in which the introns have been removed. The coding sequence of the mRNA determines the amino acid sequence in the protein that will be produced.

#### Micro RNA

MicroRNA (miRNA) are short RNA molecules, on average 22 nucleotides long, that regulate gene expression. For that purpose, miRNA is complementary to a part of messenger RNAs (mRNAs), which can be exported from the cell in macromolecular complexes with proteins: the exosomes. Tumor cells excrete exosomes containing tumor born miRNA into the microscopic vesicle of their surrounding microenvironment. Circulating tumor miRNAs are very stable and can therefore be targeted by non-invasive tests for the detection of early tumors. The miRNAs can also be used for monitoring treatment of the tumor and its prognosis.



## 2 - GENETICS AND EPIGENETICS IN THE CANCER GENOME

### Molecular alterations in the cancer genome

Cancer arises in cells of a tissue as a result of genetic changes in the basic sequence of the nucleic acid helix. There is a distinction between somatic mutations, acquired under the influence of environmental factors, and germline mutations transmitted by the ascendants. Cancer can also arise through epigenetic mechanisms during DNA duplication; molecular alterations are then superimposed upon the basic structure of the DNA helix. Genomics and epigenomics are new disciplines devoted to the study of those mechanisms. The cancerous cell develops after successive alterations on 15 to 20 genes. A double mechanism is frequently involved in the development of a cancer, when the initial genetic mutation in the basic structure of DNA leads to epigenetic mutations.

Alterations in the basal sequence of nucleic acids occur through 3 distinct mechanisms: 1 - Formation of an oncogene: the mutation concerns a positive regulator of cell proliferation which after mutation is hyperactive. This applies to the oncogene K-ras. 2 - Inactivation of a suppressor gene: this occurs after mutation in a suppressor gene, which is a negative regulator of cell proliferation. This applies to the p53 gene. 3 - Microsatellite instability (MSI) after mutations in the repair genes (Mismatch Repair or MMR genes): the defective normal DNA repair results in uncontrolled cell division and tumor growth.

### Epigenetic mechanisms in cancer

Cancer is a genetic disease and the basic structure of the genetic code, with the information contained in the genes, can be modified by point mutations in a single site of the sequence,

either under the influence of environmental factors or through transmission from the parents of a heritable germline mutation, as it occurs in familial colorectal cancer. Epigenetic alterations with modification (activation or inhibition) in the function of the genes occur independently of an alteration in the basic DNA structure, and play a major role in the molecular mechanisms of sporadic cancer. The molecular basis of epigenetics is complex, there are 3 mechanisms: 1 - DNA hypermethylation, the best known epigenetic mechanism, concerns the CpG islands in the "promoter" part of many genes; it is characterized by addition of a methyl group to the Cytosine base linked to Guanine in the CpG dinucleotide under the influence of DNA-methyltransferase. The hypermethylation of gene promoters may induce the silencing of suppressor genes and plays a role in carcinogenesis when this silencing function is suppressed. Hypermethylation of the promoter in genes is easily detected in tissue specimens by autofluorescence and is also detected in the plasma with potential application to screening tests. 2 - remodeling through translational modification of the amino acids in the histone protein component of DNA in the nuclear chromatin: this is a potential cause of cancer when there is histone deacetylation. 3 - Micro-RNA: this is the third mechanism that controls the expression of genes. MiRNA deregulation is highly targeted on oncogenes and tumor suppressors as compared to hypermethylation and histone modifications. Silencing of miRNA suppressor function will activate oncogenes resulting in malignant transformation. The expression of various mi-RNA has been shown to be altered in digestive cancer (pancreas and colon); they could act as biomarkers of cancer in blood or body fluids.

There is a relationship between the 3 major epigenetic mechanisms. The

histone modifying enzymes are under direct control of miRNAs while the expression of certain miRNA depends on methylation of their promoters. In addition, hypermethylation has an impact on the interaction of histones with the DNA expression.

## 3 - THE TUMOR INITIATING CELLS

In a normal adult tissue a small contingent of stem cells perpetuate themselves through "self-renewal". They give birth to other stem cells that have the same capacity to proliferate as the parent cells and will differentiate into specialized cell types. Normal stem cells maintain the turnover of regeneration and also act as a repair system for the body. Epigenetic modifications play an important role in the function of stem cells. The genes that regulate renewal are inactivated by epigenetic modification in normal cells whereas these self-renewal pathways are reactivated in stem cells.

The cancerous cells that constitute the bulk of the tumor mass have limited capacity to proliferate, while a small population of cells is able to self-renewal and sustaining of the tumor growth. These cells share certain common characteristics with the stem cells ensuring the stability of normal tissues and are often called cancer stem cells (CSC). On the other hand the doubt on their origin justifies their denomination as tumor-initiating cells (TICs) because their development could also result from reactivation of normal cells in the tissue. The tumor initiating cells (or cancer stem cells) differ from the large mass of the other cancerous cells by their ability to renew; in addition they may resist chemotherapy or radiotherapy, and cause recurrence or metastasis when they are not destroyed. These cells also have the capacity to transport various substrates across cellular membranes because they strongly express the ABC transporters, which rely on the energy of ATP hydrolysis.

Detection of cancer stem cells in a tumor, based on expression of epithelial cell adhesion molecules and surface markers like CD 44, CD24, EpCAM, CD133, could help in estimation of its aggressiveness and in delineating treatment options. It is critical to identify these cells in tumors, because they are a privileged target in the treatment and justify new therapeutic approaches with dormancy induced by miRNA decoys. As an example, when the miRNA (miR34) linked to p53 gene is introduced in a preparation of p53 deficient human gastric cancer cells, apoptosis of the cells occurs in relation to restoration of the p53 function in the preparation.

#### 4 - EXPECTED CONTRIBUTION OF EPIGENOMICS TO DIAGNOSIS OF DIGESTIVE CANCER

The role of genetic factors has been extensively reviewed in the detection of the most frequent form of heritable digestive cancer i.e. colorectal cancer. In this situation the study of epigenetic factors is not helpful and the identification of the point mutation by genetic testing is proposed after the initial questionnaire on family antecedents. However when digestive cancer occurs as a sporadic disease epigenetic factors play a major role and their study may contribute to diagnosis. There are two potential targets in epigenomics for the diagnosis of digestive cancer: 1. DNA tumor biomarkers for CpG hypermethylation in the promoter of various genes offering a global methylation profile.

2. Overexpression of specific categories of miRNA, which can transit to plasma as well. Such bio-markers have been first tested in stools, and then in plasma to obtain increased compliance of the tested persons. When DNA markers of multiple genes in stools or in plasma, detect a tumor further procedures of localization (endoscopic diagnostic or radiological imaging), as well as histopathologic control are required.

The efficacy of DNA biomarkers in the early detection of digestive cancer or precancerous lesions has been confirmed for esophagus, stomach, colon, pancreas, bile duct or liver across many recent publications. Most biomarkers are still in a phase of assessment in pilot studies, however a new colorectal cancer single biomarker in blood has been licensed in 2009 in the USA offering the Septin 9 methylated DNA test as a commercialized kit for colorectal cancer screening (Epigenomics AG). Biomarkers based on DNA and miRNAs are not yet cost/ effective, but the route is now open for developments in efficacy and lowering of costs.

#### 5 - EXPECTED CONTRIBUTION OF EPIGENOMICS TO THERAPY IN DIGESTIVE CANCER

The contribution of epigenetics factors to the management of digestive cancer is not limited to diagnosis and new therapeutic strategies are suggested. MiRNA may have a specific role in the control of cancer as stressed by the Nobel laureate David Balti-

more in the symposium on biological complexity recently (October 27-29) held at La Jolla in a joint action of Salk Institute, Nature, and Fondation IPSEN. The concept that only a subset of cells drives tumor formation justifies treatments that specifically target the tumor initiating cells. In the future, the treatment of cancer resistant to chemotherapy, and of relapsing or metastatic cancer, should benefit from the still experimental studies with epigenomics.

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## WGO's World Digestive Health Day

Enteric Infections: Prevention & Management, May 29, 2011



### Robert Steffen, MD, Hon. FFTM/ACTM

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University of Zurich - Epidemiology and Prevention of Communicable Diseases  
WHO Collaborating Centre for Travellers' Health and  
Adjunct Professor, Epidemiology and Disease Prevention Division  
University of Texas School of Public Health  
Houston, TX, U.S.A.

Each year the WGO encourages and welcomes the participation of its 110 national member societies to celebrate World Digestive Health Day 2011 on May 29, the day WGO was incorporated and inaugurated. This year's theme is Enteric Infections: Prevention & Management; Clean Food, Clean Water, Clean Environment. Educational and promotional activities to raise awareness to the general public and medical community on the topic of Enteric Infections have begun, and will continue throughout the year.

World Digestive Health Day (WDHD) is an annual advocacy/public awareness event hosted by WGO to increase the awareness of digestive diseases amongst member societies, government bodies, media and the general public. Traditionally held on 29th May, WDHD is WGO's key advocacy program for reaching out and engaging the general public on important digestive health issues. Although WGO is instrumental in providing overall direction, the WDHD's success will depend on the combined efforts hosted by its national member societies worldwide.

A new page on the WGO Foundation website is created each year which consists of a package of useful public

awareness materials, the featured guideline – 2011's Global Guideline is Acute Diarrhea – information for physicians and patients, an area to submit a society's event, and a page featuring what different countries and societies have done to celebrate WDHD. Events that have taken place through WGO and its member national societies include lectures, press conferences, symposia, including WDHD information on a society's website, creating a World Digestive Health Week, and much more.

The WGO Training Centers have also been active participants in past years, and have played an important role in 2011. Each Center has received the tools and resources available for this year's campaign to distribute to the many individuals, both physicians and the general public that visit the Training Centers each year. The Train the Trainer (TTT) program has also benefited from the campaign by receiving the materials during each of the Train the Trainer Programs – which took place in Chennai, India in April – which TTT attendees can take back to their respective countries and share with those that aren't yet aware of the program. The WGO looks at each way that the tools and resources can be disseminated so that the most

individuals possible can be informed and educated.

Visit [www.wgofoundation.org/wdhd-2011](http://www.wgofoundation.org/wdhd-2011) to view the compilation of tools and resources put together specifically for the 2011 WDHD Campaign, and to read about the events happening around the world to educate physicians and the general public on various enteric infections.

The WDHD campaign in 2011 has endeavored to raise global awareness of the prevalence of enteric infections in developing as well as industrialized countries. Strategies targeted at the prevention and management of enteric disease have been emphasized in developing countries where the lack of clean water, clean food and clean environment significantly impact life expectancy and give rise to a host of related health issues. In industrialized countries, where sanitation is still often at issue, we become increasingly focused toward strategies to reduce morbidity and mortality. WDHD 2011 especially considers the plight of children and travelers at risk for enteric infection.

At the national level, WDHD has taken place through WGO's national member societies, which have organized events and their individual WDHD campaign. Efforts sustained on a national basis continue to raise awareness at the grassroots level. WGO supports the national societies through the provision of related tools and promotion of local events. As anticipated, a major resource for the 2011 effort has been the WGO guidelines related to acute diarrhea.

This important initiative could not have been done without the hard work of the WDHD 2011 Steering Committee. WGO sincerely thanks

the following volunteers for their time and dedication to this important campaign:

- Dr. Robert Steffen, WDHD 2011 Campaign Director, University of Zurich, Switzerland
- Dr. Henry J. Binder, Yale University, USA
- Dr. Santanu Chatterjee, Wellesley Medicenter, India
- Dr. Herbert L. DuPont, University of Texas School of Public Health and Baylor College of Medicine, USA

Dr. Michael Farthing, University of Sussex, United Kingdom

Dr. Bernard Levin, Chair, WGO Foundation, ex-officio member, Steering Committee

Dr. Yasmine Motarjemi, Food Safety Consultant, Switzerland



Visit [www.wgofoundation.org/wdhd-2011.html](http://www.wgofoundation.org/wdhd-2011.html) for more information on World Digestive Health Day

## The Importance of YOUR Membership in WGO

The World Gastroenterology Organisation (WGO) is comprised of 110 national member societies and 4 regional associations representing over 50,000 gastroenterologists, hepatologists GI surgeons and other healthcare professionals worldwide. As a federation of national gastroenterological societies, together we project a strong and powerful voice to advance global understanding of GI, liver and related diseases through training, education and advocacy. Our one voice reflects the true global nature of the WGO and our aim to represent and support the discipline of gastroenterology worldwide and enhance the reach of our members, particularly in developing and low-resource regions.

WGO believes that it is the responsibility of societies to take an active role in promoting the growth and welfare of areas struggling to provide excellence of care in regions where available resources are at their lowest. As a member of WGO you are providing an opportunity to expand the knowledge and training of our members and increase our collective ability to truly be global guardians of digestive health. As a national society member of WGO, the dues that your organization contributes each year are channelled into training, education and advocacy in the developing world, while serving as well to strengthen these aspects in developed regions. The high level of commitment from the WGO leadership all of whom are volunteers and staff to participate in the governance, training, and development of education and other resources for your members, along with a strong belief in our mission, makes the WGO an organization of which you can be proud.

Partnership with our member organizations is the keystone of WGO's global activities. We invite you to consider the impact that your organization is able to achieve as a member of the WGO federation of national societies:

### Training Centers

*"I was able to participate in an improvement process that culminated in us changing the endoscopy practice at the national referral hospital in Uganda"*

*-Training Center Attendee*

Fourteen WGO Training Centers around the world provide training delivered by WGO volunteers working with local experts and colleagues from member societies and educational programs to hundreds of healthcare professionals every year. The Training Centers promulgate locally relevant knowledge and develop the skills of medical practitioners and healthcare workers from low-resource countries to:

- Optimize standards of patient care while ensuring a focus on regionally-relevant digestive disorders; and
- Attempt to reduce the "brain-drain" of highly skilled practitioners from developing countries by providing training close to home.

Since 2001, over 1,300 trainees have been trained at the WGO Training Centers thanks to the dedication of over 150 international volunteer trainers.

### Train the Trainers Program

*"An amazing workshop and expanded my thinking about health problems and opened the first door into clinical studies"*

*-Former TTT Participant*

2011 marks the 10th year anniversary of Train the Trainers, with over 600 trainees having participated in this TTT program since its commencement in 2001. The WGO Train the Trainers (TTT) program brings together educators from across the globe in an intensive and interactive four-day workshop, as well as two-day topic-focused workshops dedicated to the development of teaching and training skills. The TTT program creates an unparalleled forum for interaction and discussion between world leaders in gastroenterology, hepatology and GI surgery, with the universal goal being excellence in patient care through the optimal delivery of gastroenterology education and training.

### Guidelines

*"A magnificent team – very balanced & global"*

*-Guidelines Team Member*

WGO now provides a library of 23 WGO Global Guidelines which, unlike other medical guidelines which are targeted to specific regions or countries, have been written and distributed with the entire world in mind. WGO is the only international organization with this global focus. Each guideline is developed by a team of experts drawn from the ranks of our national societies. The guidelines include references to other relevant guidelines which are identified, summarized and re-published or cited by WGO for the benefit of the practitioner. WGO Global Guidelines are unique because they utilize "Cascades" which provide various evidence-based diagnostic and treatment options that are scalable to available local resources and infrastructure. Cascades make

the WGO Guidelines globally applicable by identifying multiple ways of achieving the best possible outcome by taking the available resources into account. The guidelines, which are viewed well over 20,000 times each year are widely used by practitioners around the world and are currently offered in English, French, Spanish, Portuguese, Russian and Mandarin Chinese. The guidelines are developed free of any commercial influence.

#### WDHD: World Digestive Health Day

*“We hope that this day will help unite gastroenterologists worldwide”*

The WGO engages in advocacy on a global basis as it celebrates World Digestive Health Day (WDHD) annually on May 29, the anniversary of WGO's founding in Washington, DC, USA in 1958. Each year WDHD highlights an important topic in the area of digestive health and disease for physicians, other healthcare practitioners, patients and the general public. Topics have included optimal health and nutrition, viral hepatitis, irritable bowel syndrome, and inflammatory bowel disease. In 2011 the focus will be on enteric infections and their relationship to clean water, clean food and a clean environment. Working with you, our national member societies, we make the general public and governments more aware of issues – local, national, and global – relating to digestive health, nutrition and digestive diseases. In 2009 over 60 events in 40 countries informed physicians, patients and the general public about IBS, how to live with it and how it can be treated. Information on IBD was spread in 2010 by 25 of WGO's member societies with over 50 events taking place worldwide. The WDHD campaign in the past two years alone has reached thousands through seminars, public campaigns, courses and press conferences.

WGO makes you and your members active participants in the Global Gastroenterology Community

#### Additional Benefits of Membership in WGO

As a member of WGO, you have access to other important benefits including:

- e-WGN, WGO's premier quarterly publication
- The quadrennial World Congress of Gastroenterology, the largest gathering of WGO members and committees, and the key opportunity to meet with colleagues and develop and exchange ideas and information
- Access to educational opportunities, such as Train the Trainers programs worldwide
- Global promotion of regional and national meetings as well as your own society's programs and events
- Participation and influence in the governance of WGO through ordinary and extraordinary general assemblies
- Participation in committees and input in elections of representatives to the WGO leadership and committee membership
- A platform to interact with a global network of gastroenterologists
- The WGO website, with access to additional resources such as the Ask A Librarian service, which provides access to high quality clinical and research information, along with the Graded Evidence system, which continuously provides updates on the research found in WGO's Global Guidelines. ■

As a federation of member national societies -- the WGO -- Together **WE** create a powerful mechanism by which we can meaningfully impact the ability of organizations and regions with lesser resources to grow, thrive, and serve the needs of their constituencies. Partnership extends our reach, broadens our influence, and strengthens global knowledge of digestive health.

## Training Center News

### The Cairo Training Center

Based on the 2010 Events Fact Sheet, Cairo held two annual courses this past December, the 3rd Hepatology and Gastroenterology Post Graduate Course and the 12th International Workshop on Therapeutic Endoscopy, both with great success.

Endorsed by the American College of Gastroenterology (ACG), and in collaboration with WGO, the 3rd Hepatology and Gastroenterology Post Graduate Course took place from December 10-12, and presented eight sessions geared towards improving the educational level for physicians in the Middle East and Africa. Twenty-six international speakers from fourteen countries delivered thirty-four state of the art lectures covering topics in Hepatology, Gastroenterology, and Endoscopy. Among the international speakers present were Dr. Philip Katz, Past President of ACG, and Dr. Richard Kozarek, President of WGO. This event was accredited and granted nine European CME credits.

The 12th International Workshop on Therapeutic Endoscopy featured two days of live endoscopy transmission, with 38 complex therapeutic endoscopy and ultrasonography cases executed with much success. Over 1200 physicians from 48 countries were in attendance as well as twelve world class endoscopy experts, including WGO Cairo Training Center Director Dr. Ibrahim Mostafa.

Regarding the Cairo Training Center itself, the following are quotes from former trainees:

*"Can you imagine that one doctor from the Democratic Republic of Congo said that if they have patients with bleeding varices, they refer that patient to another country (mainly South Africa) in order to do endoscopy because they lack the skills and proper materials to do band ligation or histoacryl injection? I think all efforts must be done at the CTC for the sake of the health of other African patients!"*

*-Muhammad El Zahaby, Egypt*

*"Following the training that was facilitated by the training site, I was able to participate in an improvement process that culminated in us changing the endoscopy practice at the national referral hospital in Uganda by acquiring state of the art equipment, the re-training of doctors and nurses, and adopting minimum internal guidelines for endoscopy practice."*

*-Kenny Opio, Uganda*

*"The CTC Cairo experience was truly amazing for me. My learning curve went all the way up. I am now able to perform upper GI endoscopy much better and I have been doing this in Lagos, Nigeria since returning in May 2009. This truly was the best hands-on experience I have ever had!"*

*-Ladi Hameed, Nigeria*

### Bogotá Training Center

Director: Dr. Luis Sabbagh

The XV International Gastroenterology and Advanced Endoscopy course took place this past January at the JW Marriot Convention Center in Bogotá, Colombia. According to Dr. Luis Sabbagh, "the course was a real success!"

The course received 320 gastroenterologists from several Latin American countries including Venezuela, Peru, Uruguay, Brazil and Colombia. The high quality faculty consisted of Todd Baron from USA, Manoel Galvao and Celso Ardengh from Brazil and Raul Montserrat and Roberto Fogel from Venezuela. Faculty and guest speakers gave many important lectures as well as Live Cases transmitted from the Reina Sofia Clinic to the hotel via satellite. Every trainee within the Bogotá Training Center, which consists of many various programs,



actively participated in the Live Cases demonstrations.

The VI Gastrointestinal Endoscopy course for nurses as well as the Bogotá Training Center had over 500 participants, and the Organizing Committee received very good feedback from the assistants.

Activities within the Training Center are running well. Two physicians from Venezuela and Uruguay both recently completed six months of training in Endosonography. Currently, four trainees have a fellowship in Gastroenterology and Endoscopy for a period of two years. In addition, trainees are soon expected to arrive from other universities for the duration of 2-3 months. The Center is happy to report that these trainees will receive complementary training.

### The Karachi Training Center

A one day National Workshop was recently held in 2010 titled "Acid Peptic Diseases and Functional Gut Disorders" under the auspices of World Gastroenterology Organisation, Karachi Training Center, Pakistan at Regent Plaza Hotel in Karachi.

It was chaired by Professor Khalid Mehmood and Professor Raana Q Masood of Dow University of Health Sciences. The speakers at the meeting included Professor Wasim Jafri, Dr. Saeed Hamid, Dr. Hasnain AliShah, Dr. Ashfaq Ahmed, Dr. Khalid Mumtaz, Dr. M Salih, Dr. Lubna Kamani, Dr. Col Shakil Mirza and Dr. Amna Subhan. The following topics were addressed at the meeting gastroesophageal reflux disease, functional reflux, functional dyspepsia, nonsteroidal

antiinflammatory drugs induced gastric ulcer, Helicobacter pylori associated duodenal ulcer, irritable bowel syndrome, chronic constipation and functional abdominal pain.

The meeting was well received and attended by the internists, general practitioners, and fellows in training from various regions within Pakistan. The entire workshop was interactive and was described by attendees as a "useful exercise that needs to be done more frequently." Upon completion of the workshop, certificates were distributed to the participants by WGO. ■



## GASTRO-ANTALYA 2011:

### Joint WGO-Turkish Society of Gastroenterology Meeting Announced

WGO and the Turkish Society of Gastroenterology are pleased to announce and invite you to the upcoming joint meeting, Gastro-Antalya 2011, November 16 to 20. This clinically-oriented congress will feature a two-day case-based postgraduate course, numerous symposia on critical issues in Gastroenterology, Hepatology and Endoscopy and ample opportunities for the presentation of original work.

Visit [www.wgo-turkey2011.org](http://www.wgo-turkey2011.org) regularly for updated information.

#### Symposium Topics:

- Infectious disease
- Obesity and NAFLD
- Regional Trends in IBD
- Colon cancer and prevention
- Hepatocellular carcinoma
- GI Bleeding
- Endoscopy
- Esophagus and reflux disease
- WGO symposium on training and education in GI
- Functional GI diseases

#### Postgraduate Course Topics:

- Esophagus
- IBD
- Chronic Hepatitis
- Complications of cirrhosis
- IBS and functional disorders

#### Important information to know...

**Dates:** November 16-20, 2011

**Registration** (in Euro): Physicians, 250; Residents/Nurses, 150; Accompanying Person, 150; Business Participant, 250. Cost includes participation in the scientific program, congress bag and printed materials, participation in satellite symposia, lunches, coffee breaks, welcome cocktail and gala dinner \*Prices will increase after August 15

**Hotel:** Rixos Sungate Hotel, Kemer – Antalya, Turkey. 660 Euro for 4 nights, single occupancy, includes all inclusive accommodations including breakfast, lunch, dinner, coffee breaks, snacks, and drinks \*Prices will increase after August 15

**Congress Language:** The official language of the congress will be English. Simultaneous translation service to Turkish and Russian will be provided

**Abstract Submission:** There will be oral and poster presentations during the meeting. Abstracts can be sent from the official website and will be published in the Turkish Journal of Gastroenterology. DEADLINE: July 15, 2011

**Climate:** The weather in Antalya in November is usually dry and the temperatures are around 17-19 °C.

**Currency:** Turkish Lira (TL) is used as the national currency. Major currencies can be exchanged for TL at Istanbul Ataturk Airport, Antalya Airport and all banks

**Electricity:** 240 V, 60 Hz with two-prong sockets.

Gastro-Antalya has been organized by the following individuals and organizations:

#### Presidents

Richard Kozarek, *World Gastroenterology Organisation*

Ömer Özütemiz, *Turkish Society of Gastroenterology*

#### Secretary General

Sedat Boyacıoğlu, *Turkish Society of Gastroenterology*

#### Co-Postgraduate Course Directors

Eamonn Quigley, *World Gastroenterology Organisation*

Cihan Yurdaydın, *Turkish Society of Gastroenterology*

#### President of National Meeting

Sabahattin Kaymakoglu, *Turkish Society of Gastroenterology*

You may contact the secretariats at [info@worldgastroenterology.org](mailto:info@worldgastroenterology.org) or [valor@valor.com.tr](mailto:valor@valor.com.tr), and visit [www.wgo-turkey2011.org](http://www.wgo-turkey2011.org) for more information. ■

## The Latest News in WGO Global Guidelines

The WGO is pleased to announce the launch of its newest logo for the Global Guidelines and Cascades program!

The logo brings together three key elements to this important program: The guidelines themselves, cascades, and the critical factor that makes WGO Global Guidelines especially important for our members and colleagues worldwide – *A Resource Sensitive Solution*.

As the WGO guidelines become increasingly important to low-resource countries, the guideline teams look at the chosen topic with a focus on cascades. Cascades are a hierarchical set of diagnostic or therapeutic techniques for the same disease, ranked according to the resources available. Using a team of experts, both Western and non-Western, each guideline features cascades which have a global view taking into account the available resources in various countries.

Look for the new logo on the WGO website, recently updated guidelines, and the guidelines which will be released in 2011!

### Guidelines; Present & Future

The year 2010 was a successful year for the Guidelines Program. The Endoscope Disinfection, Helicobacter Pylori and Constipation guidelines have been updated, with the Constipation Guideline now offering Cascades. Look for those on the [WGO Global Guidelines Homepage](#)

With two new guidelines currently being created – Healthy Stomach and NASH – it will be another exciting year for this program. The Healthy Stomach team is led by Professor Richard Hunt, Farncombe Family Digestive Disease Research Institute, Division of Gastroenterology, McMaster University Health Science Centre, Canada, and will be based on an integrated clinical approach covering a triad of conditions related to the Healthy Stomach: gastritis, malignancies, and NSAID ulcers. The NASH Guideline, led by Professor Doug LaBrecque, University of Iowa Healthcare, Department of Internal Medicine, Director, Liver Service, USA, has a world-renowned team covering multiple areas of the world including Mexico, Pakistan, Austria, Russia, Malaysia, Spain, Switzerland, Canada, USA and Croatia.

Watch future issues of e-WGN as well as the new monthly e-ALERT for more news and updates on Global Guidelines and Cascades, and visit <http://www.worldgastroenterology.org/global-guidelines.html> to download any of the WGO guidelines for free, in six different languages. As always, WGO invites and encourages you to provide feedback on any of our Global Guidelines, by filling out the Guideline Feedback Form found here: <http://www.worldgastroenterology.org/wgo-guideline-feedback.html>.



**A Resource Sensitive Solution**