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THE HONG KONG 香港醫訊
MEDICAL DIARY

VOL.14 NO.11 NOVEMBER 2009

*Gastroenterology &
Hepatology*

OFFICIAL PUBLICATION FOR THE FEDERATION OF MEDICAL SOCIETIES OF HONG KONG ISSN 1812 - 1691



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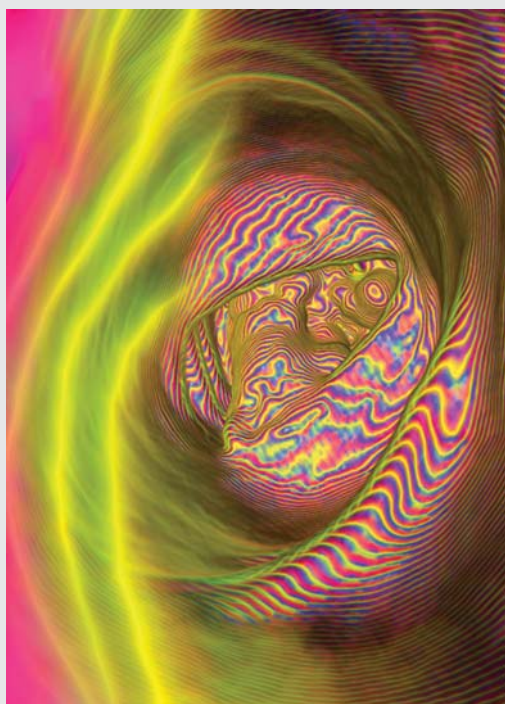
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The Cover Shot



Saying Hello to Cancer

This is an artistically rendered 3D CT scan. It represents a virtual endoscopic view inside the sigmoid colon showing a colon cancer (centre) surrounded by mucosal folds. With modern advanced medical technology, we can now see a cancer face-to-face using endoscopy or medical imaging.



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Published by
The Federation of Medical Societies of Hong Kong

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Editorial

Dr. Thomas Sik-to LAI

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Dr. Thomas Sik-to LAI

Editor

To state that the future of gastroenterology is bright is readily understandable because, for gastroenterologists, this specialty is indeed the "largest" in internal medicine. The digestive system entails the largest organ complex which is the gut together with the exuberant outgrowths such as the liver and pancreas, contains the largest number of endocrine, immune, smooth muscle and nerve cells, carries the largest cancer load, and suffers the largest varieties of acute and chronic inflammatory conditions associated with infective or non-infective causes.

As in all fields of clinical medicine, change is inevitable as practitioners and researchers become more knowledgeable about the disease states. These changes will continue to alter current practice and how gastroenterologists are trained, as well as the economics and organisation of gastroenterology practices in all settings, both private and public. Technological developments in gastroenterological imaging and testing are liable to make some common endoscopic procedures currently performed by trained gastroenterologists obsolete. To maintain the position as experts, gastroenterologists may need to offer new services such as obesity treatment, enteral / parenteral nutrition, and gastroenterological cancer chemotherapy among others. In their changing role, gastroenterologists will also have to act as the "coordinator" or "manager" of all dimensions of digestive health care in a gastroenterology patient.

Thus, gastroenterological training, through college fellowship programmes and Continuing Medical Education for those already in practice, will have to keep pace with the new directions and advancements in the field. Coupled with this trend, basic diagnostic and therapeutic competence building should remain the prime focus in our education process. I hope that our articles in the Diary can contribute, in some way, to the important mission of facilitating learning in Continuous Professional Development.

In this issue, we have gathered a strong team of knowledgeable and well known gastroenterologists to discuss various topics of current interest, with emphasis on the real life approach in daily practice and also reflection on changes and recent thinking in these particular areas. The subjects we are going to cover include management of peptic ulcer bleeding, endoscopic management of biliary obstruction, chronic constipation, hepatitis B infection in special populations, clinical application of transient elastography in liver diseases and management of ascites in cirrhosis.

It is my sincere wish that readers will find the chosen reviews useful and ultimately can translate them into benefit for our patients.

Management of Peptic Ulcer Bleeding

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Dr. Carmen Ka-man NG

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 30 November 2009.

Upper gastrointestinal bleeding (GIB) is defined as haemorrhage proximal to the ligament of Treitz. Peptic ulcer bleeding accounts for 60% of the cases.¹ Despite advances in endoscopic treatment and pharmacotherapy, the mortality of upper GIB remains unchanged. In-hospital mortality was found to be 7.1% in 3220 patients admitted for bleeding peptic ulcers from 1993 to 2003 to a teaching hospital in Hong Kong.² History taking and physical examination help to define the underlying cause. It should be followed by a detailed haemodynamic assessment. Resting tachycardia (pulse ≥ 100 /min), hypotension (sBP < 100 mmHg) and postural changes (\uparrow pulse of ≥ 20 /min or \downarrow sBP ≥ 20 mmHg on standing) represent a significant loss of intravascular volume. Fluid resuscitation is the first priority in patient management. Crystalloid should be infused via a large-bore catheter. Supplementary oxygen and supportive transfusion should be considered on a case to case basis.

Medical Therapy

The concept of clot stabilisation by raising the intragastric pH has led to the use of a high dose proton pump inhibitor (PPI) in acute GIB. A pH > 6 favours platelet aggregation, clot formation and inhibition of fibrinolysis.³

The effect of preemptive PPI before endoscopy was studied. Daneshmend had conducted a randomised study in 1147 unselected patients presenting with upper gastrointestinal bleeding. 578 patients were given omeprazole (bolus 80mg IVI, followed by 40mg IVI for three doses, then 40mg orally every 12 hours) compared to a placebo arm of 569 patients.⁴ Endoscopic signs of upper GIB in the treatment group (33%) were significantly lower than in the placebo group (45%), $p < 0.0001$. Another trial conducted in Hong Kong studied the use of PPI infusion (omeprazole 80mg IV bolus, followed by 8mg infusion / hour) before endoscopy in non-aspirin users admitted with overt signs of upper GIB.¹ The need for endoscopic treatment was lower in the PPI group (19.1%) than the placebo group (28.4%). Fewer patients had actively bleeding ulcers and more clean-based ulcers were found in the treatment group. Hospital stay was less than 3 days in 60.5% of the treatment group as compared to 49.2% in the placebo group. The Cochrane review suggested

that PPI treatment initiated prior to endoscopy in patients with upper GIB significantly reduced the proportion of patients with stigmata of recent haemorrhage at index endoscopy.⁶ It has no effect on the rate of rebleeding, surgery or mortality. In a cost-effective analysis, PPI reduced endoscopic therapy by 7.4% and resulted in a lower cost-effectiveness ratio per endoscopic therapy averted than the placebo.⁵ The approach of preemptive PPI before endoscopic diagnosis of upper GIB is still controversial, especially in countries with high prevalence of variceal bleeding.⁷

There is more evidence of using PPI as a medical adjunct after endoscopic haemostasis for peptic ulcer demonstrating high risk stigmata of bleeding. Khuroo had shown the efficacy of omeprazole (40mg given orally every 12 hours for 5 days) in decreasing the rate of further bleeding and need for surgery in a double-blind, placebo-controlled trial of 220 patients.⁸ A subgroup analysis showed positive finding in patients with non-bleeding visible vessels or adherent clots, but not in those with arterial spurting or oozing. Lau et al assessed the effect of intravenous omeprazole on recurrent bleeding after endoscopic treatment (epinephrine injection followed by thermocoagulation) of bleeding peptic ulcers.⁹ They concluded that high-dose infusion of omeprazole (80mg IV bolus, followed by infusion at 8mg per hour for 72 hours) reduced the rate of recurrent bleeding, decreased the need for endoscopic retreatment, blood transfusions, and shortened the length of hospitalisation. A systemic review of twenty-four randomised trials of PPI (oral or intravenous) compared with placebo or H₂-blocker in 4373 patients with peptic ulcer bleeding showed no difference in overall mortality (3.9% vs 3.8%).¹⁰ However, a significant reduction in rate of rebleeding (10.6% vs 17.3%) and surgery (6.1% vs 9.3%) were observed. The effect is more pronounced in studies conducted in Asian countries where all cause mortality was also found to be reduced. This may be explained by the ethnic differences in the rate of PPI metabolism, lower gastric parietal cell mass and higher prevalence of *Helicobacter pylori* infection.¹¹ An international trial conducted in 16 countries had tried to answer the question of ethnic difference in PPI response.¹² Intravenous esomeprazole 80mg bolus, followed by 8-mg/h infusion over 72 hours or matching placebo was given after successful endoscopic haemostasis to 764 patients with high-risk ulcer lesions. Recurrent bleeding



was found to be significantly less within 72 hours, at 7 days and 30 days. It showed a trend towards fewer surgery and lower all-cause mortality. The efficacy of PPIs in preventing recurrent peptic ulcer bleeding should not be race-specific and could be applied universally.

Endoscopic Therapy

Timing of endoscopy is a balance between clinical need and resources. It is usually scheduled in the following endoscopic session, within 24 hours of admission. Endoscopic intervention decreased rates of further bleeding, surgery, and mortality in patients with high-risk endoscopic features,¹³ defined as Forrest class I and IIa/b lesions. (Table 1)¹⁴

In case of torrential upper GIB, the stomach could be filled with clots. By inducing gastric emptying, 250mg erythromycin given intravenously 20 minutes before endoscopy, had resulted in an empty stomach in 82% (42/51) compared with 33% (18/54) in the placebo group ($p < 0.001$).¹⁵ Endoscopic duration was shortened. By infusion of erythromycin 30 to 90 minutes before endoscopy, at 3mg/kg over 30 minutes, image quality was significantly improved.¹⁶ Both studies showed a reduction in the need for a second-look endoscopy. It is, however, not used routinely in all upper GIB patients.

A variety of endoscopic haemostatic techniques are available. They include injection, thermal therapy and mechanical treatment. A direct comparison of the various modalities is difficult.¹⁷ The method used depends on the location of the vessels and local expertise. Adrenaline monotherapy is inferior to other monotherapies in preventing rebleeding. Adding a second haemostatic method to adrenaline injection achieves a better result than stand alone adrenaline injection therapy.¹⁸ However, dual endoscopic therapy had no advantage over thermal or mechanical monotherapy in improving patient's outcome.¹⁹

Injection Method

Diluted adrenaline (1:10 000) is the most widely used injection substance. It causes vasoconstriction and provides volume tamponade. Initial haemostasis is satisfactory but an unacceptably high rebleeding rate is observed since the injected fluid dissipates rapidly. The use of sclerosants (polidocanol, ethanolamine, alcohol and hypertonic glucose) for non-variceal bleeding is out of favour. It can cause transmural necrosis. Its injection in the proximal stomach, especially the fundus, is contraindicated due to risk of late perforation.

Thermal Method

The bipolar probe and the heater probe achieve haemostasis by occluding the vessel through compression, followed by sealing it with heat (coaptive coagulation). Arteries associated with visible vessels have a mean external diameter of 0.7mm (0.1 - 1.8mm).²⁰ Contact thermal therapy can coaptively coagulate arteries which are less than 2mm in diameter.²¹ Argon plasma coagulation is the representative non-contact thermal method for coagulation. It delivers a stream of argon gas to conduct

heat for electrocoagulation. It is especially effective in treating vascular lesions.

Mechanical Method

Endoclips provide at the spot mechanical clamping of the vessels. Newer models allow reopening and repositioning. It is difficult, if not impossible, to be placed tangentially. The deploying mechanism is weakened with the scope in retroflexion. Hence lesions in the fundus pose a challenge to therapy.

Table 1. Forrest classification of peptic ulcers in upper GIB.

Forrest class	Endoscopic appearance	Risk of rebleeding %
Ia	Arterial spurting	100
Ib	Arterial oozing	17-100
IIa	Non-bleeding visible vessel	8-81
IIb	Sentinel clot	14-36
IIc	Haematin covered flat spot	0-13
III	Clean base	0-10

Surgery

A history of peptic ulcer disease, previous ulcer bleeding, shock at presentation, active bleeding at endoscopy, large ulcers of >2cm in diameter, large bleeding vessel (≥ 2 mm) and ulcers at the lesser curvature of stomach or over the posterior / superior duodenal bulb are predictors of endoscopic treatment failures.⁷

The aim of emergency surgery is not to cure the disease but rather to stop the bleeding.⁷ It is employed in selected groups of patients. They include patients suffering from profuse blood loss rendering an unstable haemodynamics despite intravascular replacement with fluid and blood products, patients who may not tolerate recurrent or worsening bleeding and patients whose endoscopic interventions are ineffective.

Risk Score

Various risk scoring systems were designed to risk stratify patients with acute GIB into appropriate and cost-effective levels of care. The two most widely employed are the Rockall score and the Glasgow-Blatchford score.

The Rockall score (RS) was derived from 4185 admissions of patients older than 16-year old for upper GIB and validated with an additional 1625 patients' data. It was published in 1996 and revalidated a year later.^{22, 23} It comprises the pre-endoscopic clinical score and the complete score after addition of the two endoscopic variables. It has a minimum score of 0 and a maximum score of 11. (Table 2) The primary intent of the study is to predict mortality. (Table 3) At high score, it loses the discrimination power and tends to overestimate. It is useful in demonstrating low rebleeding risk and low mortality in individuals with low score.²⁴

The Glasgow-Blatchford score (GBS) assesses clinical data presented upon admission to predict the need for clinical intervention (transfusion and endoscopic intervention).²⁵ The study was conducted on 1748

patients from 19 hospitals and revalidated prospectively in another 197 adult patients. The score ranges from 0 to 23. (Table 4) From the full risk score, a fast-track screening procedure was derived. Patients fulfilling all of the following were classified as having low risk for clinical intervention, namely blood urea less than 6.5 mmol/L, haemoglobin more than 130g/L for men or 120g/L for women, systolic blood pressure 110 mm Hg or higher, and pulse less than 100 beats per min.

These two scoring systems were tested prospectively in patients admitted to four hospitals in the United Kingdom with upper GIB.²⁶ Sixteen percent (105/649) and 28% (184/657) scored 0 by GBS and RS respectively. No intervention and no death was recorded in the low-risk group identified by a GBS of 0. One death and 44 interventions (21 endoscopic or surgical) and 23

transfusions were noted in 32 (17%) of patients with an admission RS of 0. In phase 2 of this study, GBS low-risk criteria were used to assess 572 consecutive patients presenting to A&E departments at two hospitals. Overall, 123 (22%) individuals were identified as low risk, with 84 (68%) of this group managed as outpatients. All patients were offered outpatient endoscopy but only 23 (40%) attended. None of the non-attendees was readmitted for upper GIB or died in 6 months. Among those who returned for endoscopy, none had malignant disease, varices or ulcers that required intervention. GBS was superior to RS for prediction of need for intervention or death. It helps to identify patients who are safe to be managed as outpatients. GBS reduces admissions for upper GIB and allows more appropriate use of in-patient resources.

Table 2. Rockall Risk Score.

Variable	Score			
	0	1	2	3
Age	< 60 years	60 - 79 years	≥ 80 years	
Shock	'No shock' sBP ≥ 100, pulse <100	'Tachycardia' sBP ≥ 100, pulse ≥ 100	'Hypotension' sBP < 100	
Co-morbidity	No major comorbidity		Cardiac failure, ischaemic heart disease and major comorbidity	Renal / liver failure Disseminated malignancy
Diagnosis	Mallory-Weiss tear, no lesion identified and no SRH	All other diagnoses		Malignancy of upper GIT
Major SRH	None or dark spot only		Blood in upper GIT, adherent clot, visible or spurting vessel	

sBP, systolic blood pressure; SRH, stigmata of recent haemorrhage.

Table 3. Observed rebleeding and mortality by Complete Rockall

	Score								
	0	1	2	3	4	5	6	7	8+
Re-bleed (%)	4.9	3.4	5.3	11.2	14.1	24.1	32.9	43.8	41.8
Deaths (total %)	0	0	0.2	2.9	5.3	10.8	17.3	27	41.1

Table 4. Blatchford Score.

Admission risk marker	Score component value
Blood urea (mmol/L)	
≥6.5 <8.0	2
≥8.0 <10.0	3
≥10.0 <25.0	4
≥25	6
Haemoglobin (g/L) for men	
≥120 <130	1
≥100 <120	3
<100	6
Haemoglobin (g/L) for women	
≥100 < 120	1
<100	6
Systolic blood pressure (mm Hg)	
100 - 109	1
90 - 99	2
<90	3
Other markers	
Pulse ≥100 (per min)	1
Presentation with melaena	1
Presentation with syncope	2
Hepatic disease	2
Cardiac failure	2

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MCHK CME Programme Self-assessment Questions

Please read the article entitled "Management of Peptic Ulcer Bleeding" by Dr. Carmen Ka-man NG 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 30 November 2009. 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. With modern modalities of endoscopic treatment, the mortality rate of peptic ulcer bleeding is decreasing.
2. Fluid resuscitation is the first priority in managing patients with upper gastrointestinal bleeding.
3. Acidic pH is unfavourable for clot stabilisation.
4. Preemptive proton pump therapy initiated before endoscopy for patients presenting with upper gastrointestinal bleeding reduces mortality.
5. High dose proton pump therapy given after endoscopic haemostasis reduces the rate of rebleeding and surgical requirement.
6. Endoscopic intervention for ulcers demonstrating high-risk stigmata of haemorrhage can decrease further bleeding, surgical intervention and mortality.
7. Stand alone adrenaline injection therapy is as effective as other monotherapies.
8. Ulcers at the lesser curvature of stomach or over the posterior / superior duodenal bulb are predictors of endoscopic treatment failures.
9. The Rockall Score is most useful in predicting rebleeding and mortality at high scores.
10. The Glasgow-Blatchford score does not include age into its scoring system.

ANSWER SHEET FOR NOVEMBER 2009

Please return the completed answer sheet to the Federation Secretariat on or before 30 November 2009 for documentation. 1 CME point will be awarded for answering the MCHK CME programme (for non-specialists) self-assessment questions.

Management of Peptic Ulcer Bleeding

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1 2 3 4 5 6 7 8 9 10

Name (block letters): _____ HKMA No.: _____

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Answers to October 2009 Issue

Medical Treatment of Premature Ejaculation

1. F 2. T 3. T 4. F 5. F 6. T 7. F 8. T 9. F 10. T

Endoscopic Management of Biliary Obstruction

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Dr. Moon-sing LAI

Introduction

The first endoscopic retrograde cholangiopancreatography (ERCP) was performed in 1968. It is an endoscopic technique in which a specialised side-viewing upper endoscope (duodenoscope) is guided into the second part of the duodenum. A catheter can be passed through the instrument channel to cannulate the bile and/or pancreatic ducts with the help of a bridge at the tip of the duodenoscope. The bile and/or pancreatic ducts are then opacified by injection of a contrast medium, thereby permitting their visualisation under fluoroscopy and allowing for a variety of therapeutic interventions. Endoscopic sphincterotomy (EST) was subsequently introduced in 1974 as an endoscopic surgical technique facilitating therapeutic intervention for common bile duct stones and pathology during ERCP.

Causes of Biliary Obstruction

Biliary obstruction or cholestasis is a common medical or surgical problem. Broadly speaking, the causes can be divided into intrahepatic and extrahepatic (see table 1).

Table 1: Causes of Biliary Obstruction

Extrahepatic
1. Choledocholithiasis
2. Diseases of the bile ducts
<input type="checkbox"/> • Malignant - Cholangiocarcinoma
<input type="checkbox"/> • Benign - Primary sclerosing cholangitis, AIDS cholangiopathy, <input type="checkbox"/>
<input type="checkbox"/> hepatic arterial chemotherapy, post-surgical strictures
3. Extrinsic compression of the biliary tree
<input type="checkbox"/> • Malignant - Pancreatic carcinoma, metastatic <input type="checkbox"/> <input type="checkbox"/>
<input type="checkbox"/> lymphadenopathy, hepatoma
<input type="checkbox"/> • Chronic pancreatitis
<input type="checkbox"/> • Vascular enlargement (aneurysm, portal cavernoma)
3. Others: haemobilia, parasites (Ascaris)
Intrahepatic: hepatic disorders with prominent cholestasis
1. Diffuse infiltrative diseases
<input type="checkbox"/> • Granulomatous diseases (mycobacterial infection), <input type="checkbox"/>
<input type="checkbox"/> amyloidosis, malignancy
2. Inflammation of intrahepatic bile ductules or portal tract
<input type="checkbox"/> • Graft-versus-host disease, primary biliary cirrhosis, and drug <input type="checkbox"/>
<input type="checkbox"/> toxicity (chlorpromazine, erythromycin)
3. Miscellaneous
<input type="checkbox"/> • Benign recurrent intrahepatic cholestasis, drug toxicity <input type="checkbox"/>
<input type="checkbox"/> (oestrogen), total parenteral nutrition, bacterial infections, <input type="checkbox"/>
<input type="checkbox"/> uncommon manifestations of viral or alcoholic hepatitis, <input type="checkbox"/>
<input type="checkbox"/> intrahepatic cholestasis of pregnancy and postoperative <input type="checkbox"/>
<input type="checkbox"/> cholestasis

Choledocholithiasis +/- Cholangitis

ERCP plays a pivotal role in the treatment of choledocholithiasis with acute cholangitis because of its diagnostic and therapeutic capabilities and association with a lower rate of complications than surgical or transhepatic drainage. In acute cholangitis, ERCP should be done within 24 hours and the main aim of the procedure is to provide urgent biliary drainage and decompression as soon as possible¹. The bile duct is cannulated as in diagnostic ERCP. It is important to avoid injecting too much contrast during the initial cholangiogram which can result in further increase in intrabiliary pressure facilitating cholangiovenous reflux of infected materials into the hepatic venous circulation and septicaemia. Bile should be aspirated to decompress the bile ducts as soon as deep cannulation is achieved. The aspirated bile should also be sent for bacteriology study. ERCP can achieve biliary decompression by sphincterotomy and stone extraction or stent placement. In critically ill patients with coagulopathy in which sphincterotomy is contraindicated, urgent biliary drainage with a nasobiliary drain or an internal stent across the sphincter and stone should be inserted.

In patients with stable vital signs or without evidence of acute cholangitis, the extraction of the stone can be achieved within the same session. Sphincterotomy should be performed first and the stone can then be removed with a stone extraction basket or balloon (Fig 1). With multiple stones are present, the most distal stone (i.e. the one closest to the ampulla) should be removed first to reduce the risk of impaction. If a proximal stone is tried to be removed, it may create a "traffic jam" as the captured stone is pulled through the remaining distal stone. The clearance of stone extraction should then be confirmed with occlusive cholangiogram with the help of a balloon catheter.

One of the challenges is presence of giant stone(s) (stone>2 cm). The stone(s) can be fragmented by basket mechanical lithotripsy (BML), or mother and baby choledochoscopy and intraductal lithotripsy with electrohydraulic lithotripsy (EHL) or intraductal laser lithotripsy. If a stone cannot be removed, long term stenting may result in dissolution of the stone and then the stone can be removed with interval endoscopic lithotripsy. Finally, extracorporeal shock-wave lithotripsy (ESWL) or open surgery can be considered in those rare difficult cases.

Acute complications occur in 6.85% of patients with sphincterotomy. They include bleeding (1.34%),



retroperitoneal perforation (0.6%), pancreatitis (3.47%) and cholangitis (1.44%) and 30 days procedure related mortality of 0.07%². Long-term complications following endoscopic sphincterotomy include stone recurrence, papillary stenosis, and cholangitis, which occur in approximately 6 to 24 percent of patients³.

Endoscopic balloon sphincteroplasty or dilation (EBD) was introduced by Staritz et al. in 1983 as an alternative to sphincterotomy (EST). The main theoretical advantage of this technique is that it does not involve cutting of the biliary sphincter and preserves the function of it. Acute complications, especially bleeding and speculated long-term complications of EST, may be less likely. In patients for whom EST is unsuitable, such as those with coagulopathy, at risk of infection, post BII gastrectomy⁴ and probably those older patients, EBD should be considered as the alternative⁵. Recently, the combined use of EST and EBD with a large dilator balloon (ELBD) was performed. A midincision EST (m-EST) rather than a full incision is performed followed by dilatation with large balloon dilation (diameter 15-20 mm). The bile duct stones, even a large one, can be removed with ease with the standard stone extraction basket. Thus the complications due to EST and EBD are avoided or lessened while a large opening of the ampulla of Vater can be established so that the application of mechanical lithotripsy is unnecessary⁶. However, the sphincter of Oddi function is not preserved after ELBD, and results in an even worse condition than after EST. The indications and role of ELBD remain speculative and need further studies.

Benign Biliary Strictures or Extrinsic Compression

Benign biliary strictures can occur in surgical injuries, anastomotic stenoses, AIDS cholangiopathy and primary sclerosing cholangitis. The bile duct can be compressed resulting in biliary obstruction by neighbouring benign lesions like chronic pancreatitis or ampullary pathology including stenosis or muscular dysfunction.

For biliary strictures, ERCP can establish the diagnosis as well as relieve the biliary obstruction in those situations. ERCP permits the aspiration of bile for culture, biopsy of the biliary mucosa, and cholangioscopy. Endoscopic management of patients with stricture comprises endoscopic balloon dilation, placement of biliary stents, or a combination of the two. The biliary strictures can be treated by graded dilatation with catheters and balloons. Endoscopic balloon dilatation can be performed with 4-8 mm diameter balloons that are passed over a prepositioned guidewire. In the case of very tight strictures, dilating catheters can be used to facilitate advancement of the balloon catheter. Multiple procedures may be required for radiological resolution and the overall success rate of this treatment is 75 percent, a rate similar to that with surgical therapy. Long term stenting for bile duct stricture is usually required after dilatation to maintain the patency. They should be treated with at least two 10 Fr plastic stents that are electively exchanged every 3 months to prevent cholangitis due to clogging⁷. Some endoscopists suggest to insert as many stents as

possible in order to obtain maximum dilatation⁸. After a period of 12 months, the stents can be removed and observe for restenosis. There is currently no place for self-expandable metal stents for this indication.

Endoscopic therapy of chronic pancreatitis is an expanding area for the interventional endoscopist. Such strictures are a result of a fibrotic inflammatory restriction or compression by a pseudocyst. Other than stenting of bile duct to relieve the biliary obstruction, endoscopic treatment of chronic pancreatitis may be indicated. These include endoscopic sphincterotomy (bile duct and/or pancreatic duct), stricture dilatation of pancreatic duct with or without stenting, pancreatic stone extraction, ESWL, endoscopic ultrasound-guided celiac plexus block.

Benign diseases of the ampulla of Vater may also cause chronic biliary obstruction because of sphincter of Oddi dysfunction (SOD) (abnormal contractions of the sphincter of Oddi) or scarring of the ampulla. The ablation of pancreatic or biliary sphincters with sphincterotomy is highly successful in relieving the symptoms associated with ductal obstruction but remains controversial in patients in whom the disorder is manifested only by abdominal pain.

Malignant Biliary Obstruction

Malignant causes include pancreatic, gallbladder, ampullary and cholangiocarcinoma. Pancreatic, gallbladder, and cholangiocarcinoma are rarely resectable and have poor prognoses. Ampullary carcinoma has the highest surgical cure rate of all the tumours that present as painless jaundice. Hilar lymphadenopathy due to metastases from other cancers may cause obstruction of the extrahepatic biliary tree.

The role of ERCP in pancreaticobiliary malignancies is both diagnostic and therapeutic: (a) confirm the diagnosis of obstructive jaundice with suspected pancreaticobiliary malignancy; (b) obtain tissue for histopathologic diagnosis e.g. cytology brush of the biliary stricture; (c) establish the exact site of obstruction, (d) decompress the bile duct; and (e) facilitate palliative therapy such as intraluminal brachytherapy or intraductal photodynamic therapy.

For malignant biliary obstruction due to pancreaticobiliary malignancies, endoscopically placed stents can provide minimally invasive and effective reestablishment of flow of bile into the duodenum and palliation of symptoms of anorexia, pruritus and jaundice associated with biliary obstruction. Randomised trials have shown no difference in survival between endoscopic stent placement and surgical bypass for malignant obstructive jaundice but lower morbidity and procedure-related mortality⁹.

Plastic stents made of radio-opaque polyethylene or Teflon are often used to initially achieve drainage while the diagnostic work-up is ongoing or when a metal stent cannot be inserted for technical reasons. For unresectable malignancies involving the bifurcation of the bile duct causing obstruction to the right and left hepatic ducts, there is controversy about unilateral versus bilateral stents. Given that only about 25 percent

of the liver needs to be drained for adequate palliation, unilateral stenting of either the right or the left system appears to be sufficient in the absence of biliary tract sepsis¹⁰.

For long term palliation, self expandable metal stents are preferred over plastic stents because they have larger diameters. They are much less likely to become clogged by debris or tumour ingrowth and have a significantly longer patency than plastic stents¹¹. The higher cost of metal stents as compared with plastic stents is offset by a decrease in frequency of ERCP for stent exchange and hospitalisation. Therefore, for patients with pancreaticobiliary malignancies who are expected to live beyond a few months, it is preferred to replace the plastic stent with a metal one as soon as feasible. However, tumour ingrowth into the mesh of the metal stent can cause subsequent occlusion. Occluded stents are usually best managed by endoscopic insertion of a second metal stent or a plastic stent. Covered as compared to bare metal stents may have fewer problems with clogging from tumour ingrowth and they are more easily removable than are uncovered metal stents. However, one potential problem with covered stents for hilar strictures is that deployment may inadvertently result in occlusion of a major hepatic duct. Thus, covered stents are not necessarily preferred over uncovered stents.

Rarely ampullary adenoma or early cancer of ampulla without infiltration into the bile and pancreatic ducts can be cured by ERCP. Endoscopic resection therapy with endoscopic ampullectomy in a radical fashion using pure cutting current has been used as a curative treatment of adenoma or early cancer of the major duodenal papilla¹².

Conclusion

Biliary obstruction is a common medical or surgical problem. It can be caused by a variety of benign and malignant conditions and most of them can be diagnosed and managed by ERCP. With the introduction of non-invasive e.g. magnetic resonance cholangiopancreatography (MRCP)¹³ or less invasive methods e.g. endoscopic ultrasonography (EUS)¹⁴ with comparable sensitivity and specificity in the diagnosis of biliary and pancreatic pathology, the focus of ERCP has begun to shift from both a diagnostic and therapeutic modality to a mostly therapeutic interventional method. Therefore, in managing patients with biliary obstruction, diagnostic ERCP should be performed by those who are capable of proceeding with and completing the required endoscopic therapeutic interventions and should not be performed as a separate procedure.


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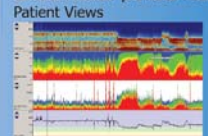
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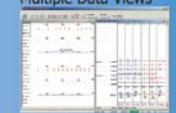
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Dermatological Quiz

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Yaumatei Dermatology Clinic, Social Hygiene Service



Dr. Ka-ho LAU



Lesions on dorsum of right hand

This 50-year-old female teacher had three months' history of this slightly itchy skin rash on the dorsum of both of her hands and fingers (Figure). She also has similar itchy rash on her face, to which her family doctors prescribed with topical steroids. It seemed to calm down her rash partially. In the last three months, she felt increasingly unwell with aches and pain in the limbs, as well as difficulty in climbing stairs to her classroom at work. In addition, she noticed a marked weight loss recently.

Questions:




1. Name the physical signs shown in the clinical photo.
What is your provisional diagnosis?
2. How will you confirm your clinical diagnosis?
3. How will you manage this woman?

(See P. 38 for answers)

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Chronic Constipation

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Introduction

Chronic constipation is a common medical problem. In the Western population, the prevalence was reported as high as 24% in elderly subjects and more commonly among women¹. A recent survey conducted in Hong Kong showed a prevalence of 14% according to the Rome criteria².

Constipation can lead to complications such as anal fissures, rectal prolapse, faecal impaction or haemorrhoids. In addition, the symptoms of constipation adversely affect the patients' psychological health and their quality of life. Despite that we are gaining more insights into the pathogenesis of functional constipation; the mechanism of colonic motility and defecation, and the associated psychological disorders are still not fully understood. In addition, the treatment available for functional constipation is still not satisfactory. This current article presents a review of the epidemiology, investigations and management for functional constipation.

Epidemiology

The prevalence of patients reporting constipation symptoms in five European countries is summarised in Table 1⁴, with the prevalence rate ranged from 6% to 23% whereas the prevalence of constipation in the US was reported to range from 2% to 28%^{3,5,6,7} depending on the definition of constipation. The Society of American Family Physicians reported in 1998 that constipation affects as many as 26% of elderly men and 34% of elderly women⁸. Exact epidemiological data however are lacking, mainly because of the difference between self-reported constipation and scientifically defined constipation. Moreover, most of the studies investigated the prevalence of constipation only, and not the incidence of constipation. We have previously conducted a population-based telephone survey in the Hong Kong Chinese population on constipation using the diagnostic criteria of Rome II². We observed that there were 14.3% among the 3,282 interviewees diagnosed to have constipation. Among these interviewees, there were 33% of them complained of incomplete evacuation, and 12% complained of bowel opening less than 3 times per week.

Diagnostic Criteria For Constipation In Adults

Definitions of constipation vary widely, and therefore true prevalence estimates are difficult to compare across studies⁹. The diagnosis of functional constipation was based on the Rome III criteria. The diagnostic criteria was two or more of the following for at least 12 weeks in the preceding 12 months:

1. Straining in more than 25% of defecations
2. Lumpy or hard stools in more than 25% of defecations
3. Sensation of incomplete evacuation in more than 25% of defecations
4. Sensation of anorectal obstruction or blockade in more than 25% of defecations
5. Manual manouvres (e.g., digital evacuation) to facilitate more than 25% of defecations
6. Fewer than three defecations per week

Loose stools are not present, and there are insufficient criteria for the diagnosis of irritable bowel syndrome.

However, these criteria may not apply when the patient is taking laxatives. In addition, the Rome III criteria do not assess the severity of constipation. The Chinese population has a different cultural background diet habit. Therefore we have designed a Chinese constipation questionnaire¹⁰. The sensitivity and specificity of the questionnaire is 91%.

Table 1 - European Survey of Bowel Symptoms (%) in Five Countries

Characteristic	Countries				
	Italy	France	Spain	Germany	United Kingdom
A. Self-perceived constipation	23	19	17	10	6
*B. Difficult defecation	16	13	11	10	13
C. Laxative use	20	19	20	20	19

*: Straining and/or hard stools and/or incomplete evacuation at least once a month.

Causes Of Constipation

The causes of constipation can be categorised into symptoms due to extraintestinal causes or intestinal and anorectal causes. For the intestinal causes, it can be further subclassified into functional or organic causes (Table 2). Functional constipation can be further subcategorised into: slow transit, normal transit, outlet blockade and mixed type. Some patients with normal transit have features of irritable bowel syndrome.



Management Of Functional Constipation

The management of patients with constipation should include a detailed medical history and physical examination to exclude secondary causes for constipation such as anatomical or systemic lesions. Laboratory evaluation does not play a large role in the initial assessment of the patient. Baseline investigations should include thyroid-stimulating hormone (TSH) levels to rule out hypothyroidism in patients refractory to dietary management, serum electrolyte profile, including potassium, calcium, glucose, and creatinine, in patients with recent-onset constipation to assess an acute electrolyte imbalance and in chronically constipated patients for whom initial medical management has failed. Faecal occult blood should be tested in the chronically constipated middle-aged or elderly adult to exclude an obstructing neoplasm of the colon (Figure 1). In those patients who have been taking laxatives, detailed assessment of their use of and the possible side-effects should be made.

Extensive testing usually is reserved for people with severe symptoms, for those with sudden changes in number and consistency of bowel movements or blood in the stool, and for older adults. Because of an increased risk of colorectal cancer in older adults, barium enema, sigmoidoscopy or colonoscopy is indicated in elderly patients.

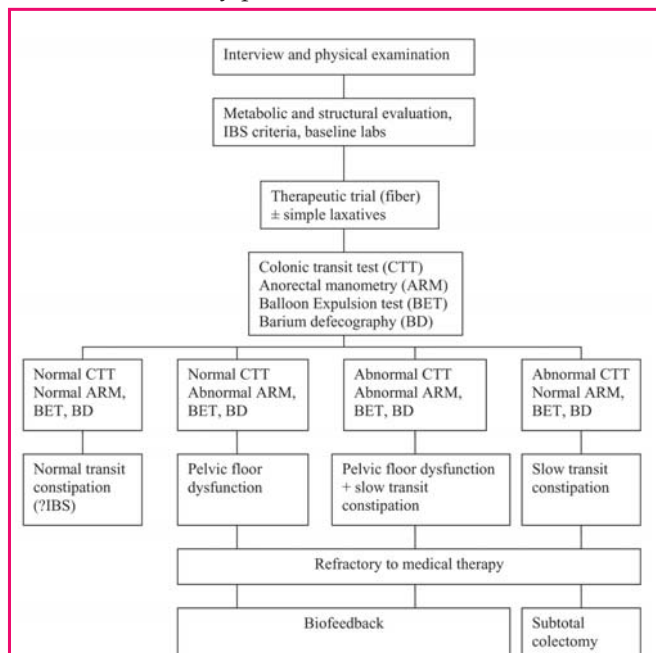


Figure 1. Flowchart for the Management of Patients with Constipation

Colonic Transit Time

Transit time studies may help differentiate colonic from pelvic floor dysfunction causing constipation. The colonic transit test quantifies the transit time of small radio-opaque markers through the colon. Subjects ingest one capsule (in which 20-24 markers have been placed) each morning for 3 days, abdominal x-rays are taken on days 4 and 7. Transit through the right, left and rectosigmoid segments of the colon can be calculated. Laxatives should be stopped prior to this test. The upper limit of normal colonic transit times ranged from 67-93 hours^{11,12,13,14}.

Balloon Expulsion Test

This is a simple office test for screening the presence of obstructed defecation. A balloon is inserted to the rectum and inflated with 50ml of air. The patient is asked to expel the balloon. If the patient fails to expel the balloon in one minute, the patient is likely to have obstructed defecation problems. However, the methodology of performing the balloon expulsion test has not been standardised.

Anorectal Manometry

Anorectal manometry evaluates the rectal propulsive force and the relaxation of the anal sphincter. A catheter or air-filled balloon inserted into the anus is slowly pulled back through the sphincter muscle to measure muscle tone and contractions. Failure to relax or presence of paradoxical contraction of the anal sphincter suggest the presence of obstructed defecation and identifies the underlying mechanism. In addition, the absence of the rectoanal inhibitory reflex suggests the presence of Hirschsprung's disease or megarectum. It is an accepted investigation by the American Gastroenterology Association for constipation and of potential value in the diagnosis and management of outlet obstruction¹⁵.

Defecography

This is an x-ray of the anorectal area that evaluates completeness of stool elimination, identifies anorectal abnormalities, and evaluates rectal muscle contractions and relaxation. During the examination, man-made stool is intilled into the rectum. The patient sits on a toilet positioned inside an x-ray machine and then relaxes and squeezes the anus and expels the solution. The detection of rectal intussusception (occult rectal prolapse) is the most important use of defecating proctography. In addition, defecating proctograms are used to calculate resting and straining anorectal angles and outlet obstruction.

Table 2. Causes of Chronic Constipation

Extraintestinal causes

- Endocrine: hypothyroidism, diabetes
- Metabolic: hypercalcemia, hypocalcemia
- Neurologic: Parkinson's disease, CVA, multiple sclerosis, spinal cord lesions, muscular dystrophies, autonomic neuropathy
- Rheumatologic: systemic sclerosis
- Psychological: depression, eating disorders
- Medications: narcotics, anticholinergics, antipsychotics, calcium channel blockers, anti-parkinson's therapy, anticonvulsants, TCA, iron, calcium, aluminium antacid, sucralfate

Intestinal and anorectal causes

- Functional disorders: slow colonic transit, anorectal dyssynergia, IBS
- Organic:
 - neoplasms, strictures
 - Anal stenosis
 - Rectocele, enterocele
 - Rectal intussusception, rectal prolapse
 - Hirschsprung's disease
 - Others: megarectum, solitary rectal ulcer

Treatment

Diet and Lifestyles

A diet with enough fibre (20 to 35 grams each day) helps form soft, bulky stool. Sufficient dietary fibre is needed to promote normality in bowel movement frequency over the long term¹⁷. Other changes that can help treat and prevent constipation include drinking enough water and other liquids, engaging in daily



exercise, and reserving enough time to have a bowel movement. Inactivity is a frequent cause of constipation in institutionalised or bedridden patients¹⁸. In addition, the urge to have a bowel movement should not be ignored.

Traditional Medicaitons

1. Bulk-forming laxatives - also known as fibre supplements, are taken with water. These laxatives are the safest but can interfere with absorption of some medicines.
2. Stimulants - increase motor activity of the bowels by direct action on the intestines.
3. Stool softeners - promote water retention in the faecal mass, thus soften the stool.
4. Lubricants - lubricate intestinal mucosa and soften stool.
5. Osmotic laxatives

It is unfortunate that most patients with chronic constipation are not satisfied with these traditional treatments.

Newer Medications

Tegaserod: Activation of 5-HT₄ receptors triggers the release of neurotransmitters from the enteric nerves resulting in increased contractility and stimulation of the peristaltic reflex^{19,20,21,22,23}. Tegaserod (Zelmac) is a classical example of 5-HT₄ agonist. It has been shown in RCTs, including one study from our team, to be effective in chronic constipation, with a responder rate of about 42-47%^{24,25,26}. However, it has been withdrawn from the market in 2006 because of potential cardiovascular side effects in patients with underlying heart disease.

Prucalopride: another 5-HT₄ agonist. It has been shown to significantly accelerate bowel transit in healthy volunteers and in patients with functional constipation^{27,28,29}. A large RCT has recently been published³⁰, demonstrating its efficacy in chronic constipation.

Polyethylene glycol: It has been previously used as a bowel cleansing agent. But recently found to be efficacious in patients with chronic constipation as demonstrated in RCT (52% in the treatment group vs 11% in the placebo group)³¹.

Lubiprostone: it is a chloride channel secretor. It has been reported that after 4-week treatment, 80% of the patients reported spontaneous bowel motions within 48 hours. Further studies on its efficacy in patients with chronic constipation are still on-going.

Biofeedback

Benefits of biofeedback in chronic constipated patients is well proven. There were reports of outpatient biofeedback therapy with success rates ranging from 50 to 90%³³. The improvement in the biofeedback group was 80% versus 22% in laxative-treated group^{34,35,36}. The benefits were sustained at 12 and 24 months. The therapy involves a number of outpatient sessions with a dedicated therapist during which the patient learns to

appropriately relax rather than contract the pelvic floor during evacuation. Progress is monitored by either electromyographic or manometric methods; other biofeedback adjuncts include sensory retraining with an intrarectal balloon, a portable home-training unit or both.

Surgery

For those refractory to any conservative or even aggressive approach, surgical treatment with colectomy and ileo-rectum anastomosis, should be taken into consideration. These patients are often young females with depressive symptoms and colonic inertia. It is necessary to ascertain that these patients have normal anorectal function, to assess whether the motor abnormality also affects the stomach and small bowel by scintigraphy or manometric studies, and whether there is underlying psychopathology³⁷. In addition, the benefits of this surgery must be weighed against possible complications, which include abdominal pain and diarrhoea.

Conclusion

Chronic constipation is one of the commonest functional gastrointestinal diseases, associates with psychological ailments and affects patients' quality of life. However, the current treatment for constipation is far from satisfactory. Further investigations directed towards the underlying pathogenesis and better treatment, both physiologically and psychologically oriented, are deemed necessary.

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Abbreviated Prescribing Information

Product Name: Zeffix™ **Active Ingredient:** Lamivudine **Indications:** treatment of patients with chronic hepatitis B (CHB) and evidence of hepatitis B virus (HBV) replication. **Dosage & Administration:** *Adults:* 100mg once daily. *Children (2-17 years old):* 2mg/kg once daily up to max. 100mg/day. *Children (<2 years old):* insufficient data to propose specific dosage recommendation in this age group. **Renal impairment:** serum lamivudine concentrations (AUC) are increased in patients with moderate to severe renal impairment due to decreased renal clearance. The dosage should be reduced for patients with a creatinine clearance of <50ml/min (see Table).

Table: Adjustment of Adult Dosage in Accordance with Creatinine Clearance

Creatinine clearance (ml/min)	First dose of Zeffix	Maintenance Dose Once Daily
30 to <50	100 mg	50 mg
15 to <30	100 mg	25 mg
5 to <15	35 mg	15 mg
<5	35 mg	10 mg

Contra-indication: Zeffix tablets are contraindicated in patients with known hypersensitivity to Zeffix or to any ingredients of the preparations. **Warnings and Precautions:** During treatment patients should be monitored regularly during treatment by a physician experienced in the management of chronic hepatitis B. If Zeffix is discontinued or there is a loss of efficacy, some patients may experience clinical or laboratory evidence of recurrent hepatitis. Exacerbation of hepatitis has primarily been detected by serum ALT elevations, in addition to the re-emergence of HBV DNA. Most events appear to have been self-limited. Fatalities are very rare and the causal relationship to discontinuation of Zeffix treatment is unknown. If Zeffix is discontinued, patients should be periodically monitored both clinically and by assessment of serum liver function tests (ALT and bilirubin levels), for at least four months for evidence of recurrent hepatitis; patients should then be followed as clinically indicated. For patients who develop evidence of recurrent hepatitis post-treatment, there are insufficient data on the benefits of re-initiation of Zeffix treatment. In patients with moderate to severe renal impairment, serum lamivudine concentrations (AUC) is increased due to decreased renal clearance, therefore the dose should be reduced for patients with a creatinine clearance of <50 ml/min. Transplantation recipients and patients with advanced liver disease are at greater risk from active viral replication. Due to marginal liver function in these patients, hepatitis reactivation at discontinuation of Zeffix or loss of efficacy during treatment may induce severe and even fatal decompensation. It is recommended that these patients are monitored for parameters associated with hepatitis B, for liver and renal function, and for antiviral response during treatment. If treatment is discontinued for any reason, it is recommended that these patients are monitored for at least 6 months post cessation

of treatment. Patients experiencing signs of hepatic insufficiency during or post-treatment should be monitored frequently, as appropriate. HBV viral subpopulations (YMDD and HBV) with reduced susceptibility to Zeffix have been identified during extended therapy. In a minority of cases this variant can lead to recurrent hepatitis. For the treatment of patients who are coinfected with HIV and are currently receiving or are planning to receive an antiretroviral treatment regimen including lamivudine, the dose of lamivudine usually prescribed for HIV infection should be maintained. There is no information available on maternal-foetal transmission of hepatitis B virus in pregnant women receiving treatment with Zeffix. The standard recommended procedures for hepatitis B virus immunization in infants should be followed. Patients should be advised that therapy with Zeffix has not been proven to reduce the risk of transmission of hepatitis B virus to others and therefore, appropriate precautions should still be taken. **Interaction:** Zeffix is predominantly eliminated by active organic cationic secretion. The possibility of interactions with other drugs administered concurrently should be considered, particularly when their main route of elimination is active renal secretion via the organic cationic transport system e.g. trimethoprim. Administration of trimethoprim/sulphamethoxazole 160 mg/800 mg increased Zeffix exposure by about 40%. Zeffix had no effect on the pharmacokinetics of trimethoprim or sulphamethoxazole. However, unless the patient has renal impairment, no dosage adjustment of Zeffix is necessary. A modest increase in C_{max} (28%) was observed for zidovudine when administered with Zeffix, however overall exposure (AUC) was not significantly altered. Zeffix may inhibit the intracellular phosphorylation of zalcitabine when the two medicinal products are used concurrently. Zeffix is therefore not recommended to be used in combination with zalcitabine. **Pregnancy and Lactation:** Use in pregnancy should be considered only if the benefit outweighs the risk. Although the results of animal studies are not always predictive of human response, the findings in the rabbit suggest a potential risk of early embryonic loss. Consequently, Zeffix administration is not recommended during the first three months of pregnancy. For patients who are being treated with Zeffix and subsequently become pregnant consideration should be given to the possibility of recurrence of hepatitis on discontinuation of Zeffix. Following oral administration of lamivudine was excreted in human breast milk at similar concentrations to those found in serum (range 1 – 8 micrograms/ml). **Undesirable effects:** In clinical studies of patients with chronic hepatitis B, Zeffix was well tolerated. The incidence of adverse events and laboratory abnormalities (with the exception of elevations of ALT and CPK, see below) was similar between placebo and Zeffix treated patients. The most common adverse events reported were malaise and fatigue, respiratory tract infections, headache, abdominal discomfort and pain, nausea, vomiting and diarrhoea. Elevations of ALT; Elevation in ALT were more common post-treatment in patients treated with Zeffix than placebo. In controlled trials in patients with compensated liver disease, however, there was no appreciable difference post treatment in clinically severe ALT elevations associated with bilirubin elevations and / or signs of hepatic insufficiency, between Zeffix and placebo treated patients. The relationship of these recurrent hepatitis events to Zeffix treatment or to the previous underlying disease is uncertain. Elevation of CPK. In addition to adverse events reported from clinical trials, the following events have been identified during post-approval use of Zeffix. Thrombocytopenia, muscle disorders (including myalgia,

cramps and rhabdomyolysis). In patients with HIV infection, cases of pancreatitis and peripheral neuropathy (or parasthesia) have been reported, although no relationship to treatment with lamivudine (3TC™) has been clearly established. In patients with chronic hepatitis B there was no observed difference in incidence of these events between placebo and Zeffix treatment patients. Cases of lactic acidosis, usually associated with severe hepatomegaly and hepatic steatosis, have been reported with the use of combination nucleoside analogue therapy in patients with HIV. There have been occasional reports of these adverse events in hepatitis B patients with decompensated liver disease, however, there is no evidence that these events were related to treatment with Zeffix. **Overdose:** If overdose occurs the patient should be monitored, and standard supportive treatment applied as required. Storage condition: Store below 30°C.

Please read the full prescribing information prior to administration. Full prescribing information is available on request Abbreviated Prescribing Information version 2.0 prepared in May 2007.

Reference: 1. Yuen MF, Fung J, Seto W-K, et al. Combination of baseline HBV DNA and ALT levels with on-treatment HBV DNA response to select HBeAg-positive patients for lamivudine therapy. (In press, 2009)

*Resistance defined as presence of YMDD mutations.

† Virological, serological and biochemical parameters assessed in 74 HBeAg-positive CHB patients receiving lamivudine 100 mg/day for 5 years without treatment interruption (including after seroconversion) or alteration. Shown are outcome data from a subset of n=10 patients with baseline HBV DNA levels <10⁹ copies/ml and ALT ≥2 x ULN and a Week 24 HBV DNA <10³ copies/ml. HBeAg seroconversion was defined as loss of HBeAg with the development of anti-HBe for at least two consecutive follow-ups and maintained as this status through to 5 years of follow-up. HBV DNA levels were determined (COBAS TaqMan™ HBV test with a lower limit of detection of 35 copies/mL (6.0 IU/mL)) at Week 4, Week 24, and every year from Year 1 to Year 5. The line probe assay (INNO-LiPA HBV DNA) was used to survey the presence of YMDD mutations at baseline and every year through to Year 5.¹

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Hepatitis B Infection in Special Populations

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Introduction

Hepatitis B virus (HBV) infection is a challenging global health problem. More than 350 million people in the world are chronically infected by the hepatitis B virus. Treatment of this infection has entered a new era with the advent of effective antiviral agents since 1998.

The treatment of hepatitis B virus infection is special in certain patient groups, who have management issues different from usual patients. The purpose of this article is to summarise, firstly, the treatment of HBV infection in haemodialysis patients and patients after kidney transplantation. Additionally, reactivation of hepatitis B and its treatment in transplant recipients and patients undergoing chemotherapy will be addressed. Other special groups like HBV-HIV and HBV-HCV co-infected patients, pregnant women and patients with extrahepatic disease will be discussed. Finally, early treatment with antiviral agents in severe acute and fulminant hepatitis B and the available evidence for preventing liver failure will be reviewed.

Haemodialysis Patients

As a result of the high infectivity of HBV and its route of transmission, many patients on dialysis have been infected with HBV in the past associated with either blood transfusion or the dialysis procedure itself¹. Active HBV vaccination is recommended for all patients with end stage renal disease (ESRD). However, non-response or incomplete response to standard HBV vaccines is more frequent in these patients. No controlled trials for the treatment of HBV with either nucleoside analogues (NUCs) like lamivudine or interferon in haemodialysis patients are currently available. Indications for treatment intervention should be similar to immunocompetent patients. Liver biopsy is recommended if transaminases are elevated. Because of side effects, NUCs appear to be superior to interferon in this patient population. Lamivudine is often chosen as it has the most data in this group² and entecavir has also been successfully used³. Adefovir, though found to be efficacious⁴, has been reported to worsen renal function. Its analogue, tenofovir, should be cautiously used in renal failure as well due to its potential nephrotoxicity.

Kidney Transplant Recipients

All patients awaiting kidney transplantation should be

vaccinated against HBV, although the likelihood of an effective antibody response is low. Chronic HBV infection can be found in a significant number of kidney recipients because of their previous dialysis. Survival of HBsAg positive kidney recipients is impaired^{5,6} and liver failure becomes the leading cause of death in HBsAg positive patients 10 years post kidney transplantation⁵. Interferon can lead to rejection precluding its use⁷. On the other hand, lamivudine leads to biochemical remission and reduction of viral load in up to 100% of treated patients⁸ but resistance can emerge. In case of resistance adefovir should be considered⁹. There is a special severe form of hepatitis B occurring in immunosuppressed patients, including kidney recipients, so called fibrosing cholestatic hepatitis (FCH)¹⁰. FCH is universally fatal within a few months after diagnosis. However, some cases of successful intervention with lamivudine have recently been reported^{11,12}.

Chemotherapy and Immunosuppressed Patients

HBsAg testing should be done in all patients before initiation of chemotherapy or immunosuppressive treatment¹³. Seronegative patients are highly recommended to receive vaccination against HBV. When the immunosuppressive is stopped, reactivation of hepatitis B infection can frequently be observed. It occurs in 21-53% of chronic HBsAg carriers^{14,15}, commonly after the first 2-3 cycles of chemotherapy. Hepatitis B flares, during or shortly after chemotherapy, are due to the return of immune competence, followed by liver damage of varying severity, including fulminant hepatitis. The use of corticosteroids among the protocol drugs has to be considered a predisposing factor for treatment-induced HBV reactivation¹⁶. Nevertheless, high baseline viral load is the most important risk factor for HBV reactivation¹⁷. It has also been reported that the frequency as well as the severity of HBV flares were higher in HBeAg-negative patients¹⁸. It is important to note that reactivation can also emerge in anti-HBc positive but HBsAg negative patients (<5%) as HBV persists even after clearance of HBsAg¹⁹. PCR based detection of HBV-DNA prior to chemotherapy is advised²⁰. Close monitoring of anti-HBc positive / HBsAg negative patients is recommended, and antiviral treatment should be started only if HBsAg turns positive or HBV-DNA levels increase.

As chemotherapy usually only lasts for a few months, suppression of HBV is only required for about half a



year. Within this short time period the development of viral resistance to currently applied nucleosides is unlikely to occur. Recombinant-interferon is not recommended because of its haemopoietic toxicity and anticipated low efficacy in immunocompromised patients. Lamivudine has been used extensively and proven effective both in the treatment and as a prevention of chemotherapy-related HBV reactivation^{21,22}. Treatment of HBV reactivation does not completely avoid the significant risk of fulminant hepatitis, particularly in HBeAg-negative patients. Primary prevention of HBV reactivation appears to be a more appropriate strategy. The only agent that has been studied during immunosuppression is lamivudine. Thus a pre-emptive antiviral treatment with lamivudine appears to be indicated for HBsAg-positive patients undergoing immunosuppressive therapy. Lamivudine (or more potent agents, if required) should be started pre-emptively in HBsAg-positive patients at least a few days before immunosuppressive therapy or chemotherapy is begun²³. There is no information to guide how long to treat such patients. For patients with HBV DNA levels of <2000 IU/mL, it would be reasonable to treat them for an additional six months after discontinuing immunosuppressive therapy or chemotherapy. Discontinuation of anti-HBV treatment after 6 months might not be sufficient for patients with high HBV DNA. It is recommended that patients with HBV DNA levels of >2000 IU/mL should continue antiviral therapy until HBV DNA is undetectable, and ALT levels become normal. Less data have been accrued with newer, more potent agents with a high barrier to resistance like entecavir and tenofovir. They may take up a more prominent position with more experience as pre-emptive treatment choices, especially if the patients have a high HBV DNA level or long-term immunosuppressive therapy is required.

HBV-HIV Co-infected Patients

Cirrhosis is more common in HBV-HIV co-infected patients^{24,25}. The indications for treatment are similar to HIV-negative patients²⁶. Flares of hepatitis B may occur during HIV treatment because of immune restitution. Most co-infected patients should receive de novo treatment for HIV and HBV simultaneously²⁷ with tenofovir and emtricitabine plus a third agent active against HIV²⁸. If HBV has to be treated before HIV in a minority of patients, adefovir and telbivudine are the preferred agents.

HBV-HCV Co-infected Patients

In HBV-HCV co-infection, HCV often suppresses HBV DNA to a low or undetectable level. Therefore, the treatment should be pegylated interferon alpha and ribavirin as for HCV²⁹. The sustained virological response is quite similar to that of patients with HCV mono-infection³⁰. HBV reactivation may occur during or after HCV clearance and NUC treatment will then be required.

Pregnant Women

The management of HBV-infected women in the child-

bearing age will start with careful planning in the pre-pregnancy stage. It includes recognition of maternal virological status, assessment of liver disease and minimisation of risks for perinatal transmission of infection. This may include simple monitoring, changes in obstetrical care or administration of antiviral therapy in late pregnancy or throughout pregnancy. For women who desire pregnancy and if their liver disease is mild with low viraemia, they are recommended to have pregnancy before treatment. For those with moderate liver disease and no cirrhosis, they can be treated before pregnancy. If they respond, treatment can be stopped before pregnancy and they are monitored closely for hepatic flare. The subset of women having advanced disease must be treated before conception, during pregnancy and after delivery³¹. Those patients with mild disease and very high viraemia should be treated in the last trimester with a category "B" agent (see below) since high maternal HBV DNA levels are likely associated with increased risk of intrauterine and perinatal transmission. The risk may increase from 0% in mothers with HBV DNA <1.1 x 10⁷ IU/mL to 32% in mothers with HBV DNA >1.1 x 10⁷ IU/mL³². Uncontrolled studies have shown the risk can be reduced by lamivudine^{33,34} but so far, no convincing prospective controlled trials have demonstrated the benefit of antiviral therapy.

All NUCs are category "C" drugs whereas telbivudine and tenofovir are category "B". Nevertheless, there is a long history of use of lamivudine during pregnancy, both for women with HIV infection and for those with chronic HBV. Safety data of tenofovir, lamivudine and emtricitabine in pregnant HIV-positive women are quite abundant³⁵. There are no standards regarding managing HBV in women who become pregnant while receiving antiviral therapy. HBV may be detected in breast milk but infants who are correctly immunised can be breastfed³¹. One caveat is NUCs can also be detected in breast milk but the significance is unknown³⁶.

The majority of HBV-infected women have no worsening of liver disease during pregnancy and the liver enzymes frequently normalise postpartum³⁷. However, cases of hepatic exacerbations/ fulminant hepatic failure have been reported³⁸. It appears prudent to monitor HBV-infected women closely for several months after delivery for hepatitis flares and seroconversion.

Patients with Extrahepatic Disease

The extrahepatic manifestations in HBsAg positive patients with active HBV replication, e.g. polyarteritis nodosa, glomerulonephropathy, essential mixed cryoglobulinemia, serum sickness-like syndrome etc., may respond to antiviral therapy. Lamivudine has been extensively used and other NUCs like entecavir and tenofovir are expected to have similar indications and higher efficacy. A useful adjunct therapy to NUCs is plasmapheresis.

Severe Acute and Fulminant Hepatitis B

No therapy is currently established for fulminant hepatitis B. Interferon is immune-stimulating and thus may be dangerous in fulminant hepatitis B, where an



overwhelming immune reaction is believed to be involved in the pathogenesis³⁹. Interferon is thus contraindicated because of the risks of worsening hepatitis and the frequent side effects. In contrast, lamivudine inhibits hepatitis B viral replication with an immediate decline of serum HBV DNA. It is a matter of debate whether lamivudine therapy should be initiated in patients with fulminant hepatitis B, as lamivudine treatment might be useless in this situation, since HBV-DNA is usually low in these patients. Anyway, studies have proved lamivudine to be safe in patients with fulminant hepatitis B, and might have the potential to prevent fatal liver failure or liver transplantation when administered early. Prospective controlled trials are necessary in order to define an established treatment for fulminant hepatitis B.

Conclusion

Major advances have been made in the management of the special populations with hepatitis B infection owing to recent increasing availability of NUCs, which have little adverse effects and are highly effective despite the presence of co-morbidities and other viral infections. The recommendations are summarised in Table 1. However, these recommendations are mainly based on small, usually uncontrolled, short-term studies. Carefully performed larger cohort studies and comparisons of various approaches to therapy should be the way forward.

Table 1. Treatment recommendations for special patient groups of hepatitis B

	Interferon- α	Nucleos(t)ide analogues
Haemodialysis patients	(+)	+#
Renal transplant recipients	—	+#
Prevention of HBV reactivation	(+)*	+++
Fulminant hepatitis B	(+)	+++

() option with reservation

* in selected cases, when interferon might be used as anti-cancer therapy

dependent on liver biopsy and biochemical disease activity

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¹ *PASL 2008*; 2, Colonna RJ, Rose RE, Pokornowski K, et al. Four year assessment of ETV resistance in nucleoside-naïve and lamivudine refractory patients: molecular mechanisms of drug resistance in chronic hepatitis B. *Gastroenterology* 2007;132:1574-1585; 5, Colonna RJ, Rose R, Baldick CJ, et al. Entecavir resistance in patients with hepatitis B virus in virus already resistant to lamivudine. *Antimicrob Agents Chemother* 2004;48:3498-3507; 7, Tenney DJ, Rose RE, et al. Two-Year Assessment of Entecavir Resistance in Patients with Chronic Hepatitis B Virus Infection.

Indication: Adults and adolescents 16 years of age or older: Nucleoside-naïve patients – 0.5 mg once daily; patients with history of hepatitis B viraemia and who are not on haemodialysis or continuous ambulatory peritoneal dialysis – 1 mg once daily. **Contraindications:** Patients with creatinine clearance < 50 mL/min, including patients on haemodialysis or continuous ambulatory peritoneal dialysis. **Warnings and Precautions:** Hepatic decompensation. **Adverse Reactions:** Common adverse reactions include headache, fatigue, dizziness, and nausea. **Use in Pregnancy and Lactation:** Safety and effectiveness in pregnancy are unknown. If BARACLUDGE treatment is determined to be necessary for a liver transplant recipient who has received or is receiving an organ transplant, the risks and benefits should be carefully considered. **Use in Children:** Safety and effectiveness in children are unknown. **Use in Elderly:** Safety and effectiveness in elderly patients are unknown. **Use in Patients with Renal Impairment:** Safety and effectiveness in patients with renal impairment are unknown. **Use in Patients with Hepatic Impairment:** Safety and effectiveness in patients with hepatic impairment are unknown. **Drug Interactions:** No clinically significant drug interactions were observed. **How Supplied:** Baraclude (entecavir) 0.5 mg/1 mg tablets are available in 100 and 200 tablets per bottle. **Storage and Stability:** Store at 20° to 25°C (68° to 77°F); excursions permitted to 15° to 30°C (59° to 86°F) for up to 6 months. See USP Controlled Room Temperature. **Excipients:** Baraclude (entecavir) 0.5 mg/1 mg tablets contain lactose monohydrate, croscarmellose sodium, hydroxypropyl methylcellulose, polyethylene glycol, and hydroxypropyl cellulose. **Other information:** Baraclude (entecavir) 0.5 mg/1 mg tablets are not for use in patients with known hypersensitivity to entecavir or any of the other ingredients. **Reference:** 1. *Journal of Hepatology* 2008;48:105-112. 2. *Journal of Hepatology* 2007;46:105-112. 3. *Journal of Hepatology* 2006;44:105-112. 4. *Journal of Hepatology* 2005;42:105-112. 5. *Journal of Hepatology* 2004;40:105-112. 6. *Journal of Hepatology* 2003;38:105-112. 7. *Journal of Hepatology* 2002;36:105-112. 8. *Journal of Hepatology* 2001;34:105-112. 9. *Journal of Hepatology* 2000;32:105-112. 10. *Journal of Hepatology* 1999;30:105-112. 11. *Journal of Hepatology* 1998;28:105-112. 12. *Journal of Hepatology* 1997;26:105-112. 13. *Journal of Hepatology* 1996;24:105-112. 14. *Journal of Hepatology* 1995;22:105-112. 15. *Journal of Hepatology* 1994;20:105-112. 16. *Journal of Hepatology* 1993;18:105-112. 17. *Journal of Hepatology* 1992;16:105-112.

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Clinical Application of Transient Elastography (Fibroscan®) in Liver Diseases

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Introduction

In patients with chronic liver diseases, determination of the severity of liver fibrosis is important for prognostic reasons, and for identifying patients who will benefit from treatment. For those patients already receiving treatment, assessment of liver fibrosis can determine their response to treatment. In addition, hepatocellular carcinoma and variceal screening can also be implemented for patients identified with underlying cirrhosis. At present, liver biopsy remains the current gold standard for assessing liver fibrosis, even though the diagnostic accuracy is limited by the specimen size and fragmentation, sampling error, and inter-observer variability. The accuracy of liver biopsy can be reduced to 80% because of these limitations.¹ Furthermore, liver biopsy is an invasive procedure which can be associated with significant morbidity and rarely mortality, rendering it less acceptable by patients.²

In the past few years, however, transient elastography (FibroscanR, Echosens, France) has been increasingly used as a non-invasive tool for the assessment of liver fibrosis by measuring liver stiffness. The probe consists of an ultrasound transducer which is located at the end of a vibrating piston (Figure 1). The piston produces a vibration of low amplitude and frequency, which generates a shear wave that passes through the skin and liver tissue. The ultrasound then detects the propagation of the shear wave through the liver (at a depth from 25 to 65 mm below the skin surface) by measuring its velocity. The shear wave velocity is directly related to the tissue stiffness, with a higher velocity equating to higher tissue stiffness, corresponding to increasing severity of fibrosis. The advantages of transient elastography are that the results are immediately available, and the procedure is painless, rapid (~3 minutes per patient), and easy to perform. The test is performed with the patient lying in the supine position, with the probe placed at the intercostal space overlying the liver (Figure 2). Ten validated measurements are required, with the median value taken as the final result, which is expressed in units of kilopascals (kPa). Transient elastography has been shown to be highly reproducible with minimal inter- and intra-observer variability.³ The range of possible liver stiffness values obtained with transient elastography is from 2.5 to 75.0 kPa, with the normal liver stiffness value for healthy individuals being around 5.5 kPa.⁴ The age of the subject does not affect liver stiffness, and males tend to have a slightly higher liver stiffness value compared to females.⁴

Although transient elastography is an easy and rapid procedure, strict adherence to quality criteria should still be followed to ensure the reliability of the results obtained. The interquartile range of all the readings should not exceed 30% of the final result (the median value), and the success rate of the scans should be greater than 60%. The results should always be interpreted by a qualified clinician according to the clinical context, taking into account the patient demographics, disease aetiology, and laboratory parameters. If the liver stiffness value appears to be discordant with the clinical scenario, then consider repeating a scan or proceed to a liver biopsy.



Figure 1. The probe of the Fibroscan



Figure 2. Positioning of patient for fibroscan

Assessment of Fibrosis

The earliest validating studies of transient elastography have been performed on patients with chronic hepatitis C.^{5,6} Many other studies have been performed since

then on other liver diseases including chronic hepatitis B, hepatitis C/human immunodeficiency virus co-infection, non-alcoholic steatohepatitis, primary biliary cirrhosis, primary sclerosing cholangitis, and recurrent hepatitis C after liver transplantation.⁷⁻¹¹ In a meta-analysis of 50 studies assessing the performance of transient elastography, the mean area under receiver operating characteristics curve (AUROC) for the diagnosis of significant fibrosis, severe fibrosis, and cirrhosis were 0.84, 0.89, and 0.94 respectively.¹² The consistent finding of the individual studies was the excellent performance of transient elastography for the diagnosis of severe fibrosis and cirrhosis. For lesser degrees of fibrosis, the performance was more heterogeneous, and dependent on the underlying liver disease.

One of the important aspects of liver stiffness measurements is the cut-off values that are adopted for different stages of fibrosis, with higher cut-off levels corresponding to higher fibrosis stages. The cut-off levels are also different for different diseases. Therefore it is important to interpret the results with the cut-off values specific for the underlying condition. A summary of the cut-off values used for specific liver diseases is shown in Table 1. Because of the variability in cut-off values (even within the same disease), the use of cut-off ranges rather than a single cut-off value should be employed. For example, in patients with liver stiffness <7.0 kPa, there is likely minimal or no fibrosis, whereas cirrhosis is likely in patients with liver stiffness >12.5 kPa (Figure 3).

Table 1.

Aetiology	F2	AUROC	F3	AUROC	F=4	AUROC	Ref
HBV ⁷	7.2	0.81	8.1	0.93	11.0	0.93	6
HCV ³⁰	7.1	0.83	9.5	0.90	12.5	0.95	
HCV ⁶	8.8	0.79	9.6	0.91	14.6	0.97	5
HCV/HIV ⁸	4.5	0.72	-	-	11.8	0.97	7
PBC or PSC ¹⁰	7.3	0.92	9.8	0.95	17.3	0.96	9
NAFLD ⁹	6.6	0.87	9.8	0.90	17.5	0.99	8

HBV=chronic hepatitis B. HCV=chronic hepatitis C. HIV=human immunodeficiency virus. PBC=primary biliary cirrhosis. PSC=primary sclerosing cholangitis. NAFLD=non-alcoholic fatty liver disease. AUROC=area under receiver operating characteristics curve.

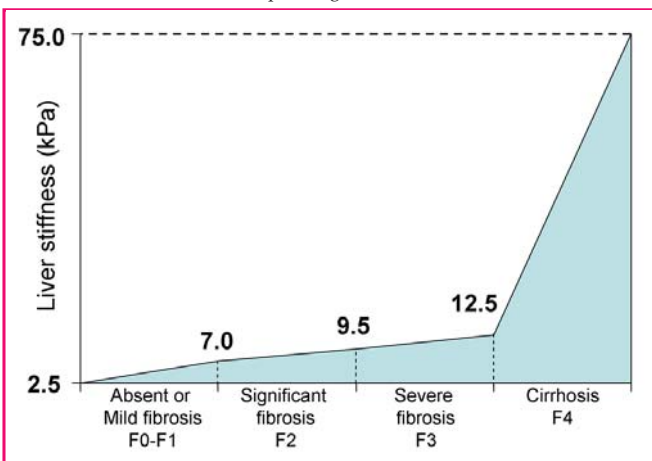


Figure 3. Example of liver stiffness cut-off values and their ranges: correlation with stages of fibrosis

Chronic Hepatitis B

In Hong Kong, chronic hepatitis B constitutes the majority of liver disease seen. One of the main reasons for determining fibrosis in these patients is to identify eligible patients for antiviral therapy. In the current Asian-Pacific guidelines for CHB treatment, liver biopsy

is recommended for patients who are over the age of forty with ALT<2x upper limit of normal (ULN) and HBV DNA >20,000 IU/mL (HBeAg-positive) or > 2,000 IU/mL (HBeAg-negative).¹³ Those patients with significant fibrosis would be candidates for antiviral therapy. According to the guidelines, these patients would be ideal candidates for transient elastography where a liver biopsy can be avoided. In patients with normal ALT and liver stiffness value <6.0 kPa, no treatment is required, whereas those with liver stiffness values >9.0 kPa should be considered for treatment. In patients with ALT 1-5x ULN, those patients with liver stiffness value <7.5 kPa can be observed, whereas those with value >12.0kPa should be considered for treatment. In patients with liver stiffness values outside these criteria, liver biopsy should be considered.¹⁴ Using this strategy, liver biopsy can be avoided in a significant proportion of patients.

Assessment of Treatment Response

On-treatment assessment of liver fibrosis has been used as a surrogate marker of treatment response and success in patients with chronic liver diseases. In CHB patients, long-term antiviral treatment has been shown to improve histological stages of fibrosis using paired liver biopsies.¹⁵ However, outside clinical trial settings, on-treatment assessment using liver biopsy is usually not feasible. A non-invasive technique such as transient elastography is ideal in this clinical setting. In chronic hepatitis C patients treated with pegylated interferon alpha-2b and ribavirin, liver stiffness values are significantly decreased (compared to pre-treatment values) in those patients with a sustained virological response compared with those that do not achieve sustained virological response.¹⁶ The preliminary study suggests a role of liver stiffness measurement to assess improvements in fibrosis stages of patients on treatment. However, the decline in liver stiffness values may be due to decline in inflammation rather than fibrosis, and further studies with histological follow-ups are required to determine the use of transient elastography in this setting.

Predictive and Prognosis Application

As described above, different cut-off values exist for the different stages of fibrosis. In patients with established cirrhosis, there is evidence that the degree of liver stiffness elevation may be predictive of underlying complications related to cirrhosis. Correlation between liver stiffness values and the presence of oesophageal varices has been reported in several studies.¹⁷⁻²⁰ However, not all studies have shown correlation between liver stiffness values and variceal size.¹⁸ In addition, the cut-off liver stiffness value for prediction of large (grade 2 or 3) varices in these studies were variable with suboptimal specificity. Without further validation studies, transient elastography is currently insufficient to predict the presence or absence of oesophageal varices in cirrhotic patients, and upper endoscopy is still required for screening.

As transient elastography is a relative new technology, the long-term prognostic application of liver stiffness



measurement is now only becoming available. In a large prospective study of over 800 patients with chronic hepatitis C followed up for a mean period of 3 years, liver stiffness was an independent predictor of subsequent development of hepatocellular carcinoma.²¹ If these findings are confirmed, then there is potential for transient elastography to be used as a screening tool to stratify patients' risk of hepatocellular carcinoma, and to implement screening and closer monitoring for high risk patients.

Screening

One of the major advantages of non-invasive investigations is their potential use as a screening tool. Using a cut-off of 7.1 kPa, significant fibrosis and cirrhosis can be excluded with a very high negative predictive value (>90%)²². This is especially useful in populations where liver disease is prevalent. In a large population study of over 1,300 patients with CHB in Hong Kong, 34% of patients were found to have severe fibrosis. Even in patients with ALT 0.5-1x ULN, 30% had severe fibrosis.²³ Identifying asymptomatic patients with significant fibrosis and cirrhosis through screening will have significant implications on the management of this disease. Other potential populations for screening include those at risk of non-alcoholic fatty liver disease, and those with significant alcohol intake or a history of intravenous drug use. Further studies are required to determine whether transient elastography is useful for population screening in other prevalent liver diseases, such as non-alcoholic fatty liver disease.

Limitations

There is an approximately 5% failure rate associated with transient elastography. The major cause of failed scans is obesity. In Asian patients, other common causes for failed scan include narrow intercostal spaces (seen mainly in young thin females) and adipose tissue overlying the thoracic area. Newer probes to address both obese patients and patients with narrowed intercostal spaces will become more widely available in the near future, and validation studies will be required to determine their diagnostic accuracy. As the pulse is not transmitted well through fluid, transient elastography is not possible in the presence of ascites.

Other factors may affect the liver stiffness value, reducing the diagnostic accuracy. One of the most important factors is with severe flares of hepatitis (ALT >10x ULN), during which the liver stiffness value may be spuriously high, returning to normal levels after resolution of the flares.^{24, 25} In our centre, 100% of our CHB patients with severe flares had abnormal liver stiffness, of which 26% had normalised their liver stiffness 3-6 months after their episode of flares.²⁶ Therefore, transient elastography performed at the time of severe flares will lead to over-diagnosis of severe fibrosis and cirrhosis. Caution should be taken into interpreting elevated liver stiffness results in patients with significant elevation of ALT. There is evidence that lesser degree of ALT elevation in both CHB and chronic hepatitis C can also increase liver stiffness values.^{27, 28}

The exact mechanism for the increase in liver stiffness seen with liver inflammation remains to be determined.

Whether steatosis increases liver stiffness is debatable. In studies of chronic hepatitis C, steatosis did not appear to affect liver stiffness values.^{5, 6} Even in a study of non-alcoholic fatty liver disease, liver stiffness correlated with fibrosis but not steatosis.⁹ However, in healthy subjects, the presence of metabolic syndrome is associated with slightly higher levels of liver stiffness.⁴ In non-diabetic patients with genotype 1 chronic hepatitis C, insulin resistance also contributed to liver stiffness independent of liver fibrosis.²⁹ Therefore, the true extent in how steatosis may affect liver stiffness remains unclear.

Conclusions

Over the past few years, significant progress has been made in the use of transient elastography in clinical practice. Despite the absence of consensus guidelines regarding the use of liver stiffness measurements in clinical practice, transient elastography is already widely used in many places, including Hong Kong. This widespread use is probably the consequence of patients and clinicians not wanting or advocating liver biopsies respectively. Transient elastography has been shown to be an excellent diagnostic tool if strict quality criteria are applied, ensuring the reliability of the results. In addition, there is now increasing evidence to suggest that liver stiffness measurements may have a longitudinal role in assessing disease progression, therapeutic response, and in predicting liver-related complications. These roles should be confirmed once long-term outcome data become available. Finally, the main focus now should be on the development of validated guidelines on the use of transient elastography, and to incorporate this new technology into current treatment guidelines.

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Management of Ascites

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Introduction

Although anti-viral treatment could delay the progression of chronic hepatitis B (CHB) infection, many patients in Hong Kong still suffer from the complications of this "silent" infection due to delayed treatment and lack of awareness. A Taiwan study showed that the annual incidence of CHB-related liver cirrhosis was 2.1% and the median age of diagnosis of cirrhosis was 35-40¹. Once cirrhosis was established, about 5-7% of cases would progress from compensated to decompensated stage annually². Ascites was usually the first sign of decompensation in this group of patients. Its occurrence was associated with a poor quality of life, increased risk of infection, and renal failure³. The cumulative survival rate 1 year and 3 years after the onset of ascites in CHB-related cirrhosis was 50.7% and 18.7% respectively in a recent Asian study⁴. The poor prognosis was related to the development of variceal bleeding, hepatic encephalopathy, spontaneous bacterial peritonitis and hepatocellular carcinoma as early as a median of 8-21 months. At low Model for End-stage Liver Disease (MELD) score (a scale of 6 to 40, with higher values indicating more severe disease) of less than 21, persistent ascites and hyponatraemia were shown to be the independent predictors of mortality⁵. In 2005, a consensus workshop on portal hypertension classified the presence of ascites in cirrhosis as stage 3 disease which carried a mortality rate of 20% per year⁶. Hence, it is recommended that all cirrhotic patients with ascites should be evaluated for liver transplantation.

Pathophysiology of Ascites (Fig 1)

The primary event that leads to portal hypertension is caused by the abnormalities in hepatic microcirculation as manifested by elevated hepatic resistance to portal flow⁷. Reduced endothelial nitric oxide (NO) production and vasodilatory response to NO are both considered as important pathogenic mechanisms. As portal hypertension develops, endothelial NO production by the arteries of the splanchnic and systemic circulation increases and leads to vasodilatation, the so-called "hyperdynamic circulatory state"⁸. When both portal hypertension and splanchnic arterial vasodilatation occur, capillary permeability and lymph formation in the splanchnic organs markedly increase and exceed the ability to return the lymph to the circulation by the thoracic duct, thus causing its accumulation in the peritoneal cavity.

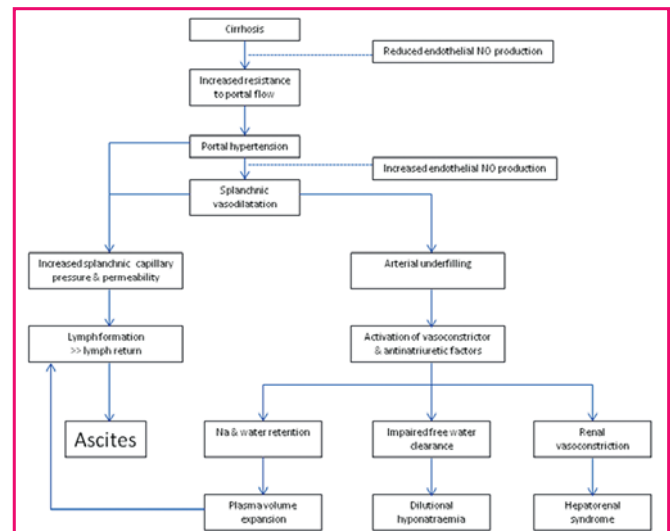


Figure 1. Pathogenesis of Ascites

Evaluation of Patients with Ascites

More than 75% of patients who present with ascites have underlying cirrhosis with the remaining being due to malignancy, cardiac failure, pancreatitis, tuberculosis and other rare causes⁹. In cirrhotic patients with ascites, physical examination may reveal splenomegaly, cutaneous venous collaterals over abdomen and other signs of chronic liver disease. Patients with gross ascites may have umbilical and inguinal hernias, leg oedema and muscle wasting due to poor nutritional status. Pleural effusion, which is known as hepatic hydrothorax, may occur in 5-12% of cirrhotic patients¹⁰. The proposed mechanism is the leakage of ascitic fluid via diaphragmatic defects facilitated by the negative intrapleural pressure. It occurs at the right-side in 65-87% of cases. During assessment, we should always look for evidence of hepatic encephalopathy, abdominal pain, fever and gastrointestinal bleeding so that prompt investigation and treatment can be initiated.

Diagnostic abdominal paracentesis (30ml) should be performed in all patients when first presented with ascites and in all patients with any evidence of clinical deterioration as stated above. Abnormal coagulation profile should not preclude paracentesis unless there is clinical evidence of hyperfibrinolysis or disseminated intravascular coagulation¹¹.

Ascitic Fluid Analysis

Ascitic fluid should be sent for cell count and differential,



albumin and total protein concentration if uncomplicated cirrhotic ascites is suspected. To diagnose ascitic fluid infection, ascitic fluid should be inoculated into blood culture bottles instead of plain bottles for higher diagnostic yield¹². An ascitic fluid neutrophil count of 250/mm³ has >90% sensitivity and specificity for the diagnosis of spontaneous bacterial peritonitis (SBP)¹³. Urine dipstick has recently been suggested to facilitate the diagnosis of SBP. However, a review of 19 studies on the use of reagent strips showed a low sensitivity and a high false-negativity rate¹⁴. The conventional concept of transudate-exudate based upon the ascitic protein concentration (<25g/L or >25g/L) should not be used due to inaccuracy in distinguishing the cause of ascites. The serum-ascites albumin gradient (SAAG= serum albumin - ascitic albumin concentration) is more specific and sensitive in classifying ascites with 97% accuracy¹⁵. Values greater than 11g/L signify cirrhotic ascites whereas values lower than 11g/L suggest other causes (Table 1).

Table 1. Serum ascites-albumin gradient (SAAG)

SAAG >11g/L	SAAG <11g/L
Cirrhosis	Malignancy
Cardiac failure (cardiac ascites)	Pancreatitis
Budd-Chiari syndrome	Tuberculosis
	Nephrotic syndrome

Stages of Ascites

In a consensus meeting report published in 1996, ascites was classified as uncomplicated ascites and refractory ascites (Table 2)¹⁶. Refractory ascites is defined as ascites that cannot be mobilised or the early recurrence of which cannot be satisfactorily prevented by medical therapy. About 5-10% of all cases of ascites fall into this category. It is frequently associated with type 2 hepatorenal syndrome and dilutional hyponatraemia.

Table 2. Stages of ascites

Stage	Severity of ascites	Treatment
1	Only detectable by ultrasound	Salt restriction
2	Moderate ascites; abdominal distension	Salt restriction,, diuretics
3	Massive ascites; marked abdominal distension	Diuretics, therapeutic paracentesis, TIPS
Refractory (5-10%)	Diuretic-resistant (unresponsive to sodium restriction and diuretics or rapid recurrence)	Therapeutic paracentesis, TIPS,
	Diuretic-intractable (develop complication due to diuretic use)	OLT

Treatment

Bed Rest

Although studies demonstrated an improved diuretic effect in patients with cirrhotic ascites when assuming a supine position, bed rest is not advisable as it may lead to muscle atrophy and prolonged hospital stay¹⁷.

Sodium Restriction

Loss of ascites can be achieved by sodium restriction alone in 10-15% of patients¹⁸. However, patient compliance is usually a problem and severe salt restriction may lead to poor nutrition. Hence moderate restriction to 5.2g/d (90 mmol) is advisable¹⁹.

Water Restriction

Many ascitic patients were advised by their physicians

to restrict water intake. However there have been no studies on its benefit or harm on the resolution of ascites. Besides, this treatment may exacerbate the severity of effective central hypovolaemia that enhances the secretion of antidiuretic hormone and results in further decline in renal function and aggravates dilutional hyponatraemia. Fluid restriction is not necessary in most patients with cirrhotic ascites.

Diuretics

Spironolactone, an aldosterone antagonist acting on the distal tubules, is more effective in cirrhotic patients with ascites than non-cirrhotics. Its major active metabolite, canrenone, has a half-life of 10-35 hours in healthy subjects (T 1/2 may be longer in cirrhotic patients). It can be started from 25-50 mg/d to a maximum dose 400mg/d. Hyperkalaemia and painful gynaecomastia are the most common side-effects. A loop-diuretic, frusemide, can be used concomitantly if the response to spironolactone is not sufficient. The recommended initial dose should be 20-40mg/d (max 160mg/d). Inadvertent use of this drug may precipitate pre-renal failure and hepatic encephalopathy due to increased renal ammonia production as a result of diuretic-induced hypokalaemia and alkalosis²⁰. Amiloride (10-40mg/d) can replace spironolactone in patients with tender gynaecomastia though it is more expensive and less effective than canrenone²¹. When diuretics are used, it is recommended that the rate of weight loss should not exceed 0.5 kg/d in the absence of oedema, or 1 kg/d when oedema is present²².

Large Volume Paracentesis (LVP)

LVP involves drainage of >5 L ascitic fluid. When compared with diuretics, it is more effective in eliminating ascites and shortening the duration of hospitalisation. If done alone, it is associated with postparacentesis circulatory dysfunction (PPCD) in 20% cases. PPCD is found to be associated with increased risk of renal failure and mortality up to 30 days after LVP²³. When compared with synthetic plasma expanders, albumin infusion before the procedure is more effective in preventing PPCD especially if >5 L ascites are removed. It is usually given at a dose of 6 to 8 g for each litre of ascites removed²³. As albumin is expensive, some studies showed that intravenous use of terlipressin, a vasopressin pro-drug, is nearly equivalent to albumin in the prevention of PPCD^{24,25}. More studies are needed to assess the long-term safety of this approach.

Aquaretic Agents

Aquaretics are specific vasopressin receptor (V2) antagonists which act on the collecting tubules of the kidney by counteracting vasopressin (AVP) and inducing free-water excretion without affecting electrolyte balance. In a short-term study, satavaptan, a highly selective non-peptide V2 receptor antagonist, when given to spironolactone treated patients with cirrhotic ascites and hyponatraemia for 14 days was shown to improve ascites control and increase serum sodium level²⁶. We await long-term studies to define the role of these agents in the management of cirrhotic ascites.

Transjugular Intrahepatic Portosystemic Shunt (TIPS)

TIPS is more effective at removing ascites as compared with paracentesis without a significant difference in

mortality, gastrointestinal bleeding, infection, and acute renal failure²⁷. However, TIPS patients develop hepatic encephalopathy significantly more often (~30%) and may be more expensive due to stent replacement for stent dysfunction (up to 75%). In general, TIPS should not be performed in patients who have a bilirubin level of greater than 3 mg/dL (51 μmol/L), prothrombin time greater than 20 seconds, and a serum creatinine level of greater than 2 mg/dL (152 μmol/L), because it is associated with a 3-month mortality exceeding 90%.

Peritoneovenous Shunts

Due to their poor long-term patency, excessive complications, and no survival advantage compared to medical therapy in controlled trials, peritoneovenous shunts (e.g. LeVeen or Denver) have little role in the treatment of refractory ascites.

Liver Transplantation

All cirrhotic patients who develop ascites should be assessed for liver transplantation due to poor long-term prognosis.

Summary

Ascites is the most common complication of liver cirrhosis which develops in 50% of patients over a 10-year period. The management of ascites is determined by the severity of the symptoms. The therapeutic options include salt restriction, diuretics, LVP, and TIPS. Newer pharmacological agents such as aquaretics are being studied. Close monitoring of both the treatment-related efficacy and adverse effects are equally important. Liver transplantation should be considered for all patients with cirrhotic ascites.

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Study Tour to Korea

Dr Shao-haei LIU

MBBS (HK), MRCP(UK), MHA(NSW)

Council Member & Hon Treasurer, HK College of Health Service Executives



Dr Shao-haei LIU

This 4-day study tour was organised by the HK College of Health Service Executives from 29 April to 2 May 2009 to provide an understanding of the health care system in S. Korea. The programme was well received with a participation of 23 members from different specialties. The delegates were doctors, nurses, administrators and allied health professionals from both the public and private sectors.

The tightly scheduled tour, consisting of hospital visits as well as attending discussion forums with 2 academic institutions, was a great opportunity to an insightful update of the evolving Korean health care system as well as getting introduced to the exemplary hospitals in the region.

We visited one of the largest leading teaching hospitals in Korea, the Seoul National University Hospital which is closely networked among a number of affiliated hospitals in the capital. Their concept is very much like the cluster hospitals of HA in Hong Kong but the independence of each hospital is much higher and there are different modes of funding. This allows individual hospital to develop their expertise with a leading edge with the latest facilities and modern advanced equipment, within a competitively as well as complementary framework. During our short encounter, the hospital's presenter impressed us on their Mission - Vision - Core Value that leads their health care professionals towards creating Korea the tomorrow of health and hope.

We were able to meet Professor Soonman Kwon from the Department of Health Policy and Management of the School of Public Health of the University. Besides teaching, Prof Kwon also worked for consultancy for the WHO and various international agencies. He first briefed us on the history of social health insurance in Korea. With the political determination of the government, the slightly over 350 health insurance societies set up post-war were all merged into one under the health care financing reform by 2000. The reform was regarded as a milestone for Korea moving away from a tax-based public funding system to a relatively sustainable national health insurance model. The reform involved a certain degree of resources injection in order to address the issues of (1) inequality in the economic burden across various scheme operators despite similar benefit packages; (2) chronic fiscal instability of the rural health insurance with increasing aged population; (3) dis-economies of scale in some insurance companies with high administrative costs and limited risk pooling.

Prof Kwon further analysed lessons for achieving universal health care coverage through the reliance on the private sector to provide health care and the government playing the role of regulator rather than financier nor service provider. In this way the government engineered the gradual change towards social insurance rather than tax-based financing together with the vision of promotion a welfare society (e.g. enhancing the role of family) in stead of a welfare state. The Korean system started their population coverage with limited benefit package and incrementally expanded. The plans allowed enrollees of different sectors with more opportunity to experience the health insurance scheme within everybody's affordability. This approach minimised drop out rate in the initial critical years and maximised social marketing. However, the system is still entangled with problems due to non-comprehensive coverage. Although the Social Health Insurance has recently introduced a ceiling for out-of-pocket payment, the protection for catastrophic medical expenses is limited. The academics commented that such policy of benefit extension was based on financial concerns rather than a rational assessment on medical necessity or cost effectiveness analysis. There were physician oppositions to such extension of coverage because of price regulation under the insurance scheme, the health care providers perceived themselves to be exploited.

The College delegation also visited a first class hospital which deployed automation and I.T. in all levels of hospital operations. This is the Bundang Hospital situated in the newly developed township with 829 specialty beds and 60 ICU beds. At its opening in 2003, the hospital successfully introduced electronic medical record system (EMR) and adopted "*informatisation*" to all its clinical and support services. The vision was to create a hospital environment which was paperless, filmless, chartless, and yet easy access to all clinical data and extending their ability to conduct remote diagnostic and treatment plans. The digitalisation of the hospital services was further enhanced with the set up of a large clinical data warehouse, a clinical decision support system, clinical indication and hospital performance evaluation framework, and clinical pathway to maximise the quality of service and judicious use of resources. The CEO of the hospital informed us that 3-4% of the annual budget was allocated for I.T. They are also ambitious for "*next generation EMR*" where technologies are heavily emphasised. One of their priority projects is on the working for "Ubiquitous Health care" which includes the employment of real time resource management system to ensure cost is



linked with safety with appropriate knowledge support; the deployment of RFID at health promotion centres for profiling community health trends; the U-health pilot which automatically transmits patients' vital data to clinical teams at hospital for continuing assessment and just in time for advice; the extensive application of robotic surgery and mobile clinical assistant, etc.

In the evening, Prof Ok Ryun Moon, an expert in health policy from the Institute of Inje Advanced Studies presented his keynote speech at our dinner symposium. He gave an analysis of Korea's past performance as compared with the OECD group in terms of health care coverage, economic development, health outcome, health resources and access to care. All in all, Korea had been performing excellently as a developing country and becoming one of economic powers in East Asia within a fairly short period. The Korean government's health policy paradigm also shifted in the past decades: from a provider centred functions centred, from treatment oriented facility building to strengthening diseases prevention and health promotion; from public health care dominance to public- private partnership. He further talked about the future direction for a healthy, efficient and sustainable health care system. The system for Koreans would consist of:

- (1) Maintaining the basic frame to further reduce dead zone through "Medicaid", identifying the complementary role of private health insurance and introducing internal market for insurers;
- (2) Streamlining the role of government to focus on essential health service (e.g. emergency services), health promotion and safety in pharmaceutical & food;
- (3) Health reform through deregulation to achieve better service competitiveness; attract diversified capital financing, and ensure adequate consumer protection through quality care;
- (4) Health industries as new driving engine for the next generation. This refers to the facilitation for enlargement of the health market, developing R&D and high tech & complex medicine industries.

The night was such an intellectual enlightenment of discussion with Prof Moon, who spoke interesting illustrations and quite understood the HK scenario, as well as the good Korean food that the whole group enjoyed almost up to the closing hour of the restaurant. After the completion of the trip, the unanimous recommendation from this group was that the College should organise another trip to another region for "comparative study" and the author was made to convey the message that an equally good itinerary in Japan would be expected next time.



Society News

News from Member Societies

Hong Kong Association of Medical Microbiologists

Updated office-bearers for the year 2009-2010 are as follows: President: Dr. Dominic Ngai-chong TSANG; Honorary Secretary: Prof. Mamie HUI; Honorary Treasurer: Dr. Bosco Hoi-shiu LAM

Hong Kong College of Health Service Executives

Updated office-bearers for the year 2009-2010 are as follows: President: Dr. Man-yung CHENG; Honorary Secretary: Ms. Tammy SO; Honorary Treasurer: Dr. Shao-haei LIU

The FMSHK would like to send its congratulations to the new office-bearers and look forward to working together with the societies.



On 1st & 2nd August, one of the Federation's associate member societies, the Hong Kong Museum of Medical Sciences Society (HKMMS) organised a health carnival cum open day (健康人生嘉年華暨博物館開放日) at the Hong Kong Museum of Medical Sciences on Caine Lane. The HKFMS Foundation Limited was invited to be one of the sixteen organisations that participated in the event.

The Foundation organised activities for two booths, one of which was to perform health checks on blood pressure, BMI and fat proportion indicators; and the other was to perform elderly fall risk screening, cognitive assessment and general physical function tests. Educational materials on home safety and injury prevention were displayed and distributed to the public to increase their awareness on the topics. The event was held with success with some 1000 participants.



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THE FEDERATION OF MEDICAL SOCIETIES OF HONG KONG

香 港 醫 學 組 織 聯 會

The Federation Annual Dinner 2009

31st December, 2009 (Thursday)

Run Run Shaw Hall
The Hong Kong Academy of Medicine Jockey Club Building

Swinging
Melodies



Tickets are now available, please contact the secretariat on 2527 8898



Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
<ul style="list-style-type: none"> ★ Joint Professional Karaoke Competition 2009 ★ HKMA Trailwalker the 8th Training Session ★ HKMA Tennis Tournament ★ OSHK A-Z Symposia Series "B" - Symposium: "B", Osteophenolate-Related Osteoporosis of the Jaw and the New OSHK Guidelines on Osteoporosis Management ★ HKMA Tennis Tournament ★ HKMA/New Mastering Your Risk - 2009 Extended Programme ★ HKMA Certificate Course on Family Medicine 2009 ★ International Symposium on Hepatology 2009 / 22nd Annual Scientific Meeting <p style="text-align: right;">8</p>	<ul style="list-style-type: none"> ★ HKMA Kowloon City & Kowloon East Community Networks CME - Management of Drug Abuse Patients on Public-Private Interface (Klin City & KECN) (Session Four) ★ Trailwalker Final Briefing Session <p style="text-align: right;">2</p>	<ul style="list-style-type: none"> ★ HKMA CME - Fish Oil in Prevention of Disease: Formulation, Uptake and Mechanism of Action ★ HKMA-Tai Po Community Network - Management Approach of Gastro-oesophageal Reflux Disease ★ HKMA/New Mastering Your Risk - 2009 Extended Programme ★ HKMA Tai Po Community Network - CME Course on Maintaining Bone Health and Preventing Falls and Fractures in the Elderly (I) <p style="text-align: right;">3</p>	<ul style="list-style-type: none"> ★ HKMA/New Mastering Your Risk - 2009 Extended Programme ★ HK Neurosurgical Society Monthly Academic Meeting - Special Lecture: Management of Diabetes Mellitus in Hospital <p style="text-align: right;">4</p>	<ul style="list-style-type: none"> ★ HKMA/New Mastering Your Risk - 2009 Extended Programme ★ HKMA Council Meeting ★ 17th Asia Pacific Optometric Congress (APOC) <p style="text-align: right;">5</p>	<ul style="list-style-type: none"> ★ 17th Asia Pacific Optometric Congress (APOC) ★ Joint Surgical Symposium - Complications - Avoidance & Management ★ HKPGA Psychotherapy Workshop: Contemporary Psychotherapies for Older Adults <p style="text-align: right;">6</p>	<ul style="list-style-type: none"> ★ HKMA/New Mastering Your Risk - 2009 Extended Programme ★ 17th Asia Pacific Optometric Congress (APOC) ★ HKPGA Annual Scientific Symposium and Annual General Meeting ★ 2nd HKMA Table-Tennis Training Course <p style="text-align: right;">7</p>
<ul style="list-style-type: none"> ★ HKMA Tennis Tournament ★ HKMA/New Mastering Your Risk - 2009 Extended Programme ★ HKMA Certificate Course on Family Medicine 2009 ★ International Symposium on Hepatology 2009 / 22nd Annual Scientific Meeting <p style="text-align: right;">8</p>	<ul style="list-style-type: none"> ★ HKMA Kowloon City & Kowloon East Community Networks CME - Management of Drug Abuse Patients on Public-Private Interface (Klin City & KECN) (Session Four) ★ Trailwalker Final Briefing Session <p style="text-align: right;">9</p>	<ul style="list-style-type: none"> ★ HKMA Tai Po Community Network - CME Course on Maintaining Bone Health and Preventing Falls and Fractures in the Elderly (II) <p style="text-align: right;">10</p>	<ul style="list-style-type: none"> ★ HKMA/New Mastering Your Risk - 2009 Extended Programme ★ HK Neurosurgical Society Monthly Academic Meeting - Special Lecture: Management of Diabetes Mellitus in Hospital <p style="text-align: right;">11</p>	<ul style="list-style-type: none"> ★ HKMA/New Mastering Your Risk - 2009 Extended Programme ★ Programme with Hong Kong Sanatorium & Hospital Year 2009 - Chinese Child Health Problems "華裔兒童的健康問題" <p style="text-align: right;">12</p>	<ul style="list-style-type: none"> ★ 17th Asia Pacific Optometric Congress (APOC) ★ Joint Surgical Symposium - Complications - Avoidance & Management ★ HKPGA Psychotherapy Workshop: Contemporary Psychotherapies for Older Adults <p style="text-align: right;">13</p>	<ul style="list-style-type: none"> ★ HKMA/New Mastering Your Risk - 2009 Extended Programme ★ 2nd HKMA Table-Tennis Training Course ★ Refresher Course for Health Care Providers 2009/ 2010 <p style="text-align: right;">14</p>
<ul style="list-style-type: none"> ★ HKMA Tennis Tournament ★ HKMA/New Mastering Your Risk - 2009 Extended Programme <p style="text-align: right;">15</p>	<ul style="list-style-type: none"> ★ HKMA Kowloon City & Kowloon East Community Networks CME - Management of Drug Abuse Patients on Public-Private Interface (Klin City & KECN) (Session Four) ★ Trailwalker Final Briefing Session <p style="text-align: right;">16</p>	<ul style="list-style-type: none"> ★ HKMA Tai Po Community Network - CME Course on Maintaining Bone Health and Preventing Falls and Fractures in the Elderly (III) <p style="text-align: right;">17</p>	<ul style="list-style-type: none"> ★ HKMA/New Mastering Your Risk - 2009 Extended Programme <p style="text-align: right;">18</p>	<ul style="list-style-type: none"> ★ HKMA/New Mastering Your Risk - 2009 Extended Programme ★ FMSHK Executive Committee Meeting & Council Meeting ★ FMSHK & Foundation Annual General Meeting <p style="text-align: right;">19</p>	<ul style="list-style-type: none"> ★ 17th Asia Pacific Optometric Congress (APOC) ★ Joint Surgical Symposium - Complications - Avoidance & Management ★ HKPGA Psychotherapy Workshop: Contemporary Psychotherapies for Older Adults <p style="text-align: right;">20</p>	<ul style="list-style-type: none"> ★ HKMA/New Mastering Your Risk - 2009 Extended Programme ★ 2nd HKMA Table-Tennis Training Course ★ Advanced Trauma Care for Nurses (ATCN) Provider Course ★ Advanced Trauma Care for Nurses (ATCN) Student Course ★ Oxfam Trailwalker 2009 from Sai Kung to Tai Tong ★ HKMA HKE Network - PPI Lecture on Update on Neurosurger ★ 2nd Guangdong, Hong Kong and Macau Sports Meet <p style="text-align: right;">21</p>
<ul style="list-style-type: none"> ★ HKMA Tennis Tournament ★ Advanced Trauma Life Support (ATLS) Student Course ★ Oxfam Trailwalker 2009 from Sai Kung to Tai Tong ★ 2nd Guangdong, Hong Kong and Macau Sports Meet ★ HKMA Structured CME Programme with PMH Year 2009 (10) - Common ENT Infections <p style="text-align: right;">22</p>	<ul style="list-style-type: none"> ★ HKMA Kowloon City & Kowloon East Community Networks CME - Management of Drug Abuse Patients on Public-Private Interface (Klin City & KECN) (Session Four) ★ Trailwalker Final Briefing Session <p style="text-align: right;">23</p>	<ul style="list-style-type: none"> ★ HKMA Tai Po Community Network - CME Course on Maintaining Bone Health and Preventing Falls and Fractures in the Elderly (III) <p style="text-align: right;">24</p>	<ul style="list-style-type: none"> ★ HKMA/New Mastering Your Risk - 2009 Extended Programme <p style="text-align: right;">25</p>	<ul style="list-style-type: none"> ★ HKMA/New Mastering Your Risk - 2009 Extended Programme <p style="text-align: right;">26</p>	<ul style="list-style-type: none"> ★ 17th Asia Pacific Optometric Congress (APOC) ★ Joint Surgical Symposium - Complications - Avoidance & Management ★ HKPGA Psychotherapy Workshop: Contemporary Psychotherapies for Older Adults <p style="text-align: right;">27</p>	<ul style="list-style-type: none"> ★ HKMA/New Mastering Your Risk - 2009 Extended Programme ★ 2nd HKMA Table-Tennis Training Course <p style="text-align: right;">28</p>
<ul style="list-style-type: none"> ★ HKMA Tennis Tournament ★ HKMA Family Sports Day <p style="text-align: right;">29</p>	<ul style="list-style-type: none"> ★ HKMA Kowloon City & Kowloon East Community Networks CME - Management of Drug Abuse Patients on Public-Private Interface (Klin City & KECN) (Session Four) ★ Trailwalker Final Briefing Session <p style="text-align: right;">30</p>					



Date / Time	Function	Enquiry / Remarks
1 SUN 2:00 pm 7:00 am 8:00 pm (8,15,22,29) 10:00 am - 4:00 pm	Joint Professional Karaoke Competition 2009 Organised by: The Hong Kong Medical Association, Venue: Backstage Live Restaurant HKMA Trailwalker the 8th Training Session Organised by: The Hong Kong Medical Association, Venue: MacLehose Stage 1-5 HKMA Tennis Tournament Organised by: The Hong Kong Medical Association, Venue: Kowloon Tong Club OSHK A-Z Symposia Series "B" - Symposium: "B" Isphosphonate-Related Osteonecrosis of the Jaw and the New OSHK Guidelines on Osteoporosis Management Organised by: The Osteoporosis Society of Hong Kong, Venue: Shanghai Room, Level 8 Langham Place Hotel, Mongkok, Kowloon	Ms. Dora HO Tel: 2527 8285 Ms. Dora HO Tel: 2527 8285 Ms. Dora HO Tel: 2527 8285 Secretariat Tel: 2881 4295 Fax: 2159 7242
2 MON 1:15 pm 8:00 pm	HKMA Kowloon City & Kowloon East Community Networks CME - Management of Drug Abuse Patients on Public-Private Interface (Kln City & KECN) (Session Four) Organised by: HKMA Kowloon City & Kowloon East Community Networks, Speakers: Dr. LEE Che Kin & Dr. FUNG Wai Ching, Venue: To Kwa Wan Trailwalker Final Briefing Session Organised by: The Hong Kong Medical Association, Venue: The HKMA Dr. Li Shu Pui Professional Education Centre, 2/F, Chinese Club Building, 21-22 Connaught Road Central, Hong Kong	Miss Alice Tang Tel: 2527 8285 Ms. Dora HO Tel: 2527 8285
3 TUE 1:00 pm 1:00 pm 6:00 pm (4,5,7,8,11,12,14,15,17,18,19,21)	HKMA CME - Fish Oil in Prevention of Disease: Formulation, Uptake and Mechanism of Action Organised by: The Hong Kong Medical Association, Speaker: Prof. Lise MADSEN, Venue: The HKMA Dr. Li Shu Pui Professional Education Centre, 2/F, Chinese Club Building, 21-22 Connaught Road Central, Hong Kong HKMA-Tai Po Community Network - Management Approach of Gastro-oesophageal Reflux Disease Organised by: KMA-Tai Po Community Network, Speaker: Dr. IP Shing Fai, Venue: Chiuchow Garden Restaurant, Uptown Plaza, Tai Po, N.T. HKMA/New Mastering Your Risk - 2009 Extended Programme Organised by: The Hong Kong Medical Association, Speakers: Dr. Justin CHENG & Dr. Andy CHEUNG, Venue: Langham Place Hotel, Mongkok, 555 Shanghai Street, Mongkok, Kowloon	Miss Viviane LAM Tel: 2527 8452 1 CME Point Ms. Carol LEUNG Tel: 8209 9152 Miss Viviane LAM Tel: 2527 8452 2.5 CME Points
4 WED 1:00 pm 8:00 pm - 10:00pm	HKMA CME - Symposium on Medical Experts Organised by: The Hong Kong Medical Association, Chairman: Dr. CHOI Kin Gabriel, Speakers: Dr. TEOH Ming Keng; Dr. LEONG Kwon On Harold & Dr. Bernard J. MURPHY, Venue: Mongkok FMSHK Officers' Meeting Organised by: The Federation of Medical Societies of Hong Kong, Venue: Gallop, 2/F., Hong Kong Jockey Club House, Shan Kwong Road, Happy Valley, Hong Kong	Miss Viviane LAM Tel: 2527 8452 1.5 CME Point Ms. Paulina TANG Tel: 2527 8898 Fax: 2865 0345
5 THU 8:00 pm (6,7)	HKMA Council Meeting Organised by: The Hong Kong Medical Association, Chairman: Dr. H.H. TSE, Venue: HKMA Head Office, 5/F., Duke of Windsor Social Service Building, 15 Hennessy Road, Hong Kong 17th Asia Pacific Optometric Congress (APOC) Organised by: Asia Pacific Council of Optometry, The Hong Kong Society of professional Optometrists, Zhongshan Ophthalmic Center, Sun Yat-sen University & The Hong Kong Polytechnic University, Venue: The Hong Kong Polytechnic University and Hong Kong Convention and Exhibition Centre	Ms. Christine WONG Tel: 2527 8285 Ms. Ivy YEUNG Email: secretariat@asiapacificoptometry.org Website: http://www.asiapacificoptometry.org/17thapoc.html
6 FRI 8:00 am - 9:00 am 9:00 am - 5:00 pm	Joint Surgical Symposium - Complications - Avoidance & Management Organised by: Department of Surgery, The University of Hong Kong & Hong Kong Sanatorium & Hospital, Venue: Hong Kong Sanatorium & Hospital, Chairman: Prof. William WEI, Speakers: Prof. William WEI & Dr. Ambrose HO HKPGA Psychotherapy Workshop: Contemporary Psychotherapies for Older Adults Organised by: HKPGA, Venue: Royal Park Hotel, Shatin	Department of Surgery, Hong Kong Sanatorium & Hospital Tel: 2835 8698 Fax: 2892 7511 1 CME Point (Active) Email: info@hkpga.org Website: http://www.hkpga.org
7 SAT 9:00 am - 1:00 pm 4:00 pm (14,21,28)	HKPGA Annual Scientific Symposium and Annual General Meeting Organised by: HKPGA, Venue: Royal Garden Hotel, Tsim Sha Tsui East, Kowloon 2nd HKMA Table-Tennis Training Course Organised by: The Hong Kong Medical Association, Venue: Kowloon Park Sports Centre	Email: info@hkpga.org Website: http://www.hkpga.org Ms. Dora HO Tel: 2527 8285
8 SUN 2:00 pm	HKMA Certificate Course on Family Medicine 2009 Organised by: The Hong Kong Medical Association, Speakers: Dr. CHAN Wing Yan Loretta & Prof. Albert LEE, Venue: Queen Elizabeth Hospital, Kowloon International Symposium on Hepatology 2009 / 22nd Annual Scientific Meeting Organised by: The Hong Kong Association for the Study of Liver Diseases, Venue: Hong Kong Convention and Exhibition Centre	Miss Viviane LAM Tel: 2527 8452 3 CME Points Ms. Melissa LEUNG CMPMedica Pacific Limited Tel: 2116 4348 Email: melissa.leung@asiacmpmedica.com
10 TUE 1:45 pm (17, 24)	HKMA Tai Po Community Network - CME Course on Maintaining Bone Health and Preventing Falls and Fractures in the Elderly (I), (II) & (III) Organised by: HKMA Tai Po Community Network and Department of Orthopaedics and Traumatology of Prince of Wales Hospital of CUHK, Speakers: Various, Venue: Chiuchow Garden Restaurant, Uptown Plaza, Tai Po, N.T.	Ms. Candy CHAN Tel: 2632 3074
11 WED 7:30 am	HK Neurosurgical Society Monthly Academic Meeting - Special Lecture: Management of Diabetes Mellitus in Hospital Organised by: HK Neurosurgical Society, Speaker: Dr. Annette TSOI, Venue: Seminar Room, G/F, Block A, Queen Elizabeth Hospital, Kowloon	Dr. Y.C. PO Tel: 2990 3788 Fax: 2990 3789 2 CME Points



Date / Time	Function	Enquiry / Remarks
12 THU 2:00 pm	HKMA Structured CME Programme with Hong Kong Sanatorium & Hospital Year 2009 - Chinese Child Health Problems "華裔兒童的健康問題" Organised by: The Hong Kong Medical Association, Chairman: Dr. WONG Bun Lap Bernard, Speaker: Dr. YEUNG Chap Yung, Venue: The HKMA Dr. Li Shu Pui Professional Education Centre, 2/F, Chinese Club Building, 21-22 Connaught Road Central, Hong Kong	Miss Viviane LAM Tel: 2527 8452 1 CME Point
14 SAT 2:30 pm	Refresher Course for Health Care Providers 2009/ 2010 Organised by: The Hong Kong Medical Association and Our Lady of Maryknoll Hospital, Speaker: Dr. TSANG Mei Ling, Venue: Training Room II, 1/F., OPD Block, Our Lady of Maryknoll Hospital, 118 Shatin Pass Road, Wong Tai Sin, Kowloon, Hong Kong	Ms. Clara Tsang Tel: 2354 2440 2 CME Points
19 THU 7:00 pm - 8:00 pm 8:30 pm - 10:00 pm	FMSHK Executive Committee Meeting & Council Meeting Organised by: The Federation of Medical Societies of Hong Kong, Venue: Council Chambers, 4/F., Duke of Windsor Social Service Building, 15 Hennessy Road, Wanchai, Hong Kong FMSHK & Foundation Annual General Meeting Organised by: The Federation of Medical Societies of Hong Kong, Venue: Council Chambers, 4/F., Duke of Windsor Social Service Building, 15 Hennessy Road, Wanchai, Hong Kong	Ms. Paulina TANG Tel: 2527 8898 Fax: 2865 0345 Ms. Paulina TANG Tel: 2527 8898 Fax: 2865 0345
20 FRI (21) (21,22) 9:00 am (21,22)	Advanced Trauma Care for Nurses (ATCN) Provider Course Organised by: Department of Surgery, Queen Mary Hospital & Hong Kong Chapter of the American College of Surgeons # The Jockey Club Skills Development Centre, C3, Main Block, Queen Mary Hospital, Pokfulam, Hong Kong Advanced Trauma Life Support (ATLS) Student Course Organised by: Department of Surgery, Queen Mary Hospital & Hong Kong Chapter of the American College of Surgeons, Venue: The Jockey Club Skills Development Centre, C3, Main Block, Queen Mary Hospital, Pokfulam, Hong Kong Oxfam Trailwalker 2009 from Sai Kung to Tai Tong Organised by: The Hong Kong Medical Association, Venue: MacLehose Trail	Course Administrator Tel: 2855 4885 / 2855 4886 Fax: 2819 3416 Email: hnsrg@hkucc.hku.hk Web site: http://www.hku.hk/surgery Course Administrator Tel: 2855 4885 / 2855 4886, Fax: 2819 3416 Email: hnsrg@hkucc.hku.hk, Web site: http://www.hku.hk/surgery Ms. Dora HO Tel: 2527 8285
21 SAT 2:00 pm (22)	HKMA HKE Network - PPI Lecture on Update on Neurosurger Organised by: HKMA HKE Network & HA HKE Cluster, Chairman: Dr. LAM See Yui Joseph, Venue: HKEC Training Centre for Healthcare Management & Clinical Technology, Pamela Youde Nethersole Eastern Hospital 2nd Guangdong, Hong Kong and Macau Sports Meet Organised by: The Hong Kong Medical Association, Venue: Guangzhou	Miss Alice TANG / Miss KWONG WL Tel: 2527 8285 / 2595 6941 Ms. Dora HO Tel: 2527 8285
22 SUN 2:00 pm	HKMA Structured CME Programme with PMH Year 2009 (10) - Common ENT Infections Organised by: The Hong Kong Medical Association, Speaker: Dr. LAM Chiu Wing, Venue: G8 Hall, Princess Margaret Hospital, Kowloon	Miss Viviane Lam Tel: 2527 8452 2 CME Points
29 SUN 1:30 pm	HKMA Family Sports Day Organised by: The Hong Kong Medical Association, Venue: Stanley Ho Sports Centre	Ms. Dora HO Tel: 2527 8285

Meetings

9/1/2010	Hong Kong Surgical Forum - Winter 2010 Organised by: 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 Secretariat, Tel: 2855 4855 / 2855 4886, Fax: 2819 3416, Email: hksf@hkucc.hku.hk, Website: http://www3.hku.hk/surgery/forum/php
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Courses

12-13/12/2009	Advanced Medical Life Support (AMLS) Provider Course Organised by: Department of Surgery, Queen Mary Hospital & Hong Kong Chapter of the American College of Surgeons, Venue: The Jockey Club Skills Development Centre, C3, Main Block, Queen Mary Hospital, Pokfulam, Hong Kong, Enquiry: Course Administrator, Tel: 2855 4885 / 2855 4886, Fax: 2819 3416, Email: hnsrg@hkucc.hku.hk Web site: http://www.hku.hk/surgery
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Upcoming Certificate Courses of the Federation of Medical Societies of Hong Kong

Date	Course No	Course Name	Target Participants	CME/CNE
4 Nov 09 - 9 Dec 09 (Every Wed)	C145	Certificate Course on Sports Medicine & Emergencies	Medical and Health Professionals	9 CNE Points / CME Accreditation in application
17 Nov 09 - 29 Dec 09 (Every Tue)	C152	Certificate Course in Obstetrics 2009	General Practitioners, Midwives, Nurses and Health Care Providers who are interested in Obstetrics	9 CNE/PEM Points / CME Accreditation in application



Answer to Dermatological Quiz

1. There are multiple erythematous violaceous lichenoid papules confluence into poikilodermatous patches and plaques at the knuckles of the hands and dorsum of the fingers in this middle age woman. These are often referred to as Gottron's papules. The presence of periungual erythema, telangiectasia and cuticular infarct are also very useful cutaneous clues to the diagnosis of an underlying connective tissue disease. In this patient, coupled with the history of facial rash with similar violaceous heliotrope nature and symptoms suggestive of proximal myopathy, a clinical diagnosis of dermatomyositis should be considered.
2. Skin biopsy of lesional skin shows interphase dermatitis with basal vacuolar degeneration at the epidermis. The basement membrane is thickened by mucin deposition. The component of myositis, as evidenced by proximal muscle weakness on physical examination, can be confirmed by the elevated muscle enzymes. Further investigations with electromyography, MRI and muscle biopsy, if necessary, may show myositic/ myopathic changes.
3. Late onset dermatomyositis, as in our patient, is reported to have a 6.5 fold increase in risk of internal malignancy. The reported frequency of internal malignancy in adult dermatomyositis varies from less than 10% to over 50%. Commonly associated malignancies in local patients include nasopharyngeal carcinoma (commonest), breast, lung, stomach and other female genital cancers. The approach in managing adult late onset dermatomyositis is thorough malignancy screening upon diagnosis and detailed laboratory evaluation as directed by clinical finding. Systemic steroid is the first line treatment for dermatomyositis, especially when myositic component of the disease is prominent. Adjunctive systemic treatment such as antimalarial or low dose methotrexate may also be helpful. Significant resolution of dermatomyositis after treatment of associated malignancy is seen, while relapse of cutaneous disease may herald relapse of underlying malignancy.

Dr. Ka-ho LAU

MBBS(HK), FRCP(Glasg), FHKCP, FHKAM(Med)
Yaumatei Dermatology Clinic, Social Hygiene Service

The Federation of Medical Societies of Hong Kong

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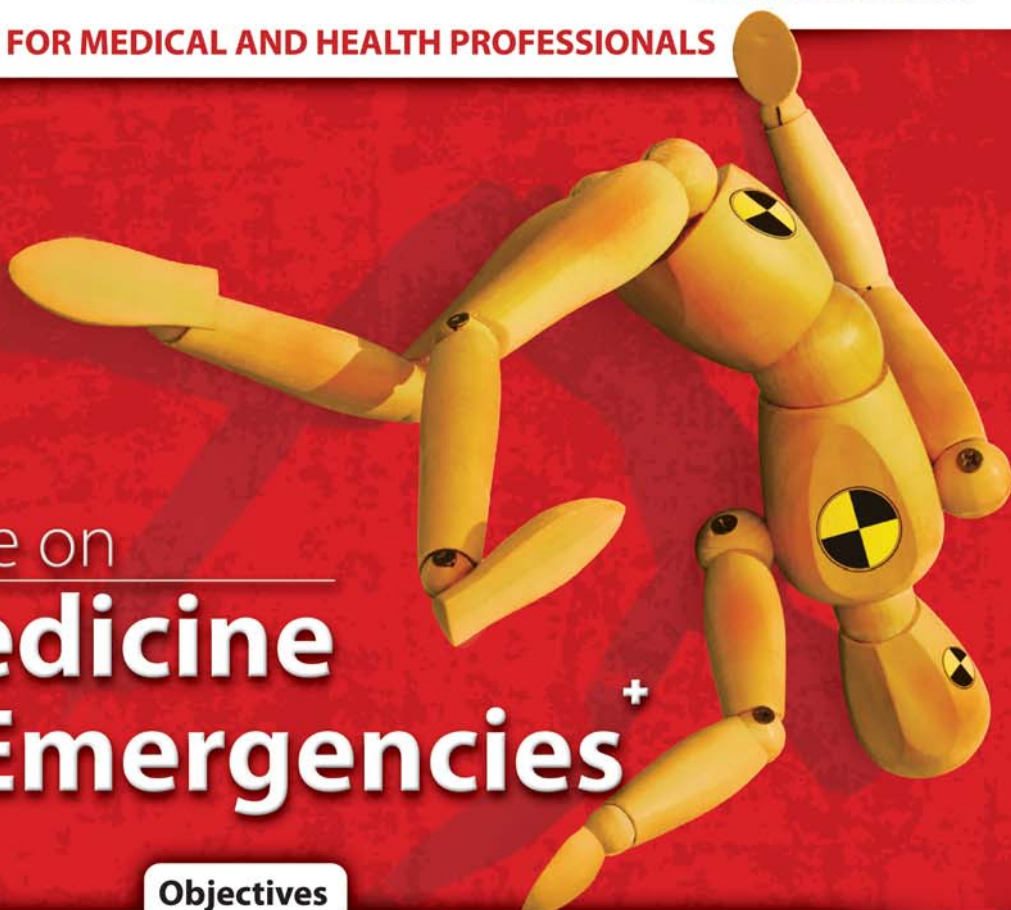
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Certificate Course on Sports Medicine & Emergencies⁺



Jointly organised by



The Federation of Medical
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香港醫學組織聯會



Hong Kong Society for
Emergency Medicine and Surgery
香港急症醫學會

Objectives

Want to know what Sports Medicine is about?

We are a group of emergency physicians who are interested in sports medicine. We will present an overview of many aspects of Sports Medicine and related Emergencies. You will learn the role of pitch-side doctor, basic knowledge of sports injuries and their management.

Dates	4 November 2009 – 9 December 2009 (Every Wednesday)
Time	7:00 p.m. – 8:30 p.m.
Venue	Lecture Hall, 4/F, Duke of Windsor Social Service Building, 15 Hennessy Road, Wanchai, Hong Kong
Language Media	Cantonese (Supplemented with English)
Course Fee	HK\$750 (6 sessions)
Certificate	Awarded to participants with a minimum attendance of 70%
Enquiry	The Secretariat of The Federation of Medical Societies of Hong Kong
Tel.	2527 8898
Fax	2865 0345
Email	info@fmshk.org

Date	Topic	Speaker
4 November 2009	Introduction to Sports Medicine and Common Injuries in Contact Sports	Dr. Ken WU
11 November 2009	Mind your head !	Dr. Kwan-Leong AU YEUNG
18 November 2009	Challenges to your leg's limit: Marathon runner and Trailwalker	Dr. Man-Kam HO
25 November 2009	Pitch-side assessment and management	Dr. Chi-Wai CHAU
2 December 2009	Medical Emergency in Sporting Grounds	Dr. Willis KWOK
9 December 2009	Theory and practical tips for weight training	Dr. Ben Siu-Pan NG

CME / CPD Accreditation in application

A total of **9 CNE points** for the whole course and the points will be awarded according to the number of hours attended.