JUNE 2004

The Hong Kong Society of Gastroenterology

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Scientific Updates

Molecular Pathology of Gastric Cancers

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Gastric cancer is the second most common cancer worldwide. Its prevalence is still on the rise in developing countries due to the ageing population. Like many cancers, the pathogenesis of gastric malignancy is believed to be a multiple steps development from chronic inflammation to metaplasia/dysplasia and finally malignant transformation. In the last decade, two major milestones in the studies of gastric cancers have been laid. They are 1. recognition of a cascade of gastric carcinogenesis and 2. identification of Helicobacter pylori as an important cause of the disease. Correa put forward a multi-steps and multi-factorial process in the development of gastric cancer; originated from chronic gastritis, glandular atrophy, intestinal metaplasia, dysplasia and gastric cancer [1]. And in just 10 years after the discovery of Helicobacter pylori, a Gram-negative curved bacterium that was originally thought to be a contaminant in gastric biopsy, the International Agency for Research on Cancer (IARC) has proclaimed that this infective agent is a Class I carcinogen [2].

Yet, there is a big missing gap in the understanding of pathogenesis between the gastric microbe, histopathology and molecular mechanisms. Thanks to the advent of modern molecular biology, the sophisticated process of cancer development has been gradually unveiled. There is strong evidence to support the notion that carcinogenesis resulted from a series of mutations in important genes occurring in specialized cell type. This multi-step process is well illustrated by colorectal cancer research and, the same principle also applies to gastric cancer.

In the last 5 years, our group has endeavored to study the molecular mechanisms of gastric pathogenesis. Our studies started from investigating whether eradication of Helicobacter pylori would be able to prevent malignant transformation of the gastric mucosa. We chose to study a cohort from Yantai of the Shangdong Province, a region of high gastric cancer prevalence in China. Subjects were recruited in an endoscopic surveillance study. Those who were confirmed to have H. pylori infection were randomized to receive a one-week course of omeprazole, clarithromycin and amoxicillin (OAC) for the treatment of the infection or placebo [3]. One year after the treatment, 515 out of 587 subjects returned for follow-up. Endoscopic biopsy of the gastric mucosa was repeated and the histology before and after the therapy was compared. There was no obvious improvement in atrophy and intestinal metaplasia despite eradication of H. pylori. Recently, we returned to Yantai five years after the randomization to repeat endoscopy and biopsy. Gastric cancer and/or severe dysplasia were found in 5 subjects from the OAC group and 9 subjects in the placebo group. Compare to the placebo group, those who received OAC had significantly milder degree of glandular atrophy and intestinal metaplasia in the antrum at the 5-year follow-up [4]. Subjects in the OAC group had retarded progression of glandular atrophy (odds ratio, 1.89; 95% CI 1.29 to 2.76) and intestinal metaplasia (odds ratio, 3.59; 95% CI 2.47 to 5.23) compared with subjects in the placebo group (odds ratio for intestinal metaplasia, 3.66; 95% CI 2.38 to 5.63; odds ratio for glandular atrophy, 6.99; 95% CI 4.58 to 10.68).

Since glandular atrophy and intestinal metaplasia are considered to be the precursors of gastric cancer, we studied the molecular events during these pre-malignant stages in relation to H. pylori infection. First, we looked at bacterial virulence factors and their correlation with glandular atrophy and intestinal metaplasia. Blood group antigen binding adhesin (BabA) has been shown to mediate bacterial adherence to human blood group antigens on gastric epithelium [5]. We correlated the cytotoxin associated gene A (cagA), vaculoating toxin (vacA) and blood group binding adhesion (babA2) genotypes of H. pylori with the severity of gastric inflammation and epithelial cell turnover [6]. 104 subjects from the Yantai cohort were studied and found that the great majority of them (98.1%) were cagA+ strains and all had vacA s1 genotype. This came as no surprise because it is a well-known fact that most Asian patients are infected by cagA and vacA positive (so-called Type I) H. pylori strains. Interestingly, the babA2 strain was found in 79.8% and was associated with higher lymphocytic infiltration, presence of glandular atrophy (odds ratio 7.5, 95% CI 2.3-24.3) and intestinal metaplasia (odds ratio 7.4, 95%CI .2-25.3). We believe that adhesion to

gastric epithelial cells via BabA may facilitate the effective delivery of bacterial products such as the CagA protein into the host cells and the subsequent tyrosine phosphorylation process [7]. None the less, babA2 is probably only one of the mediators for the attachment process and other unidentified factors are also likely to be involved.

The disturbance of cellular kinetics plays an instrumental role in cancer development. Inhibition of apoptosis and increased cellular proliferation leads to cellular accumulation and increased the risk of mutation and malignant transformation. From our previous study, we know that H. pylori infection induces cellular apoptosis and proliferation in normal gastric epithelium [8]. This increased cellular turnover with parallel accentuation of proliferation and apoptosis in inflammation is relatively harmless. It can be reversed by the eradication of H. pylori infection at the resolution of inflammation. However, when we studied the cellular kinetics of the Yantai cohort with intestinal metaplasia, a different behavior was observed. We found that the apoptotic activity was significantly lower in intestinal metaplasia when compared to non-intestinal metaplasia tissue in the antrum of the stomach [9]. On the other hand, the level of cellular proliferation was comparable. Thus, the apoptotic index/proliferation index ratio of the gastric epithelium was markedly reduced in intestinal metaplasia, favoring cellular accumulation and malignant transformation. After successful eradication of H. pylori, significant drop in proliferation in both intestinal metaplasia and normal mucosa was observed. A similar fall in apoptosis was detected in normal gastric tissue but not in intestinal metaplasia tissue.

We attempted to understand these changes in cellular kinetics by studying the regulators of cell cycles, cyclins and cyclin-dependent kinase inhibitors. While cyclins and cyclin-dependent kinases are promoters of cell cycle progression, cyclin-dependent kinase inhibitors have been identified as potential tumor suppressors. Cyclin D promotes cellular proliferation through the G1 phase of the cell cycle by regulating the activity of CDK4 and CDK6 [10]. On the other hand, cyclin-dependent kinase inhibitors $p27^{kip1}$ (p27) binds to a wide variety of cyclin/cyclin-dependent kinase complexes including CDK2 and CDK4, inhibits kinase activity and blocks the cell cycle progression [11]. From our cohort study, we have demonstrated that cyclin D2 was over-expressed in H. pylori associated chronic gastritis, intestinal metaplasia and gastric cancer tissues [12]. On the other hand, diminished p27 expression was found in intestinal metaplasia and gastric cancer associated with H. pylori infection. Furthermore, we found that the up-regulated expression of cyclin D2 and down-regulated expression of p27 often go hand-in-hand in H. pylori-induced intestinal metaplasia. Potentially, these alterations will drive cell cycle transition and increase the risk of malignant transformation. These changes in cell cycle regulators are not only due to inflammation as the same phenomenon could be demonstrated when gastric cell lines were co-cultured with H. pylori without inflammatory cells. Similar observation between p27 and cyclin D1 had been reported in gastric cancer. Recently, we also found that the reduced cyclin D2 expression in a subset of gastric cancer is associated with promoter hyper-methylation in cyclin D2 gene [13].

Disturbance of apoptosis can also be a result of inhibitor proteins. Inhibitor of apoptosis proteins (IAP), a family of proteins that directly inhibits caspase and pro-caspase molecules, have been demonstrated to function as potential mediators of the terminal effect phase of cell death and survival [14]. Survivin is a member of the IAP family recently identified as a novel anti-apoptotic protein that bind specifically to caspase 3 and caspase 7 inhibiting apoptosis [15]. We evaluated survivin expression in normal gastric mucosa, gastric cancer cell line, gastric cancer tissue using reverse transcriptase-polymerase chain reaction, immunohistochemistry and Western blot. Survivin is absent in normal gastric tissue but expressed in 68% of gastric cancer tissues and all gastric cell line tested [16]. Gastric cancer with survivin expression displayed significantly reduced apoptosis. For the first time, survivin mRNA was also detected in the gastric mucosa of 27% non-cancer first degree relatives of patients with gastric cancer in association with H. pylori infection [16]. As first-degree relative have an approximately three-fold increase in risk of developing gastric cancer, the presence of survivin, which may or may not be related to H. pylori infection, could offer a potential explanation.

Another area of interest is the role of cyclooxygenase-2 (COX-2). COX-2 is an inducible enzyme which converts arachidonic acid into prostaglandin in response to inflammation. There is a wealth of evidence to support that COX-2 is strongly expressed in gastrointestinal tumors. In gastric cancer, COX-2 up-regulated expression was first described by Ristimaki et al [17]. COX-2 over expression is also associated with angiogenesis, tumor invasion and distant metastasis. The study of COX-2 is potentially of great importance because of its therapeutic implications. If eradication of H. pylori alone cannot prevent progression of pre-malignant conditions such as glandular atrophy and intestinal metaplasia sufficiently to halt malignant transformation, COX-2 inhibitors such as celecoxib and rofecoxib may be a potential chemo-prophylactic agent in the prevention of gastric cancer. We started with studying the gastric biopsy of the Yantai cohort. While only weak expression of COX-2 could be found in non-infected subjects, intensive expression of COX-2 was found predominantly in the foveolar and glandular epithelium of the gastric mucosa and to a lesser extent in the lamina propria [18]. With eradication of H. pylori, COX-2 expression in the laminar propria was reduced. On the other hand, in the gastric epithelium, there was only a modest reduction in COX-2 expression in intestinal metaplasia and glandular atrophy. This dissociation of COX-2 expression between the laminar propria and the epithelium implies that the presence of COX-2 is not merely a reaction to inflammation. Nonetheless, the mechanism leading to COX-2 overexpression in gastric tumor remains elusive. A recent in vitro study suggested that wild-type p53 inhibits the binding of TATA-binding proteins (TBP) to the promoter region of Cox-2 gene [19]. Thus, levels of prostaglandin E2 were 10 times lower in cells with wild-type p53 than in those with mutated p53, suggesting the potential interaction of p53 and COX-2 in cancer cells. We investigated the interaction between p53 and COX-2 in gastric cancer. In 39 cases of gastric cancers, COX-2 over-expression was seen in 19 (49%). These tumors had more lymph node metastasis and a poorer survival. Missense mutations of p53 were detected in 20 (51%) patients. In this study, we showed that tumor with p53 missense mutations, which leads to amino acid substitution, had a higher level of COX-2 expression when compared to tumor with wild-type p53 [20].

To complicate the issue further, we have also demonstrated an inverse association between cyclooxygenase-2 overexpression and microsatellite instability in gastric cancer [21]. Microsatellite instability (MSI) is a form of genomic instability reported in a variety of familial as well as sporadic cancers. Microsatellites are ubiquitous, short, repetitive DNA sequences widely distributed throughout the human genome with an unknown function [22]. When intestinal metaplasia tissues were taken out from patients with or without gastric cancer by microdissection, Leung et al discovered that there was a progressive accumulation of MSI from the premalignant to malignant stage of the disease [23]. Furthermore, H. pylori gastritis was found to occur more frequently in individual with MSI-positive than MSI-negative gastric cancers implying the role of H. pylori infection in affecting DNA mismatch repair. The same group then proceeded to study the effects of co-culturing H. pylori with gastric cell lines and determined the MutS (hMSH2, hMSH6) and MutL (hMLH1, hPMS2 and hPMS1) DNA mismatch repair (DNA MMR) proteins. In this study, H. pylori infection was found to reduce the DNA MMR proteins and decreased mRNA levels of repair genes through production of a heat labile protein [24]. This important finding suggests that H. pylori infection lead to a deficiency of DNA MMR in gastric epithelial cells that may increase the risk of mutation accumulation in gastric mucosa cells and the risk of gastric cancer during chronic H. pylori infection.

So far, we have identified several molecular pathways underlying progression of intestinal metaplasia including p53 mutation, microsatellite instability, cyclooxygenase-2 overexpression. There are also reports on overexpression of transforming growth factor alpha (TGF$\propto$) and epidermal growth factor (EGF) receptor involved in the process. However, all these changes are only present in a subset of intestinal metaplasia. While chromosomal changes may be an important pathway leading to malignant transformation, epigenetic changes have

recently emerged as an important cause of tumorigenesis. Of particular importance is that hypermethylation of the CpG island of tumor-related genes can result in transcriptional silencing of the gene with subsequent loss of protein expression. Hypermethylation of CpG island has previously been detected in gastric cancer [25]. We microdissected tissues with foci of intestinal metaplasia and examined for gene promoter hypermethylation in DAP-kinase, E-cadherin, GSTP1, p14, p15, p16, RASSFIA and hMLH1 by methylation-specific-PCR. Three different patterns of methylation were found [26]. Aberrant methylation in tumor-related genes was detected in high frequency in gastric intestinal metaplasia of both cancer and non-cancer patients. Hypermethylation was more frequent in cancer than intestinal metaplasia in DAP-kinase, p14, p15, p16, with comparable frequency in E-cadherin and hMLH1 and no methylation was found in GSTP1. Furthermore, concurrent methylation of multiple tumor-related genes were found in gastric cancer tissues as well as adjacent normal gastric tissues [27]. Some of these aberrant gene promoter methylation can be detected in the sera of patients with gastric cancer, this study opens a possibility of using this test in early diagnosis of the malignancy [28]. Interestingly, methylation of CpG island of the Cox-2 gene can also be found in a subset of gastric cancer, adding to the heterogeneity of gastric cancers [29].

There are other unexplored areas in gastric carcinogenesis which might open new doors of intervention. Wnt signaling pathway activation leads to inactivation of the adenomatous polyposis coi (APF)/Axin/GSK3 complex which suppresses the activity of β-catenin by promoting its degradation. Recently, a gene called Frizzled (Fz) was clone. This gene encodes a protein with a cysteine rich domain (CRD) which is a binding site and receptor for Wnt. One member of the Frizzled gene family, FzE3, is found to be over-expressed in oesophageal carcinoma leading to translocation of β-catenin [30]. This observation suggested that Wnt pathway can be activated by overexpression of FzE3. We studied expression of FzE3 and secreted Frizzled related proteins (hsFRP). All 12 cases of gastric cancer showed upregulated expression of FzE3 and down-regulated expression of hsFRP [31]. These alterations in FzE3 and hsFRP may provide alternative mechanism for the activation of Wnt signaling pathway in gastric carcinogenesis. Trefoil factor family (TFF) domain peptides are synthesized and secreted by mucin-secreting epithelia cells lining the gastrointestinal tract. There are at least 3 members in the TFF family. TFF1 is located in the foveolar cells of the gastric mucosa and TFF2 in the mucus neck cells of the pylori glands of the normal stomach. TFF3 or intestinal trefoil factor is normally expressed in the small and large intestine but not in the stomach. We studied the pattern of expression of trefoil peptides in gastric cancer, intestinal metaplasia and non-cancer tissues. TFF1 and TFF2 expression were reduced in intestinal metaplasia and cancer tissue. On the contrary, TFF3 expression was up-regulated in metaplasia and cancer [32].

We are beginning to unveil the molecular mechanisms of gastric carcinogenesis. Thus far, there are several concepts shaping up. First, gastric cancer is not a homogenous condition but possess various pathways in its development. Second, Helicobacter pylori infection triggers the initial events in the cascade of mutagenesis and they interact at various stages in the development. Finally, beyond a certain point of cellular transformation, removal of the stimulating factor, namely H. pylori, may not be sufficient to prevent progression of pathology. More work will be needed to explore interventions at cellular and subcellular levels to halt the process of gastric carcinogenesis.

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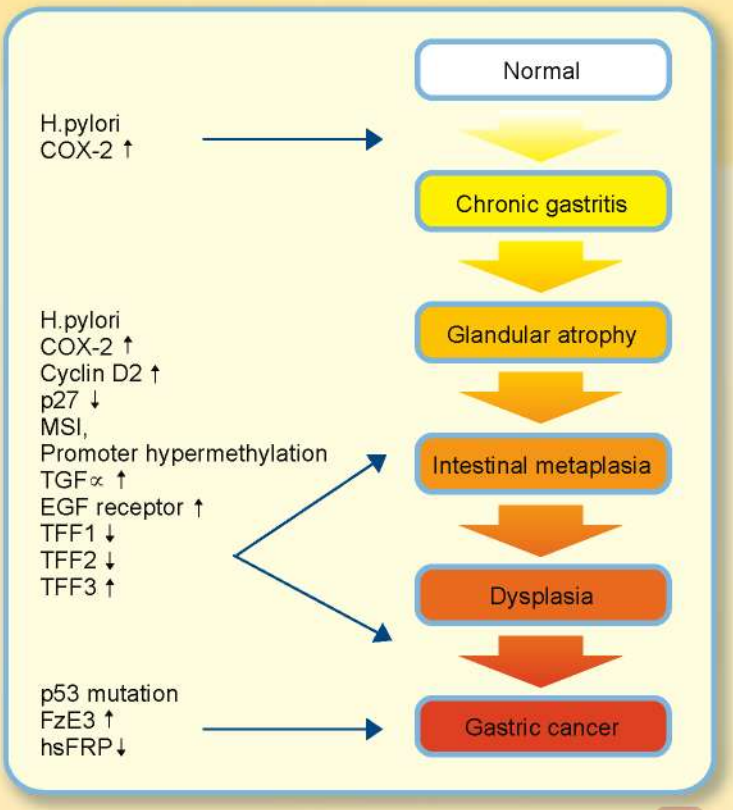
Fig 1. The multi-step gastric carcinogenesis pathway and its molecular mechanisms



Nonalcoholic steatohepatitis

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Non-alcoholic steatohepatitis (NASH) is a form of chronic hepatitis with histological features of alcohol-induced liver disease that occurs in individuals who do not consume significant amounts of alcohol. It is part of a broad spectrum of non-alcoholic fatty liver disease (NAFLD) that includes patients with pure steatosis. NAFLD is increasingly recognized as a potentially serious condition. Conservative estimation suggests that 6.4 million US adults have NAFLD and the prevalence of the disease is likely to increase with time.[1]

Diagnosis of NAFLD and NASH

By definition, diagnosis of NAFLD requires exclusion of alcohol as an aetiological factor. The acceptable level of alcohol consumption is variable but can be reasonably taken as weekly intake not greater than 14 units (20g/day).[2] Because there are no specific tests for NAFLD, exclusion of other co-existing liver diseases is also needed before establishing the diagnosis. Clinically, while some patients may present with symptoms such as fatigue and right upper quadrant discomfort, many more are recognized by abnormal liver enzyme levels detected at routine evaluations. Although ultrasound, computed tomography and magnetic resonance imaging have all been used to diagnose fatty liver, none of them is sensitive enough to detect degree of steatosis less than 30%.[2] These radiological modalities are not capable of differentiating simple fatty liver from NASH. Furthermore, they are not able to detect liver fibrosis reliably, which is essential in staging the disease.

Liver biopsy permits histological diagnosis of NAFLD and NASH. NAFLD is defined as fat accumulation in the liver exceeding 5% to 10% by weight, but it is estimated practically as the percentage of fat-laden hepatocytes observed by light microscopy. As the name implies, NASH encompasses a more severe form of liver injury with the presence of inflammation. The necessary histological components for NASH include macrovesicular steatosis (diffuse or mainly pericentral), lobular inflammation and hepatocellular ballooning typically in pericentral area. Other features that may be present but are not necessary for diagnosis are perisinusoidal fibrosis, hepatocellular glycogenated nuclei and Mallory bodies. It should however be noted that evidence remains inconclusive on whether liver biopsy should constitute an essential part of management of patients suspected of having NAFLD.[2] On the one hand, it provides histological diagnosis with useful information on the grade and stage of the disease. On the other hand, it is associated with a finite albeit small risk of complication, patient discomfort and costs. The value of liver biopsy is further limited by the lack of a definite effective treatment option, as discussed below.

Risk factors, pathogenesis and natural history of NAFLD

A number of retrospective and population studies identified obesity, type II diabetes mellitus and hypertriglyceridemia as the main risk factors of NAFLD. More recent work further demonstrates that NAFLD is a feature of insulin-resistance syndrome.[3, 4] As a result, NAFLD is increasingly considered part of a multifaceted metabolic disease that has insulin resistance as a common, primary factor, in addition to obesity, hypertension, and high triglyceride and low HDL-cholesterol concentrations. The importance of NAFLD in this so-called metabolic syndrome should not be underestimated. A recent study showed that in patients with type II diabetes, the standardized mortality rates for liver disease were even greater than those for cardiovascular disease.[5]

The pathogenesis of NAFLD is a subject of intensive research. Current opinions suggest that insulin resistance leads to accumulation of fat in liver (steatosis). A second hit by oxidative stress, free fatty acid toxicity and other injurious stimuli then result in necroinflammation (steatohepatitis) and fibrosis.[2] Further studies are undoubtedly needed to unravel the underlying cellular and molecular pathways.

The natural history of NAFLD and NASH is gradually being understood. Although no major prospective longitudinal clinical studies have been carried out, combined results from reports of small series provide useful hints. An important finding in recent years is that NAFLD may be an aetiological factor in cryptogenic cirrhosis and hepatocellular carcinoma (HCC). Poonawala et al. examined 65 patients with advanced cryptogenic cirrhosis and found that these patients were more likely to be obese or diabetic, the important risk factors of NAFLD.[6] Two studies published in 2002 provided evidence that NAFLD may be an importance cause of HCC in patients with underlying non-viral hepatitis related cirrhosis.[7, 8]

Research has also been performed to determine the predictors of more severe histological disease on the initial diagnostic biopsy. The most consistent factors that have been identified so far include age greater than 40 to 50 years, severity of obesity, diabetes or hypertriglyceridemia.[2] Elevation of aspartate transaminase (AST), alanine transaminase (ALT) and an AST:ALT ratio greater than 1 have also been reported as predictors of advanced disease. Nevertheless, a recent study also demonstrated that among NAFLD patients, the histological spectrum in individuals with normal ALT is not significantly different from those with elevated ALT levels.[9] More severe histological disease in initial biopsy in turn may predict progression of liver injury. In severe disease (presence of hepatocyte ballooning, Mallory bodies or fibrosis), the risk of progression to severe fibrosis is 25% and to cirrhosis is 15% over 5 years. Though by no means conclusive, patients with simple steatosis or steatosis with minimal inflammation are likely to have relatively stable disease without significant histological deterioration.

Treatment

There is no consensus on effective treatment of NASH. Therapeutic trials have mostly been conducted in uncontrolled settings with small sample size. Modification of clinical conditions associated with NASH appeared to be effective in some reported series. Weight loss in obese patients resulted in improvement of liver enzyme abnormality and degree of steatosis.[10] However, the optimal amount and rate of weight loss are still uncertain. Treatment trials using lipid-lowering drugs yielded mixed results. Use of insulin-sensitising agents like metformin or thiazolidinediones appeared to be promising but large randomised studies are needed to demonstrate the benefits convincingly.[2, 11]

Local perspective

In Asia, there has not been any comprehensive study on the clinical significance of NAFLD. Although chronic viral hepatitis is likely to remain the most important cause of chronic liver disease and cirrhosis in the foreseeable future, there is increasing circumstantial evidence to suggest that the prevalence of NAFLD will rise. Extensive research already showed an increasing incidence of type II diabetes in Hong Kong, partly related to improving affluence and Westernised life style. The latest age-standardised prevalence of undiagnosed diabetes and impaired glucose tolerance are 2.8% and 7.3% respectively, which are similar to the corresponding figures in the US.[12] Such secular trend has been faithfully translated into the rising incidences of cardiovascular disease and diabetic renal complication locally. Overweight and obesity is another problem associated with affluence. The cut-off values of body mass index (BMI) used to define overweight (25<BMI<23) and obesity (BMI>25) in Chinese are lower than those for Caucasians.[13] Using such cut-off values, the prevalence of these disorders was found to be similar to that of Western countries. The implication is that the Chinese population is perhaps just as likely to suffer from NAFLD and its complications as our Caucasian counterparts.

Conclusion

While significant progress has been made in our understanding of NAFLD in recent years, many issues remain unresolved. More research is needed especially on its pathogenesis, natural history and treatment. In Hong Kong, a project supported by a grant from HKSGE is currently underway to investigate the prevalence and natural history of the disease in our Chinese population. The data generated will serve to provide useful information and guidance in our management of local NAFLD patients in future.

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Highlights from The Annual General Meeting and Scientific Meeting 2004

Dr. Vincent Leung, Senior Medical Officer
Department of Medicine & Geriatrics, United Christian Hospital

March 23, 2004 (6:15-10:00 p.m.)
Ballroom, 3/F Sheraton Hotel & Towers

The Scientific Meeting began with a captivating presentation by our distinguished guest Prof. David Graham on *Helicobacter pylori and Gastric Cancer: The Problem – The Solution*. Members found the talk highly interesting and informative and raised a number of questions on the subject. Following this, Prof. Sung gave excitations on the outstanding work and contributions of Society's two new honorary fellows: Prof. S K Lam and Prof. David Y Graham and presented to each an honorary fellowship certificate.

The Interactive Digestive Disease Case Discussion: Two Patients with Variceal Bleeding formed the second half of the Scientific Meeting. It started with an introduction by Dr. Vincent Leung, the Organizing Chairman. There were two cases this year:

Case 1 from United Christian Hospital
A young lady with recurrent oesophageal variceal bleeding was presented by Dr. Chan Wai Hong. Dr. Li Ting Ho and Dr. Tsang Woon Choy were the panel discussants for this case.
Case 2 from Prince of Wales Hospital
A middle aged lady presented with melaena and fresh blood hemetemesis was presented by Dr. Hung Cheung Tsui. The two panel discussants were Dr. Lee Yuk Tong and Dr. Li Kin Kong.

Dr. Vincent Leung and Dr. Francis Mok were the panel co-chairmen for the case discussion session. The two cases : congential hepatic fibrosis (Case 1) and traumatic hepatic arterioportal fistula (Case 2), were well presented with good illustrations and usefully evaluated. Participants responded with great interest.

Eight exhibition booths by pharmaceutical companies were set up: Abbott Laboratories, Takeda, Altana Pharma, AstraZeneca, Eisai, GlaxoSmithKline, Roche and SciClone. Participants were interested in the exhibits and talked to the company representatives both at registration time and during recess.

The Annual General Meeting went very well. 59 members and fellows were present. Chairman and Hon. Treasurer reported briefly the important events and financial statements for 2003. Election of Council Members took place smoothly. 8 Council Members were elected.

It was a successful Scientific Meeting. About 300 doctors attended the scientific session. Majority of the participants stayed for the after-meeting dinner. As a token of thanks to contributing parties: the guest speaker, panel discussants, case presenters and the sponsors, this Society presented at dinner to each a souvenir in the form of a Society plaque. A presentation was also made to Society's retiring Councillor Professor S K Lam in appreciation of his long service in the Council and remarkable contributions for the past 22 years.

Sixth Joint Annual Scientific Meeting

Programme

Venue: Sheraton Hotel & Towers

Date & Time: October 9, 2004 (2:00-9:00 p.m.)

Co-organizers: The Hong Kong Society of Gastroenterology
Hong Kong Society of Digestive Endoscopy
Hong Kong Society for Coloproctology
The Hong Kong Association for the Study of Liver Diseases
The Hong Kong Society of Gastrointestinal Motility

Sessions:
Research Forum
CA Stomach
Colorectal Cancer
Hepatitis B

Co-sponsors: AstraZeneca GlaxoSmithKline

Welcome! New members & fellows

Honorary Fellow

Prof. David Y. Graham
VA Medical Center
Houston, USA

Prof. Lam Shiu Kum
Department of Medicine
Queen Mary Hospital

Fellow

Dr. Tsang Woon Choy Steven
Department of Medicine
Tseung Kwan O Hospital

Member

Dr. Li Wing Heng Simon
Department of Medicine
Pamela Youde Nethersole Eastern Hospital

Major Meetings

June 19-20, 2004
Advances in Medicine 2004
Organizer: Department of Medicine & Therapeutics, The Chinese University of Hong Kong
Location: Hong Kong Convention and Exhibition Centre
Website: http://cuhk.edu.hk/med/mect/aimProgramme.htm

July 3-7, 2004
2nd World Congress of Pediatric Gastroenterology Hepatology and Nutrition
Organizer: American Gastroenterological Association
Location: Paris, Francis
Website: www.gastro.org

July 15, 2004
The Evolution of PPI Therapy - an Ongoing Story
Organizers: The Hong Kong Society of Gastroenterology and Hong Kong Society of Digestive Endoscopy
Location: InterContinental Hotel
Website: www.hksge.org

2004年 8月16-19日
中日消化內鏡會議
組織者: 中華醫學會消化病學分會
地方: 廣西桂林
網址: www.csge.org

September 9-12, 2004
14th World Congress of the International Association of Surgeons, Gastroenterologists (and Oncologists)
Organizer: International Association of Surgeons, Gastroenterologists
Location: Zurich, Switzerland
Website: www.iasg2004.ch

September 18-19, 2004
Alimentary Disease Weekend
Co-organizers: Departments of Medicine and Surgery, The University of Hong Kong
Location: Cheung Kung Hai Conference Centre, Academic and Administration Block, Faculty of Medicine Building, The University of Hong Kong
Tel: (852) 2818 0232
Email: ADW2004@hku.hk

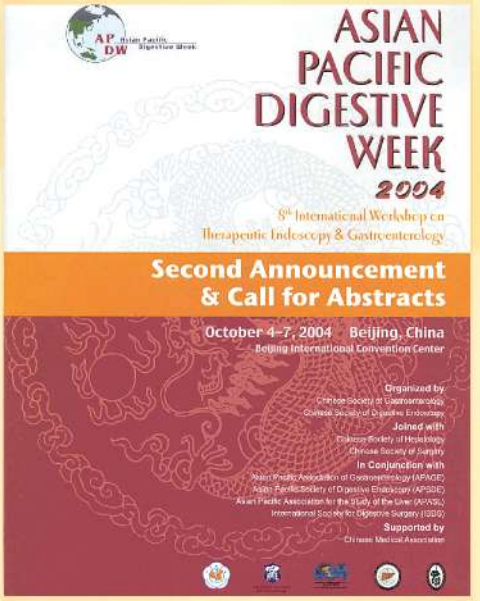
October 1-6, 2004
Annual Meeting of the American College of Gastroenterology (ACG)
Organizer: American College of Gastroenterology
Location: Orlando, Florida, USA
Website: www.acg.gi.org

October 4-8, 2004
Australian Gastroenterological Week
Organizer: Gastroenterological Society of Australia
Location: Brisbane, Australia
Website: www.gesa.org.au

October 9, 2004
6th Joint Annual Scientific Meeting
(Please see the programme on P. 6)

October 21-24, 2004
Digestive Disease Week
Organizer: The Japanese Society of Gastroenterology
Location: Fukuoka, Japan
Website: www.ddw.jp

October 29 - November 2, 2004
Annual Meeting and Postgraduate Course of the American Association for the Study of Liver Disease (AASLD)
Organizer: American Association for the Study of Liver Diseases
Location: Boston, Massachusetts, USA
Website: www.aasld.org



www.chinamed.com.cn/apdw2004

November 26-27, 2004
International Symposium on Hepatology 2004
Organizer: The Hong Kong Association for the Study of Liver Diseases
Location: Hong Kong Convention and Exhibition Centre

December 8-11, 2004
19th World Congress of International Society of Digestive Surgery (ISDS 2004)
Organizer:
International Society for Digestive Surgery
Location:
Website: Yokohama, Japan www.19isds.com

December 15-16, 2004
4th International Meeting of Hepatocellular Circinoma: Eastern and Western Experiences
Organizer: The Centre for the Study of Liver Disease, The University of Hong Kong, Queen Mary Hospital
Location: Hong Kong Convention and Exhibition Centre
Website: www.hcc-ewe.org

UNITED EUROPEAN GASTROENTEROLOGY FEDERATION
www.uegf.org

12th United European Gastroenterology Week in Prague, Czech Republic
September 25-30, 2004

APASL 04 India
www.apaslindia2004.com

Asian Pacific Association for the Study of the Liver Biennial Congress in Vigyan Bhawan, New Delhi, India
December 11-15, 2004

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