Hepatitis C - How to choose the right candidate for treatment? When should liver biopsy be performed?

Chee-Kin Hui, Annie OO Chan, George KK Lau
Department of Medicine, Queen Mary Hospital, Hong Kong

Hepatitis C virus (HCV) has an estimated prevalence of 3% in the general population all over the world. Epidemiological studies have shown that although 40% of these subjects are asymptomatic, they can still have significant histological lesions on liver biopsies. In Europe and the United States, HCV infection accounts for 20% of all cases of acute hepatitis, 70% of chronic hepatitis, 40% of decompensated cirrhosis, 25-60% of hepatocellular carcinoma and 30-40% of all liver transplantation [1].

The aims of chronic HCV treatment are to prevent liver failure and hepatocellular carcinoma, to stop the development of liver cirrhosis by arresting the progression or even the reversion of hepatic fibrosis and to improve general well-being. The best treatment for chronic HCV is combination pegylated interferon-α-2a (180 μg/week) or pegylated interferon-α-2b (1.5 μg/kg/week in genotypes 1 and 4 and 1 μg/kg/week in genotypes 2 and 3) plus ribavirin (800 mg/day for body weight <65 kg and 1000 mg/day for 65-85 kg and 1200 mg/day for >85kg patients). The treatment duration varies between 24 weeks for patients with genotype 2 or 3 and 48 weeks for patients with genotype 1, 4, 5 or 6. Continuation of therapy after 12 weeks of treatment for patients with genotype 1 should be based on whether a reduction of serum HCV RNA by more than 2 log drop at week 12 has been achieved. Therapy for patients with genotype 1 should be stopped if the decrease in serum HCV RNA at this time is less than 2 log drop.

Who should be treated?

Naive patients

Treatment is recommended for patients who are most likely to have progressive liver disease, such as those with persistently elevated serum alanine aminotransaminase (ALT) level, detectable serum HCV RNA level and portal fibrosis with moderate inflammation on liver biopsy. Currently, the accepted criteria for treatment are: (i) elevation of serum ALT level for at least 6 months, (ii) detectable serum HCV RNA, (iii) portal or bridging fibrosis and/or moderate liver inflammation, (iv) compensated liver disease, (v) good compliance to treatment and (vi) abstinence from alcohol and/or illegal drugs for more than 6 months before therapy and (vi) no contraindication for treatment (Table 1).
The need for histological assessment of fibrosis stage should be considered in patients with more than 10 years of infection and in whom serum ALT level is raised. From the results of studies on the natural history of chronic HCV, those with no (F0) or minimal (F1) fibrosis are very unlikely to develop major complications within 10-20 years, particularly if they are aged below 35 [2,3,4]. Therefore, if these patients are asymptomatic, then treatment is not required.

On the other hand, those with fibrosis stage F2 or F3 have a high risk of progression to cirrhosis, and usually progress to liver cirrhosis over a 10 year period [5]. These patients, therefore, has a strong indication for antiviral treatment. However, the need for a liver biopsy in patients who are infected with genotype 2 or 3 is debatable and some investigators have suggested that these patients can proceed to treatment without the need for a liver biopsy.

**Patients with normal ALT level**

The decision whether to treat patients with normal ALT level needs to be individualized and should take into account factors such as age, liver histology, extra hepatic manifestations of chronic HCV, comorbid states and patient motivation. Patients with HCV genotype 2 or 3 have excellent response rates and treatment should be considered in these patients, even if they have normal serum ALT level.

Furthermore, studies have shown that the outcome of patients with normal ALT level is not as benign as first suspected [6] and that 1 in 6 of chronic HCV patients with normal ALT level have evidence of significant, progressive liver disease that can only be identified by liver biopsy [7]. The results of these two studies suggests, that perhaps, liver biopsy should be considered in normal ALT level who have risk factors for non-alcoholic steatohepatitis, history of alcoholism, features of portal hypertension and co-infected with human immunodeficiency virus (HIV) in order to determine their fibrosis stage and need for antiviral therapy. The presence of these concomitant factors may be associated with an increase in the severity of liver disease.

**Cirrhotic patient**

This response of patients who have developed liver cirrhosis is lower. This may be due to intrinsic viral factors or the low amount of interferon given in the presence of leucopenia and thrombocytopenia. Pegylated interferon has been shown to be effective either as monotherapy or in combination with ribavirin [8]. One study has even shown that decompensated patients awaiting liver transplantation showed an on treatment viral response of 33% [9]. The consensus guideline from European Association for the Study of Liver Disease has recommended treatment for patients with fibrosis stage 4 in order to stabilize the disease and reduce the risk of hepatocellular carcinoma.

**Co-Infected patients**

Chronic HCV and HIV are usually associated with a more severe disease even in the presence of normal serum ALT level. It is also associated with a higher risk of hepatocellular carcinoma. Thus, patients with HCV-HIV co-infection are considered for therapy if their T4 lymphocytes are more than 350/mm3 with an HIV viremia of less than 30,000 copies/ml [10]. Co-infected patients should be treated for 48 weeks regardless of their genotypes. However, careful monitoring of adverse events must be undertaken.

### Summary

In summary, antiviral therapy should be considered for immunocompetent chronic HCV patients with F2 to F4 fibrosis. Liver biopsy should be considered in patients who have been infected for more than 10 years even in the presence of persistent normal serum ALT level.

### References


### Table 1. Contraindications to interferon and ribavirin.

<table>
<thead>
<tr>
<th>Antiviral</th>
<th>Absolute contraindications</th>
<th>Relative contraindications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interferon or pegylated interferon</td>
<td>Psychosis (present or past)</td>
<td>History of depression</td>
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<td></td>
<td>Severe depression</td>
<td>Hypertensive retinopathy</td>
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<td></td>
<td>Pregnancy</td>
<td>Psoriasis</td>
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<td></td>
<td>Poorly controlled seizure</td>
<td>Symptomatic heart disease</td>
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<tr>
<td></td>
<td>Poorly controlled diabetes mellitus</td>
<td>Autoimmune disorders</td>
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<td></td>
<td>Impaired marrow function</td>
<td>Neuromuscular disorders</td>
</tr>
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<td></td>
<td>Poor compliance to therapy</td>
<td>Anemia</td>
</tr>
<tr>
<td>Ribavirin</td>
<td>Renal failure</td>
<td>Risk factors for coronary artery disease</td>
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<td></td>
<td>Unstable heart disease</td>
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<td></td>
<td>Pregnancy</td>
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</tbody>
</table>

### Table 2. Physician’s checklist prior tocommencing hepatitis C virus antiviral therapy.

<table>
<thead>
<tr>
<th>Clinical</th>
<th>Laboratory</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full medical history</td>
<td>Hepatitis C virus RNA (qualitative PCR), genotypic and viral load (quantitative PCR)</td>
</tr>
<tr>
<td>Physical examination</td>
<td>Complete blood count</td>
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<tr>
<td>Cardiac evaluation if there is history suggestive of ischemic heart disease</td>
<td>Renal function</td>
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<td></td>
<td>Liver biochemistry</td>
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<td></td>
<td>Thyroid function tests (thyroid stimulating hormone)</td>
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<td></td>
<td>Fasting blood glucose</td>
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<td></td>
<td>Pregnancy test</td>
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</table>
Molecular genetics in GI cancers - Pathogenesis and clinical application

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INTRODUCTION

The human gut harbors approximately 20% of all cancers. In Hong Kong, cancers from the gastrointestinal tract accounts for half of the ten major causes of cancer deaths in the recent few years: liver, colon, and stomach cancer rank the second, third, and forth respectively. Colorectal cancer accounts for 9.3% of all newly diagnosed cancers and 7.8% of all cancer deaths between 1995 and 1996 in Hong Kong (1,2). Gastric cancer remains the second major cause of cancer related deaths in the world (3,4).

It is now widely accepted that cancer evolves through several histological stages: eg. adenoma-carcinoma sequence in colorectal cancer, the gastritis-intestinal metaplasia-dysplasia-adenocarcinoma sequence in gastric cancer. The morphological progression is associated with the accumulation of multiple genetic and epigenetic events. Understanding of the genetic changes along with the histological progression in carcinogenesis allows the discoveries of potential screening, monitoring and therapeutic strategies.

It is now increasingly recognized that epigenetic silencing of gene expression by CpG island methylation is an important alternative mechanism in inactivating tumor suppressor genes. Targeting at the epigenetic changes such as CpG island methylation that occur before the development of frank malignancy as chemopreventive intervention offers the maximal impact. Hence, our group is interested in the methylation changes in GI cancers. The current article summarizes the work from our group on genetic aspects in GI cancer, with emphasis on the work on CpG island methylation. In addition, the potential clinical applications from our studies are discussed.

COLORECTAL CANCER (CRC)

Hyperplastic polyps in CRC

Despite that hyperplastic polyps are frequently considered to be ‘bystander’ in colorectal carcinogenesis, there is growing recognition of the importance of an alternative pathway to sporadic CRCs in which serrated polyps, including HPs, are the precursor lesions. In addition, patients with hyperplastic polyposis, characterized by the presence of numerous HPs and/or large HPs, have increased risk of colorectal cancer (5). We studied CpG island methylator phenotype (CIMP) in hyperplastic polyps in patients with hyperplastic polyposis. We observed that there was concordant methylation status of hyperplastic polyps within the same patient (odds ratio, 5.92; P = 0.0001). Importantly, CIMP-high (two or more methylated loci) hyperplastic polyps were present primarily in patients with a predominance of hyperplastic polyps in the right colon and/or serrated adenomas (P = 0.0009), and were associated with the absence of K-ras proto-oncogene mutations (odds ratio, 5.08; P = 0.03) (5).

We also observed in another study that BRAF mutation was present in 43% of HPs (P = 0.01 versus sporadic HPs), 75% of serrated adenomas, and 33% of carcinomas from patients with hyperplastic polyposis. BRAF mutation status in patients with hyperplastic polyposis correlated with HPs from the same patient (odds ratio, 5.5; P = 0.0002) but associated with younger age (odds ratio, 0.83; P = 0.006 compared to older age), with a large HP (odds ratio, 22.5; P = 0.01), with location of HPs in the right colon (odds ratio, 3.0; P = 0.03), and with methylation of the p16 gene and the MINT31 locus [odds ratio, 12.2 (P = 0.0001) and 4.4 (P = 0.02), respectively] (6).

Aberrant crypt foci in CRC

We studied CpG island methylation in aberrant crypt foci (ACF) from patients with familial adenomatous polyposis (FAP) and those with sporadic colorectal cancer. The associations between CpG island methylation and ACF histopathology, K-ras proto-oncogene mutation, loss of heterozygosity at chromosome 1p, and microsatellite instability, respectively, were investigated. Methylation was more frequent in sporadic ACF than FAP ACF (P = 0.002), especially dysplastic sporadic ACF (P = 0.004). Strong associations of ACF methylation with K-ras mutation (P = 0.007) and with loss of chromosome 1p (P = 0.04) were observed in hyperplastic type ACF. Methylation was the only molecular abnormality identified in 16% (10 of 61) of ACF. Our findings suggest that methylation in ACF is an early event in the pathogenesis of a subset of colorectal carcinomas, and that ACF from FAP patients and patients with sporadic colorectal cancer have distinct epigenetic changes that reflect differences in molecular pathogenesis, with a subset of hyperplastic ACF in sporadic CRC characterized by dysplasia -ve, methylation +ve and K-ras mutation +ve (7).

The above two studies lead to the proposal of two alternative pathways for CRC, in addition to the dysplastic adenoma-carcinoma sequence (8). Firstly, there exists a ‘hyperplastic polyp-serrated poly-polypt-neoplasia pathway’, this appears to play particularly important role in the development of sporadic cancers with MSI. Secondly, a ‘hyperplastic ACF-adenoma-carcinoma’ pathway might also exist.

Potential clinical application: Gastroenterologists should be become aware of the presence of these alternative pathways as this poses important implication in the future development of screening and surveillance strategies (8, 9). Currently, stool DNA for CRC screening is being widely studied (9, 10). However, it is still not used clinically because of its low sensitivity. This may be partially explained by that the genetic changes that were being analyzed were mutations in K-ras, APC and p53 genes, and the microsatellite-instability marker BAT-26. On the other, our studies on ACF and hyperplastic polyposis showed that CpG island methylation is one of the earliest genetic changes. Hence, by detecting methylation change, in particular, using the methylation panel from our previous studies, in stool may increase the sensitivity of CRC screening. A large scale stool DNA study for CRC screening is currently under progress in our laboratory. The result will be available shortly.
Our studies on ACF and hyperplastic polyposis also pose further clinical questions on surveillance. Since a subset of hyperplastic polyps with molecular changes, especially those associated with serrated adenomas, may have the potential to progress into CRC, should these patients with hyperplastic polyps be surveyed like those with adenomas? Patients with hyperplastic ACF that are associated with methylation changes and K-ras mutation probably represent another high risk group, should these patients be subjected to routine colonoscopy screening? Further studies are needed to answer these questions to allow better CRC screening and prevention.

**Hormonal replacement therapy (HRT) and CRC**

Meta-analysis on evaluating the relation between current or recent HRT use and its effect on colorectal cancer have demonstrated a decreased risk in postmenopausal women, up to a 34% reduction (11). In a recent study evaluating sex, reproductive factors, and hormone exposure in relation to the presence or absence of MSI in tumors, women were found to be less likely then men to have MSI+ tumors at a young age and more likely to have unstable tumors at an older age. The data suggest that estrogen exposure in women protects against MSI, whereas the lack of estrogen in older women increases risk of instability. HRT in these older women may, again, reduce the risk of unstable tumors. In addition, HRT use was associated with a reduction in risk for recurrence of distal adenomas.

**Potential clinical application:** Methylation at ER in colonic mucosa increases as age increases. In addition, a possible relationship between CIMP and MSI exists. Western blot analysis revealed that malignant colon tissue showed a selective loss of ER-beta protein expression when compared to normal colon tissue in the same patient (12). Based on the above evidences, we postulated that reversing ER methylation is one of the possible mechanisms that could account for the protective effect of estrogen on colorectal cancer/adenoma. A study on the methylation analysis at ER beta in post-menopausal women receiving HRT is undergoing in our laboratory. Any positive finding will have potential impact on the future development of CRC chemoprevention.

**GASTRIC CANCER**

**Gastritis and intestinal metaplasia in gastric cancer**

E-cadherin was one the most important candidate gene in the development of gastric cancer (13). We investigated the change of E-cadherin complex expression along the Correa's cascade. We showed that the expression of E-cadherin and alpha- and beta-catenins decreased early in intestinal metaplasia and followed by a progressive decrease along the Correa's pathway (14). We subsequently showed that the early decrease in E-cadherin expression was likely to be due to the hypermethylation at the E-cadherin gene (15). Our study showed that methylation was present in 57% of intestinal metaplasia, 65% of the tumors lesions and 68% of the metastatic lymph nodes in patients with gastric cancer. The methylation status was highly concordant with the immunohistochemistry of E-cadherin result (15).

**Methylation at E-cadherin gene and Helicobacter pylori in gastric cancer**

In our previous study, we have shown that E-cadherin methylation was present in 37% of the gastric mucosa in patients with dyspepsia but without gastric cancer. We then investigated if there was any external factor associated with the methylation at E-cadherin gene in the gastric mucosa in these patients. Our study showed that methylation at E-cadherin gene was associated with H pylori infection by multivariate analysis (p=0.002), but was independent of the age of the patient or presence or absence of gastritis. We concluded that E-cadherin methylation is an early event in gastric carcinogenesis, and is initiated by H pylori infection (15).

In order to further confirm the etiologic role of H. pylori in causing methylation at E-cadherin gene, we performed a prospective randomized controlled trial. Patients with dyspepsia and H. pylori positive were randomized to receive H. pylori eradication therapy (Group 1, n = 41) or no treatment (Group 2, n = 40) and followed up prospectively. Gastric mucosae were taken for methylation assay at Week 0 (before treatment) and Week 6 (after treatment). Methylation at E-cadherin was detected in 46% (19/41) and 17% (7/41) at Week 0 and 6, respectively in Group 1 (P = 0.004). 78.9% (15/19) specimens turned unmethylated after eradication of H. pylori. Methylation was detected in 47.5% (19/40) and 52.5% (21/40) at Week 0 and 6, respectively in Group 2 (P = 0.5). On the other hand, there was no difference in methylation frequency at E-cadherin in intestinal metaplasia with or without the presence of H. pylori (16).

**Potential clinical application:** It has been demonstrated that H. pylori eradication therapy may be protective for the development of gastric cancer in patients without precursor lesions, but not in patients with the presence of precursor lesions (17). Our methylation study in gastric cancer may partially explain the observation. In addition, eradicating H. pylori in every patient may not be cost-effective to prevent gastric cancer (18, 19). Targeting the subset population with the presence of E-cadherin methylation but without advanced precursor lesions may enhance the cost-effectiveness.

**Interleukin 1 beta polymorphism, methylation and H. pylori in gastric cancer**

It has been reported that patients with polymorphisms in IL-1B gene (carriers of IL-1B-511T) and in the IL-1 receptor antagonist gene (IL-1RN*2/2) were found to be associated with an increased risk of gastric cancer (20). It has also been shown that IL-1B-511T carriers (IL-1B-511T/T or IL-1B-511T/CT) homozygous for the short allele of IL-1RN (IL-1RN*2/2) associating with vacAs1-, vacAam1-, and cagA-positive strains of H. pylori had an increased gastric cancer risk (21). On the other hand, it has been reported that methylation-dependent gene silencing can be induced by interleukin 1 beta via the action of nitric oxide (22). Therefore, we postulated that the association of H. pylori infection and methylation at E-cadherin could be explained by the fact that patients with interleukin 1β polymorphism and infected with H. pylori will have up-regulation of interleukin 1β, which will lead to the production of nitric oxide and the subsequent activation of DNA methyltransferase, hence induce E-cadherin gene methylation (23).

**Potential clinical application:** We are currently investigating the association among methylation pattern, interleukin 1β polymorphism and H. pylori in patients with chronic gastritis. Potentially, this may be a targeted group for screening for future development of gastric cancer, if any association can be identified.

**Soluble E-cadherin in gastric cancer**

Soluble E-cadherin was found in the circulation of normal subjects, but was found to be markedly elevated in patients with cancers (13).

**Potential clinical application:** We investigated the clinical application of soluble E-cadherin as a prognostic factor in patients with gastric cancer. We found that soluble E-cadherin concentrations were significantly more elevated in patients with gastric cancer than healthy subjects (p = 0.0001), and in palliative/inoperable cancers than operable cancers (p = 0.012). The concentrations correlated with tumor size (p = 0.017). The cut-off value calculated from discriminant analysis.
on the operability and inoperability/palliative treatment was 7221 ng/ml. Soluble E-cadherin concentration higher than this cut-off value predict lymph node (N2) metastasis (p = 0.039, C.I. 1.008-1.902) and palliative/inoperable tumors (p = 0.027, C.I. 1.042-2.719) (24).

We further investigate the long term prognostic value of soluble E-cadherin. We found that on multivariate analysis, soluble E-cadherin is an independent factor predicting long-term survival. Ninety percent of patients with serum level of E-cadherin greater than 10000 ng/ml had survival less than 3 years (P = 0.006) (25).

We also analyzed if soluble E-cadherin could predict tumor recurrence in patients received curative resection of gastric cancer. We prospectively followed up these patients. Median follow up of the patients with (n = 14) and without recurrence (n = 58) were 24 and 36 months, respectively (p = 0.007). The optimal cut-off level of E-cadherin was 10.000ng/ml. The sensitivity in the prediction of recurrence using this value at months 3 and 6 post-operation were 50% and 64% respectively, significantly better than that of CEA using conventional cut-off (14% and 14%, p = 0.039 and p = 0.005 respectively). The median time between the elevated E-cadherin level and documented disease recurrence was 12 months (range, 4 to 20 months), as compared to 4 months (range, 1 to 20 months) for CEA. The early prediction of tumor recurrence by soluble E-cadherin allows time for vigilant surveillance or chemotherapy (26).

OTHER GASTROINTESTINAL TUMORS

Duodenal and biliary tumors

Duodenal carcinomas were more frequently methylated than biliary carcinomas at p14, MGMT, MINT1, MINT25, MINT27, RARj, and ER, and than ampullary carcinomas at p14, RARj, and ER. In contrast the methylation profiles of biliary and ampullary carcinomas were not different. Site-specific concordant methylation of different sets of genes and loci was present in bile duct and duodenal cancers suggesting the presence of a hypermethylator phenotype. MGMT methylation was associated with G-to-A mutation in K-ras (P = 0.001) and p53 (P = 0.048), and hMLH1 methylation was associated with MSI-high (P = 0.001). Our findings indicate that the methylation profile and genetic alterations of duodenal carcinomas are distinct from biliary and ampullary carcinomas, and that tumor-specific concordant methylation influences gene mutations and MSI-high (27).

Carcinoid and pancreatic endocrine tumors

Carcinoid tumors were frequently methylated at RARj, MGMT, p16, COX2, p14, THBS1, and ER ranging from 25% to 63% of tumors. By contrast, PETs and normal pancreas were frequently methylated only at ER. Methylation was more frequent in carcinoid tumors than PETs at MGMT, THBS1, p14 and RARb, respectively. Our study indicates that methylation profile of carcinoid tumors differs from PETs, reflecting different molecular pathogenesis (28).

CONCLUSION

Our series of molecular studies on GI cancer demonstrated an understanding of molecular alterations in the morphological progression, interaction between methylation, environment and other molecular changes; and offers potential clinical application.
Scientific Meetings

Annual General Meeting & Scientific Meeting 2005

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

March 21, 2005 (6:15-10:00 p.m.)
Ballroom, 3/F Sheraton Hotel & Towers

On behalf of The Hong Kong Society of Gastroenterology, Dr. Szeto Ming-leung, the President of the Society, welcomed all participants to the Scientific Meeting, and started the meeting with the presentation of Honorary Fellowship Certificates to two distinguished guests, Prof. Roy Pounder from the United Kingdom, and Prof. Hu Pin-jin from China. Prior to this, the President and Dr. Benjamin Wong commended Prof. Pounder and Prof. Hu on their outstanding work and contributions to the field of gastroenterology. The two Professors thanked the Society for the honour given to them, and undertook to continue their best to promote the advancement of gastroenterology in Hong Kong and in other places.

Afterwards, two stimulating and enlightening presentations entitled Gastroenterology - now you see it, now you don’t and NERD - known and unknown were delivered by Prof. Pounder and Prof. Hu respectively. Participants took an active role in the following discussions led by Dr. Vincent Leung, the Organizing Chairman of the Meeting, and raised a number of thought-provoking questions on each topic. Doctors and medical professionals who attended the Meeting found the scientific updates generally very interesting and useful. About 200 participants attended this highly successful scientific meeting.

The subsequent EGM and AGM were attended by 55 members. A special resolution was passed at the EGM. At the AGM, Chairman and Hon. Treasurer reported the Society’s activities and its budget for the year 2004. These were endorsed. A election then took place. Four members were successfully elected to the Council for the period 2004-06.

Eight exhibition booths by pharmaceutical companies were set up. These included Abbott Laboratories, Alanta Pharma, AstraZeneca, Eisai, GlaxoSmithKline, Roche, Takeda, and Novartis. In appreciation of their support, a Certificate of Appreciation from the Society was presented to each of the sponsors. A Society plaque was also presented to Dr. Mok Puk Tim, the retiring Councillor, in appreciation of his outstanding service and contributions in the past 12 years.

Majority of the participants stayed for dinner during which informal discussions and exchange of views continued. It was a remarkable evening for all who attended the Scientific Meeting and AGM 2005.

Advances in Clinical Management of Upper Disorders

Dr. Hui Wai Mo, Specialist (Gastroenterology)

April 25, 2005 at 7:30 p.m. in Ballroom, JW Marriott

Co-organizer: The Hong Kong Society of Gastroenterology
Hong Kong Society of Digestive Endoscopy

Co-Chairmen: Dr. Hui Wai Mo
Dr. James Y W Lau

Sponsor: AstraZeneca

This meeting was well attended. 3 stimulating lectures were presented. These included GERD - Defining the Standards of Management, Strategic Questions in Management of Bleeding Peptic Ulcers and Aspirin and Coxibs: Balancing Risks and Benefits by Dr. Benjamin Wong, Prof. Joseph Sung and Dr. Francis Chan respectively.

Participants found the topics highly interesting and useful.

They took part actively in the panel discussion, exchanging views and raising a number of questions for thoughts. Majority of the 200 participants stayed and enjoyed the after-meeting dinner. The event was a successful one.

Seventh Joint Annual Scientific Meeting

Date & Time : August 27, 2005 (2:00 - 9:00 p.m.)
Venue : Sheraton Hotel & Towers
Co-organizer : The Hong Kong Society of Gastroenterology
Hong Kong Society of Digestive Endoscopy
Hong Kong Society of Coloproctology
The Hong Kong Association for the Study of Liver Diseases
The Hong Kong Society of Gastrointestinal Motility

Research Forum:
NASH
Acid suppression vs dupidogrel

Presentation:
Investigation for esophageal dysmotility
GERD
Advances in esophageal cancer therapy
(chemoradiation vs surgery)
Non-alcoholic Fatty Liver Disease
Lamivudine for HBV Cirrhosis
RFA vs Liver resection for HCC
Obesity - endoscopy & surgery
Surgical management of hilar cholangiocarcinoma
Role of enteroscopy in small bowel diseases
### Honorary Fellow

- **Prof. Hu Pin Jin**  
  Department of Gastroenterology  
  The First University Hospital  
  Sun Yat Sen University, Guangzhou, China

- **Prof. Roy Pounder**  
  Professor of Medicine  
  Royal Free & University College Medical School  
  University College London, UK

### Fellow

- **Dr. Cheung Ting Kin**  
  Specialist in Gastroenterology and Hepatology  
  Private Practice

- **Dr. Hung Hui Gong**  
  Department of Medicine & Geriatrics, Tuen Mun Hospital

- **Dr. Ng Ching Yan Annie**  
  Department of Medicine & Geriatrics, Caritas Medical Centre

### Member

- **Dr. Chan Wai Hong**  
  Department of Medicine, United Christian Hospital

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### Major Meetings

#### June 23-25, 2005
- **2nd International Congress on Gastrointestinal Oncology**
  Organizer: Hellenic Society of Gastrointestinal Oncology
  Location: Santorini Island, Greece  
  Website: www.gi- oncology.com

#### July 7-9, 2005
- **5th Shanghai International Conference of Gastroenterology**
  Organizer: Shanghai 2nd Medical University Renji Hospital, Shanghai Institute of Digestive Disease, John Hopkins University GI Department  
  Location: Shanghai International Convention Center, China

#### July 8-9, 2005
- **Hong Kong Surgical Forum - Summer 2005**
  Organizer: Department of Surgery, The University of Hong Kong, Queen Mary Hospital  
  Location: SFE, Lecture Theatre, Professorial Block, Queen Mary Hospital  
  Website: www.hku.hksurgery

#### July 16-17, 2005
- **10th HK Medical Forum**
  Organizer: Department of Medicine, Faculty of Medicine, The University of Hong Kong, Queen Mary Hospital  
  Location: Rm 201, 2/F., New Wing, Hong Kong Convention & Exhibition Centre  
  Website: www.hku.hk/medicine

#### August 17-19, 2005
- **7th Asia Pacific Congress of Endoscopic Surgery (ELSA 2005)**
  Organizer: Endoscopic & Laparoscopic Surgeons of Asia Hong Kong Society of Minimal Access Surgery, The Chinese University of Hong Kong  
  Location: Hong Kong Convention and Exhibition Centre  
  Website: www.elsa2005.org

#### August 19-21, 2005
- **Asian Pacific Association for the Study of the Liver (APASL) 2005 Conference**
  Organizer: Asian Pacific Association for the Study of the Liver (APASL)  
  Location: Jakarta, Indonesia  

#### August 27, 2005
- **7th Joint Ann. Scientific Meeting**
  The Hong Kong Society of Gastroenterology, The Hong Kong Society of Digestive Endoscopy, The Hong Kong Society of Gastrointestinal Motility, The Hong Kong Association for the Study of Liver Diseases and Hong Kong Society for Coloproctology  
  Location: Sheraton Hong Kong Hotel & Towers  
  Website: www.hksage.org

#### September 28-30, 2005
- **6th International Meeting on Therapy in Liver Diseases**
  Organizer: Oasis, Viajes  
  Location: Barcelona, Spain  
  Website: www.viajesoasis.com/en/index.asp

#### October 5-8, 2005
- **Digestive Disease Week Japan**
  Location: Kobe, Japan  
  Website: www.ddw.jp

#### October 19-22, 2005
- **Australian Gastroenterological Week**
  Organizer: Gastroenterological Society of Australia  
  Location: Brisbane, Australia  
  Website: www.agw2005.com

#### November 25-26, 2005
- **International Symposium on Hepatology 2005**
  Organizer: The Hong Kong Association for the Study of Liver Diseases  
  Location: Hong Kong Convention & Exhibition Centre  
  Enquiry: CMP Medics Pacific Ltd.  
  Tel: +65 2259 5888  Fax: +65 2259 6910

#### December 5-8, 2005
- **20th International Workshop on Therapeutics Endoscopy**
  Organizer: The Chinese University of HK, HK Society of Digestive Endoscopy  
  Location: Shaw Auditorium Postgraduate Education Centre, Prince of Wales Hospital  
  Website: www.surgery.chem.eduhk/events.htm

#### December 8-10, 2005
- **12th Hong Kong International Cancer Congress & 2nd Annual Meeting of Research Centre of Cancer**
  Location: Faculty of Medicine Building, The University of Hong Kong, Pokfulam Road, Hong Kong  
  Website: www.hkcic.org

#### September 25-28, 2005
- **Asian Pacific Digestive Week**
  Website: www.apdx2005.org

#### September 10-14, 2005
- **World Congress of Gastroenterology in Montreal, Canada**
  Website: www.wcog2005.org

#### October 15-19, 2005
- **13th United European Gastroenterology Week in Copenhagen-Malmö**
  Website: www.uegf.org