Gastroenterology and Hepatology
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### The Cover Shot

The solitary worshipper walks in quiet solitude across the grand halls of Istanbul’s St Sophia Cathedral, now a mosque. As he hold a steady pace, he is praying to god.

The many candlelights highlight the grandeur of this house of worship.

f8, 1/50sec, ISO 800, at 55mm

Dr. Amy LM PANG  
MBBS(HK),  
FRCR, FHKCR,  
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Specialist in Radiology

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The Lone Faithful
In this issue, we have picked some hot topics in gastroenterology and hepatology for review. Dr. Benjamin CY Wong wrote on the update in H. pylori infection and the available options when resistance was encountered. Dr. James YY Fung took a review on the current management of chronic HCV infection, and the new therapeutics for non-responders. Prof. Bernard MY Cheung summarised the current indications and concerns regarding proton pump inhibitors. Prof TP Poon highlighted the various treatment modalities on inoperable hepatocellular carcinoma.

Common GI symptoms and diseases could be managed in the primary care setting. We need to apply evidence based medicine to patient care. Judicious use of clinical care research results is important in the management of individual patients.

In this issue there is an invited article by Prof. Geoffrey Lieu on the Healthcare Reform Second Stage Public Consultation. A voluntary and Government-regulated Health Protection Scheme (HPS) is proposed. The HPS aims to provide more choices with better protection in private health insurance and private healthcare services. The deadline of the consultation is 7 Jan. 2011. Your views may be given to these contacts: Email: mychoice@fhb.gov.hk and Website: www.MyHealthMyChoice.gov.hk.
Triad of Neuropathic Pain

3 Different Problems
1 Simple Solution

**LYRICA**

- **Pain**
- **Sleep**
- **Anxiety**

---

**Advanced Treatment for Neuropathic Pain**
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**A New Class for Generalized Anxiety Disorder (GAD)**
Rapid relief of both psychic and somatic symptoms at week 1

**Novel Sleep Architecture Benefits**
Significantly reduced sleep onset latency and increased slow-wave sleep proportion compared with placebo

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*Symptoms of neuropathic pain

References:

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Pfizer Corporation Hong Kong Limited

Total Pain Management

Lyrica®
Pregabalin
Proton Pump Inhibitors – a Sting in the Tale?

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This article has been selected by the Editorial Board of the Hong Kong Medical Diary for participants in the CME programme of the Medical Council of Hong Kong (MCHK) to complete the following self-assessment questions in order to be awarded one CME credit under the programme upon returning the completed answer sheet to the Federation Secretariat on or before 31 December 2010.

Why then, can one desire too much of a good thing? William Shakespeare, ‘As You Like It’

The proton pump inhibitors (PPIs) are potent inhibitors of gastric acid production. Omeprazole was the first PPI introduced. Subsequently, lansoprazole, pantoprazole, rabeprazole and the S-enantiomer of omeprazole became available. As they suppress acid more efficaciously than H2-receptor antagonists, they are now widely used for the treatment of conditions such as peptic ulcer disease,1,2 gastro-oesophageal reflux disease (GERD),3 nonsteroidal anti-inflammatory drug (NSAID)-induced gastrointestinal lesions,4,5 Zollinger-Ellison syndrome, dyspepsia and, together with two antibiotics, eradication of Helicobacter pylori infection.6

PPIs are more expensive than H2-receptor antagonists; the current difference in price is about 10-fold. Therefore, cost-effectiveness could be an issue. While PPIs are superior to H2-receptor antagonists in the resolution of symptoms and healing of ulceration,7 there are not much significant differences among different PPIs.7,8 In high risk patients with peptic disease, e.g. a patient with fresh melaena, PPI given intravenously has been shown to be effective in downstaging the endoscopic lesion and decreasing the need for endoscopic intervention.7 Intravenous PPI reduces rebleeding and mortality after endoscopic treatment.7 Complicated peptic diseases should also be treated with a course of PPI for 6-8 weeks. In uncomplicated helicobacter-negative peptic disease, an H2-receptor antagonist may suffice, with PPI as second line treatment if the ulcer fails to heal after 8 weeks. PPI is also used for the prevention of gastrointestinal bleeding in patients on long term NSAIDs and aspirin (table 1).1,3

In general, PPIs are very well tolerated. Side-effects are uncommon and usually minor. However, there are recent concerns about osteoporotic fractures, susceptibility to infections and interaction with clopidogrel diminishing its antiplatelet effect.

The suppression of gastric acid by a PPI can be up to 99%. While this facilitates the healing of ulcers and reduces the pain due to acid in the stomach or oesophagus, the lack of gastric acid, hypochlorhydria, may affect the digestion of proteins and the absorption of vitamin B12 and calcium. It is also thought that insufficient acid may lead to bacterial overgrowth and increase the risk of pneumonia.10 Therefore, it has been suggested that patients at high risk of pneumonia should be prescribed PPI only when necessary and at a lower dose.11 Similarly, prolonged treatment with a PPI may increase the risk of Clostridium difficile infection substantially.12

There are also concerns that prolonged use of PPIs might cause osteoporosis and increase the risk of fractures of the hip, wrist, and spine. In a study of 135,000 people aged 50 or above, those taking high doses of PPI for longer than a year were 2.6 times more likely to have sustained a hip fracture.13 The risk of a fracture increases with dose and duration. The precise reasons for this are unclear, but it is thought that a rise in pH may reduce the solubility of calcium and consequently its absorption. The Food and Drugs Administration of the United States has requested a change in the drug labelling to include the possible increased risk of fractures.14

Table 1A. Patients at increased risk of gastrointestinal toxicity due to NSAID

<table>
<thead>
<tr>
<th>Risk Group</th>
<th>Gastrointestinal complication</th>
</tr>
</thead>
<tbody>
<tr>
<td>High risk</td>
<td>Gastro-oesophageal reflux</td>
</tr>
<tr>
<td>Moderate risk (1-2 risk factors)</td>
<td>Gastro-oesophageal reflux</td>
</tr>
<tr>
<td>Low risk</td>
<td>Gastro-oesophageal reflux</td>
</tr>
</tbody>
</table>

Adapted from American College of Gastroenterology Guidelines for prevention of NSAID-related ulcer complications15

Table 1B. Summary of recommendations for prevention of NSAID-related ulcer complications

<table>
<thead>
<tr>
<th>Gastrointestinal risk</th>
<th>Low</th>
<th>Moderate</th>
<th>High</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low cardiogenic risk</td>
<td>NSAID alone (the least ulcerogenic)</td>
<td>NSAID + PPI/ misoprostol</td>
<td></td>
</tr>
<tr>
<td>High cardiogenic risk</td>
<td>Misoprostol required)</td>
<td>NSAID + PPI/ misoprostol</td>
<td></td>
</tr>
<tr>
<td>Alternative therapy</td>
<td>if possible or COX-2 inhibitor + PPI/ misoprostol</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Avoid NSAIDs or COX-2 inhibitors. Use alternative therapy.
The interaction of PPI with clopidogrel has come under the spotlight recently. Clopidogrel is an antiplatelet agent that has a marginally superior cardiovascular outcome and better gastrointestinal side-effect profile compared to aspirin. It is used together with aspirin in acute coronary syndrome and after percutaneous coronary intervention. Clopidogrel is inactive and requires metabolism by cytochrome P450 enzymes to achieve its therapeutic effect. People with a variant in CYP2C19 metabolise clopidogrel poorly and therefore the antiplatelet effect is diminished. In Hong Kong, about 18% of the population are poor metabolisers in this respect. Patients on long term clopidogrel, especially those also taking aspirin, may require an acid suppressing agent. In this situation, a PPI could be hazardous as it might block the metabolism of clopidogrel into its active form. This can lead to an increase in the risk of myocardial infarction. Whereas similar findings were observed only in retrospective studies, other post hoc analyses, prospective studies and a randomised controlled trial revealed no increase in major cardiac events related to cotherapy. In the face of conflicting evidence, the current recommendation is not to use PPI in a patient on clopidogrel unless it is essential to do so. If PPI is indicated, then a PPI with a lower likelihood of interaction should be considered, as the potential for interactions among these agents varies. Omeprazole and esomeprazole are metabolised mainly via CYP2C19 and therefore have the highest potential for interaction. Rabeprazole is also metabolised via this isoenzyme, but possesses significant affinity for CYP3A4 resulting in fewer clinically significant interactions. Pantoprazole, on the other hand, is primarily metabolised via CYP2C19 O-demethylation rapidly followed by sulfate conjugation. As a result, pantoprazole has the lowest potential for P450 metabolism and drug-drug interaction and should be the preferred PPI for patients on clopidogrel. Ticagrelor and prasugrel, two new antiplatelet drugs, do not require metabolism to be active and may have an advantage over clopidogrel if they are proven to be clinically as effective. Like all drugs classified as poisons, PPIs carry risks as well as benefits. In the United States, they are the third best-selling class of drugs, suggesting a large degree of overprescribing. The appropriate use of PPIs should be promoted. This would include using alternative drugs for dyspepsia and uncomplicated peptic ulcer disease, and limiting the duration of PPI treatment.

References

23. Ho PM, Maddox TM, Wang L, Fihn SD, Jesse RL, Peterson ED, Rumsfeld JS. Risk of adverse outcomes associated with concomitant use of clopidogrel and proton pump inhibitors following acute coronary syndrome. JAMA 2009;301(9):937-44.
MCHK CME Programme Self-assessment Questions

Please read the article entitled “Proton Pump Inhibitors – A Sting in the Tale?” by Prof. Bernard M.Y. Cheung, Dr. Ivan F.N. Hung and Dr. S.Y. Wong and complete the following self-assessment questions. Participants in the MCHK CME Programme will be awarded 1 CME credit under the Programme for returning completed answer sheets via fax (2865 0345) or by mail to the Federation Secretariat on or before 31 December 2010. Answers to questions will be provided in the next issue of The Hong Kong Medical Diary.

Questions 1-10: Please answer T (true) or F (false)

1. Proton pump inhibitors (PPIs) suppress acid more efficaciously than H2-receptor antagonists (H2RAs).
2. PPIs and H2RAs are equally effective in symptom resolution and ulcer healing.
3. Intravenous PPIs or H2RAs have shown to be equally effective in down staging endoscopic lesions and decreasing the need for endoscopic intervention.
4. PPIs and H2RAs are commonly used for the prevention of GI bleeding in patients on long term NSAIDs and aspirin. They are of similar efficacy.
5. Prolonged treatment with PPIs may increase the risk of C. difficile infection substantially.
6. The risk of pneumonia is not related to the degree of gastric acid suppression.
7. Prolonged use of PPIs might increase the risk of fractures.
8. The risk of fracture increases with dose and duration of PPIs.
9. Concomitant use of an PPI and clopidogrel could be hazardous as PPIs might block the metabolism of clopidogrel into its active form.
10. Pantoprazole has the highest potential for P450 metabolism.

PROTON PUMP INHIBITORS – A STING IN THE TALE?

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HKID No.: ________________________________
HKDU No.: ________________________________
Contact Tel No.: ________________________________
CDSHK No.: ________________________________

Answers to November 2010 Issue

Update on Management of Helicobacter Pylori Infection

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Introduction

The discovery of Helicobacter pylori led to the award of the Nobel Prize to two scientists Dr Robin Warren and Dr Barry Marshall in 2005. Although there has been intense research on this bacterium which affects half of the world’s population, there are still areas of controversy and the ideal simple regime of treatment is yet to come. This article summarises some of the important issues related to indication, diagnosis and treatment of H. pylori.

Indications

Three indications for treatment are supported by definite evidence with clinical benefits (Table 1). Most physicians are aware of these conditions. Patients with active or past history of gastric or duodenal ulcers with or without ulcer complications (bleeding, perforation, gastric outlet obstruction) should be tested for H pylori, and if positive, be treated. The treatment not only heals the ulcer but will prevent relapse of the ulcer in the long run. Patients with gastric MALT lymphoma and those with early gastric cancer after endoscopic or surgical resection should also be tested and treated if positive.

Table 1. Indications for treatment

<table>
<thead>
<tr>
<th>Definite evidence of clinical benefits</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Active or past history of gastric and/or duodenal ulcers/ erosions, with or without complications</td>
</tr>
<tr>
<td>2. Gastric mucosa-associated lymphoid tissue (MALT) lymphoma</td>
</tr>
<tr>
<td>3. Early gastric cancer after resection</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Supportive evidence of clinical benefits</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Gastric cancer prevention in high risk populations</td>
</tr>
<tr>
<td>2. Uninvestigated dyspepsia</td>
</tr>
<tr>
<td>3. Functional dyspepsia</td>
</tr>
<tr>
<td>4. Patients’ wishes</td>
</tr>
<tr>
<td>5. Family history of gastric cancer</td>
</tr>
<tr>
<td>6. Atrophic gastritis</td>
</tr>
<tr>
<td>7. Patients on aspirin or non-steroidal anti-inflammatory drugs</td>
</tr>
<tr>
<td>8. Patients with GERD requiring long term proton pump inhibitors</td>
</tr>
<tr>
<td>9. Other intestinal and extra-intestinal diseases: unexplained iron deficiency anaemia, idiopathic thrombocytopenic purpura, lymphocytic gastritis, gastric hyperplastic polyps, Menetrier’s disease</td>
</tr>
</tbody>
</table>

Other indications are not so well supported, including patients with atrophic gastritis or intestinal metaplasia, patients with gastro-oesophageal reflux disease requiring long term proton pump inhibitors, and those with extra-intestinal diseases as listed in Table 1.

Diagnosis

The choice of test for pre-treatment or never treated patients consists of non-invasive tests and invasive tests (Table 2). The non-invasive tests include carbon-13 urea breath test, serology for anti-H. pylori antibody, stool for H. pylori antigen, and urine for anti-H. pylori antibody. The invasive tests used during an upper endoscopy and biopsy include rapid urease test [with the commercial CLO test most commonly used], histology, culture, and polymerase chain reaction, with the later two very seldom performed.

Table 2. Diagnostic tests for Helicobacter pylori infection

<table>
<thead>
<tr>
<th>Principle</th>
<th>Post-treatment</th>
<th>Cost*</th>
<th>Near patient testb</th>
<th>Remarksb</th>
</tr>
</thead>
<tbody>
<tr>
<td>Invasive Tests</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Rapid urease test</td>
<td>urease activity</td>
<td>+/-</td>
<td>+++</td>
<td>Yes</td>
</tr>
<tr>
<td>2. Histology</td>
<td>pathology assessment</td>
<td>+</td>
<td>+++</td>
<td>No</td>
</tr>
<tr>
<td>3. Culture</td>
<td>microbiology</td>
<td>+</td>
<td>+++</td>
<td>No Antibiotic sensitivity</td>
</tr>
<tr>
<td>4. PCR</td>
<td>genome</td>
<td>+</td>
<td>+++</td>
<td>No Research</td>
</tr>
<tr>
<td>Non-invasive Tests</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. 13C-Urea breath test</td>
<td>urease activity</td>
<td>+</td>
<td>++</td>
<td>Yes/No</td>
</tr>
<tr>
<td>2. Stool</td>
<td>Hp Antigen</td>
<td>+</td>
<td>+</td>
<td>No</td>
</tr>
<tr>
<td>3. Serology</td>
<td>Hp antibody</td>
<td>-</td>
<td>+</td>
<td>No Need validation</td>
</tr>
<tr>
<td>4. Whole blood</td>
<td>Hp antibody</td>
<td>-</td>
<td>+</td>
<td>Yes Need validation</td>
</tr>
<tr>
<td>5. Urine</td>
<td>Hp antibody</td>
<td>-</td>
<td>+</td>
<td>Yes Need validation</td>
</tr>
</tbody>
</table>

a. Cost of invasive tests includes cost of upper endoscopy.
b. Near patient test means test that can be done within the doctor’s office and can provide immediate result.
c. Tests that rely on antibody need to be locally validated in Hong Kong. The accuracy may vary widely.

The method of choice for non-invasive tests include urea breath test and stool antigen test. The serology tests rely on the accuracy of the test kit and not all test kits perform with the same accuracy. These tests are based on the ELISA method that requires the use of antigen epitopes from H pylori during production. Unfortunately H pylori from different countries or races have very diverse genomic variations. So some of the tests manufactured in USA or Europe based on Caucasian H pylori strains yield a very low accuracy for testing in Hong Kong12. The other form of serology test is the whole blood near patient test. The test uses only one drop of blood to be placed onto the test kit and the
The method of choice for invasive tests include the rapid urease test and histology. Since the density of H pylori in the gastric antrum is the highest in normal patients without drugs, an antral biopsy is usually taken. However in patients on proton pump inhibitors, there is reduced density of H pylori in the antrum but with a higher density in the body and fundus. Therefore patients on PPIs should have biopsies from both the antrum and body to increase the accuracy.

Recent intakes of PPIs and/or antibiotics produce false negative results for all tests except serology. False negative tests may result from these drugs that suppress bacterial growth. PPIs should be stopped at least 2 weeks before performing the tests. Nowadays more and more patients are already receiving long term PPIs and cannot be withheld for various reasons. In this case, a locally validated serology test should be used.

Post-treatment testing is generally performed 4-8 weeks after stopping all PPIs and antibiotics, the longer the better. Hence if there is no urgent need to perform the test, it should be done at 8 weeks after stopping treatment. For patients who have used both bismuth and PPIs in the treatment regime, most commonly in a second line treatment of H pylori, the test should be performed 8-12 weeks after stopping treatment, preferably 12 weeks. The test of choice is the urea breath test. An alternative is the stool Hp antigen test. Serology tests should never be used in post-treatment testing, as the antibody level will only be decreasing slowly despite successful treatment. In post-treatment testing for patients on long term PPIs, we still should not use serology test for the above mentioned reason. There is no single best method for these patients and clinical judgement is required in each scenario.

### Treatment

#### Standard First Line Treatment

For years, the use of triple therapy is the gold standard for first line treatment of H pylori infection. There are several recent guidelines with detailed description of the different regimens. In principle, the eradication rate of any first line regimen should be above 90% by per protocol analysis (PP), or 80% by intention to treat analysis (ITT). The best regimen for most Asian countries is probably a PPI plus amoxicillin plus clarithromycin (Table 3). We have recently completed a local study and the combination of a PPI plus amoxicillin plus clarithromycin for 7 days is still the best regimen in Hong Kong with an eradication rate of 92.7%. Some guidelines recommend the treatment period be extended from 7 days to 10 days or even 14 days, hoping to increase the eradication rate. Meta-analysis has shown that this approach yields only small benefit, and yet the cost effectiveness, side effects and cost may need to be considered carefully.

#### Treatment for Patients Allergic to Penicillin

For patients allergic to penicillin, the regime of choice will be a PPI plus clarithromycin plus metronidazole for 7 days. Due to increasing use of clarithromycin or metronidazole in monotherapy against other bacterial infections, it leads to increasing prevalence of antibiotic resistance in H. pylori. In Hong Kong, the antibiotic resistance of H pylori to clarithromycin and metronidazole is around 10% and 40% respectively and has remained stable in recent years. However we should be closely monitoring the pattern of resistance in future. The alternative for patients allergic to penicillin will be to use the quadruple therapy in the first line setting for 7 days. This will avoid the problem of resistance to clarithromycin and metronidazole, but carries a risk of very limited options remaining if the treatment is not successful.

#### Other Options

In view of increasing prevalence of resistance to clarithromycin and metronidazole, some countries have advocated the use of levofloxacin-containing triple therapy in first line treatment. We have completed a local study to assess the use of PPIs twice daily plus amoxicillin twice daily plus levofloxacin 500mg once daily. The eradication rate was 85.3% only. Hence we concluded that levofloxacin-containing triple therapy is not suitable for use in Hong Kong as first line treatment at this moment.

#### Second Line Treatment

For second line treatment of H pylori infection, the classical quadruple therapy is still the regimen of choice (Table 3). Our local study showed that the classical quadruple therapy with PPIs, bismuth subcitrate 240mg bid, metronidazole 400mg tds and tetracycline 500mg qds has an eradication rate of 88%. The use of a PPI plus bismuth plus amoxicillin 1000mg bid and levofloxacin 500mg bid has an eradication rate of only 73% (P<0.05). The other rescue therapy is a PPI, rifabutin 300mg daily, levofloxacin 500mg daily for 7 days. It had an eradication rate of 91%. However rifabutin may have a rare chance of neutropenia and thrombocytopenia which restrict its use in this setting.

### Table 3. Treatment regimes for H. Pylori infection

<table>
<thead>
<tr>
<th>First line treatment</th>
<th>Second line treatment for H. Pylori infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. PPI standard dose + amoxicillin 1 gram + clarithromycin 500mg, all twice daily for 7 days (up to 14 days)</td>
<td>1. PPI standard dose twice daily + bismuth 240mg twice daily + metronidazole 400mg three times daily + tetracycline 500mg four times daily for 7 days (up to 14 days) (for patient allergic to penicillin)</td>
</tr>
<tr>
<td>2. PPI standard dose + metronidazole 400mg + clarithromycin 500mg, all twice daily for 7 days, (up to 14 days)</td>
<td>PPI standard dose: Omeprazole 20mg, Lansoprazole 30mg, Pantoprazole 40mg, Rabeprazole 20mg, Esomeprazole 20mg</td>
</tr>
<tr>
<td>3. PPI standard dose + amoxicillin 1 gram + metronidazole 400mg, all twice daily for 7 days, (up to 14 days)(for patients allergic to clarithromycin, or cost concern)</td>
<td></td>
</tr>
<tr>
<td>4. PPI standard dose twice daily + bismuth 240mg twice daily + metronidazole 400mg three times daily + tetracycline 500mg four times daily for 7 days (up to 14 days)</td>
<td></td>
</tr>
</tbody>
</table>

In this regard, it is of importance to emphasise good compliance during both first and second line treatment. Most of the drop outs are usually due to minor adverse effects such as loose stool, altered taste, malaise etc. It is important to encourage the patients to complete the whole course of treatment and reassure them that these minor adverse effects are tolerable, and will disappear after finishing the regimen. It is still important to be
on the alert for pseudo-membranous colitis due to the use of amoxicillin. Patients should be reminded to contact the physician urgently if there is profuse watery diarrhoea during the course of treatment.

Conclusion

Although there are several new regimens proposed for the treatment of H pylori infection, the classical triple and quadruple therapy are still the best for first and second line treatment respectively. It is important to ensure patient compliance to enhance the high eradication rate.

References

For nucleoside-naïve patients with chronic hepatitis B

Helps Hold back resistance year after year¹*

Baraclude maintains minimal resistance long-term²,*

Choose BARAQUOTE first for your nucleoside-naïve chronic hepatitis B patients. Powerful viral suppression and a high genetic barrier protect against resistance long-term.*²⁻⁶⁻⁷

Experience The Baraclude Effect

* In nucleoside-naïve patients, the cumulative probability of genotypic resistance to BARAQUOTE (entecavir) is 1.7% through 5 years.¹

¹ 93% of patients in year 5 had HIV DNA ≤ 320 copies/mL. In years 1 through 5, respectively, 665, 279, 149, 129 and 128 nucleoside-naïve patients were treated and monitored in studies 564030202, and the subsequent roll over study 901. In studies 022/027, patients received 0.5 mg of ETV (year 0), patients initially received a combination of ETV 1 mg and lamivudine 100 mg daily and subsequently 1 mg ETV monotherapy. The nucleoside-naïve resistance cohort reflects the use of a 1 mg dose of ETV for 147 of 149 patients in year 3, and all patients in years 4 & 5. ¹ Baraclude (entecavir) requires multiple mutations (M204V/I/V1). In HBV and additional substitution at nt 1764, nt 3082 or nt 3510 for emergence of resistance.⁴⁻⁷

References:

INDICATIONS AND IMPORTANT SAFETY INFORMATION about BARAQUOTE (entecavir) tablets:

INDICATIONS: Treatment of chronic hepatitis B virus infection in adults with evidence of active viral replication and evidence of persistent elevations in serum aminotransferases (ALT or AST) or histologically active disease. Dosage: Adults and adolescents 16 years of age or older: Nucleoside-naïve patients – 0.5 mg once daily; patients with history of hepatitis B virus infection or on HIV therapy – 0.5 mg once daily. Hepatitis IMPAIRMENT: No dose adjustment required. LIVER TRANSPLANT RECIPIENTS: The safety and efficacy of BARAQUOTE in liver transplant recipients are unknown. If BARAQUOTE treatment is determined to be necessary for a liver transplant recipient who has received or is receiving immunosuppressant that may affect renal function, renal function must be carefully monitored both before and during treatment with BARAQUOTE. PREGNANCY: There are no adequate or well controlled studies in pregnant women. Use during pregnancy only if clearly needed and after careful consideration of the risks and benefits.

CONTRAINDICATIONS: BARAQUOTE is contraindicated in patients with previously demonstrated hypersensitivity to entecavir or any component of the product. WARNINGS: LACTIC ACIDOSIS and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of nucleoside analogues alone or in combination with antiretrovirals. Severe acute exacerbations of hepatitis B have been reported in patients who have discontinued antiviral therapy, including entecavir. Hepatic function should be monitored closely with both clinical and laboratory follow-up for at least several months in patients who discontinue antiviral therapy. If appropriate, treatment of antiviral hepatitis B therapy may be warranted. Limited clinical experience suggests a potential for the development of resistance to HIV (human immunodeficiency virus) nucleoside reverse transcriptase inhibitors if BARAQUOTE is used to treat chronic hepatitis B virus infection in patients with HIV infection that is not being treated. Therapy with BARAQUOTE is not recommended for HIV/HBV co-infected patients who are not also receiving highly active antiretroviral therapy (HAART). See WARNINGS: Co-infection with HIV. ADVERSE REACTIONS: Based on four studies, the most common adverse events in relation to study drug for BARAQUOTE-treated patients were headache, fatigue, diarrhea, and nausea. PRESENTATIONS: Tab 0.5 mg x 30’s; 1 mg x 30’s. (presentation may vary and/or not be available in some countries). For further information please refer to BARAQUOTE Prescribing Information.

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Standing strong against resistance
Updates in the Treatment of Chronic Hepatitis C

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Background

An estimated 170 million people worldwide are infected with the hepatitis C virus (HCV).1 The majority of these people will remain asymptomatic at the time of acute infection; therefore HCV infection is rarely diagnosed during the acute phase.2 In those subjects acutely infected with HCV, approximately 50-85% will become chronically infected, of which around 20% will progress to cirrhosis over the course of 15-20 years.3 In fact, HCV has become one of the major indications for liver transplantation in the Western world.

Currently Available Agents

The current standard treatment for chronic hepatitis C (CHC) is pegylated interferon (peg-IFN) α-2a or α-2b in combination with ribavirin (RBV). In a randomised trial (the IDEAL study) of these two forms of peg-IFN, efficacy and side-effect profiles were similar.4 The ultimate goal of antiviral therapy is the achievement of sustained virological response (SVR), which is defined by undetectable HCV RNA by a sensitive molecular assay at 6 months after the completion of antiviral therapy, and is considered as a cure. Achievement of SVR is associated with improvement of fibrosis stage, reduced incidence of hepatocellular carcinoma, and decreased morbidity and mortality.5 The exact antiviral mechanism of peg-IFN-α is not known. RBV is a guanosine analog with low antiviral potency against HCV when used alone.6 However, its antiviral effect is augmented when used together with IFN although the mechanism of this synergism is not known.6,10

HCV can be divided into 6 major genotypes, numerically named from 1 to 6 according to their time of discovery. These genotypes display differences in their geographical distribution, with genotype 1 and 6 being the most prevalent in Hong Kong.11 The majority of genotype 1 patients are infected through blood transfusion, whereas a larger proportion of genotype 6 patients are infected through the use of intravenous drug abuse.12 Apart from their differences in distribution, the other major difference between the genotypes is their responses to antiviral therapy.

Genotype 1

In patients infected with HCV genotype 1, the recommended duration of treatment is 48 weeks, with a SVR of approximately 50-55%.13-15 The level of HCV RNA is assessed at week 12 for early virological response (EVR), which can be defined as complete (undetectable HCV RNA) or partial (≥2 log decrease in HCV RNA from baseline). For those patients who cannot achieve EVR, the negative predictive value for treatment outcome is high at 97%, and the chance of going on to achieving SVR with 48 weeks of therapy is unlikely.13 In patients who fail to reach EVR at week 12, early treatment discontinuation is recommended as these patients are likely to be non-responders. For those patients who achieved EVR, an estimated 65-72% will go on to achieve SVR.13,16

More recently, the use of rapid virological response (RVR), defined by undetectable HCV RNA at week 4 using sensitive molecular tests, has been evaluated to identify a subgroup of patients who may benefit from a shorter duration of therapy. Several trials have shown that in genotype 1 patients who achieve RVR, a high SVR rate of over 70% can be achieved with peg-IFN plus ribavirin with a shorter duration of treatment for 24 weeks, which was comparable to those that were treated for 48 weeks.17-21 The major factor determining the outcome in patients with RVR and shorter duration of therapy was the level of viraemia at baseline. However, there is currently no consensus as to the baseline cut-off HCV RNA level that can be adopted to select out those who will be sufficiently treated with 24 weeks, although various cut-offs of 400,000, 600,000, and 800,000 IU/mL have been evaluated. Further trials are needed to identify an optimal cut-off level before shorter duration of therapy can be implemented.

On the opposite end of the spectrum, there have been studies evaluating longer duration of treatment. In an earlier trial looking at 48 vs 72 weeks of treatment in genotype 1 patients, there was no significant difference observed in SVR rates, although a higher SVR rate was observed in those who failed to achieve complete EVR at 12 weeks with 72 weeks of treatment.22 Those patients who did not achieve RVR also had a higher SVR rate when treated for 72 weeks compared to 48 weeks.23 However, more recent trials have not shown the benefits of 72 weeks of treatment when compared with 48 weeks.24 In patients who achieve partial EVR (but not complete EVR), there was no significant increase in SVR observed with 72 weeks of therapy compared with 48 weeks.24 Another study also showed no significant difference in SVR rates between 48 and 72 weeks of therapy in patients with genotype 1/4 who achieved either partial or complete EVR.25-27

Genotypes 2 and 3

In patients infected with HCV genotype 2 or 3, the recommended treatment length is 24 weeks, with a
SVR rate of 70–75%. Given that most patients will achieve EVR, and coupled with a shorter duration of therapy (compared to genotype 1), the use of EVR at week 12 to determine treatment outcome has not been adopted. Similar to the recent approaches for genotype 1 patients, both shortening and extending the duration of therapy have been evaluated in patients infected with genotype 2/3.

In the ACCELERATE trial comparing 16 vs 24 weeks of therapy, those treated for 16 weeks resulted in a lower SVR rate. For patients with HCV genotype 2/3 (the NORDynamiC study), treatment length of 12 weeks was inferior to 24 weeks of therapy. However, in patients who achieved RVR at week 4, 12 weeks of therapy was shown to be as effective as 24 weeks of therapy. Another study showed similar results with 16 weeks of therapy, although those patients infected with HCV genotype 3 and a high baseline viral load (>800,000 IU/mL) showed a lower SVR with 16 weeks of therapy compared with 24 weeks. Patients infected with HCV genotype 2 who achieved RVR appeared to show equal efficacy when treated for either 16 or 24 weeks. A meta-analysis of trials evaluating shorter duration of 12-16 weeks in genotype 2/3 patients with RVR showed an association with a lower SVR rate and higher relapse rates. Given the heterogeneity of these studies it is difficult to recommend a shorter duration of therapy for patients infected with genotype 2/3, although those who achieve RVR would appear to benefit most.

**Genotype 6**

There is currently no randomised controlled trial for genotype 6, therefore the recommendation is to treat these patients for 48 weeks. In retrospective studies comparing genotypes 6 and 1, the SVR rates were significantly higher in genotype 6 compared to genotype 1 when treated for 48 weeks. However, another retrospective study showed that 24 weeks of treatment was inferior to 48 weeks of treatment for genotype 6.

**Non-responders to Therapy**

In patients who do not respond to peg-IFN plus RBV therapy, the HALT-C study showed that further prolonged maintenance therapy with low-dose peg-IFN did not significantly reduce the rate of disease progression despite significant decline in HCV RNA. However, studies of re-treatment with a limited duration have shown some benefits. In the REPEAT study, re-treatment with peg-IFN-a2a + RBV for 72 weeks achieved a higher SVR rate compared to 48 weeks, although the SVR rate was still low at 16%. The EPIC3 study also showed a SVR of 22% in patients re-treated for 48 weeks with peg-IFN-a2b + RBV. Therefore, re-treatment appears to be beneficial in subgroups of patients who have failed previous treatments with peg-IFN. However, there is no current recommendation for retreatment of patients who have completed a full course of peg-IFN + RBV therapy.

**Side-effects of Current Therapy**

Prior to commencing antiviral therapy, a full medical history and examination must be obtained as there can be potential for serious adverse effects. Since immune stimulation by peg-IFN may induce severe liver injury, treatment for patients with established cirrhosis should be considered carefully, and is contra-indicated in those with decompensated cirrhosis. The side-effects of hepatitis C therapy are summarised in table 1. Because of the possible serious adverse events, patient selection is of utmost importance, and the decision to treat requires a careful assessment of the risk to benefit ratio for each individual patient. Patients should also be aware of the possible worsening of their quality of life during the course of the treatment.

**Table 1. Common side effects of pegylated interferon and ribavirin therapy**

<table>
<thead>
<tr>
<th>Flu-like symptoms</th>
<th>Haematological</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td>Anaemia</td>
</tr>
<tr>
<td>Myalgia</td>
<td>Leucopenia</td>
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<tr>
<td>Pyrexia</td>
<td>Thrombocytopenia</td>
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<tr>
<td>Rigours</td>
<td>Autoimmune</td>
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<tr>
<td>Headache</td>
<td>Thyroid disorder</td>
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<tr>
<td>Arthralgia</td>
<td>Other autoimmune disorders</td>
</tr>
<tr>
<td>Mood disturbances</td>
<td>Dermatological</td>
</tr>
<tr>
<td>Depression</td>
<td>Rash</td>
</tr>
<tr>
<td>Irritability</td>
<td>Exacerbation of psoriasis</td>
</tr>
<tr>
<td>Memory loss</td>
<td>Injection site reaction</td>
</tr>
<tr>
<td>Mood swings</td>
<td>Alopecia</td>
</tr>
<tr>
<td>Insomnia</td>
<td></td>
</tr>
</tbody>
</table>

**Interferon**

Patients who experience flu-like symptoms may respond to treatment with acetaminophen or non-steroidal anti-inflammatory drugs, whereas those with insomnia may be treated with sleeping medications. Although neutropenia is commonly observed in patients treated with IFN, the risk of infection is low, and careful monitoring usually suffices. The use of granulocyte colony-stimulating factor is only rarely considered. Thrombocytopenia is commonly observed in patients with liver disease secondary to both hypersplenism and insufficient hepatic production of thrombopoietin. This can be further compounded by the administration of IFN-based therapy, which is associated with a rapid and sustained reduction in peripheral platelet count. Currently there is no approved agent available for the treatment of thrombocytopenia, although thrombopoietin-mimetic agents such as eltrombopag may become available in the near future.

**Ribavirin**

The most significant adverse effect of ribavirin is haemolytic anaemia, which is commonly observed in patients undergoing treatment. Management includes reducing the dose of ribavirin if the haemoglobin level falls below 10 g/dL, or stopping therapy if it falls below 8.5 g/dL. Ribavirin may need to be avoided in patients who cannot tolerate anaemia, such as those with pre-existing cardiovascular or cerebrovascular diseases. The use of erythropoietin is effective in treating anaemia and ameliorating the need for dose reduction of ribavirin, and in improving the quality of life of patients. However, the effect on improved SVR is yet to be demonstrated. As there is associated teratogenicity with ribavirin, it is contra-indicated during pregnancy, and adequate contraception must be adopted for both male and female patients.
**Future Therapeutic Agents in HCV Treatment**

As described previously, with the current standard of care using peg-IFN and ribavirin, only around 50% of patients with genotype 1 may achieve SVR. Newer agents are much anticipated to improve the modest cure rate. Newer types of IFN are undergoing evaluation, including consensus IFN and albuferon. Novel deliveries of IFN include controlled release formulations and the uses of nanoparticle delivery systems are also being explored.

Currently, there are many promising agents known as specifically targeted antiviral therapy for hepatitis C (STAT-C) compounds which target the HCV replication cycle are undergoing phase I to III trials. Two of these STAT-C agents, telaprevir and boceprevir, are in advance stages of development, and should become available in the following 1-2 years.

**Telaprevir**

Telaprevir is an oral NS3 protease inhibitor currently undergoing phase III evaluation. In the initial phase I studies, an optimal dose of 750mg q8h following an initial loading dose of 1250mg was identified. Selection of telaprevir-resistant mutations was observed with telaprevir monotherapy, although the rate was significantly lower when combined with peg-IFN. In the phase II trial of treatment-naïve genotype 1 patients (PROVE 1 study in USA and PROVE 2 study in Europe), those treated with 12 weeks of telaprevir had a significantly higher SVR rate when treated with 24 or 48 weeks or Peg-IFN + ribavirin compared to standard therapy of 48 weeks of peg-IFN + ribavirin without telaprevir. Two of these trials also showed that 12 weeks of therapy using telaprevir, peg-IFN, and ribavirin was associated with a high relapse rate. The PROVE 2 trial also showed that those treated without ribavirin was associated with a lower SVR rate. In the trial of treatment-experienced patients (the PROVE 3 study), re-treating non-responders with 12 weeks of telaprevir + peg-IFN + ribavirin for 12 weeks followed by a further 12 weeks of peg-IFN + ribavirin resulted in a SVR rate of 51%, compared to 14% in patients retreated with peg-IFN + ribavirin without telaprevir. A number of phase III trials are currently in progress for treatment-naïve patients (the ADVANCE and ILLUMINATE study) and for patients with previous treatment failure (the REALISE study). The most common side effects of telaprevir include rash, gastrointestinal disorders, and anaemia.

**Boceprevir**

Boceprevir is a NS3 protease inhibitor, another STAT-C compound that is currently undergoing phase III evaluation. In the phase II trial (the SPRINT 1 study) of treatment-naïve genotype 1 patients, those patients receiving boceprevir had higher rates of SVR compared to patients treated with peg-IFN + ribavirin without boceprevir. Common side-effects included anaemia and gastrointestinal symptoms. Boceprevir is currently being evaluated in phase III trial of treatment-naïve genotype 1 patients (the SPRINT 2 study) using boceprevir 800mg tds + peg-IFN α-2b + ribavirin for 28/48 weeks versus standard treatment with peg-IFN α-2b + ribavirin for 48 weeks. The other phase III trial is on relapers and non-responders (the RESPOND-2 study) using boceprevir 800mg tds + peg-IFN α-2b + ribavirin for 36/48 weeks versus standard treatment with peg-IFN α-2b + ribavirin for 48 weeks. Similar to telaprevir, there are also mutations associated with boceprevir treatment.

Apart from telaprevir and boceprevir, there are currently a host of other NS3/4A protease inhibitors undergoing phase I and II evaluations. In addition to the NS3/4A protease inhibitors, other classes of antiviral compounds undergoing phase II and II development include the NS5B polymerase inhibitors and NS5A inhibitors.

**Summary**

Over the recent years, there has been a shift towards individualisation of treatment according to their initial responses to therapy. There have been many studies evaluating shortening of therapy in patients who achieve RVR and also those with lower baseline viral load. However, further studies are still needed to clarify the optimal modified duration of therapy and also the optimal baseline viral load at which these truncated treatment regimens can be implemented. For those patients who do not respond to therapy, extending the duration of therapy may not improve the chance of achieving SVR. Fortunately there are now many newer agents in various stages of development to treat patients infected with genotype 1 and those patients who have failed peg-IFN + RBV therapy. Both telaprevir and boceprevir are undergoing phase III evaluation and should become available in the very near future. Because of the high risk of resistant mutations when used as monotherapy, these newer agents will be used in combination with peg-IFN + RBV or with other newer STAT-C compounds as they become available.

**References**


催眠治療
臨床應用課程
（基礎訓練）

課程目的:
1. 協助參加者掌握正確的催眠治療知識及自我催眠的運用
2. 學習運用自我催眠技巧於相關的臨床工作
   - 改善睡眠質素
   - 舒緩情緒
     - 平衡與轉化情緒
     - 舒緩壓力

課程內容:
- 一般人對催眠的誤解
- 催眠的定義、歷史及用途
- 催眠對身心的效用
- 催眠與意識
- 認識潛意識的力量
- 催眠能力的測試
- 自我催眠的基本概念及運用技巧
- 導入催眠意境的基本技巧
- 循環式放鬆技巧
- 催眠治療提示的應用（直接提示）
- 改善睡眠質素的技巧
- 平衡與轉化情緒的方法
- 舒緩壓力的技巧

導師：尹婉萍小姐
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服務，善於情緒輔導、家庭關係、親子溝通及宗教等。
尹小姐亦為香港大學行為健康及研究中心臨床實習導師，
於「催眠治療」學科輔導碩士課程的學生。

日期/節數
2011年1月6日（第一節）
認識催眠治療：催眠治療的導入方法
- 導入催眠意境的製作
- 自我催眠與改善睡眠質素

2011年1月13日（第二節）
自我催眠與情緒調節（一）催眠提示的應用
- 平衡情緒的方法
- 情緒的轉化：收納與釋放

2011年1月20日（第三節）
自我催眠與情緒調節（二）催眠提示與身心反應的運用
- 自我催眠與壓力的舒緩

2011年1月27日（第四節）
自我催眠與情緒調節（三）催眠提示與身心反應的運用
- 專注力的提升及耐力的增加

日期：2011年1月6日至1月27日（逢星期四）
時間：晚上7:00至9:30
地點：香港灣仔軒尼詩道15號
溫莎公爵社會服務大樓4字樓演講廳
教學語言：廣東話
名額：40人
課程收費：$1,000

整個課程共4節，每星期1節，每節2.5小時

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Recent Advances in Management of Hepatocellular Carcinoma

Prof. Ronnie Tung-ping POON

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Introduction

Hepatocellular carcinoma (HCC) is one of the most common malignancies, ranking fifth in frequency among all malignancies in the world.¹ HCC is characterised by rapid tumour growth and a high propensity of vascular invasion. Furthermore, 80% of patients with HCC have associated liver cirrhosis related to hepatitis B or C viral infection, which often restricts treatment options because of impaired liver function. The prognosis of untreated HCC is poor, but the management approach of HCC has changed from a previously nihilistic approach to a more aggressive one with recent advances in management, resulting in improved prognosis. The wider utilisation of screening programme in high-risk patients has resulted in early detection of small HCCs, and thus improved chance of treatment.² Compared with other gastrointestinal cancers, management of HCC is more complicated because of the wide range of treatment modalities available and the underlying liver disease. Appropriate selection of patients for individual treatment according to tumour status and liver function is critical to optimise treatment outcome, and some patients may require combination of modalities in management. Treatments for HCC can be classified into curative (resection, transplantation or ablation) or palliative (transarterial chemoembolisation, radioembolisation or systemic therapy).

Surgical Resection

Hepatic resection is the treatment of choice for patients with HCC and preserved liver function. Even for patients with a large HCC > 10 cm in diameter, resection is safe and offers favourable long-term survival results.³ The presence of multiple tumour nodules or vascular invasion in major intrahepatic venous branches may be associated with worse prognosis. However, surgical resection is still considered the best treatment in terms of long-term survival.⁴ Extended right or left hepatic resection can be performed even in the presence of cirrhosis, provided patients are carefully selected in terms of liver functional reserve.⁵ In patients with inadequate remnant liver volume for a right or extended right hepatectomy, preoperative right portal vein embolisation can be employed to induce atrophy of the right lobe and hypertrophy of the liver remnant before resection. In centres specialised in hepatobiliary surgery, liver resection for HCC is now a safe operation with an operative mortality 2-5%.⁶ Major complications such as massive bleeding or postoperative liver failure are rare with careful patient selection and modern operative techniques.

In recent years, laparoscopic liver resection has become feasible with the development of laparoscopic instruments that allow liver transection without major bleeding. Tumours in anterior segments or left lateral segments can be resected using a laparoscopic approach, with the benefit of less postoperative wound pain, better cosmetic result, shorter hospital stay and faster recovery (Figure 1). A meta-analysis of retrospective comparison of laparoscopic and open approach has shown reduced blood loss with the laparoscopic approach, while oncologic clearance in terms of resection margin was similar between the two groups.

Bilobar HCC was used to be a contraindication for resection. However, with the advent of thermal ablation therapy, it is now possible to perform combined resection of predominant tumour mass(es) in one lobe and ablation of small tumour nodule(s) in the other lobe (Figure 2). Such an aggressive approach has increased the chance of patient receiving curative therapy for HCC and could achieve similar survival results compared with resection alone.
Liver Transplantation

In the 1980s, advanced unresectable HCC was a common indication for transplantation but the results were disappointing, with a 5-year survival rate of around 20%. The presence of circulating tumor cells associated with large HCC leads to a high incidence of postoperative recurrence in the setting of immunosuppressive therapy used to prevent graft rejection. A landmark study published in 1996 showed that for solitary HCC < 5 cm or < 3 tumor nodules each of size < 3 cm, the long-term survival rate of liver transplantation was favorable. It is now well-accepted that Child’s cirrhotic patients with HCC < 5 cm or < 3 tumor nodules each of size < 3 cm (Milan criteria) and without radiological evidence of venous invasion or distant metastasis should be treated by transplantation, as hepatic resection is usually contraindicated in this group of patients with poor hepatic function. Some centers adopted expanded criteria of solitary tumour ≤ 6.5 cm or ≤ 3 nodules with the largest lesion ≤ 4.5 cm and total tumour diameter ≤ 8 cm (UCSF criteria) for liver transplantation. With such stringent selection criteria, the 5-year survival rate is about 60-75%. Tumor recurrence is an important cause of long-term mortality after liver transplantation. Currently there is no effective adjuvant therapy to reduce the risk of tumor recurrence.

Whether Child’s cirrhotic patients with preserved liver function and a small HCC should be treated with transplantation or resection is a controversial issue. Some Western centers recommended liver transplantation for small HCC even in child’s patients because of the lower tumor recurrence rate compared with resection. However, in most Asian centers including Hong Kong where there is a severe shortage of liver graft donors, hepatic resection remains the first-line treatment for such patients because similar overall survival results of about 70% in 5 years can be achieved for small HCCs. A significant proportion of HCC patients listed for liver transplantation may drop out of the waiting list because of tumor progression. Furthermore, specific long-term complications of liver transplantation such as recurrent viral hepatitis, graft rejection, opportunistic infection or secondary malignancies as a result of immunosuppression may lead to mortalities. Resection followed by salvage transplantation for intrahepatic recurrence or deterioration of liver function may be a more effective strategy for patients with small HCC and preserved liver function.

Adult live donor liver transplantation is an appealing alternative for patients with HCC because it reduces the chance of dropout from the waiting list for deceased donor liver grafts. However, the benefit of live donor liver transplantation for HCC patients has to be balanced against a risk of about 0.5% mortality and 20% morbidity in the live donor undergoing right lobe donor heptectomy. Furthermore, there is some concern of the effect of regeneration of the partial liver graft in stimulating the growth of microscopic metastasis, although there are not enough clinical data on this issue. Hence, most centers consider that the selection criteria for HCC patients to undergo live donor liver transplantation should be similar to that of deceased donor liver transplantation. Even with the use of live donor liver transplantation, less than 5% of HCC patients at the author’s institution are treated by liver transplantation.

Local Ablative Therapies

Local ablation is a potentially curative therapy for small HCCs not amenable to resection. Patients with HCC ≤ 5 cm and up to 3 nodules are the best candidates for ablative therapies, although larger tumors can also be ablated in selected cases. While there is some preliminary evidence suggesting that ablative therapies may achieve similar survival results compared with surgical resection, the evidence is not yet strong enough to recommend local ablation as the first-line therapy for patients with a resectable small HCC. However, for patients with borderline liver function, local ablation is a safer option especially if the tumors are centrally located. Local ablative therapies are useful in treating recurrent HCC after previous resection, which occurs mostly in the liver remnant. Local ablative therapy may also be employed as a bridging therapy for control of tumors before a liver graft is available even if liver transplantation is contemplated.

Percutaneous ethanol injection therapy was used to be the main local ablative therapy in the 1990s. However, radiofrequency ablation (RFA) has replaced ethanol injection to be the most widely used ablative modality for HCC. Randomised controlled trials have demonstrated that RFA is superior to ethanol injection in that it requires fewer treatment sessions, and it achieves a higher complete ablation rate, lower tumor progression rate and higher overall survival rate. RFA is associated with a mortality rate of 1% or lower, and it can be performed through percutaneous, laparoscopic, and open approaches. The choice of treatment approach depends on the size and location of the tumor(s) and patients’ comorbid condition. Patients with tumor ≤ 3 cm in diameter located in the periphery of the liver are the best candidates for percutaneous RFA under ultrasonographic...
or computed tomography guidance. Laparoscopic RFA allows the ablation of liver tumours in close contact with the surrounding organs, such as bowel, kidney, gallbladder and diaphragm, for which percutaneous RFA carries the risk of bowel perforation or visceral damage. Open surgical approach is indicated in patients with large tumours or multiple tumour nodules located at the superior or posterior portion of the liver (Figure 3). There is a higher degree of freedom for accurate introduction of the RF needle into the tumour in open RFA compared with other approaches, so that more effective ablation can be carried out to minimise the chance of residual tumour at the treatment site. For HCC > 3 cm in diameter, a previous study by the author showed that open approach achieved better long-term survival compared with percutaneous RFA. Recent studies have shown that 5-year survival of 40-60% can be achieved with RFA for small HCCs, but the recurrence rate remains high. The author is conducting randomised controlled trials to evaluate the benefit of combining transarterial chemoembolisation (TACE) or heat-activated liposomal doxorubicin (Thermolox) in combination with RFA to reduce recurrence rate. Thermolox contains doxorubicin encapsulated in a heat-sensitive layer of liposome that releases the doxorubicin at temperature > 42°C. This allows delivery of high concentrations of doxorubicin to the ablation zone with minimal systemic toxicity. An early phase trial jointly conducted by the author and the National Cancer Institute of the USA showed that this is a promising strategy in enhancing cancer killing at the ablation zone.

High intensity focused ultrasound (HIFU) is a new modality of ablation that is totally non-invasive. Ultrasound focused by a transducer can kill cancer cells by cavitation effect in addition to thermal ablation effect. Currently, Queen Mary Hospital is the only hospital in Hong Kong with a HIFU system for treatment of liver cancer. Since 2007, more than 100 cases of HIFU for HCC have been performed under ultrasound imaging guidance, with complete ablation rate close to that of RFA. As no electrode needle puncture is required, it eliminates the small risk of bleeding or needle track tumour cell seeding associated with RFA. Furthermore, the ablation is more precise than RFA and it may be used in tumours located near major bile duct or vessels. It is also possible to ablate large tumours > 5 cm (Figure 4).

Transarterial Therapies

For patients with large tumour or multifocal tumours confined to the liver but not suitable for resection, transplantation or ablation because of inadequate liver function reserve or poor general condition, transarterial chemoembolisation (TACE) is the standard of care. In this treatment, cisplatin or doxorubicin mixed with Lipiodol is injected to the hepatic artery supplying the tumour(s) via a catheter placed through the femoral artery, followed by embolisation using gelfoam or embosphere particles. Meta-analyses of prospective randomised trials have demonstrated the efficacy of TACE in prolonging the survival of patients compared with conservative management, but the tumour response rate is only about 35%. Revascularisation by angiogenesis in the periphery of tumour after initial response leads to disease progression. Molecular targeting agents such as bevacizumab, which is a monoclonal antibody against vascular endothelial growth factor, have been developed to inhibit angiogenesis. Anti-angiogenic therapy has been proven to be a useful treatment to inhibit cancer growth in several human cancers. The author is conducting a trial of combining bevacizumab with TACE to enhance its efficacy.

Doxorubicin-eluting bead is a new development that aims to enhance the efficacy of TACE and reduce its toxicity. The beads are microspheres pre-loaded with doxorubicin that releases the doxorubicin slowly in the tumour when injected transarterially and the beads also serve as embolising particles. A phase I/II study conducted by the author showed that doxorubicin-eluting bead could significantly reduce the systemic exposure to doxorubicin while delivering higher concentration of doxorubicin to the tumour compared with conventional Lipiodol-doxorubicin TACE, and the tumour response rate appeared superior. A randomised trial in Europe has shown that doxorubicin-eluting beads reduced liver toxicity and increased tumour response in more advanced HCC compared with conventional Lipiodol-TACE.

Transarterial radioembolisation using Yttrium-90 labelled spheres is an alternative to TACE that has become more popular in recent years, though its use is still limited compared with TACE. The efficacy and safety of transarterial radioembolisation appears to be similar to TACE, but there are no randomised trials comparing it with TACE in the literature. Transarterial radioembolisation appears to be more effective in inducing shrinkage of tumour thrombus in the portal vein compared with TACE. The author prefers to use transarterial radioembolisation rather than TACE in patients with portal vein tumour thrombus and has experience of successful shrinkage of tumour thrombus in main portal vein followed by resection.

Systemic Therapy

For patients with advanced HCC that is not amenable to locoregional therapy, systemic chemotherapy has so far demonstrated low efficacy and toxicity is significant because of the underlying cirrhosis in most patients. Systemic chemotherapy suing conventional agents
such as 5-FU, doxorubicin and cisplatin either alone or in combination has not been shown to prolong patient survival in prospective randomised trials.\(^\text{25,26}\) HCC is a highly vascularised tumour, and previous studies by the author have demonstrated that significance of angiogenesis and vascular endothelial growth factor in HCC.\(^\text{27,28}\) Recently, a molecular targeting agent that inhibits receptor of vascular endothelial growth factor and a signalling protein Raf kinase in the HCC cells has been shown to be effective in prolonging survival of patients with advanced HCC in two large phase 3 randomised placebo-controlled trials.\(^\text{29,30}\) The drug Sorafenib prolonged patient survival by approximately three months in these trials, but tumour response rate was less than 3%. Hence, the benefit is limited. The use of Sorafenib is also hindered by significant side effects such as hand-foot skin reaction and the high cost.

Currently many other molecular targeting drugs that target different pathways such as the mTOR pathway, c-MET and fibroblast growth factor are under clinical trials in direct comparison with Sorafenib, in combination with Sorafenib or as a second-line therapy after Sorafenib failure.\(^\text{31}\) Some novel drugs such as Everolimus and Brivanib have demonstrated favourable safety and also efficacy in phase II trials in HCC and are now being evaluated in phase III trials.\(^\text{32}\) In the author’s institution, several clinical trials on the novel drugs are on-going (information available on www.livercancer.hku.hk) and provide an alternative option for patients who cannot afford Sorafenib or who have failed Sorafenib therapy. The author has also completed a phase II trial of combining Sorafenib with newer chemotherapeutic agents Capecitabine and Oxaliplatin (SECOX) for advanced HCC. Our data showed that the regimen is well-tolerated in HCC patients and appears to be substantially superior to Sorafenib monotherapy in tumour response rate, disease stabilisation rate and overall survival. An international multi-centre phase III randomised controlled trial will be conducted to further evaluate the benefit of this regimen compared with Sorafenib monotherapy. Finally, the role of molecular targeted agents in earlier stage HCC is also being evaluated. The author is participating in a large-scale international multi-centre phase III randomised trial of Sorafenib versus placebo as adjuvant therapy after resection or ablation of HCC, with a target sample size of 1100 patients. There are also on-going trials of combination of Sorafenib or novel targeting agents such as Brivanib with transarterial chemoembolisation for intermediate stage HCC.

Conclusions

The management of HCC has changed dramatically in recent years with improved outcomes. The improved safety and long-term survival after hepatectomy for HCC and the development of minimally invasive liver resection have reinforced the role of liver resection as the first-choice treatment. Local ablative therapies have provided an important alternative for curative treatment for patients who have inadequate liver function reserve for resection. Recurrence after resection or ablation remains a major problem, but active studies are being conducted to evaluate novel adjuvant therapies to improve the prognosis of patients. TACE or radioembolisation is the mainstay of palliation for patients whose HCCs are confined to the liver that is not amenable to resection or ablation. Occasionally, patients with initially unresectable disease can be down-staged to resectable disease after transarterial therapies. Development of novel techniques such as drug-eluting beads and combination with molecular targeting drugs may further enhance the efficacy of TACE. Molecular targeted therapy is an important break-through that has shown for the first time as a systemic therapy to improve survival of patients with advanced HCC. It has triggered major interests in development of new drug therapies that hopefully will help conquer a disease once deemed to be associated with uniformly grim prognosis.

References


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Voluntary Health Protection Scheme: the right choice for the next step of Hong Kong’s healthcare reform?

Prof. Geoffrey LIEU
DBA, MHA, LFACHE, FACHSE, LFHKCHSE
Chairman Emeritus and Founder
The Institute for Health Policy and Systems Research

The voluntary Health Protection Scheme (hereafter, the Scheme) proposed by the Hong Kong Special Administrative Region Government (HKSARG) in the consultation document *My Health My Choice* is a form of the traditional individual private indemnity health insurance or fee-for-service plan that many healthcare systems in the world are shunting or have dropped in favour of other forms of health insurance. In the United States, for example, where private indemnity health insurance dominated between the 1960s to 1980s, such traditional plans have dwindled and are now rarely offered in its original form due mainly to its high cost arising from, among other things, warped incentives for both consumers and providers.

As it is presented for public consultation, it should be relevant to review the pros and cons of the Scheme and focus on the question: Is the proposed scheme the right choice for the next step of Hong Kong’s healthcare reform? To answer this question, one should need to have at least two other questions answered first: What kind of future healthcare financing and payment systems do we want or should best befit Hong Kong in the long term, say 20 or 30 years from now? What or how will the proposed Scheme address Hong Kong residents’ current and future healthcare concerns?

The right healthcare financing and payment systems for Hong Kong

What healthcare financing arrangements Hong Kong should adopt should fundamentally be premised on the healthcare system that we want in the future. Although it has never been precisely clear, it is suggested in the current as well as previous consultation documents that we should want an effective and sustainable healthcare system that:

- ensures equitable access with the public system providing a safety net for all; and
- provides adequate choice through a private sector that is equally professional and transparent (as the public sector) to consumers in both quality and service fees.

The right words are mostly there. But what do they mean and how do they work in practice? What conjures up in our minds as the way it will and should work may be very different. Our concerns, thoughts and behaviours, including those of our close ones, are very different before we are sick and while we are sick. Then, of course, consumers, patients and providers can have divergent perspectives, wants, needs and demands that may be difficult to align.

The vision of the healthcare system that we should want has largely been defined top down. We have been persuaded to share the view that a comprehensive reform is needed because:

“...ageing demographic profile of the population and rising medical costs due to advancement in medical technology would pose significant challenges to the healthcare system. The ageing population would lead to rapid increase in healthcare needs and services demands on the healthcare system, particularly the public system. The cost of healthcare would also likely continue to rise in view of the advancement of medical technology and medical inflation....The significant public-private imbalance in our healthcare system... could lead to deterioration of service quality and lengthening of waiting queue for highly-subsidised public healthcare services, where the elderly, chronic disease patients and the under-privileged group would likely be most affected.”

There can be different views and hence arguments about the aforementioned scenarios. Even given these scenarios to be probable, what financing arrangements should be implemented to address the presupposed challenges? That is, how financial resources in healthcare should best be pooled and distributed, in particular how providers should be paid? Unfortunately, these questions have not been fully deliberated, at least not at the community level.

The public at large know little about the importance and implications of the various financing and payment arrangements to the cost, access and quality of healthcare services delivery. But they deserve to know.

How resources are best pooled for healthcare and distributed is fundamentally an issue of societal and humanistic values. The current debate in healthcare reform elsewhere is increasingly torn between market orientation (based on economic considerations) and social responsibility. Hong Kong has traditionally exhibited a strong social responsibility for the health and healthcare of its residents. Free A&E services and nominal fees and charges in other services in the public healthcare sector were clear evidence. The formation of the Hospital Authority in 1991 was a sign of its further commitment towards that end.
That commitment, however, seems to have shifted when fees were levied for A&E services in public hospitals on 29 November 2002. But what do Hong Kong residents prefer for their future public health system and what should policymakers do: more social responsibility, more market orientation, or a hybrid of the two?

One of the aims of the Scheme is to enable more people to access private healthcare. While that obviously could facilitate movement from the public to the private sector, it is uncertain if in practice the reverse is also true. Will this then mean a move towards further market orientation? Not until we have clarity and public support of the long view of the type of public healthcare system that we want and should have, it could be counterproductive to introduce initiatives to move the system away from its stronghold of health as a right and social responsibility.

Healthcare economics, financing and policy issues aside, it seems that most retirees, elderly, patients and families should prefer and want a health system free of avoidable and unnecessary worries or where they could have ease of access to quality healthcare with affordable and justifiable financial outlay and where healthcare costs will not wipe out most of their hard earned savings or assets or drive them to economically deprived conditions. Will the Scheme help us move towards achieving a health system that we can feel safe, confident, secure and trusted?

What will the Scheme likely do and not do?

The objective of the scheme, as stated in the Chief Executive’s 2010-11 Policy Address, is “to provide the public with wider choices and better protection through government-regulated private health insurance and health care services.” This is to be achieved by:

- encouraging the public to take-out health insurance and savings to enhance access to private healthcare services and to facilitate greater use of private services as an alternative to public services; and
- increasing the transparency of service standards and price levels in the private health insurance and healthcare markets through the offering of packaged charging for common medical procedures.

The benefits design of the Scheme is to provide cover for mainly hospitalisation and selected admission associated specialist outpatient consultations, investigations or procedures. Maternity services are not covered. To prevent abuse or overuse, the Scheme incorporates various utilisation management controls such as deductibles and co-payments that are common among private health insurance policies. On the other hand, how the Scheme will incentivise individual providers for improved performance and in helping patients stay healthy are visibly lacking.

To ensure that the Scheme is attractive to the public to join and stay, especially those who already have private health insurance coverage, the Government will consider using the HK$50 billion earmarked for supporting healthcare reform to provide no-claim discounts of up to 30 percent for the public to join the scheme in the initial period and to offer premium rebates at age 65 or above based on the participant’s savings and length of continuously staying insured under the Scheme.

It seems that the Scheme is designed primarily to lure patients away from using public hospital services, to incentivise them to stay insured and remain in the private sector. By enabling more people to use private healthcare on a sustained basis, it is anticipated that the Scheme will help public healthcare better focus on queue relief, being a safety net for all, serving the needy and providing acute and emergency care as well as catastrophic care.

Very little, if any, is provided in the consultation document for how the Scheme may contribute to lowering healthcare costs, enhancing equity of access and improving quality. In fact, there is limited evidence, based on international experience, that the Scheme, being a voluntary indemnity health insurance plan, will improve efficiency of the health system, reduce overall healthcare costs pressure, or relieve over-crowding in the public healthcare sector. On the contrary, it will likely:

- bring access inequity to plan benefits for consumers.
- exacerbate healthcare cost increases.
- stimulate demand or even abuse and overuse of healthcare services.
- lead to adverse selection.

To mitigate the down-side risks, the Scheme will need, as proposed, extensive regulation, supervision and monitoring, including a strong supporting infrastructure and claims arbitration mechanism. These suggest that it will be an expensive system to implement and administer.

Is the Scheme the right choice for Hong Kong?

Hong Kong already has private health insurance in varying forms for decades. Around 3.5 million policies, comprising 2.0 million individual memberships and 1.5 million group memberships, were in force in 2009. This represents 34 percent of the population having private health insurance and the number of individuals purchasing private health insurance has grown significantly in recent years.

The contribution of private health insurance to Hong Kong’s healthcare financing has stayed at 12 percent to 13 percent between 1998/90 and 2006/07. In terms of share of total expenditure on health, private health insurance grew at an average rate of nearly 9 percent per year during this period. In 2006/07, private hospitals incurred about a quarter of the expenditure on inpatient care, about half of which was financed by private health insurance.

So, what is the point of introducing the proposed Scheme?

The study commissioned by the Food and Health
Bureau on private health insurance outlined a number of inadequacies or challenges confronting insurers, consumers and providers in the existing private health insurance sector:

**For insurers:**
- anti-selection and non-disclosure during underwriting.
- moral hazard and unnecessary admissions due to investigations.
- limited private providers and limited application of clinical guidelines and audits.
- non-transparent and rising medical fees.
- private health insurance’s attractiveness dimmed by public services.

**For consumers:**
- uncertainty of coverage and charges.
- disputes over policy terms and conditions and their application.
- non-transparent medical fees and lack of quality assurance.
- non-portability of private health insurance.

**For private hospitals and doctors:**
- inadequate coverage.
- coverage of outpatient procedures.

If the Scheme is to address the inadequacies of the current private health insurance market, then perhaps the ones worth the Government’s attention would be mainly those confronting consumers. Yet, these are issues that other health systems with private health insurance have long addressed successfully through regulation or policy changes.

Does Hong Kong really need the force and weight of the huge designated HK$50 billion healthcare reform fund and the potentially high administrative cost of the proposed Scheme to institute such improvements in the private health insurance sector?

The cost benefit of the proposed Scheme is uncertain and appears unjustified. It is also not evident that the proposed Scheme can efficiently and effectively mobilise resources to help build an effective and sustainable healthcare system that ensures equitable access and provides adequate choice. If the objective is to put forward a voluntary supplementary healthcare financing scheme with wider choice and continuous protection, surely other viable options should be explored and presented for consultation. Unfortunately, this is not the case.

**Conclusion**

After two decades of consultation after consultation, Hong Kong deserves something more refreshing, precise, understandable and practical in revamping its healthcare system. We want a health system that gives us a brighter future about improving and sustaining our health and healthcare, not one that is suppressed by our own pessimism in its inevitable and insurmountable burdens or that which we strive to solve its problems by using the same kind of thinking that had created them.

We cannot and should not allow prolonged malaise or more muddling through. Perhaps, a completely fresh and inclusive approach backed by renewed political determination to craft a clear new vision and innovative strategies to more efficiently mobilise existing and future resources is what is needed instead.

**References**


Geoffrey Lieu is Founder and Chairman Emeritus of The Institute for Health Policy and Systems Research (http://www.ihpsr.org.hk), a private not-for-profit voluntary think-tank based in Hong Kong. He may be reached at glieu@ihpsr.org.hk.

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Questions:
1. What is your clinical diagnosis and differential diagnoses?
2. What are the possible related aetiological agents and which one is the commonest nowadays?
3. How do you manage this condition?

(See P. 33 for answers)
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<td>Joint Surgical Symposium – Recurrences and Prognostication for Esophageal and Gastric Cancer</td>
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<td><strong>WED</strong> 1:00 pm</td>
<td>HKMA HK East Community Network – New Treatments in LDL and HDL for CV Risk Reduction</td>
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<td><strong>THU</strong> 12:30 pm</td>
<td>HKMA CME Series on Chronic Hepatitis B and its Complications (Hong Kong Island Series)</td>
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<td><strong>FRI</strong> 8:00am – 9:00am</td>
<td>Joint Surgical Symposium – Recurrences and Prognostication for Esophageal and Gastric Cancer</td>
<td>Department of Surgery, Hong Kong Sanatorium &amp; Hospital Tel: 2835 8696 Fax: 2892 7511 1 CME Point</td>
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<td>HKMA Kowloon City &amp; Kowloon East Community Networks - From Evidence to Action - Achieving Target Lipid Goal to Reduce Cardiovascular Risk</td>
<td>Mr. Patrick TSANG Tel: 2971 2940</td>
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<td><strong>SUN</strong> 9:00am</td>
<td>Seminar on Doping Control in Sports</td>
<td>Ms. Sonia Cheung Tel: 2527 8998 Fax: 2865 0345</td>
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<td><strong>SUN</strong> 2:00pm</td>
<td>HKMAPS 4th photo competition &amp; sharing session</td>
<td>Ms. Peony CHAN Tel: 2527 8285</td>
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<td>HKMA Tennis Tournament</td>
<td>Miss. Peony CHAN Tel: 2527 8285</td>
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<td><strong>MON</strong> 8:00pm</td>
<td>HKMA Choir Voice Training Course 2010</td>
<td>Dr. Hing-hoi HUNG / Ms. Taminy HUNG Tel: 2958 6066 / 9609 6064 Fax: 2958 6076 / 8344 5113 CME Accreditation: 1 Point (The College of Surgeons of Hong Kong)</td>
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<td><strong>TUE</strong> 1:00pm</td>
<td>HKMA HK East Community Network – 2010 RA Classification Criteria: Importance of Early Diagnosis and Effective Treatment</td>
<td>Ms. Kandy WAN Tel: 2811 9711 1.5 CME Point</td>
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<td><strong>TUE</strong> 8:00pm</td>
<td>FMSHK Officers’ Meeting</td>
<td>Ms. Sonia Cheung Tel: 2527 8898 Fax: 2865 0345</td>
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<td><strong>WED</strong> 7:30am</td>
<td>Hong Kong Neurosurgical Society Monthly Academic Meeting – Brain Edema</td>
<td>Dr. Gilberto LEUNG Tel: 2255 3368 Fax: 2818 4350</td>
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<td>HKMA Kowloon West Community Network - Erectile Disorder* (PENDING)</td>
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<td>HKMA Structured CME Programme with Hong Kong Sanatorium &amp; Hospital Year 2010 – Diagnosis of head and neck cancer: “look, feel and what else!”</td>
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<td><strong>SAT</strong> 2:30pm</td>
<td>Refreshor Course for Health Care Providers 2010/2011</td>
<td>Ms. Viviane LAM Tel: 2527 8452 2 CME Point</td>
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<td><strong>SUN</strong> 1:00 pm</td>
<td>HKMA - Diagnosing and Assessing Lung Diseases in the Office (YTM Series)</td>
<td>Ms. Alice TANG; Miss Carman WONG Tel: 2527 8285</td>
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<td><strong>SUN</strong> 7:30pm</td>
<td>HKMA Tennis Tournament</td>
<td>Ms. Peony CHAN Tel: 2527 8285</td>
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Calendar of Events

Date / Time | Function | Enquiry / Remarks
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14 **TUE** | 1:00 pm | HKMA Hong Kong East Community Network – The Role of TZDs in the Management of Type 2 Diabetes
Organiser: HKMA Hong Kong East Community Network; Chairman: Dr. YOUNG Ying Nam; Dominic; Speaker: Dr. WONG Bin Lap, Bernard; Venue: 慈信大廈復康村梅華道100合和商場203號
Ms. Alice TANG | Tel: 2527 8285

16 **THU** | 1:00 pm | HKMA New Territories West Community Network – Infant Nutrition (PENDING)
Organiser: HKMA New Territories West Community Network; Chairman: Dr. TSUI Fung; Speaker: TBC; Venue: Plentiful Delight Banquet (元朗美高慕吃茶), 1/F, Ho Shun Tai Building, 10 Tai Ching Street, Yuen Long, N.T.
Ms. Sonia Cheung | Tel: 2527 8898; Fax: 2865 0345

17 **FRI** | (18,19) | 2010 Asian Chinese Quality of Life Conference
Organiser: International Society for Quality of Life Research – Asian Chinese Chapter; Family Medicine Unit, Department of Medicine, Li Ka Shing Faculty of Medicine, The University of Hong Kong & Hong Kong Society for Quality of Life; Co-Chairmen: Prof. Peng-bin LIU, Prof; Cindy LAM & Mr. Kwok-tai LEUNG; Speakers: Various; Venue: Li Ka Shing Faculty of Medicine, The University of Hong Kong, 21 Sassoon Road,Pokfulam, Hong Kong
Ms. Candy LAW | Tel: 6509 6842; Fax: 3528 5727, Email: candy@hksosqol.org; Website: http://www.hksosqol.org/conf2010

18 **SAT** | 1:30pm | HKMA Kowloon East Community Network – Joint CME Course for Health Personnel 2010 on “Type 2 DM and Insulin Management”
Organiser: HKMA Kowloon East Community Network; Hong Kong College of Family Physicians; United Christian Hospital; Chairman: Dr. MA Ping Kwan, Danny; Speaker: Dr. TSANG Man Wo; Venue: Crystal Ball Room, 2/F, Cityview Hotel (formerly YMCA International House), 23 Waterloo Road, Kowloon (Yau Ma Tei MTR Exit A2)
Ms. Winniea LEE | Tel: 2861 0220

19 **SUN** | 7:30pm | HKMA 90th Anniversary Ball
Organiser: The Hong Kong Medical Association; Venue: Kowloon Tong Club
Ms. Peony CHAN | Tel: 2527 8285

31 **FRI** | 8:00pm | FMSHK 45th Anniversary Annual Dinner - Sensational 45th Anniversary with Music of the Eras
Organiser: The Federation of Medical Societies of Hong Kong; Venue: Run Run Shaw Hall, The Hong Kong Academy of Medicine Jockey Club
Ms. Sonia Cheung | Tel: 2527 8898; Fax: 2865 0345

Courses / Meetings

12/1/2011 | Seminar on Wound Care – Integrative Perspectives from Western and Chinese Medicine
Organiser: Association for Integrative Aesthetic Medicine, Hong Kong (AIAM); Chairman: Dr YU Chau Leung; Speaker: Dr. CHIU Kai Ming, Leo; Dr S.K. HUI & CMP EU Wen Shu; Venue: Lecture Hall, 4/F Duke of Windsor Social Service Building, 15 Hennessy Road, Wanchai, Hong Kong; Tel: 3575 8600, Fax: 2301 2414, Email: aiam.hk@yahoo.com, CME Accreditation: pending

14-16/1/2011 | Hong Kong International Acupuncture Conference – Neurological and Mental Illness
Organiser: Hong Kong Association for Integration of Chinese-Western Medicine & Hospital Authority; Chairman: Dr. Vivian Taam Chi Woon WONG; Speakers: Various; Venue: Hong Kong Academy of Medicine Jockey Club Building; Enquiry: Ms. Joy CHOW & Ms. Y.C. YEUNG, Tel: 2871 8787, 2871 8897 / 3119 1850, Fax: 2871 8898

22/1/2011 | Hepatobiliary & Pancreatic Surgery and Liver Transplantation
Organiser: Department of Surgery, The University of Hong Kong; Queen Mary Hospital & Hong Kong Chapter of American College of Surgeons; Venue: Underground Lecture Theatre, New Clinical Building, Queen Mary Hospital, Pokfulam, Hong Kong; Enquiry: Forum Secretary, Hong Kong Surgical Forum, Tel: (852) 2255 4885 / (852) 2255 4886, Fax: (852) 2819 3416, E-mail: hksf@hku.hk; Web-site: http://www3.hku.hk/surgery/forum.php

12-14/5/2011 | 18th Asian Congress of Surgery & 37th Philippine College of Surgeons Mid-year Convention
Organiser: Asian Surgical Association; Venue: Waterfront Cebu City Hotel & Casino, Lahug, Cebu City, Philippines; Enquiry: Congress Secretariat, Tel: (632) 9274973-74; (632) 9281083; (632) 9292359, Fax: (632) 9292297, E-mail: secretariat@acs2011.org, Website: www.acs2011.org

Society News

1. Osteoporosis Society of Hong Kong
Updated office-bearers for the year 2010-2012 are as follows: President: Dr. Tai-pang IP; Honorary Secretary: Dr. Ka-kui LEE; Honorary Treasurer: Dr. Eddie Siu-lun CHOW

The FMSHK would like to send its congratulations to the new office-bearers and look forward to working together with the society.
Conceptual issue on QOL
1. Prof John Ware (USA) will conduct a 3 hour workshop on Conceptualizing and Measuring Patient Reported Outcomes.
2. Prof Fang Ji (China) will talk on new insight on Patent Reported Outcome
3. Mona Martin (USA) will talk on claiming benefit from the regulatory authority perspective.

QOL Research Statistics
1. Dr. Daniel Fong (HK) will conduct a workshop on the use of structural equation model in QOL research
2. Prof Benny Zee (HK) will lecture on Quality of life analysis approaches in clinical trials
3. Dr. Donald McKnight BUSHNELL (USA) will lecture on clinical significance and minimal importance changes in QOL research
There are also invited plenary and symposium sessions on QOL in Chinese medicine, palliative care, mental health, chronic illness and other special population. Please check out the program.

www.hksqoql.org/conf2010

Organizers
International Society for Quality of Life Research – Asian Chinese Chapter
Department of Family Medicine and Primary Care, The University of Hong Kong
Hong Kong Society for Quality of Life
Co-Organizers
First Affiliated Hospital, Guangzhou University of Traditional Chinese Medicine
School of Nursing, Li Ka Shing Faculty of Medicine, The University of Hong Kong
The Nethersole School of Nursing, Faculty of Medicine, The Chinese University of Hong Kong
Department of Applied Social Studies, College of Humanities & Social Science, The City University of Hong Kong

Supporting Organization
The Federation of Medical Societies of Hong Kong
Answer to Dermatological Quiz

1. Papular acrodermatitis (Gianotti-Crosti syndrome). The main differential diagnoses are scabies, arthropod bite, papular urticaria, drug eruption, molluscum contagiosum and other viral exanthema.

2. Hepatitis B virus was originally quoted as its aetiological agent, but is actually an uncommon link. Epstein-Barr virus is now the commonest reported cause. Other agents reported include cytomegalovirus, coxsackie viruses B, respiratory syncytial virus, parainfluenza, poliovirus and beta-haemolytic streptococcus. Post-immunisation with vaccinia or BCG has also been reported as related cause.

3. As the natural course of this condition is benign, the treatment is mainly supportive. A thorough history and physical examination should be performed, but evaluation for hepatitis or other specific viral agents (e.g. hepatitis B virus) should be performed only if indicated. Although this condition mainly occurs in children, it has been reported in adults as well, but exclusively in women. The prognosis is good with spontaneous resolution, usually within 3-4 weeks, although the eruption may occasionally persist for up to several months. If lesions persist, other diagnosis should be considered.

Dr. Lai-yin CHONG

MBBS(HK), FRCP(Lond, Edin, Glasg), FHKCP, FHKAM(Med)
Private Dermatologist
For initial and adjunct use in patients with type 2 diabetes,*  

**JANUVIA®** for **substantial efficacy** in a broad range of patients†  

**In clinical studies:**  
- **Substantial HbA1c reduction** through a physiologic mechanism of action‡  
- **Generally weight neutral** therapy with a **low risk of hypoglycemia** §, ‡  
- **Once-daily** oral treatment‡  

*Before prescribing, please consult the prescribing information.  
† JANUVIA® is indicated for initial use or as monotherapy or in combination with metformin, sulfonylurea, PPAR agonist.  
‡ As typical with other antihyperglycemic agents (e.g., metformin, thiazolidinediones) used in combination with a sulfonylurea, adding JANUVIA increased the incidence of sulfonylurea-induced hypoglycemia compared to a placebo. A lower dose of sulfonylurea may be considered to reduce the risk of sulfonylurea-induced hypoglycemia.  
§ JANUVIA® is contraindicated in patients who are hypersensitive to any components of this product. A dosage adjustment is recommended in patients with moderate or severe renal insufficiency or with end-stage renal disease requiring hemodialysis or peritoneal dialysis. The adverse experiences reported regardless of causality assessment in >5% of patients and more commonly than placebo or the active comparator included hypoglycemia, diarrhea, dyspepsia, flatulence, and headache.  

For appropriate patients with type 2 diabetes,  

**JANUMET®** provides **powerful HbA1c reductions** to help patients who need more than metformin alone  

**In clinical studies:**  
- **Powerful HbA1c, PPG, and FPG reductions** to help patients get to goal (HbA1c goal <7%)  
- **Comprehensive mechanism of action targets 3 key defects** of type 2 diabetes  

*Before prescribing, please consult the prescribing information.  

* HbA1c goal <7%.  
JANUMET® is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus when treatment with both sitagliptin and metformin is appropriate.  
JANUMET® is contraindicated in patients with: Renal disease or renal dysfunction, e.g., serum creatinine levels >2.5 mg/dL (males); >1.4 mg/dL (females); Known hypersensitivity to any other component of JANUMET®; acute or chronic metabolic acidosis, including diabetic ketoacidosis with or without coma. In clinical studies as monotherapy and in combination with other agents, the adverse experiences reported regardless of causality assessment in >5% of patients and more commonly than placebo or the active comparator included: hypoglycemia, orthostatic hypotension, upper respiratory tract infection, headache, and peripheral edema. There have been postmarketing reports of serious hypersensitivity reactions, including anaphylaxis, angioedema, and exfoliative skin conditions including Stevens-Johnson syndrome. When JANUMET® is used in combination with a sulfonylurea, a lower dose of the sulfonylurea may be considered to reduce the risk of hypoglycemia. For additional adverse experience information, see the product circular.