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New Scope in Risk Factor Control for Diabetic Patients & those with Renal Disease

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Coronary heart disease, stroke and renal failure are the most devastating complications in type 2 diabetes. Prevention of diabetic complications involves not only tight glycaemic control but also global metabolic risk factors such as reduction in LDL-c, blood pressure, albuminuria and elevation of HDL-c. One important risk factor that warrants special attention in the management of diabetes is elevated arterial pressure. It has recently been shown in the ADVANCE trial that aggressive reduction in blood pressure irrespective of the initial blood pressure or whether diabetic patients are already on anti-hypertensive drugs, addition of perindopril-indapamide combination helps to reduce cardiovascular mortality[1]. In this issue of the Hong Kong Medical Diary, Dr. Godwin Leung (Specialist in Cardiology) gives an insightful commentary to this landmark trial, the findings of which may have an impact on future hypertension treatment guidelines in the diabetic population.

An important group of diabetic patients at very high cardiovascular risk is those with diabetic nephropathy. The presence of proteinuria and impaired renal function substantially increases cardiovascular mortality in this group of patients. Interestingly, in diabetic patients with advanced renal disease, conventional risk factors do not appear to be important predictors of mortality compared to those without nephropathy. Indeed the 4D study failed to show improved cardiovascular mortality with LDL reduction by atorvastatin in haemodialysis diabetic patients[2]. One of the non-traditional risk factors is anaemia. It has been shown in the RENAAL study to be an independent predictor for progression of diabetic nephropathy to end-stage renal disease[3]. In this issue, Dr. Felix Li (Specialist in Nephrology) discusses the management of anaemia in patients with diabetic kidney disease. Furthermore, Dr. Angela Wang (Specialist in Nephrology) addresses the importance of other non-traditional risk factors in the pathogenesis of cardiovascular disease in ESRD patients. Finally, the management of these very high-risk diabetic renal patients requiring comprehensive and integrated care with multi-faceted approach is emphasised by Professor van Biesen in his paper presented in a recent Neprohrology meeting in Japan. Indeed, combined endocrine and renal management in these high risk diabetic patients may greatly reduce their cardiovascular mortality.

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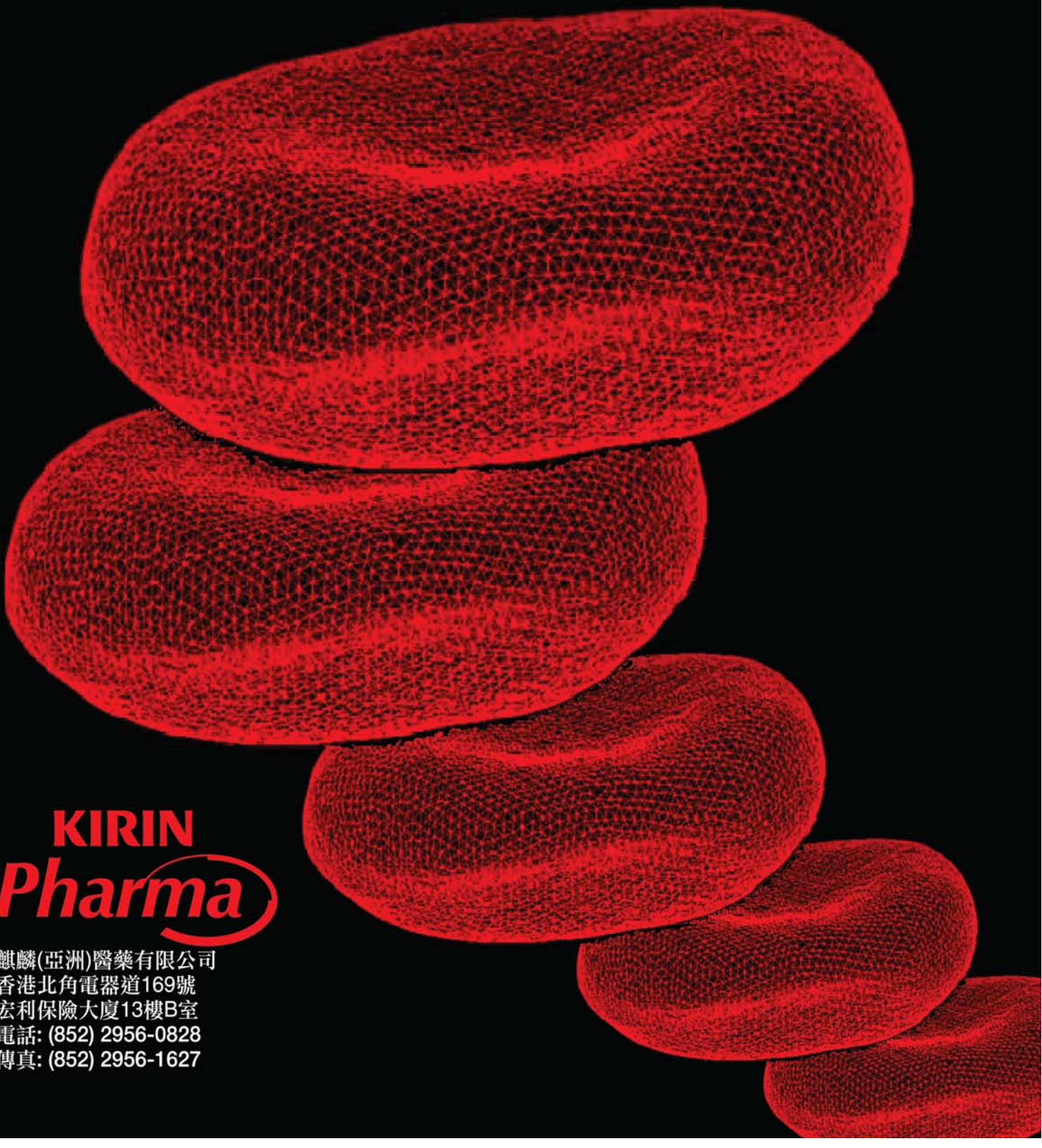

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Management of Hyperprolactinaemia

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Prolactin is solely secreted by the lactotroph cells of the pituitary gland. Hyperprolactinaemia therefore either results from hyper-secretion of lactotroph cells or decreased clearance. The regulation of secretion of prolactin differs from other pituitary hormones in that it is mainly suppressive in nature by the dopamine pathway. Hyperprolactinaemia per se can cause hypogonadotropic hypogonadism and is closely related to the reproductive axis. However, the management of hyperprolactinaemia relies heavily on the underlying causes and extends beyond its biochemical correction[1].

The upper normal range of prolactin is usually around 500 mIU/l. Stress and nipple stimulation are known to increase prolactin production. However, stress usually leads to a mild increase of prolactin level only, and rarely exceeds 2 fold of upper normal range. The magnitude of increase by nipple stimulation relies heavily on pre-existing lactotroph hyperplasia. Prolactin level increases during pregnancy and peaks at delivery. However, it falls rapidly after delivery and normalises usually in around 6 week's even if the mother breastfeeds.[1,2] Apart from these physiological processes, hypothalamic and pituitary diseases, and drugs interfering with the dopamine pathway are the most important causes of hyperprolactinaemia. It is obvious that prolactinomas will cause an increase in prolactin. However, it is important to realise that other pituitary adenomas, pituitary and hypothalamic diseases cause increases in prolactin as well due to disruption of dopamine inhibition.[3] Antipsychotic drugs such as haloperidol, phenothiazine and antiemetic drugs such as metoclopramide, domperidone are the two main categories of drugs which cause increases in prolactin due to dopamine receptor blockade. Verapamil and methydopa are the two antihypertensive drugs which cause increases in prolactin.[4] Although oestrogen in large amounts such as that occurring in pregnancy causes an increase in prolactin, contraceptive pills generally do not. Other miscellaneous causes include chronic renal failure, hypothyroidism, chest wall injury (similar to nipple stimulation), etc.[1]

The effect of hyperprolactinaemia alone depends on the gender and age of the patients. In premenopausal women, hyperprolactinaemia causes hypogonadotropic hypogonadism through inhibition of FSH and LH secretion, the severity of which depends on the prolactin level. The clinical features can range from shortened luteal phase, to oligomenorrhoea, to amenorrhoea. Even mild hyperprolactinaemia can cause infertility even when there is no abnormality in the menstrual cycle.[5,6] Overall, hyperprolactinaemia accounts for 10-20 percent of amenorrhoea and 20% of infertility. Hyperprolactinaemia also causes galactorrhoea, which is one of the common presenting features.[3] Women with amenorrhoea due to hyperprolactinaemia have lower bone mineral density. However, it is not clear whether women with hyperprolactinaemia but without menstrual problems have lower BMD.[7] Post-menopausal women are hypogonadal by definition and hyperprolactinaemia does not cause galactorrhoea in these women due to lack of oestrogen, though they may give a history of previous galactrrhoea[8]. In men, hyperprolactinaemia also causes hypogonadotropic hypogonadism, which is manifested by decreased libido, impotence and infertility. Galactorrhoea is much less common compared with women.[9] Due to less prominent clinical features of hyperprolactinaemia in post-menopausal women and men, hyperprolactinaemia due to prolactinoma, though less common in these two groups of people, is more likely to present with visual disturbances caused by the mass effect of the tumour rather than the hormonal effects.

There are two pitfalls in biochemical assessment of hyperprolactinaemia, namely the hook effect and macroprolactinaemia. The hook effect refers to the effect that when prolactin is very high, e.g. up to 100,000 mIU/l, the signal and capture antibodies are saturated and hence gives rise to a falsely low result. This can be avoided by repeating the assay with dilution.[10] This is particularly relevant when the prolactin level is only modestly raised while MRI pituitary shows a large pituitary adenoma, and the physician needs to differentiate a true prolactinoma from raised prolactin from stalk effect. Macroprolactinaemia is the presence of "big prolactin" which has decreased clearance and hence a falsely raised level of prolactin. This can be distinguished by gel filtration or polyethylene precipitation. The prevalence of macroprolactinaemia in patients found to have hyerprolactinaemia is as high as 10%.[11]

Prolactin should be checked when patients present with symptoms of galactorrhoea, oligomenorrhoea, amenorrhoea, infertility, impotence and known pituitary problems. The assessment should concentrate on a detailed assessment of sexual function, especially plans for pregnancy for women of reproductive age; detailed drug history, especially history of taking anti-emetic and antipsychotic drugs; previous insult to the hypothalamic pituitary region such as a history of radiotherapy to the head and neck region and neurological assessment of vision. The most readily identifiable causes are a history of taking drugs

interfering with the dopamine pathway or a history of previous radiotherapy involving the head and neck region[12]. The presence of macroprolactin interfering with the assay should be excluded since further investigation is no longer necessary if it is confirmed.[13] If raised prolactin is confirmed and no obvious causes can be found from history, thyroid stimulation hormone level and renal function test will be needed to exclude hypothyroidism and renal impairment causing a raised prolactin. Sex hormone assessment will be needed to assess the effect of raised prolactin on the reproductive axis. Magnetic resonance imaging of the pituitary will always be needed to look for a mass lesion in the pituitary region unless the patient is taking any drug known to increase prolactin.[14] If a mass in the pituitary hypothalamic region is found, referral to an endocrinologist for further assessment and treatment will be needed. For patients with raised prolactin, no other obvious causes and normal pituitary on MRI, they are often labelled as idiopathic hyperprolactinaemia.

It is a common pitfall to label any pituitary adenoma with raised prolactin as a prolactinoma or to treat the prolactin level alone without adequate assessment. In fact, pituitary adenomas other than prolactinoma also lead to raised prolactin due to the stalk effect, interfering with the inhibitory effect of dopamine from the hypothalamus[3, 14]. The differentiation relies on the feature that most prolactinomas secret prolactin proportionally, i.e. the level of prolactin is usually proportional to the size of the prolactinoma. Prolactinomas of <1cm size are usually associated with prolactin levels less than 10 fold of upper normal range, while prolactinomas of 1-2 cm size are associated with prolactin levels of around 10-50 fold of normal upper range, though there are occasional exceptions[1,15]. Therefore, if a large pituitary macroadenoma(>1cm) with modestly raised prolactin is found and the hook effect has been excluded, it suggests that the tumour is not a prolactinoma. This differentiation is important because prolactinomas, even of large size, mostly respond well to pharmacological treatment; while other pituitary tumours do not. MRI assessment is mandatory since if we treat the prolactin level alone without proper assessment, there is always the chance of missing a pituitary tumour which needs surgical intervention.

The treatment of hyperprolactinaemia relies heavily on the underlying causes, natural course of the disease and the aim of treatment. Prolactinomas can be divided into microprolactinomas (<1cm) and macroprolactinomas. Studies showed that 95% of microprolactinomas do not enlarge during the first four to six year of observation[16,17]. Therefore, the indication of treatment will be the relief of symptoms (galactorrhoea), normalisation of menses and improvement of fertility. For women who have hyperprolactinaemia, but are not planning for pregnancy and are asymptomatic, they can just be put on observation. For those who need treatment, dopamine agonists such as bromocriptine and carbegoline are the first line treatment. More than 90% of patients respond well to treatment. However, for macroprolactinoma, there is a high chance of tumour progression; therefore treatment is almost always indicated. Again, a dopamine agonist is the first line treatment, which leads to both reduction in prolactin level, and more importantly shrinkage of the tumour.[18-20] In fact, even for macroprolactinoma patients with visual field defects, treatment with dopamine agonists leads to rapid improvement in the visual field within days, well before imaging shows a shrinkage of the tumour in the majority of patients.[21,22] Transphenoidal surgery is considered when the patient does not show satisfactory response to medical treatment or tolerate medical treatment poorly. For patients with pituitary or hypothalamic diseases other than prolactinoma, the underlying causes should be treated if possible. Dopamine agonists can be used if necessary. However, it is always important to monitor such patients closely. Pituitary function also shows improvement upon treatment. For patients with drug induced hyperprolactinaemia, we should seriously consider whether the offending drug can be discontinued or substituted. If this is not possible, then the hypogonadism can be treated with sex hormones. One should use dopamine agonists with extreme caution since they may counteract the original therapeutic action of the drug.

In conclusion, hyperprolactinaemia needs thorough assessment and management should include not only biochemical normalisation, but also management of fertility, sexual function and visual problems.

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Laparoscopic Adrenalectomy

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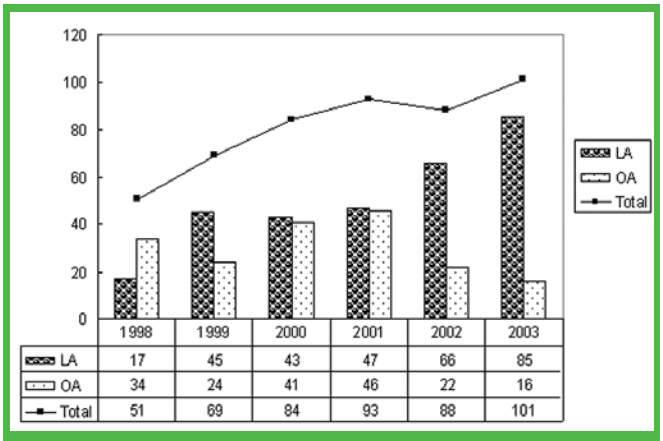
This article has been selected by the Editorial Board of the Hong Kong Medical Diary for participants in the CME programme of the Medical Council of Hong Kong (MCHK) to complete the following self-assessment questions in order to be awarded one CME credit under the programme upon returning the completed answer sheet to the Federation Secretariat on or before 30 April 2008.

Introduction

Adrenal masses are one of the most prevalent of all human tumours. The prevalence of adrenal masses approaches 3% in middle age, and increases to as much as 7% in the elderly[1]. It is anticipated that the management of adrenal masses will be a growing clinical challenge in our aging society because of its high prevalence in the elderly and the increased use of abdominal imaging studies. The significance of this clinical entity is also reflected by a recently published population-based study on adrenalectomy in Hong Kong[2]. A 2-fold increase in the total number of adrenalectomies performed in all public hospitals has been observed between 1998 and 2003, and the number of adrenalectomies performed by the laparoscopic approach in 2003 was 5 times than that in 1998 (Fig. 1).

The aim of this review is to present the recent developments of the surgical management of this common entity, and to update the clinicians the indications for surgical referral, the different surgical approaches and the potential complications.



	1998	1999	2000	2001	2002	2003
LA	17	45	43	47	66	85
OA	34	24	41	46	22	16
Total	51	69	84	93	88	101

Figure 1
The total number of adrenalectomies performed by public hospitals and the proportion of each approach adopted each year in all public hospitals in Hong Kong.

Indications for surgery

Not all adrenal masses are of clinical importance and candidates for surgery. When an adrenal mass is discovered incidentally, the clinician must decide between an operative and a non-operative management strategy. The indication for operation depends on hormonal activity and the likelihood of malignancy.

A. Functional adenoma

If history or physical examination of a patient with a unilateral adrenal mass shows signs and symptoms suggestive of glucocorticoid, mineralocorticoid, adrenal sex hormone that is confirmed biochemically, adrenalectomy is often considered the treatment of choice.

In the absence of clinical symptoms, treatment decisions for patients with biochemical evidence of cortisol hypersecretion present a vexing problem. While adrenalectomy has been demonstrated to correct biochemical abnormalities, its effect on long-term outcome and quality of life is unknown. Either adrenalectomy or careful observation has been suggested as a treatment option.

B. Phaeochromocytoma

Phaeochromocytoma is among the most life-threatening endocrine diseases, particularly if it remains undiagnosed. In a review of 40,078 autopsies at the Mayo Cliic between 1928 and 1977, phaeochromocytoma was found in 0.13% and had not been diagnosed in 76% of the patients while alive[3]. Patients even with "silent" phaeochromocytomas are at risk for a hypertensive crisis and should undergo adrenalectomy.

C. Adrenocortical carcinoma

In patients with nonfunctioning adrenal masses, distinguishing between malignant and benign primary adrenal tumours guides subsequent management. Variables to consider are the size of the lesion, its imaging characteristics, and its growth rate. Traditionally, the size of the lesion has been considered to be the major determinant of the presence of a malignant tumour. More than 60% of the adrenal masses less than 4 cm are benign adenomas, while less than 2% represent primary adrenocortical carcinomas. In contrast, the risk for carcinoma increases to 25% in lesions that are greater than 6 cm, while benign adenomas account for less than 15%. Therefore, the generally accepted recommendation is to excise lesions that are larger than 6 cm. Lesions that are less than 4cm and are defined as low risk by imaging criteria are unlikely to have malignant potential and are generally not resected. For lesions between 4 cm and 6 cm, either

close follow-up or adrenalectomy is considered a reasonable approach. Adrenalectomy should be strongly considered if the imaging findings suggest that the lesion is not an adenoma.

D. Metastases

The adrenal glands are frequent sites for metastases from many cancers. Lymphoma and carcinoma of the lung and breast account for a large proportion of adrenal metastases. Other primary cancers include melanoma, leukaemia, and kidney and ovarian carcinoma. In a review of 1000 consecutive autopsies of patients with carcinoma, the adrenal glands were involved in 27% of the cases[4]. The incidence of adrenal metastases in patients with breast and lung cancer is approximately 39 and 35%, respectively[4,5]. Among cancer patients, 50-75% of clinically inapparent adrenal masses are metastases[6].

There is no established clinical benefit to be derived form adrenalectomy in those patients who are diagnosed with a metastasis from a known primary neoplasm. Nevertheless, long term survival has been reported in selected patients, after resection of isolated adrenal metastases[7]. Since then, many series have confirmed that when metastasis is isolated to the adrenal gland, adrenalectomy by open or laparoscopic approach can achieve long term survival[8].

E. Others

Generally, myelolipoma and adrenal cyst are benign lesions that require no therapy. Larger, symptomatic or rapidly growing tumours are treated with adrenalectomy, which is usually curative. Infections, especially tuberculosis and histoplasmosis, can also manifest themselves as an adrenal mass. Surgery may be indicated if medical treatment is ineffective.

Adrenalectomy

Initially, all adrenalectomies were performed via the open, transabdominal route. In the 1980s, the posterior approach was adopted by the majority of surgeons due to a perceived decreased in surgical morbidity. The posterior approach was first used for small tumours and later for large tumours, phaeochromocytomas, and metastases. In addition, lateral retroperitoneal and thoracoabdominal approaches have also been described for open adrenalectomy, each having its specific merits and disadvantages (Fig 2).

In the early 1990s, Gagner et al reported the first laparoscopic adrenalectomy[9] and documented the feasibility of this new surgical technique in the first small series of adrenal tumours[10]. As with the open posterior approach, initial indications were limited. As surgeons gained experience, indications for laparoscopic adrenalectomy expanded to include large tumours, phaeochromocytomas, and metastases. In just a few years, the laparoscopic technique has become the 'new gold standard' for benign adrenal lesions up to 6 cm. Similar to the open procedure, the laparoscopic adrenalectomy can be performed by lateral transperitoneal (Fig 3) and posterior retroperitoneal approaches.

For invasive carcinomas and very large tumours, the best approach has yet to be determined. Few reports have examined these specific indications, and many authors consider them contraindications to laparoscopy. Others, however, have challenged these limitations, operating on large tumours and potential carcinomas, although the latter are usually converted to open procedures once they are definitely identified. In this situation the anterior transperitoneal and rarely the thoracoabdominal approach are preferable.

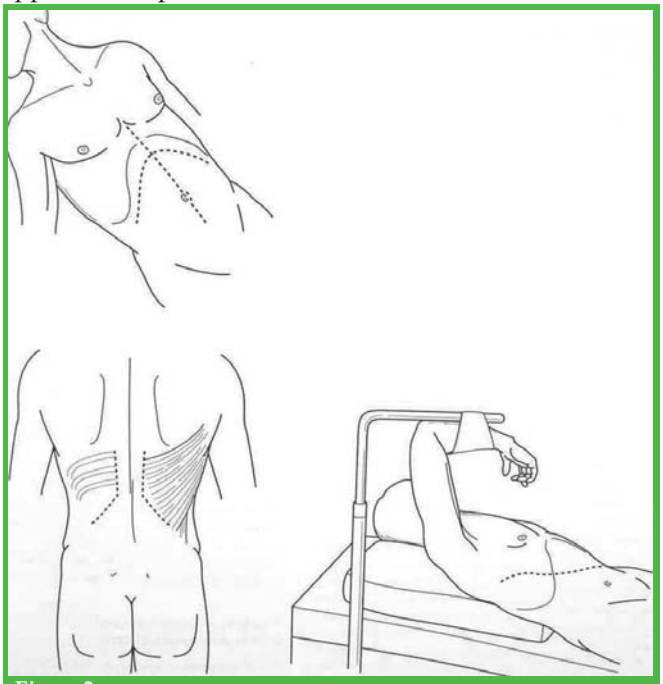


Figure 2
Different approaches of open adrenalectomy (Top: anterior transperitoneal, bottom right: posterior, bottom left: thoracoabdominal).

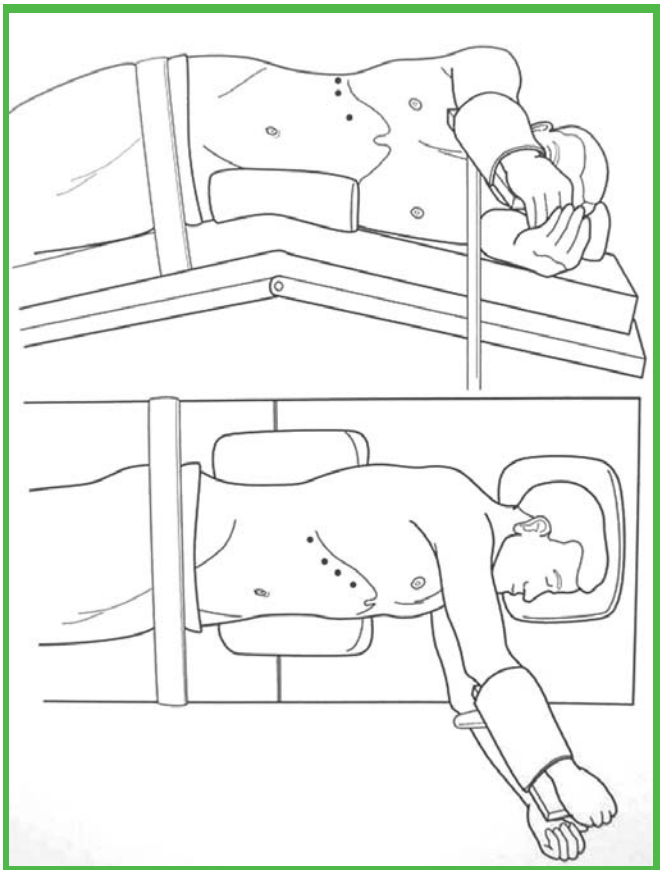


Figure 3
Position of patient undergoing laparoscopic right adrenalectomy and the position of port sites

Open or laparoscopic adrenalectomy

Either open or laparoscopic adrenalectomy is an acceptable procedure for resection of an adrenal mass. Despite the large number of studies involving thousands of patients, the quality of the evidence comparing different surgical approaches is poor. Randomised, controlled trials are lacking, and nonrandomised series risk a significant selection bias because surgeons routinely assign more difficult cases, larger tumours, and invasive cancers to the control group. In general, the laparoscopic approach usually takes longer, but results in less blood loss, less postoperative pain and late morbidity, a shorter hospital stay, earlier return to normal activity, and improves cosmetic results[11-13] (Fig 4).

Complications

The advent of laparoscopy for advanced surgical procedures has given rise to specific risks of intraoperative complications. Complications being reported in the literature included tissue injury (liver, spleen, pancreas, kidney, duodenum and colon), vascular injury (hepatic artery, splenic artery, venal cava and adrenal veins), and major haemorrhage. Post-operative complications such as haematoma, infection and port-site herniation have also been reported. The overall complication rates reported in various literatures, including the local one, were around 4%, and the mortality was less than 1%.[2,11-13]

The conversion rate was around 4-5% for various approaches of laparoscopic adrenalectomy. In most cases, the reason for conversion was bleeding, difficult dissection, or intraoperatively suspected malignancy.

Conclusion

As our population ages, the management of adrenal masses is becoming an increasingly important aspect of health care. Moreover, advances in imaging may reveal an even higher incidence, making the management of adrenal masses a challenge for modern medicine. Proper work-up by physicians, particularly endocrinologists, is recommended. In spite of all the advantages offered by the new minimally invasive operating techniques, one should not widen the indication for operation itself. When surgery is indicated, a careful selection of patients for all types of adrenal surgery, and experience with an adequate number of patients with different types of adrenal tumours guarantee optimal early and long-term results.

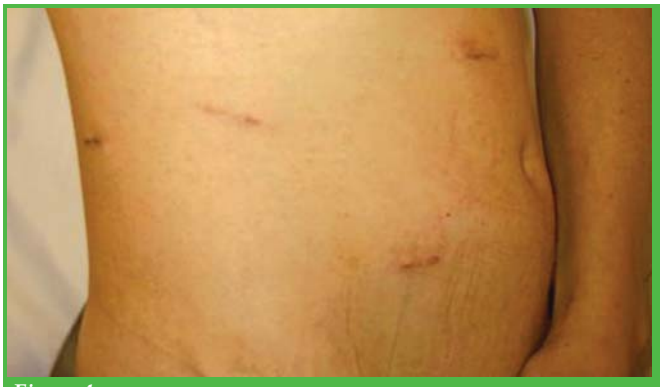


Figure 4
Post-operative photo shows the surgical wounds 1 month after right laparoscopic adrenalectomy.

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MCHK CME Programme Self-assessment Questions

Please read the article entitled "Laparoscopic Adrenalectomy" by Dr Wai-fan Chan , 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 April 2008. 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. Conn's adenoma is a common indication for adrenalectomy.
2. Surgery is not indicated in patients with asymptomatic phaeochromocytoma.
3. Adrenal gland is a common site of metastasis in patients with lung cancer.
4. Resection of isolated adrenal metastasis may prolong the survival.
5. Adrenalectomy is indicated in patients with growing or complicated myelolipoma or adrenal cyst.
6. Adrenocortical carcinoma is an indication for laparoscopic adrenalectomy.
7. The risk of adrenocortical carcinoma is lower in large adrenal mass (> 6cm).
8. Bilateral adrenalectomy should be performed by open approach.
9. Patients following laparoscopic adrenalectomy, generally, have a faster recovery, comparing to open approach.
10. Bleeding is the most common intra-operative complication of laparoscopic adrenalectomy.

ANSWER SHEET FOR APRIL 2008

Please return the completed answer sheet to the Federation Secretariat on or before 30 April 2008 for documentation. 1 CME point will be awarded for answering the MCHK CME programme (for non-specialists) self-assessment questions.

Laparoscopic Adrenalectomy

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1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10 ☐

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

HKID No.:___ ___ - ___ ___ ___ ___ X X (x)

Other Membership No. (please indicate): _____

Contact Tel No.:_____

Answers to March 2008 issue

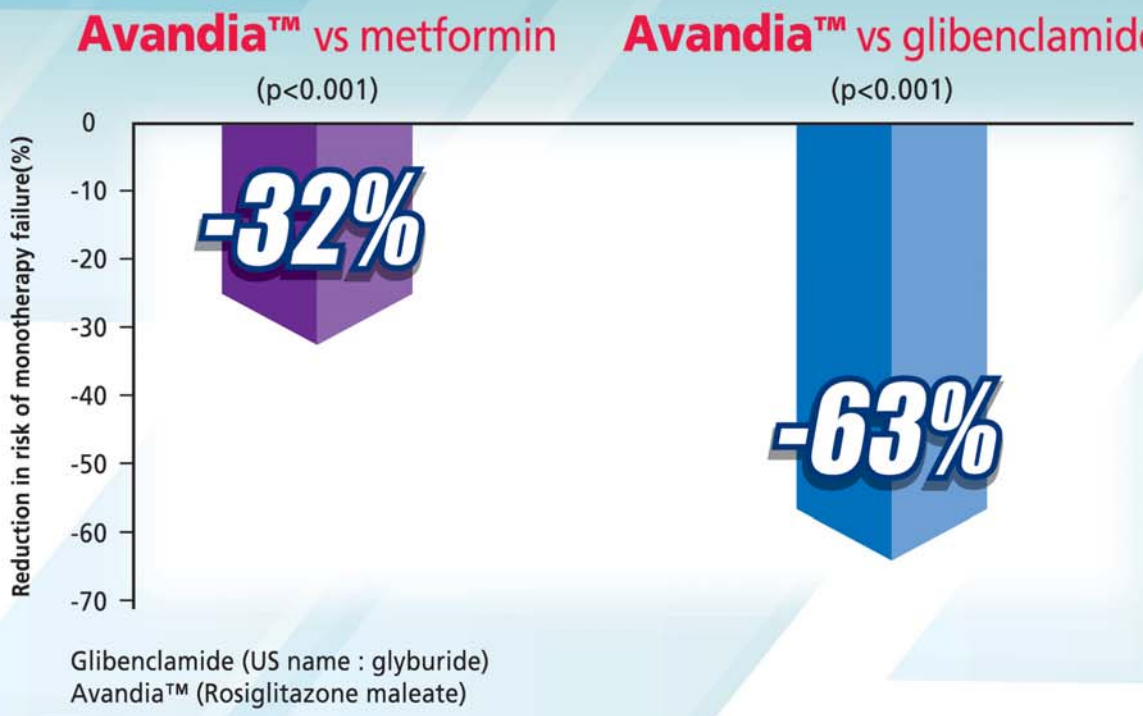
On Gastro-oesophageal Reflux-Induced Diseases

1. C 2. D 3. D 4. E 5. A 6. E 7. C 8. A 9. A 10. C

ADOPT

A Diabetes Outcome Progression Trial

Landmark ADOPT study shows Avandia™ (rosiglitazone) is superior to both sulphonylurea and metformin in sustaining long-term glycaemic control in type 2 diabetes



Kahn SE, Haffner SM, Heise MA, et al. N Eng J Med 2006; 355: 2427-2443

Avandia™
rosiglitazone maleate

ACTIVE INGREDIENT: Rosiglitazone maleate. **INDICATIONS:** AVANDIA is indicated as an adjunct to diet and exercise to improve glycemic control in patients with type 2 diabetes mellitus. AVANDIA is indicated as monotherapy and in combination with a sulfonylurea, metformin, or insulin. AVANDIA is also indicated for use in combination with a sulfonylurea plus metformin.

DOSAGE AND ADMINISTRATION: AVANDIA may be administered either at a starting dose of 4 mg as a single daily dose or divided and administered in the morning and evening. For patients who respond inadequately following 8 to 12 weeks of treatment, as determined by reduction in FPG, the dose may be increased to 8 mg daily as monotherapy or in combination with metformin, sulfonylurea, or sulfonylurea plus metformin. AVANDIA may be taken with or without food. **Monotherapy:** The usual starting dose of AVANDIA is 4 mg administered either as a single dose once daily or in divided doses twice daily. In clinical trials, the 4 mg twice daily regimen resulted in the greatest reduction in FPG and HbA1c. **Combination Therapy:** When AVANDIA is added to existing therapy, the current dose(s) of the agent(s) can be continued upon initiation of AVANDIA therapy. **Sulfonylurea:** When used in combination with sulfonylurea, the usual starting dose of AVANDIA is 4 mg administered as either a single dose once daily or in divided doses twice daily. **Metformin:** The usual starting dose of AVANDIA in combination with metformin is 4 mg administered as either a single dose once daily or in divided doses twice daily. It is unlikely that the dose of metformin will require adjustment due to hypoglycemia during combination therapy with AVANDIA. **Insulin:** For patients stabilized on insulin, the insulin dose should be continued upon initiation of therapy with AVANDIA. AVANDIA should be dosed at 4 mg daily. Doses of AVANDIA greater than 4 mg daily in combination with insulin are not currently indicated. **Sulfonylurea Plus Metformin:** The usual starting dose of AVANDIA in combination with a sulfonylurea plus metformin is 4 mg administered as either a single dose once daily or divided doses twice daily. **Maximum Recommended Dose:** The dose of AVANDIA should not exceed 8 mg daily. Doses of AVANDIA greater than 4 mg daily in combination with insulin are not currently indicated. No dosage adjustments are required for the elderly or when AVANDIA is used as monotherapy in patients with renal impairment. Since metformin is contraindicated in such patients, concomitant administration of metformin and AVANDIA is also contraindicated in patients with renal impairment. Rosiglitazone is not recommended in patients with moderate to severe hepatic impairment, and in patients under 18 years of age.

CONTRAINDICATIONS: History of hypersensitivity to rosiglitazone or any other ingredient of the preparation.

WARNINGS AND PRECAUTIONS: AVANDIA is active only in the presence of insulin and should not be used in the treatment of type 1 diabetes. AVANDIA is not recommended in patients with severe cardiac failure unless the expected potential benefit is believed to outweigh the potential risk. AVANDIA, like other thiazolidinediones, can cause fluid retention, which can exacerbate or lead to signs or symptoms of congestive heart failure. The fluid retention may very rarely present as rapid and excessive weight gain. All patients, particularly those receiving concurrent sulphonylurea or insulin therapy, those with mild to moderate heart failure (NYHA class I and II), and those at risk for heart failure, should be monitored for signs and symptoms of adverse reactions relating to fluid retention, including heart failure. Postmarketing reports of new-onset or worsening diabetic macular oedema with decreased visual acuity have been reported with AVANDIA. Many of these patients reported concurrent peripheral oedema. In some cases the visual events resolved or improved following discontinuation of the drug. Prescribers should be alert to the possibility of macular oedema if patients report disturbances in visual acuity. Patients taking AVANDIA may be at risk of dose-related hypoglycaemia if receiving combination regimens that contain a sulphonylurea or insulin. A reduction in the dose of the concomitant agent may be necessary. Close monitoring of glycaemic control and rosiglitazone dose adjustment may be needed when AVANDIA is co-administered with CYP2C8 inhibitors or inducers.

INTERACTIONS: In vitro data demonstrate that rosiglitazone is predominantly metabolised by CYP2C8, and to a lesser extent, CYP2C9. Co-administration of AVANDIA with CYP2C8 inhibitors (e.g. gemfibrozil) resulted in increased rosiglitazone plasma concentrations. Since there is a potential for an increase in the risk of dose-related adverse reactions, a decrease in AVANDIA dose may be needed when CYP2C8 inhibitors are co-administered. Co-administration of AVANDIA with a CYP2C8 inducer (e.g. rifampicin) resulted in decreased rosiglitazone plasma concentrations. Therefore, close monitoring of glycaemic control and changes in diabetic treatment should be considered when CYP2C8 inducers are co-administered.

PREGNANCY AND LACTATION: AVANDIA may result in resumption of ovulation in premenopausal, anovulatory women with insulin resistance. These patients may be at risk for pregnancy. AVANDIA has been reported to cross the human placenta and to be detectable in foetal tissues. There are no adequate data to support the use of AVANDIA during pregnancy and lactation in humans. AVANDIA should be used during pregnancy only if the potential benefit justifies the potential risk to the foetus. AVANDIA should be used during lactation only if the potential benefit justifies the potential risk to the infant.

ADVERSE REACTIONS: *Clinical Trials:* Oedema was generally dose-related, mild to moderate in nature and was more frequently observed when AVANDIA was used in combination with a sulphonylurea or insulin. Anaemia was generally dose-related and mild to moderate in nature. Hypercholesterolaemia. Weight gain was generally dose-related. Hypoglycaemia was generally mild to moderate in nature and was dose-related when AVANDIA was used in combination with a sulphonylurea or insulin. Increased appetite. Congestive heart failure/pulmonary oedema - An increased incidence of heart failure has been observed when AVANDIA (at both 4 mg and 8 mg) was added to treatment regimens that include a sulphonylurea or insulin. There were too few events to confirm a dose relationship; however, the incidence of heart failure appeared higher with 8 mg AVANDIA compared to 4 mg AVANDIA (total daily dose). Events typically associated with cardiac ischaemia - A small number of events typically associated with cardiac ischaemia was observed with AVANDIA in combination with insulin and these events occurred at a higher frequency with the combination (2.77%) compared with insulin alone (1.36%). In a retrospective analysis of data from pooled clinical studies, the overall incidence of events typically associated with cardiac ischaemia was higher for AVANDIA containing regimens, 1.99% versus comparators, 1.51% [Hazard ratio 1.31 (95% confidence interval 1.01 - 1.70)]. In a large observational study where patients were well-matched at baseline, the incidence of the composite endpoint of "myocardial infarction and coronary revascularization" was 1.75 events per 100 person years for AVANDIA containing regimens and 1.76 events per 100 person years for other anti-diabetic agents [Hazard ratio 0.93 (95% confidence interval 0.80 - 1.10)]. A causal relationship between cardiac ischaemic events and AVANDIA has not been established. Constipation is generally mild to moderate. *Postmarketing Data:* Anaphylactic reaction. Congestive heart failure/pulmonary oedema- AVANDIA as monotherapy and in combination with other antidiabetic agents. Hepatic dysfunction, primarily evidenced by elevated hepatic enzymes- A causal relationship to AVANDIA has not been established. Angioedema, urticaria, rash, pruritis, macular oedema, bone fractures.

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Treatment Choices of Childhood Graves' Disease

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Introduction

Graves' disease is a common endocrine disorder in adults. It also accounts for most cases of hyperthyroidism in children and adolescents. The incidence increases with age and peaks during adolescence. It seems that Hong Kong children have more Graves' disease than Caucasian children with the incidence of 6.5/100000/year and 0.79 to 2/100000/year respectively,(1-6) and the incidence seems to be increasing.[7] Girls are usually affected 4-5 times more frequently than boys. In a local series, the female to male ratio was up to 9.7.[7]

Graves' disease is characterised by diffuse goitre, hyperthyroidism and ophthalmopathy.

In Graves' disease there is spontaneous development of thyroid stimulating antibodies (TSAbs) which mimic TSH action, and lead to the excessive production and release of thyroid hormones. The main clinical presentations of Graves' disease in children are similar to those in adults, including weight loss, sweatiness, palpitation, enlarged goitre and proptosis. Sometimes children might present as deterioration in school performance due to poor attention and hyperactivity. Typical clinical features and biochemical hyperthyroidism can confirm the diagnosis in most of the cases. In doubtful cases, TSAbs can be of help since it is elevated in most cases.[8]

Current Treatment Modalities

Medication

Antithyroid medications, surgery and radioactive iodine are the currently used modalities to manage Graves' disease either in adults or in children. Antithyroid drugs are still the commonest used choice. It was introduced in early 1940s by Astwood. Current therapies include the thioamide derivatives: Propylthiouracil (PTU), Methimazole and Carbimazole. They reduce the thyroid hormone synthesis by inhibiting the oxidation of iodide and block the coupling of iodotyrosyl residues in thyroglobulin. Furthermore, PTU inhibits the peripheral conversion of T4 to T3. The recommended doses for PTU is 5-10 mg/kg/day, and for Carbimazole and Methimazole is 0.5-1.0 mg/kg/day. Because of its shorter half-life, PTU is better given as twice a day especially in the early treatment course. The maximal clinical responses occur after about 4-6 weeks. Before that, the signs and symptoms can be controlled by beta blockers such as propranolol. Saturated potassium iodide (Lugol's solution) blocks the release of thyroid hormones and is usually used prior to surgery to reduce the vascularity of the thyroid gland.

The remission rate for antithyroid drugs ranged from 21-42% according to different studies.[9-13] Dr. Raza and Brook in Great Ormond Street Hospital analysed 76 paediatric patients with thyrotoxicosis and showed a remission rate of 38% after drug therapy for a mean period of 3.3 years.[14] Two large series involving nearly 200 children each done by Hamburger JI et al and Glaser NS et al showed that only 20% and 30% achieved remissions lasting more than 2 years respectively.[9] The remission rate had been shown to be even lower in prepubertal kids (17%) than pubertal kids (30%).[13] Data from adult patients showed that the remission rate is inversely related with serum level of TSAbs and goitre size[15-19]. Furthermore long-term remission rate is less likely also if hyperthyroidism persists after short term (4-6 months) of drug treatment.[20,21]

It has been reported that 20-30% of patients will develop complications such as mildly increased liver enzymes, mild leucopenia, skin rash and agranulocytosis.[9,22] Some respond well with switching to the other thioamide derivatives while others require discontinuation of all thionamide drugs.

Surgery

Surgery is an alternative, especially in those who failed the medical treatment. Subtotal thyroidectomy is the older form of therapy which has been described in 1909. Total thyroidectomy is increasingly recommended to reduce the risk of recurrent hyperthyroidism. The success rate largely depends on the skills and experience of the surgeon. Long-term cure rate after subtotal thyroidectomy is shown to be 80%. 60% of them developed hypothyroidism and 10-15% remained hyperthyroidism.[22,23] Apart from pain, transient hypocalcaemia (10%), keloid formation (2.8%), permanent hypopara-thyroidism (2%) and vocal cord paralysis (2%) are the main complications associated with thyroidectomy. ([24,25] incidence shown in the brackets.)

Radioactive iodine

Radioactive iodine was first introduced in 1942 at the Massachusetts General Hospital . After iodine-131 has been taken orally, most of it is localised in the thyroid gland. It is the beta radiation which destroys the follicular cells. There would be epithelial swelling,

necrosis, oedema and leukocyte infiltration of the thyroid gland following the irradiation. At the end, the thyroid gland becomes fibrotic. The dose of iodine-131 is usually from 50 to 200 microCi per gram of thyroid tissue calculated according to the formula below [26]

Dose (mCi)=50-200microCi of I-131/gm of thyroid X estimated thyroid weight

It has been suggested that doses delivering 10,000-20,000 cGy may result in complete or partial destruction of the thyroid. Usually, a dose of 150 microCi/g of thyroid tissue yields radiation doses of 12,000 cGy to the thyroid.[27] Symptoms of hyperthyroidism may appear 4-10 days after iodine-131 administration because more thyroid hormone is released from degenerating follicular cells. It can be controlled by beta-blockers or Lugol's solution.

The long term cure rate has been reported in different studies. Hyperthyroidism persists in 25-40% if a dose of 50-100 microCi/g thyroid tissue is given.[28] It would be only 5-20% if 150-200 microCi/g thyroid tissue is administered. In the later group, 60-90% of the patients become hypothyroid.[26, 29] The success rate is inversely related to the size of the thyroid gland and the circulating levels of TSAb.[30,31]

Very few acute adverse responses to iodine-131 have been reported in children.[29,32-34] In adults, the main short term side effects would be transient thyroid pain in about 5%, worsening of eye disease in about 3-5%, others such as nausea, thyroid storm and transient hypocalcaemia are rare.[32,35,36] Worsening of thyroid ophthalmopathy, another potential side effect of iodine-131 treatment in adults, however, has not been well studied or reported in paediatric age group.

In children, the risk of thyroid cancer and the other cancers are the main worries for iodine-131 therapy. It has been shown that when used diagnostically, a dose of 60 microCi (6.5 cGy) iodine-131 resulted in no increased risk of thyroid or nonthyorid cancers in adults.[37,38] But there is an increased risk of thyroid neoplasia when the thyroid gland is exposed to 20-2000cGy.[39] Most of our experiences for radiation induced malignancy came from nuclear weapon use in world war II, radiation leakage or disaster. After the atomic bomb explosions in Japan, there is 3-10 fold increase in the rates of both benign and malignant thyroid neoplasms. And the estimated dose received from the bomb explosion is about 150cGy for adults, about 700-1400cGy for children.[40,41] The Chernobyl disaster also resulted in an increased rate of thyroid cancer, with children under 10 years old being affected most.[42,43] CTSG(Collaborative Thyrotoxicosis Study Group) has performed a large scale epidemiological survey involving more than 36,000 patients in USA. They reported that when the thyroid gland was exposed to high levels of radiation, rates of thyroid cancer were not increased. Follow up studies done by the same group of people for children showed that the incidence of thyroid neoplasms was not increased when the children were treated with high doses of iodine-131 (100-200 microCi/g).[44] In other reports, children were followed up from less than 5 years to 15 years after iodine-131 treatment. They have not found increased risk of thyroid malignancy.[9, 32,35] There are several studies which showed that the risk of leukaemia and breast cancer does not differ significantly from control populations.[45-47] It has been reported that the risk of stomach cancer was slightly higher (1.14 relative risk) in adults.[45] CTSG follow-up studies in adults showed that non-thyroid cancer mortality after iodine-131 therapy was not significantly elevated.[48]

Up to year 2004, only four cases of thyroid malignancy in children treated with iodine-131 were reported. They were all treated with low to moderate doses of iodine-131.[25] The use of high dose was further justified by Ron et al.[48] It is because when a high dose is used, it totally ablates the thyroid gland. When there is no thyroid tissue remains, there would be no chance to develop thyroid cancer.

The radiation to the gonads is comparable to that from barium enema.[49] Data showed that the incidence of congenital anomalies among the offspring of patients who had received iodine-131 did not differ from the general population. [9, 29,32,50]

Summary

Childhood Graves' disease is a rather common disease in our locality. There are different preferences among paediatricians for the choice of treatment. Although the remission rate after antithyroid drug alone is lower when compared to the adult population, it remains the first line of treatment in almost all clinical centres. However, surgical treatment under experienced hands should be considered when medical treatment fails and the patient has a large goitre (>80g) or in those with severe thyroid eye diseases. With more and more promising long term data coming out, radioactive iodine aiming at thyroid ablation should also be one of the treatment choice in older children above 12-15 years, especially for those who could not tolerate antithyroid drugs.

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Management of Anaemia in Diabetic Kidney Disease

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Patients with chronic kidney disease (CKD) have a high burden of cardiovascular (CV) morbidity and strategies to modulate CV risks are needed in this population. Anaemia has been recognised as a frequent complication of diabetic nephropathy, appearing earlier than in non-diabetic renal disease[1]. Recent data suggest that anaemia is a potentially modifiable risk factor and its correction could improve outcome in CKD patients[2]. The potential benefit of erythropoietin treatment in patients with diabetic renal disease is also emerging[3].

Aetiology of Anaemia in Diabetic Nephropathy

In type I diabetic patients, a series of observations have documented very convincingly that the onset of anaemia occurs early. Bosman et al. compared 27 type I diabetic patients with diabetic nephropathy and an average serum creatinine concentration of 96 umol/L (maximum 160 umol/L) with 26 non-diabetic patients with glomerulonephritis and persistent proteinuria[4]. Thirteen of the 27 diabetic patients were anaemic (haemoglobin 10.6 ± 0.9 g/dL), but none of the patients with glomerulonephritis (haemoglobin 13.7 ± 1.4 g/dL, $P<0.005$) was. When the erythropoietin concentration in the diabetic patients was compared with reference values measured in patients with microcytic anaemia (mostly caused by iron deficiency), it became obvious that the erythropoietin concentrations were clearly inappropriate to the low haemoglobin concentrations. The authors proposed the interesting hypothesis that the inadequate secretion of erythropoietin in response to anaemia was due to autonomic polyneuropathy causing efferent sympathetic denervation[4]. This idea was based on animal studies showing that renal denervation interferes with erythropoietin secretion[5] and that anaemia may occur in patients with primary failure of the autonomic nervous system[6]. When these were combined with damaged erythropoietin-producing fibroblasts in the renal cortex, early development of anaemia will result in the patients with diabetes. Other confounding factors are iron deficiency and therapy with angiotensin-converting enzyme inhibitors or angiotensin receptor blockers[7]. Resistance to erythropoietin, on the other hand, has not been demonstrated in diabetic patients[8].

Consequences of Anaemia in Patients with Diabetes

Diabetes and anaemia are each associated with significant morbidity and mortality. While the contribution of anaemia to the development of diabetic complications is not completely understood, it is imperative that both be managed to limit negative outcomes. Patients with diabetes are two to four times more likely to have heart disease or suffer a stroke than non-diabetics, and approximately 75% of patients with diabetes die of CVD-related causes[9]. Anaemia is associated with a greater incidence of left ventricular hypertrophy[10, 11], de novo or recurrent cardiac failure[12], and increased cardiac-related hospitalisations and deaths[13].

Anaemia in patients with diabetes is also associated with diabetic retinopathy and macular oedema, both of which result in accelerated vision loss[14]. Patients with retinopathy and low haemoglobin levels were more than five times as likely to have severe rather than mild retinopathy, suggesting that anaemia plays a significant role in retinopathy development and progression[15]. The Early Treatment Diabetic Retinopathy Study confirmed that anaemia was an independent risk factor for proliferative retinopathy or vision loss with a hazard ratio of 1.52[14].

In a seperate analysis of the Reduction of Endpoints in NIDDM with the Angiotensin II Antagonist Losartan (RENAAL) study by Mohanram[16], anaemia was shown to be an independent predictor for progression to end-stage renal disease in type 2 diabetics with nephropathy. Anaemia may worsen the renal function by directly causing renal tissue hypoxia and consequently renal scarring. Additionally, it may activate the renal sympathetic activity, resulting in reduction in renal blood flow and glomerular filtration rate.

Benefical Effects of Anaemia Management

In studies in which investigators explored the connections between diabetic neuropathy and anaemia, the haemoglobin levels of patients with diabetes improved with erythropoietin administration. Rarick and colleagues showed that the administration of erythropoietin improves haematocrit values and quality of life in patients with diabetes, anaemia and clinically normal renal function[17]. Although this study was too small to determine the causes of early anaemia in patients with diabetes, it provided preliminary evidence

of the need for early anaemia screening and treatment in patients with diabetes.

In the The Anaemia CORrection in Diabetes (ACORD) Study[18], one hundred seventy-two patients with type 1 or 2 diabetes mellitus, mild to moderate anaemia, and stage 1 to 3 chronic kidney disease were randomly assigned to attain a target haemoglobin level of either 13 to 15 g/dL (group 1) or 10.5 to 11.5 g/dL (group 2). The primary end point was change in left ventricular mass index (LVMI). Secondary end points included echocardiographic variables, renal function, quality of life, and safety. Median haemoglobin level and left ventricular mass index (LVMI) were similar in groups 1 and 2 (haemoglobin 11.9 and 11.7 g/dL; LVMI, 113.5 and 112.3 g/m^2, respectively). At study end, haemoglobin levels were 13.5 g/dL in group 1 and 12.1 g/dL in group 2 ($P < 0.001$). No significant differences were observed in median LVMI at month 15 between study groups (group 1, 112.3 g/m^2; group 2, 116.5 g/m^2). Multivariate analysis showed a non-significant decrease in LVMI ($P = 0.15$) in group 1 versus group 2. Anaemia correction had no effects on the rate of decrease in creatinine clearance, but resulted in significantly improved quality of life in group 1 ($P = 0.04$).

The Trial to Reduce Cardiovascular Events with Aranesp (darbepoetin alpha) Therapy (TREAT) is a randomised controlled trial designed to determine the impact of anamia correction on mortality and non-fatal cardiovascular events in patients with type 2 diabetes and stage 3-4 nephropathy[19]. 4000 patients will be randomised in a 1:1 manner to achieve a target haemoglobin of 13 g/dL or ≥ 9 g/dL with darbepoetin alfa therapy. Placebo will be given for a haemoglobin of >9 g/dL in the low-haemoglobin group. TREAT, when completed, will provide data that are critical to the management of cardiovascular risk in this high-risk population.

Whether anaemia correction may be beneficial to the progression of diabetic nephropathy remains unknown. One study demonstrated that the reversal of anaemia by recombinant erythropoietin was able to slow down the progression of chronic renal disease but this effect is less prominent in diabetics compared to non-diabetic patients[20]. In another open uncontrolled study in which 179 patients with chronic heart failure were treated with recombinant erythropoietin and iron to maintain a target haemoglobin of 12.5 gm/dL throughout the study, the mean serum creatinine and creatinine clearance (assessed with the Cockcroft-Gault formula) did not change significantly in either group during the study, whereas the mean rate of fall in creatinine clearance in the period before the study (untreated anaemia) was >1 ml/min/month in both groups[21].

Diabetic kidney disease is an increasingly common clinical entity. Despite the considerable advances, many issues including the prevalence, pathophysiology and consequences of anaemia in diabetic patients remain unsettled. Further prospective and controlled studies are urgently needed to clarify these issues.

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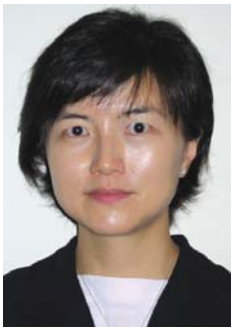
Cardiovascular Risk Factors in End-Stage Renal Disease: Beyond Framingham



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Introduction

Cardiovascular disease is the leading cause of mortality in patients with end-stage renal disease (ESRD). According to the report from the National Kidney Foundation Task Force on Cardiovascular Disease in Chronic Kidney Disease, ESRD patients treated by dialysis had at least 10 to 30-fold higher risk of cardiovascular mortality compared to age, gender and race-matched control population[1]. Data from the Hong Kong Renal Registry showed that over half of the mortality in ESRD patients was accounted by cardiovascular causes. Background atherosclerotic vascular disease increased mortality and cardiovascular death risk in ESRD patients by nearly three-fold and having a previous history of heart failure increased the subsequent cardiovascular mortality by at least three fold[2].

Apart from considering the traditional Framingham risk factors, there is an increasing recognition of 'non-traditional' risk factors in predisposing ESRD patients to cardiovascular complications. These include abnormalities in mineral metabolism with resulting hyperphosphatemia, secondary hyperparathyroidism, inflammation, extracellular volume overload, anaemia, increased asymmetric dimethylarginine, sympathetic overactivity, insulin resistance and increased oxidative stress. In this article, we will provide an overview on some of these risk factors.

Hyperphosphatemia

Hyperphosphatemia is highly prevalent in ESRD patients on maintenance dialysis. The United States Renal Data System showed that 70% of chronic haemodialysis patients had hyperphosphatemia[3]. A local survey[4] and a survey from Europe[5] showed that around 40% of chronic peritoneal dialysis patients had serum phosphorus above the Kidney Disease Outcome Quality Initiative (KDOQI) recommended target of 1.78 mmol/L and the prevalence increased further with loss of residual renal function[4].

Hyperphosphatemia not only contributes to secondary hyperparathyroidism but is an important predictor of mortality in dialysis patients[3,5]. Analysis from two large national databases from the United States revealed that hyperphoshatemia, elevated calcium*phosphorus product and elevated parathyroid hormone were specifically associated with death from coronary artery disease and sudden cardiac death in ESRD patients[6].

One of the major mechanisms whereby hyperphosphatemia contributes to an increased cardiovascular mortality relates to the development of vascular and valvular calcification. Hyperphosphatemia is capable of inducing a phenotypic change of vascular smooth muscle cells to 'osteoblast-like cells' which further lay down calcium and phosphorus loaded matrix vesicles, leading to calcium deposition[7-8]. Vascular calcification that develops secondary to hyperphosphatemia classically occurs in the media and is also known as the 'Monckeberg's calcinosis'. It has a tram-line appearance on plain radiographs and is associated with generalised arterial stiffening which increases the afterload and results in left ventricular (LV) hypertrophy[9-10]. This may reduce coronary flow reserve and increase risk of myocardial ischaemia. Hyperphosphatemia may also increase cardiac fibrosis, hypertrophy and aggravate microvascular disease[11] and predispose to sudden cardiac death in dialysis patients. On the other hand, vascular calcification that occurs in the intima is typically atherosclerotic in nature and may lead to obstructive lesions with resulting ischaemia. ESRD patients frequently exhibit both intimal and medial type of calcification but the intimal calcification is usually more extensive and severe as compared to non-uraemic subjects[12].

Vascular and valvular calcification is an important predictor of mortality and cardiovascular death in ESRD[13-14]. There is evidence that valvular calcification also represents a marker of generalised atherosclerosis as shown by its strong association with carotid intima-media thickness and plaque calcification[15] and atherosclerotic vascular disease[16] in ESRD. This suggests that calcification and atherosclerosis are indeed closely associated phenomena.

Coronary artery calcification (CAC) is a highly prevalent complication in ESRD with a prevalence ranging from 40% to almost 100% in different dialysis cohorts[17-19]. The prevalence of valvular calcification ranged from 30% to over 50%[17,20]. The degree of coronary artery calcification was at least 2.5 to 5-fold higher in dialysis patients compared to age and gender-matched non-dialysis controls with coronary artery disease[17]. Coronary calcification was rapidly progressive in dialysis patients[21]. A recent longitudinal study showed that serum phosphorus and calcium*phosphorus product predict the progression of coronary calcification in dialysis patients[19]. Other factors that predisposed to coronary calcification included increasing age, increasing duration of dialysis and cumulated dose of calcium-based binders[21].

There is recent concern that calcium-based binders may increase risk of vascular calcification when mineral metabolism was not well controlled[22]. However, the evidence regarding this issue has remained inconclusive. In the 'Treat to Goal' Study, sevelamer hydrochloride, a non-calcium based binder, has been shown to attenuate the progression of CAC[23] and is associated with better survival compared to calcium-based binder in haemodialysis patients[24]. However, this observation is contrary to the recent 'Dialysis Clinical Outcome Revisited (DCOR)' Trial which showed no overall survival benefit with sevelamer hydrochloride compared to calcium-based binder[25].

Inflammation

Inflammation plays a pivotal role in the initiation and progression of atherosclerosis[26] and is considered one of the major non-traditional risk factors for accelerated atherosclerosis in dialysis patients. Using C-reactive protein (CRP) as the prototype marker of inflammation, inflammation was detected in 20 - 50% of ESRD patients[27]. According to a previous local survey, around 35% of dialysis patients were inflamed as denoted by a CRP 5mg/L[2]. The prevalence was somewhat lower compared to that reported in Caucasian population[27]. An elevated CRP was not only associated with greater prevalence of atherosclerotic vascular disease but also more severe cardiac hypertrophy and dilatation[2]. CRP is a powerful predictor of all-cause mortality and cardiovascular death in ESRD patients[2,28]. The risk associated with an elevated CRP appears to be independent of other parameters including background cardiovascular disease, cardiac hypertrophy and residual renal function[2]. CRP has also been shown to contribute to the progression of carotid atherosclerosis in dialysis patients[29]. Cellular adhesion molecule which is involved in leukocyte-endothelial activation and plays a pivotal role in inflammation has also been shown to be associated with carotid atherosclerosis[30] and predicts mortality and cardiovascular events in ESRD[31]. Recent study suggested that interleukin-6 may be a stronger predictor of mortality and cardiovascular death in ESRD patients as compared to CRP[32].

Inflammation may also be involved in the calcification process as evidenced by the strong link between inflammation and valvular calcification[20]. Increased inflammatory proteins have been shown to predict a worse prognosis of valvular calcification in ESRD[33]. The finding of a more rapid annualised progression of coronary artery and aortic calcification in dialysis patients with higher CRP was additional evidence to support a causal role of inflammation in calcification[34]. In this context, serum fetuin-A, being a negative acute phase protein and calcification inhibitor, was negatively associated with valvular calcification independent of CRP and calcium*phosphorus product[35].

Loss of residual renal function is an important contributing factor to inflammation in ESRD patients. As shown in previous studies, residual renal function showed an important inverse relationship with inflammation[2,31]. The exact mechanism underlying this association is not clear. There is some suggestion that loss of residual renal function or uraemia per se may enhance an inflammatory response via increased oxidative stress and that may lead to monocyte activation and cytokine production[36]. The other possible mechanism may be that the kidneys are involved in cytokine handling as evidenced by impaired cytokine clearance in nephrectomised rats [37].

Extra-cellular Volume Overload

Left ventricular (LV) hypertrophy is one of the most prevalent cardiovascular complications and is a powerful predictor of mortality and cardiovascular death in ESRD patients[38]. According to a cross-sectional survey in incident dialysis patients, the prevalence of LV hypertrophy was around 75%[39]. Our previous survey showed that over 90% of the prevalent peritoneal dialysis patients had LV hypertrophy[38]. There are numerous risk factors responsible for LV hypertrophy in ESRD patients. Hypertension and arteriosclerosis result in pressure overload and give rise to concentric LV hypertrophy. Anaemia, chronic volume expansion, hyperparathyroidism and arteriovenous fistula which result in a volume overload state are associated with ventricular dilatation with LV hypertrophy or so-called eccentric LV hypertrophy. In a previous study, we observed greater LV hypertrophy and dilatation as well as more diastolic dysfunction among peritoneal dialysis patients who had previous history of volume overload[40], suggesting the importance of extra-cellular volume overload in predisposing ESRD patients to greater LV hypertrophy.

Close to 40% of chronic peritoneal dialysis patients have extra-cellular volume overload or more appropriately termed 'circulatory congestion'[41]. The causes of circulatory congestion are usually multi-factorial including non-compliance with fluid intake, low ultra-filtration volume and high transporter status. Diabetes and background atherosclerotic vascular disease increased the risk of circulatory congestion[41]. Extra-cellular volume overload may also be partly attributed to decline in residual renal function which by itself is an important predictor of mortality in PD patients[42-43] and shows an important link with LV hypertrophy[44]. Furthermore, loss of residual renal function was closely interrelated with inflammation and cardiac hypertrophy and these three key risk factors combined adversely to enhance the overall mortality and cardiovascular death of ESRD patients[38].

Conclusions

Mortality of ESRD patients has remained high due to an excessive cardiovascular risk burden resulting in a very high incidence of coronary artery disease, vascular and valvular calcification, LV hypertrophy and circulatory congestion. To improve the cardiovascular outcomes of these patients, we believe a more proactive approach is required and attention should be focused not only on modifying the traditional Framingham risk factors but more importantly the 'non-traditional' cardiovascular risk factors in ESRD.

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Blood Pressure Lowering with Perindopril and Indapamide - an ADVANCE in Improving Diabetic Mortality

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Original article:

Effects of a fixed combination of perindopril and indapamide on macrovascular and microvascular outcomes in patients with type 2 diabetes mellitus (the ADVANCE trial). Lancet 2007;370(9590):829-40.[1]

Summary

The effects of the routine administration of an angiotensin converting enzyme inhibitor (ACEI)-diuretic combination on serious vascular events in patients with diabetes were assessed, irrespective of initial BP levels or the use of other BP lowering drugs . A total of 11,140 patients with type 2 diabetes were randomised to treatment with a fixed combination of perindopril and indapamide or matching placebo in addition to existing therapy. The use of concomitant treatments during follow-up remained at the discretion of the responsible physician, with two exceptions - the use of thiazide diuretics was not allowed, and open-label perindopril, to a maximum of 4 mg a day, was the only angiotensin-converting enzyme (ACE) inhibitor allowed, thus ensuring that the maximum recommended dose of 8 mg for perindopril could not be exceeded by patients randomly assigned to active treatment. The primary endpoints were composites of major macrovascular and microvascular events, defined as death from cardiovascular (CV) disease, non-fatal stroke or non-fatal myocardial infarction (MI), and new or worsening renal or diabetic eye disease.

The results showed that after a mean duration of 4.3 years, compared with patients assigned placebo, those assigned active therapy had a mean reduction in systolic BP of 5.6 mm Hg and diastolic BP of 2.2 mm Hg. The relative risk of a major macrovascular or microvascular event was significantly reduced by 9%. There was a 14% reduction in total mortality which was mainly due to an 18% reduction in CV deaths in the active treatment group. There was no evidence that the effects of the study treatment differed by initial BP level or concomitant use of other treatments at baseline. By the end of follow-up, antihypertensive drugs were being used by more than three-quarters of participants. The results suggest that for every 66 patients commencing long-term treatment with perindopril and indapamide, one patient would avoid at least one major vascular event in five years. Over five years, one death would be averted in every 79 patients commencing treatment with the study drug. In summary, the results of ADVANCE indicate that the routine administration of a fixed combination of perindopril and indapmide to a broad range of patients with diabetes reduces the risks of death and major macrovascular or micrvascular complications, irrespective of initial BP level or ancillary treatment with many other preventive treatments typically provided to diabetic patients today. The authors concluded that if the benefits seen in ADVANCE were applied to just half the population with diabetes worldwide, more than a million deaths would be avoided over five years

Comment

ADVANCE, the largest-ever randomised trial of the prevention of diabetes complications, is a very important study that supports the idea that lower mortality rates could be achieved with lower blood pressures in diabetic patients. ADVANCE confirmed that more aggressive BP reduction in type 2 diabetics provides greater protection against both micro- and macrovascular events.

In the past, the United Kingdom Prospective Diabetes Study (UKPDS)[2] established that reducing BP produced benefits in diabetics. It demonstrated that each 10 mmHg decrease in systolic BP was associated with average reductions in rates of diabetes-related mortality (15 percent), myocardial infarction (11 percent), and the microvascular complications of retinopathy or nephropathy (13 percent). Mean systolic BP was lowered from 155 mmHg to 145 mmHg in UKPDS, and the ADVANCE study extended these findings to patients with lower pressures. In ADVANCE, the average BP at baseline was 145/81 mm Hg, and this was reduced to 135/75 mm Hg in the active-treatment group vs 140/77 in the placebo group over 4.3 years. This greater reduction in BP in the active-treatment arm was associated with significant improvement in outcomes. These benefits were achieved on top of aggressive ancillary drug therapy, with the majority of patients in both arms also taking other blood-pressure-lowering agents. Most guidelines[3,4] recommend lower blood-pressure targets for diabetics (130/80mmHg) than the normal population (140/90mmHg), and this study reinforces this recommendation. There was no direct evidence in the past because the recommendation was mainly based on data largely generated from subgroup analyses within the more general hypertensive populations[5]. ADVANCE provides new and more solid evidence to support the recommendations already in the guidelines for lower target blood pressures in diabetic patients. An important message from this trial is that diabetic patients should be treated aggressively to lower their BP below 130/80 mmHg.

It is generally believed that the link between reducing BP and improving mortality shown in this study may be generalisable to other antihypertensive medications[6]. However, the tolerability and benefits of ACEI-diuretic combination were well shown in this trial, with only 3.6% of patients withdrawn because of suspected side effects during the pre-randomisation run-in period. At the end of the study, adherence to active treatment was 73%, only 1% less than adherence to placebo. Whether this excellent tolerability will apply in Chinese patients remains to be seen because Chinese patients may be more susceptible to ACEI-related cough.

This finding also indicates that a short course of active treatment is able to identify the small proportion of patients who are intolerant. This result has important implications for health service delivery, since only one follow-up visit is needed to establish patient's suitability for long-term treatment with this regimen. Thereafter, follow-up visits can be maintained at 3 to 6-month intervals with minimum requirement for titration. This simple strategy may prove more practical and affordable in most clinical circumstances.

This trial also supports the recommendation that in treatment-naive high-risk diabetic patients, initiation of combination treatment immediately to reduce BP is beneficial and well tolerated. The rationale of commencing combination treatment right at the beginning is that even short periods of uncontrolled hypertension can translate into additional risks of cardiovascular events and more than one anti-hypertensive agents will often be required to lower BP to the target in majority of diabetic patients[4,7]. The use of fixed-dose combination treatment is more convenient and simplify the treatment regimen and may cost less than the individual components prescribed separately. Greater BP reduction can usually be achieved at lower doses of the component agents, resulting in fewer side effects. [8,9]

Lastly, optimal care for diabetic patients should include global risk reduction [10]. In this cohort of patients, only about half of them were on aspirin or statin. Hence optimising anti-platelet and lipid lowering therapies may achieve even greater cardiovascular risk reduction in addition to intensive BP control.

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Dermatological Quiz

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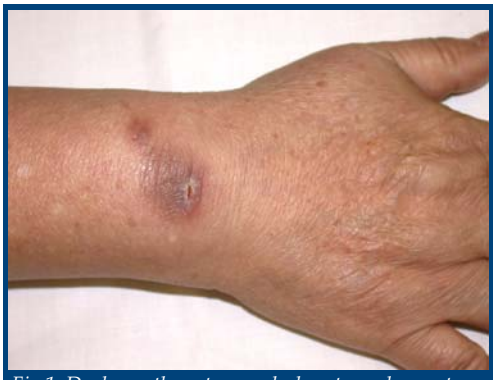

Fig 1: Dusky erythematous and edematous plaque at dorsum of right forearm

A 50-year-old lady complained of recurrent episodes of non-pruritic skin lesion near right wrist for two years. The lesion usually appeared at similar site and lasted for about 1-2 weeks before subsiding and leaving some pigmentation. Her past health was good except that she had rheumatism, which she treated herself by buying some pain killer occasionally over the counter. She was a right-handed person and wore her watch at the left wrist.

Questions:

1. What is your preliminary diagnosis or differential diagnosis?
2. What are the main clues in the diagnosis?
3. How do you confirm your diagnosis if necessary?
4. What is the mainstay of treatment?

(See P. 31 for answers)

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The 3rd Asia Chapter of the International Society for Peritoneal Dialysis - Hiroshima, Japan November 2007


Dr. Norman Chan Prof. W. Van Biesen

Is Glucose a Problem in the Dialysate for Diabetic PD Patients?

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Diabetes is commonly present in the patients with end-stage renal disease (ESRD) requiring regular renal replacement therapy. In continuous ambulatory peritoneal dialysis (CAPD) patients, supraphysiological concentration of dextrose has been widely used as dialysate in the peritoneal dialysis (PD) fluid for the past two decades. Depending on the period of exposure and the strength of the dextrose solution used, 320-700 kCalories of additional energy daily intake may result from peritoneal dialysis. Not surprisingly, this has caused some concern, not least due to the direct glucose toxicity to the peritoneum membrane but also the possible adverse metabolic consequences, such as obesity, increased insulin resistance and dyslipidaemia. However, is this concern regarding metabolic effect as a result of dextrose dialysate justified?

Body mass index & mortality in ESRD patients

Malnourishment as reflected by low BMI has been linked with increased mortality in patients with ESRD[1]. Numerous studies have shown that patients undergoing chronic peritoneal dialysis do not have adequate dietary protein and energy intake[2-4]. For instance, Wang and colleagues studied nutritional intake in 266 ESRD patients (31% had diabetes) and found that 75% of patients had energy intake <126kJ/kg/day. Even with the addition of peritoneal glucose intake, only 20% of patients achieved the recommended intake of 146 kJ/kg/day[2]. In another study, Jacob et al found that in 61 CAPD patients, over 63% had inadequate energy intake, as assessed by a low triceps skinfold thickness or a reduced midarm muscle circumference[3]. Hence additional calories from glucose through PD fluid could potentially be beneficial if appropriate therapy is given to maintain euglycaemia in those with diabetes.

The concern about possible weight gain as a result of chronic PD therapy is not well established. Studies from Korea, Sweden and America have shown that PD patients have either normal or only slightly high BMI[5,6]. In these studies, data on waist circumference (marker of visceral obesity) were not provided. On the other hand, data from large-scale studies showed a trend towards "reverse epidemiology" with regard to obesity and mortality in ESRD patients[1,6]. Whether this is a true phenomenon remains a subject of debate. Meanwhile, there is no clear evidence that obesity (as reflected by increased BMI) confers extra risks in PD patients. It is very likely that it is the loss of lean muscle weight (as a result of malnutrition) which determines the short-term mortality in ESRD patients and these patients do not survive long enough for high BMI to have an impact.

Does dextrose dialysate worsen glycaemic control?

The claim that dextrose dialysate worsens insulin resistance is also unproven. Szeto and colleagues studied a cohort of 60 Chinese insulin-treated diabetic patients who have just been started on PD therapy. They found that slightly increased subcutaneous insulin (0.103 unit/kg/day) was required over a period of 6 months,; there was no change in glycaemic control. This increase in insulin was mainly confined to patients on higher dextrose dialysate concentration. There was no evidence that extra glucose loading from PD leads to deterioration in glycaemic control if insulin therapy is appropriately titrated. Given that ESRD patients with diabetes are often insulin resistant, the use of insulin sensitisers such as thiazolidinedione therapy in diabetic PD patients may have a role. Another study of Chinese diabetic patients by the same research group examined this issue. Fifty-two insulin-treated diabetic patients were randomised to receive either add-on rosiglitazone therapy or remained on insulin alone. After 24 weeks, total insulin dosage was significantly decreased in the rosiglitazone group compared to the control group (-21.5% vs +0.5%). Furthermore, the rosiglitazone therapy was associated with significant reduction in C-reactive protein[8]. These results are certainly promising but long-term outcome studies would be required. While glycaemic control is important in preventing micro- and macrovascular complications, in ESRD patients, it has been shown that pre-dialysis glycaemic control is an important determinant of mortality[9]. Intra-peritoneal insulin therapy has been advocated by some nephrologists in the past which was thought to be more physiological. Literature on the comparison between peritoneal insulin and subcutaneous insulin has been sparse. Torun and co-investigators compared the use of peritoneal insulin and subcutaneous insulin in a small

number (n=14) of diabetic patients. They found that when compared with subcutaneous insulin, intraperitoneal insulin was associated with significantly greater weight gain, higher triglyceride levels, higher glucose load in dialysate and higher insulin dosage. Furthermore, 5 out of the 8 patients on intraperitoneal insulin developed hepatic subcapsular steatosis[10]. Currently, most centres are using subcutaneous rather than intraperitoneal insulin. The impact of diabetes education should be emphasised as it has been shown to improve glycaemic control and patient outcomes in ESRD patients[11] just like those without chronic kidney disease.

Dyslipidaemia and glucose loading

Worsening of dyslipidaemia occurs in PD patients with a gradual rise in triglyceride and total cholesterol[12,13]. Several studies have considered glucose loading in PD fluid as a contributory factor but results have been conflicting. In a retrospective study of 102 CAPD patients, Olivaries et al found an initial rise in serum triglycerides related to glucose load which was not sustained and began to normalise after 2 years of CAPD[14]. In another study, Little et al found that in a prospective cohort of 124 ESRD patients, serum triglyceride and total cholesterol were elevated after PD when compared to baseline but more so in the group with pre-existent cardiovascular disease[15]. This is most likely to be due to a genetic predisposition in this group of patients. In this study, the strongest predictor of worsening of dyslipidaemia was weight gain and was not associated with glucose loading[15]. Similarly, a study of 22 non-diabetic PD patients from Sweden also confirmed the lack of effect of PD glucose loading on worsening of dyslipidaemia[16].

Summary

In summary, dextrose dialysate fluid has not been shown to result in derangement in metabolic parameters. Alternative dialysate fluids such as icodextrin and amino acid PD fluids have been developed which are generally more expensive and have their own limitations. Good glycaemic control pre-dialysis is paramount in reducing mortality in diabetic PD patients. Well-designed large-scale outcome studies are required to determine the most appropriate PD fluid for diabetic ESRD patients.

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PD First Strategy for Diabetic Patients

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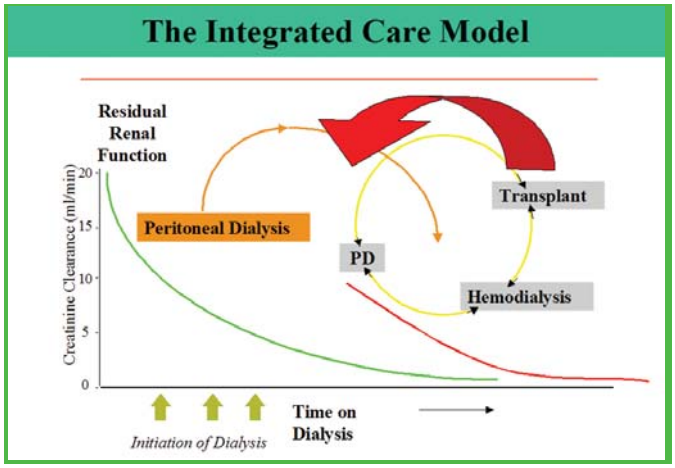
Until some years ago, each renal replacement therapy (RRT) was considered as a separate entity, an approach that neglected completely the fact that most patients transfer between the different modalities over time. The concept of integrated care (figure) aims at providing the most optimal therapy at each time of the disease process for each patient[1]. The question is thus not "which treatment is best" but " which succession of treatments will give the best outcome in the long term". Also for diabetics, this integrated care concept makes sense, and presenting PD as a very good starting modality for RRT should be encouraged.



PD as a first line therapy

Outcome on PD in diabetics

The first question when advocating a RRT modality is of course whether this choice would impact on the survival of the patient.

Survival analysis of PD vs haemodialyis (HD) shows a different picture in the US as compared to Europe and Asia. In European studies, almost all report a survival benefit or a comparable survival on HD vs PD in diabetic patients, especially in the first 3-4 years of the treatment[2;3].

The data of the USRDS database seem to indicate that mortality is lower in PD vs HD in younger diabetics, but worse in older diabetics, especially if they are female[4;5]. This interpretation can be seriously questioned because of different reasons[6]. First, the USRDS database only includes patients after 90 days, favouring the "worst" modality by selecting only the fittest patients. Second, the patient numbers in USRDS are very high, making that statistically significance does not equal clinical significance. This was neatly shown by Vonesh et al[4;5], who found alternating superiority of HD and PD in consecutive and overlapping cohorts of USRDS. Third, both the approach to PD as the patient mix is quite different in the US as compared to the rest of the world. It is thus well accepted these days that well performed PD results in an at least as good outcome as HD also in diabetic patients.

Advantages of PD first in diabetic patients

There are several reasons why PD should be a good option to start RRT in diabetic patients (table 1).

Table 1: factors in favour of PD as a first line treatment

• **Vascular access**
• **Residual renal function**
• **Cardiovascular mortality**
• **Infectious (Viral) contamination**
• **Outcome after transplantation**
• **Cost/benefit**
• **Quality of life**

The most prominent advantage is the lack of need for vascular access. It is well established that creation of vascular access can be quite cumbersome in diabetic patients, especially when they are older or female or have cardiovascular comorbidity. In DOPPS for example, diabetics were 25% less likely to be dialysed with a native fistula than non-diabetics[7]. The risks and perils of the use of permanent catheters are well recognised. Although most realise that the infection risk for a patient with a catheter is twice that of a patient with an AV fistula, fewer people will know that the infectious risk for a PD patient is equal to that of an AV fistula[8], as most consider infection to be "the" problem of PD.

A second important advantage of PD first is the preservation of residual renal function (RRF). Diabetic patients tend to lose their RRF more rapidly than non diabetics[9], whereas preservation of RRF might just be of greater importance for them. There is more and more evidence that the accumulation of advanced glycation end products plays an important role in the emergence of diabetic complications like micro-angiopathy and polyneuropathy. Levels of AE's are directly related to RRF. There is also evidence that in diabetics, further deterioration of RRF can be delayed substantially by starting them on PD on a somewhat earlier level than a residual GFR of 15ml/min[10], probably because the PD removes uraemic waste products that are nephrotoxic by themselves. In this regard, it is expected that the new low GDP containing solutions might even perform better than the old solutions. Some studies seem to support this hypothesis[11], whereas others, though different in set up and with different brands of solutions, did not find a difference.

It also seems logical that the risk of sudden cardiac death should be lower in PD as compared to HD, because of the continuous nature of the treatment. Indeed, after the weekend, HD patients have accumulation of fluids and potassium, leading to arrythmias and sudden death[12]. Also the rapid changes in volume status during the HD session seem to predispose to arrythmias. It is quite conceivable that diabetics are even more prone to this type of complication: diabetics gain more weight in between dialysis sessions, because of their (hyperglycaemia driven) higher fluid intake, and they tolerate ultrafiltration less well, because of autonomous polyneuropathy and stiffer blood vessels.

Other advantages of PD first are just comparable for diabetics and non diabetics: cost-effectiveness, better quality of life, better employment, lower risk of (viral) nosocomial infection[1].

Extending technique success in diabetic PD patients

Major reasons for technique failure still remain membrane failure and peritonitis/ infection. It is not clear whether the peritoneal membrane has different properties in diabetics, as some authors do find a faster transport status, whereas others do not. There is evidence that a good control of blood glycaemia nearly completely abolishes the negative impact of diabetes in experimental models[11]. Comparably, it might be that in centres not using hypertonic bags, and stressing good glycaemic control, no differences in membrane characteristics are present, whereas in centres using hypertonic exchanges, there are. Clinical studies reveal that control of serum glycaemia becomes more problematic when more hypertonic exchanges are being used[11]. Worse glycaemic control in its turn will lead to hyperosmolarity, thirst and thus more fluid intake, which by itself forces the patient to use more hypertonic exhanges. This vicious circle can only be broken by correct control of serum glycaemia, salt restriction and avoidance of hypertonic bags.

There is animal and human evidence that the peritoneal membrane "wears off" during time on peritoneal dialysis, by two distinct processes: thickening of the membrane by fibrosis, and neo-angiogenesis , leading to increased solute transport rates and ultrafiltration failure.

As the underlying processes driving these findings slowly emerge, it also is apparent that we can prevent these changes from happening to a large extend.

Second, exposure of the membrane to glucose leads by itself to upregulation of TGF beta and epithelial to mesenchymal transition: avoidance of glucose as much as possible is thus of importance. Again, care should be

taken to avoid the vicious circle of using hypertonic bags to control fluid overload. Salt restriction is again the cornerstone of the treatment. Salt intake increases hyperosmolarity, leading to thirst and volume intake. Besides these volume mediated effects, salt has also direct negative influences: there is an upregulation of pro-fibrotic growth factors in the heart, and in the kidney, leading to hypertrophy of the left ventricle and to enhanced glomerular sclerosis respectively.

Also for peritonitis, the literature is somewhat conflictive whether diabetics should have higher incidence rates than non-diabetics. Again, tight glycaemic control might play a role, as hyperglycaemia might create the ideal environment for micro-organisms. More important however to my opinion is the presence of polyneuropathy and diabetic rethinopathy, leading to touch contamination. A thorough training process, with special attention to adapt the exchange to the needs and skills of the individual patient, and a fail proof connectology are therefore crucial to avoid peritonitis in diabetic patients.

Patient empowerment and PD first

One of the big advantages of PD first (and also of other home therapies) is that there is an absolute need of patient education and involvement. There is rising evidence that these "educated patients" have better outcome as compared to patients who just have a more passive approach to their disease. Jones et al demonstrated that in patients who took part in a well structured pre-dialysis educational programme, the risk related to "diabetes" on outcome was abolished. This is not quite surprising, as other large trials like UKPDS have clearly shown that good control of blood pressure and glycaemia substantially improves outcome. In contrast to general belief, good control of blood pressure and glycaemia has more to do with life style changes, like salt restriction, physical exercise, weight control, than just with "prescription of medication". In this context, the importance of an educational team, like a PD training team, can not be overestimated. There is also evidence that patients in such well structured programmes have a slower decline or residual renal function, probably again related to better blood pressure control.

Conclusion

The concept of integrated care is the ideal treatment paradigm for diabetic patients. It offers them the multi-disciplinary approach of their disease they deserve.

PD first is a valuable option that should be recommended to the diabetic patient during his/her educational process, because of the preservation of vascular access, and of residual renal function, and the lower risk of sudden cardiac death.

Good glycaemic control, salt restriction and absolute avoidance of hypertonic exchanges should preserve the peritoneal membrane as long as possible. A safe and easy to use connectology and a tailored training programme taking into account eventual polyneuropatic and visual disturbances should be provided to avoid infection.

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2008 - 2009 Part-time Postgraduate Diploma in

Community Psychological Medicine

社區精神醫學深造文憑

- **Quotable qualification by the Medical Council of Hong Kong**
- **Clinically orientated**
- **Multiple learning modes**
- **Clinical teaching at sites across Hong Kong**

This programme, organized in conjunction with the Department of Psychiatry, aims to improve your knowledge and skills in the care of patients with psychological problems. It will include seminars, case discussion, clinical training in psychotherapy and clinical attachment.

"In the 21st century, everybody deserves to be cared by doctors who can appreciate the complexity of human sufferings, assess health problems biopsychosocially, provide quality psychological care and use medications rationally. This diploma course has been designed to empower you to face these challenges."

Dr LAM Wing Wo Edmund (2004 Graduate)

2008 - 2009 Part-time Postgraduate Diploma in

Community Geriatrics

社區老年醫學深造文憑

- **Quotable qualification by the Medical Council of Hong Kong**
- **Clinically orientated**
- **Multiple learning modes**
- **Flexible teaching hours**
- **Clinical teaching at sites across Hong Kong**

This programme, developed in conjunction with the Hong Kong Geriatrics Society, aims to upgrade your knowledge and skills in the care of the elderly. Different modes of study including distance learning, interactive workshops and clinical attachment will be employed to enhance your learning.

"After taking this course, I have become more capable of treating and managing elders both at my clinic, and in old age homes. I strongly recommend this course to all primary care physicians."

Dr TSOI Lai To Sammy (2002 Graduate)

2008-09

The two programmes will commence in September and last for one year on a part-time basis of half a day per week. Tuition fee for each programme is HK$42,000, subject to adjustment in 2008/09.

Closing Date for Application

30th April 2008

Application forms for the above programmes can be downloaded from our websites:
www.hku.hk/fmunit/psychiatry
www.hku.hk/fmunit/geriatrics

For further information, please contact Magdalene Tang, Executive Assistant at 2518 5688 (voice mail) or 2814 7475 (fax) or email to magtang@hku.hk. Address: Family Medicine Unit, 3/F, Ap Lei Chau Clinic, 161 Main Street, Ap Lei Chau, Hong Kong.

Liquid Assets: Laying Down a Cellar and Investing in Wine

Ms. Tiffany Ip

Ms. Tiffany Ip

Senior Wine Consultant
Berry Bros. & Rudd, Hong Kong

How does a novice go about investing in wine? A few simple steps will put anyone with a nose for a good wine and a good investment on the right track.

Firstly, choose what you like to drink. Whilst some wines will perform better than others, most people choose to buy wine for *drinking* and *investment*. Therefore, it is sensible to decide where your tastes lie.

Most people opt for Grand Cru Classe red Bordeaux. Bordeaux red wines tend to be the best investment, and are best bought for laying down as an "*en primeur*". The exact process is a simple purchase of a wine whilst it is still in the cask, and the main area in the world for *en primeur* sales is Bordeaux.

Whilst *en primeur* still remains quite unknown to many buyers of everyday wine, it is becoming more popular as merchants make it part of their annual offerings. It is not only popular for collectors, but also for people who enjoy wines to buy their favourite wines at good prices. *Primeurs* release prices tend to be the lowest price the wine commands, thus giving the greatest value.

The process is quite simple: wine merchants buy the wines from chateaux and offer the wines to end users in an annual campaign, which usually begins in the middle of June in the year following the vintage.

As the wines remain in cask for 18 months or so prior to bottling, customers simply place orders with reputable merchants. The wine will not be delivered until 18 months later, but usually is stored for longer. Very few of these wines will be ready to drink for at least 3 more years. The wines are then stored (preferably under bond to avoid paying duties and taxes immediately) prior to drinking. They can be stored by the merchant, on behalf of the purchaser; or by the purchaser himself.

Good wine merchants will offer to store the wines for the customer until they are ready to drink, removing the trouble from the purchaser, who can request a stock sheet similar to that of investments, to see the maturity of the wines. Always choose to leave the wines in bond (i.e. free of duty) until you want to drink them, that ensures there are a more attractive purchase should you wish to sell them.

The second step is to establish a drinking window. How soon would you like to drink the wines, or sell them? From an investment perspective, a minimum of 5-7 years allows the wine to approach maturity and thus the price to rise. The secondary market views wines as considerably more attractive if they have been well-stored and they are from an impeccable source.

Is it a good investment? Definitely, wine is an international commodity; there is only a limited supply of the greatest wines. As mentioned the wines are at their lowest prices, and may not even be available after the *en primeur* campaign. There is always a secondary market, and most good merchants also act as brokers for their clients' wines.

For investment, the top 30 Bordeaux chateaux are always the best buys, as they hold their value well, and there are always more buyers when selling. If you are buying for drinking wines to lay down and keep, bear in mind that not all vintages are suitable for very long-term keeping.

Choose styles of wines you enjoy drinking, and always ensure you buy from a reputable and long-established merchant, such as the bigger London merchants. London is still the centre of the international wine trade, and top merchants will store and insure your wines for you.

The last step is to sit back and wait. Even if the price does not rise as much as you hope, you still have a cellar full of wine, waiting to be drunk. Certainly more fun than eating those share certificates!

香港鐳射醫學會
HONG KONG SURGICAL LASER ASSOCIATION

2008 Annual General Meeting of the Hong Kong Surgical Laser Association
&
Combined Scientific Meeting of the Hong Kong Surgical Laser Association and The Hong Kong Medical Association

香港醫學會
THE HONG KONG MEDICAL ASSOCIATION

LASERS IN UROLOGY

Date: 16th April 2008 (Wednesday)
Venue: HKMA, Dr. Li Shu Pui Professional Education Centre, Second Floor, Chinese Club Building
21-22 Connaught Road, Central, Hong Kong
Time: 7:00 pm - 7:30pm
AGM 2008
7:30 pm - 8:45 pm
Scientific Meeting
Chairman : Dr. Li Shu Keung
Specialist in Urology, Director, Urology & Endo-urology Centre, Hong Kong Baptist Hospital
Speakers: (1) Laser Applications in Urology - An Overview
Dr. Bill Wong
Specialist in Urology, Pedder Clinic, Hon. Consultant Urologist, Queen Elizabeth Hospital
(2) Trends of Laser BPH Treatment
Dr. Richard K. Lo
Consultant Urologist, Pedder Clinic
(3) Large Prostate Obstruction Treatment - Open Surgery or Minimally Invasive Treatment by Laser
Dr. Szeto Yiu Kwai
Specialist in Urology, Institute of Medical Specialists
Discussion

CME accredited by various colleges of the Hong Kong Academy of Medicine and various institution in Hong Kong for Specialists and Non-Specialists

R.S.V.P. by fax to Ms. Karen Chu at 2865 0345
LIMITED SPACE - FIRST COME FIRST SERVE

Sponsored by: 東靈醫療有限公司 SINO SPIRIT MEDICAL LIMITED

Faculty of Medicine
The Chinese University of Hong Kong

Postgraduate Diploma in End-of-Life Care

September 2008 admission

The First Postgraduate Diploma course on end-of-life care in Hong Kong

This one year part-time programme provides knowledge base on the theories, principles and approach needed for those involved in end of life care in different specialties and health care settings. The course will provide a broad coverage of wide ranging aspects, from global issues and concerns of end of life, to the care for physical, psychological, social and spiritual needs of dying patients and the challenging clinical and ethical dilemma; from basic principles of communication, counseling with terminally ill patients, to bereavement support and care for carers. The programme consists of lectures, case studies and written examinations.

Following the successful commencement of this diploma last year, further topics on paediatrics perspectives, surgical perspectives, non-cancer perspectives in organ failures & frailty syndromes, funeral and last office arrangements etc will also be added in the curriculum.

Admission requirements: Bachelors degree in health or social sciences from a recognised university, with honours not lower than second class, or course equivalent to honours degree. Fulfilled "English Language Proficiency Requirement" as stipulated by the Graduate School before being considered for admission.

Course duration and fees: One year part time. HK$35,000 for the academic year 2008-2009.

Course Director: Prof Jean Woo

Deputy Course Director: Dr Raymond Lo

***Information Seminar:**
21 April 2008, 6:30 pm -7:30 pm
Seminar Room 1, 2/F, Clinical Sciences Bldg
Prince of Wales Hospital, Shatin, N.T.

Application Deadline:
31 May 2008

*Please contact us to reserve a place

Forms and relevant materials are obtainable by post from us at Rm 426, School of Public Health, Prince of Wales Hospital, Shatin, N.T. or you can make an online application through our Graduate School at http://www.cuhk.edu.hk/gss.

Enquiries:
Ms F Chan/Ms M Yu
Tel: 2252 8765/ 2252 8885
Fax: 2604 8091
Email: fayechan@cuhk.edu.hk
Website: http://www.mect.cuhk.edu.hk/diploma.asp

Answer to Dermatological Quiz

Answer

1. The most likely diagnosis judged on the clinical ground is fixed drug eruption. The main differential diagnosis in this patient is contact dermatitis, commonly due to nickle of the watch.

2. The well demarcated dusky violaceous plaques or patches, together with a history of recurrence at same site whenever exposed to the same drug, are the main clues in the diagnosis.

3. The diagnosis is mainly based on clinical ground. If indicated, drug re-challenge can be performed. Fixed drug eruption usually does not have systemic involvement and is the only type of drug eruption that can be re-challenged safely in clinical practice.

4. Identification of the culprit drug by taking a careful and thorough history and its avoidance in the future is the mainstay of treatment. NSAIDs, sulphur-containing antibiotics, tetracyclines, phenolphthalein, narcotics, barbiturates, etc are the common culprits.

Dr. Lai-yin Chong
MBBS(HK), FRCP(Lond, Edin, Glasg), FHKCP, FHKAM(Med)
Yaumatei Dermatology Clinic, Social Hygiene Service

Departure of Ms. Sue Cheng - Executive Manager, FMSHK

Ms. Sue S.Y. Cheng, Executive Manager has left FMSHK on 13 February 2008. We wish her all the best in her future endeavours.

Certificate presentation for students of IVE, Shatin

A certificate presentation was held on 23 February 2008 at the Lecture Hall, Institute of Vocational Education, Shatin for all student volunteers who helped in the Federation events of 2007 such as Annual Scientific Meeting, Central & Western District Health Festival and the Federation Annual Dinner.

Society News

News from Member Societies:

College of Nursing, Hong Kong
Updated office-bearers for the year 2008-2009 are as follows: President: Ms. LUI Wing Mui, June; First Secretary: Ms. KU Wai Yin, Ellen; First Treasurer: Ms. HUNG Tao Ying, Gloria

Hong Kong Society of Clinical Chemistry Limited
Updated office-bearers for the year 2007-2009 are as follows: President: Dr. Michael HM CHAN; Vice President: Mr. Eric LK LAW; Honorary Secretary: Ms Judy PS LAI; Honorary Treasurer: Ms Heidi YP IU

Obstetrical and Gynaecological Society of Hong Kong


Dr. Lam Siu Keung

Formed in 1961, the Obstetrical and Gynaecological Society of Hong Kong (OGSHK) was running into her 46th year of service to its members. We have around 380 life, regular and associate members and the objectives of the society was three fold. Firstly to stimulate interest in, to exchange views in the field of, and to provide co-operation and facilitate relationship among those who are interested in obstetrics and gynaecology. Secondly, to organize scientific meetings in connection with obstetrics and gynaecology. Thirdly, to represent the obstetricians and gynaecologists of Hong Kong in international organizations.

All year round, we held academic meetings on the various topic of obstetrics, gynaecology, women's health, contraception, oncology etc. The perinatal symposium which was held annually by the Hong Kong Perinatal Chapter was a joint venture between the OGSHK and the Hong Kong Society of Neonatal Medicine. OGSHK is representing Hong Kong in the AOFOG (Asia Oceanic Federation of Obstetrics and Gynaecology) and FIGO (International Federation of Obstetrics and Gynaecology) thus ensuring the continuous presence and influence of Hong Kong internationally. Although OGSHK lost its bid for the 2011 AOFOG meeting in Hong Kong, we will continue to explore other ways of national and international collaboration.

Obstetrics and gynaecology are undergoing tremendous change and challenge in Hong Kong especially with the influx of mainland mothers and the high manpower turnover in public hospitals. With the increasing expectation of patients and relatives and the rapid advancing medical technology, clinicians must keep abreast of the current development in our field and Medical Diary can help to keep our members informed on the current development.

Dr. Lam Siu Keung
President
Obstetrical and Gynaecological Society of Hong Kong
(www.ogshk.org)

The Hong Kong Society of Sleep Medicine

The Hong Kong Society of Sleep Medicine was formed in November 1993 with the aim of promoting clinical practice, knowledge and training in Sleep Medicine. The current president is Prof. Yun Kwok Wing from the Department of Psychistry, The Chinese University of Hong Kong. The society organizes regular clinical meeting whereby interesting and educational topics / cases are discussed. Our Annual Scientific Meeting usually takes place in September of each year, and the event is always well attended and received by all personnel involved in Sleep Medicine. We encourage all interested parties to join our young and yet energetic society. Full membership is eligible for doctors and associate membership for non-medical, health professionals.

香港疼痛學會
Hong Kong Pain Society

HKPS Mission

The Hong Kong Pain Society aims to advance professional knowledge and expertise in managing pain through education, training and research; and aspires to improve public understanding towards pain and promote a positive attitude in persons with pain.

The Hong Kong Pain Society (HKPS)

The Hong Kong Pain Society (HKPS) is a multi-disciplinary organisation with over 330 members from over 16 different medical specialties and healthcare disciplines. Membership is opened to all medical practitioners, dentists, nurses, psychologists, physiotherapists, occupational therapists, pharmacists, medical social workers and scientists, and any person who has real and substantial interests in the objects of the Society. The HKPS aims to advance professional knowledge and expertise in managing pain through education, training and research, foster exchanges and collaborations among different healthcare disciplines involved in pain management, and aspire to improve public understanding towards pain and promote a positive attitude in persons with pain.

The HKPS was inaugurated on 16 October 2007. In the last 12 months, we have participated in the RTHK talk-show (香港電台第一台: 精靈一點), conducted public lectures, workshops and CME lectures for healthcare professionals and in the September we celebrated our first birthday with our first Annual Scientific Meeting on 22-23 September 2007. For more information, please visit our website at www.hkpainsociety.org. The HKPS invites you to share with us your interest and experience in clinical pain management, education and research.

Council 2007-2009

Dr CHEN Phoon Ping (President), Dr CHUI Tak Yi (Vice-President), Ms LAW Ka Yee, Rainbow (Secretary), Dr WONG Ho Shan, Steven (Treasurer), Dr CHAN Miu Han, Anne, Professor CHEUNG Tak Fai, Raymond , Professor CHAN Che Hin, Chetwyn , Dr CHIN Ping Hong, Raymond, Dr KWOK Oi Ling, Annie , Ms HO Shui Wan, Ruby, Dr LI Ching Fan, Carina, Ms POON Yee Hung, Priscilla, Ms LEE Wing Ming, Mary, Dr WONG Kam Hung

The Pharmaceutical Distributors Association of Hong Kong (PDA)

The Pharmaceutical Distributors Association of Hong Kong (PDA) was established in 3/2005. Our main objectives are :

1. To promote and advance the interest, character, status and efficiency of the wholesale distribution of pharmaceuticals
2. To promote and educate supply chain management in relation to pharmaceutical and healthcare products
3. To enhance, promote and safeguard business interest of members in a professional and lawful manner
4. To assist in the promotion or opposition of legislations affecting the distribution and sale of pharmaceutical products and services.
5. To advance and support innovations in technology and logistics in the wholesale business of pharmaceutical products and services
6. To represent the views of the pharmaceutical wholesale profession in all matters affecting the interests of members of the Association

Executives of committee 2007-2009 :

Chairman : Ms. Tina WT YAP
Vice-Chairman : Mr. William TSUI
Hon Secretary : Mr. Nelson LC LAM
Hon Treasurer : Mr. James CHAN

The PDA look forward to cooperating and affiliating with other bodies and organisations in the promotion of medical, pharmaceutical and other allied health professions.

Medical Diary of April

Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
		★ Management of Haemorrhoid ★ HKMA Choir Talent Show **1**	★ CME Lecture in Dermatology Lecture I: Psoriasiform Dermatoses **2**	★ Update on Obstetrics ★ HKMA Council Meeting **3**	**4**	★ Friendly Table-Tennis Tournament **5**
★ HKMA Structured CME Programme at Queen Elizabeth Hospital Year 08/09 (I) - Medicine ★ HKMA Snooker Tournament ★ Friendly Badminton Tournament with Craigengower Cricket Club ★ Dragon Boat Practice Session **6**	★ HKMA Choir Rehearsal **7**	★ FMSHK Officers' Meeting ★ 8 Lessons in Practical Psychiatry for General Practitioners: A Certificate Course ★ CME Lecture on 常見頭頸腫瘤 **8**	★ Hong Kong Neurosurgical Society Monthly Academic Meeting - Interesting Cases in Epilepsy Surgery **9**	★ HKMA Structured CME Programme with Hong Kong Sanatorium & Hospital Year 2008 (IV) ★ Update on Obstetrics **10**	★ CME Lecture on Ocular Emergency **11**	★ Refresher Course for Health Care Providers 2007/2008 (VIII) - Pre-travel Health Service and Update **12**
★ HKMA Snooker Tournament ★ Dragon Boat Practice Session **13**	★ HKMA Choir Rehearsal **14**	★ 8 Lessons in Practical Psychiatry for General Practitioners: A Certificate Course ★ CME Lecture on 常見中、內耳疾病 ★ CME Lecture in Dermatology Lecture II: Contact Dermatitis in Hong Kong **15**	★ Joint Scientific Meeting of the Hong Kong Surgical Laser Association and the Hong Kong Medical Association "Lasers In Urology" & Annual General Meeting of the Hong Kong Surgical Laser Association **16**	★ FMSHK Executive Committee Meeting **17**	★ HKMA Wine Dinner **18**	**19**
★ Dragon Boat Practice Session **20**	★ HKMA Choir Rehearsal **21**	★ 8 Lessons in Practical Psychiatry for General Practitioners: A Certificate Course ★ CME Lecture on 社區兒科耳鼻喉疾病 **22**	★ CME Lecture in Dermatology Lecture III: Onychomycosis and Fungal Infections **23**	★ FMSHK Foundation Meeting ★ Update on Obstetrics **24**	**25**	**26**
★ 5th Exercise Prescription Course ★ Dragon Boat Practice Session **27**	★ HKMA CME on Psychiatry - Recent Advances in the Management of Attention Deficit Hyperactivity Disorder ★ HKMA Choir Rehearsal **28**	★ 8 Lessons in Practical Psychiatry for General Practitioners: A Certificate Course **29**	★ CME Lecture in Dermatology Lecture IV: Acne: Anything New? **30**			

Medical Diary of April

Date / Time	Function	Enquiry / Remarks
1 TUE 1:00 pm	**Management of Haemorrhoid** Organised by: The Hong Kong Medical Association Tai Po Community Network Speaker: Dr. LAM Chung Wa Steve # Grand Capital Banquet Hall	Joyce Tel: 2666 0868 2.5 CME Points
8:00 pm	**HKMA Choir Talent Show** Organised by: The Hong Kong Medical Association # Sai Wan Ho Civic Centre Threatre	Ms. Candy YUEN Tel: 2527 8285
2 WED 1:30 pm	**CME Lecture in Dermatology Lecture I: Psoriasiform Dermatoses** Organised by: The Hong Kong Medical Association Speaker: Dr. HO Ka Keung # Shanghai Room 1, 8/F, Langham Place Hotel, 555 Shanghai Street, Mongkok, Kowloon	Miss Viviane LAM Tel: 2527 8452 1 CME Point
3 THU *(10,24)*	**Update on Obstetrics** Organised by: The Federation of Medical Societies of Hong Kong # Lecture Hall, 4/F, Duke of Windsor Social Service Building, 15 Hennessy Road, Wanchai, Hong Kong	Ms. Karen CHU Tel: 2527 8898 Fax: 2865 0345
8:00 pm	**HKMA Council Meeting** Organised by: The Hong Kong Medical Association Chairman: Dr. K CHOI # HKMA Head Office, 5/F., Duke of Windsor Social Service Building, 15 Hennessy Road, Wanchai, Hong Kong	Ms. Christine WONG Tel: 2527 8285
5 SAT 3:00 pm	**Friendly Table-Tennis Tournament** Organised by: The Hong Kong Medical Association # Kowloon Tong Club	Ms. Dora HO Tel: 2527 8285
6 SUN 2:00 pm *(13)*	**HKMA Snooker Tournament** Organised by: The Hong Kong Medical Association # Prat Billiard Club	Ms. Dora HO Tel: 2527 8285
2:00 pm	**HKMA Structured CME Programme at Queen Elizabeth Hospital Year 08/09 (I) - Medicine** Organised by: The Hong Kong Medical Association & Queen Elizabeth Hospital Speaker: Dr. WU Tak Chiu Dr. NG Ying Wai Dr. HUI Yee Tak # Lecture Theatre, G/F., Block D, Queen Elizabeth Hospital, Kowloon	Miss Viviane LAM Tel: 2527 8452 (Registration Fee is required) 3 CME Points
2:00 pm	**Friendly Badminton Tournament with Craigengower Cricket Club** Organised by: The Hong Kong Medical Association # Craigengower Cricket Club	Ms. Dora HO Tel: 2527 8285
3:00 pm *(13,20,27)*	**Dragon Boat Practice Session** Organised by: The Hong Kong Medical Association # Sai Kung	Ms. Dora HO Tel: 2527 8285
7 MON 8:00 pm *(14,21,28)*	**HKMA Choir Rehearsal** Organised by: The Hong Kong Medical Association # Sai Wan Ho Civic Centre Cultural Activities Hall	Ms. Candy YUEN Tel: 2527 8285
8 TUE 8:00 pm - 10:00 pm	**FMSHK Officers' Meeting** Organised by: The Federation of Medical Societies of Hong Kong # Gallop, 2/F., Hong Kong Jockey Club Club House, Shan Kwong Road, Happy Valley, Hong Kong	Miss Paulina Tang Tel: 2527 8898 Fax: 2865 0345
1:00 pm	**CME Lecture on 常見頭頸腫瘤** Organised by: The Hong Kong Medical Association Tai Po Community Network Speaker: Dr. TSANG Kin Yin Raymond # Grand Capital Banquet Hall	Dr. CHAN Wing Kwan Tel: 2664 3382 2.5 CME Points
2:00 pm *(15,22,29)*	**8 Lessons in Practical Psychiatry for General Practitioners: A Certificate Course** Organised by: The Hong Kong Medical Association Speaker: Various # Harbour Plaza Resort City, 18 Tin Yan Road, Tin Shui Wai, New Territories	Miss Jo WONG Tel: 2527 8285 1 CME Point
9 WED 7:30 am	**Hong Kong Neurosurgical Society Monthly Academic Meeting - Interesting Cases in Epilepsy Surgery** Organised by: Hong Kong Neurosurgical Society Chairman: Dr. X.L. ZHU Speaker: Dr. Benadice TAW # Seminar Room, G/F, Block A, Queen Elizabeth Hospital, Kowloon	Dr. Y.C. PO Tel: 2990 3788 Fax: 2990 3789 2 CME Points
10 THU 2:00 pm	**HKMA Structured CME Programme with Hong Kong Sanatorium & Hospital Year 2008 (IV)** Organised by: The Hong Kong Medical Association & Hong Kong Sanatorium & Hospital Speaker: Dr. CHAU Mo Chee Elaine # 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 (Registration Fee is required) 1 CME Points
11 FRI 1:00 pm	**CME Lecture on Ocular Emergency** Organised by: The Hong Kong Medical Association Shatin Community Network Speaker: Dr. Jackson WOO #新界沙田白鶴汀八號帝都酒店2/F 帝都軒	Ms. Kandy WAN T: 2963 5521 1 CME Point
12 SAT 2:30 pm	**Refresher Course for Health Care Providers 2007/2008 (VIII) - Pre-travel Health Service and Update** Organised by: The Hong Kong Medical Association & Our Lady of Maryknoll Hospital Speaker: Dr. FAN Pang Yung # 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
15 TUE 1:00 pm	**CME Lecture on 常見中、內耳疾病** Organised by: The Hong Kong Medical Association Tai Po Community Network Speaker: Dr. TSANG Kin Yin Raymond # Grand Capital Banquet Hall	Dr. CHAN Wing Kwan Tel: 2664 3382 2.5 CME Points
1:30 pm	**CME Lecture in Dermatology Lecture II: Contact Dermatitis in Hong Kong** Organised by: The Hong Kong Medical Association Speaker: Dr. LAM Wai Sun # Ching Room, 4/F, Sheraton Hotel, 20 Nathan Road, Tsimshatsui, Kowloon	Miss Viviane LAM Tel: 2527 8452 1 CME Point
16 WED 7:00 pm - 9:00 pm	**Joint Scientific Meeting of the Hong Kong Surgical Laser Association and the Hong Kong Medical Association "Lasers In Urology" & Annual General Meeting of the Hong Kong Surgical Laser Association** Organised by: Hong Kong Surgical Laser Association & Hong Kong Medical Association Chairman: Dr LI Shu Keung, Speakers: Dr Richard K. LO, Dr SZETO Yiu Kwai, Dr Bill T.H. WONG # Dr. Li Shu Pui Professional Education Centre, Second Floor, Chinese Club Building, 21-22 Connaught Road, Central, Hong Kong	Ms. Karen CHU Tel: 2527 8898 Fax: 2865 0345

Date / Time	Function	Enquiry / Remarks
17 THU 8:00 pm - 10:00 pm	**FMSHK Executive Committee Meeting** Organised by: The Federation of Medical Societies of Hong Kong # Council Chambers, 4/F, Duke of Windsor Social Service Building, 15 Hennessy Road, Wanchai, Hong Kong	Miss Paulina Tang Tel: 2527 8898 Fax: 2865 0345
18 FRI 7:30 pm	**HKMA Wine Dinner** Organised by: The Hong Kong Medical Association # HKMA Dr. LI Shu Pui Professional Education Centre, 2/F., Chinese Club Building, 21-22 Connaught Road Central, Hong Kong	Ms. Dora HO Tel: 2527 8285
22 TUE 1:00 pm	**CME Lecture on 社區兒科耳鼻喉疾病** Organised by: The Hong Kong Medical Association Tai Po Community Network Speaker: Dr. CHAN Wing Kwan # Grand Capital Banquet Hall	Dr. CHAN Wing Kwan Tel: 2664 3382 2.5 CME Points
23 WED 1:30 pm	**CME Lecture in Dermatology Lecture III: Onychomycosis and Fungal Infections** Organised by: The Hong Kong Medical Association Speaker: Dr. HO Man Hon # Shanghai Room 1, 8/F, Langham Place Hotel, 555 Shanghai Street, Mongkok, Kowloon	Miss Viviane LAM Tel: 2527 8452 1 CME Point
24 THU 8:00 pm - 10:00 pm	**FMSHK Foundation Meeting** Organised by: The Federation of Medical Societies of Hong Kong # Council Chambers, 4/F, Duke of Windsor Social Service Building, 15 Hennessy Road, Wanchai, Hong Kong	Miss Paulina Tang Tel: 2527 8898 Fax: 2865 0345
27 SUN 2:00 pm	**5th Exercise Prescription Course** Organised by: The Hong Kong Medical Association	Miss Sophia LAU Tel: 2527 8452 (Registration Fee is required)
28 MON 2:00 pm	**HKMA CME on Psychiatry - Recent Advances in the Management of Attention Deficit Hyperactivity Disorder** Organised by: The Hong Kong Medical Association Chairman: Dr. the Hon. KWOK Ka Ki Speaker: Dr. HO Ting Pong # 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 (Free of charge, capacity: 80, first come, first serve) 1 CME Point
30 WED 1:30 pm	**CME Lecture in Dermatology Lecture IV: Acne: Anything New?** Organised by: The Hong Kong Medical Association Speaker: Dr. LEUNG Chi Yan # Churchill Room, 26/F, The Park Lane Hong Kong, 310 Gloucester Road, Causeway Bay, Hong Kong	Miss Viviane LAM Tel: 2527 8452 1 CME Point

Meetings

2-4/5/2008	**16th Annual Scientific Congress of Hong Kong College of Cardiology** Organised by: Hong Kong College of Cardiology Chairman: Dr. CHIANG Chung Seung # Sheraton Hong Kong Hotel & Towers, 20 Nathan Road, Tsimshatsui, Kowloon Enquiry: Ms. Dora HO Tel: 2527 8285 Fax: 2865 0943 Email: dorahkma@hkma.org Website: http://www.hkcchk.com/scientificcongress.php
17-18/5/2008	**9th Regional Osteoporosis Conference** Organised by: Osteoporosis Society of Hong Kong & Hong Kong College of Radiologists Speaker: International and Regional Experts # Hong Kong Convention & Exhibition Centre, Wanchai, Hong Kong Enquiry: Ms. Lenora YUNG Tel: 2871 8787 Fax: 2871 8898
24-25/5/2008	**Annual Scientific Meeting "Family Physicians and Our Community"** Organised by: Hong Kong College of Family Physicians Chairman: Dr. Winnie W.Y. CHAN # HKAM Jockey Club Building, 99 Wong Chuk Hang Rood, Aberdeen, Hong Kong Enquiry: Ms. Erica SO Tel: 2528 6618 Fax: 2866 0618
11-12/7/2008	**Hong Kong Surgical Forum, Summer 2008** Organised by: Department of Surgery, Li Ka Shing Faculty of Medicine, University of Hong Kong Medical Centre; Queen Mary Hospital & Hong Kong Chapter of the American College of Surgeons # Underground Lecture Theatre, New Clinical Building, Queen Mary Hospital, Pokfulam, Hong Kong Enquiry: Forum Secretary Tel: 2855 4885 Fax: 2819 3416 Email: hksf@hkucc.hku.hk Website: http://www.hku.hk/surgery
22-25/11/2008	**2nd Asian Preventive Cardiology & Cardiac Rehabilitation Conference cum 7th Certificate Course in Cardiac Rehabilitation** Organised by: Hong Kong College of Cardiology Co-Chairman: Prof. LAU Chu Pak & Dr. LAU Suet Ting Speaker: Various # Hong Kong Convention & Exhibition Centre, 1 Expo Drive, Wanchai, Hong Kong Enquiry: Secretariat Tel: 2527 8285 Fax: 2865 0943 Email: dorahkma@hkma.org Website: http://www.apccrc.com
20-22/2/2009	**CardioRhythm 2009** Organised by: Hong Kong College of Cardiology & Chinese Society of Pacing and Electrophysiology Co-Chairman: Prof. LAU Chu Pak Enquiry: Secretariat Tel: 2899 2035 Fax: 2899 2045 Email: info@cardiorhythm.com Website: http://www.cardiorhythm.com

Courses

2,9,16,23,30/5/2008 6,13,20,27/6/2008 6:30 pm to 9:30 pm	**Certificate Course in Ward Management - Module III: "Managing risk at workplace" (Code No. TC-WM-0107III)** Organised by: College of Nursing, Hong Kong Enquiry: Secretariat Tel: 2572 9255 Fax: 2838 6280
16,17/5/2008	**ISCD Bone Densitometry Course** Organised by: Osteoporosis Society of Hong Kong Chairman: Prof. Annie KUNG Speaker: International & Local Experts # Hong Kong Convention and Exhibition Centre, Wanchai, Hong Kong Enquiry: Ms. Lenora YUNG Tel: 2871 8787 Fax: 2871 8898 CME Accreditation for HKCP, HKCFP, HKCR, HKCOS, HKCOG, HKCCM, HKDU, HKMA
23/5/2008	**9th Refresher Course on Colposcopy** Organised by: The Hong Kong Society for Colposcopy and Cervical Pathology & The Family Planning Association of Hong Kong Chairman: Dr. T.S. WONG Speaker: Dr. WONG Ching Yin Grace # The Auditorium, 8/F, Southern Centre, 130 Hennessy Road, Wanchai, Hong Kong Enquiry: Ms. Michelle LEE Tel: 2919 7738 Fax: 2919 7790 CME Accreditation: 2 Points for HKCOG, HKCPath, MCHK, CNE

香港醫學組織聯會

網球訓練班

宗旨： 提供專業途徑予會員，灌輸正確網球基本技術知識， 教授正確手法， 步法基本功，給與適量體能訓練，戰術運用及比賽細則，務求令學員享受網球運動之餘，提高其專業水平。

Elementary 初班	Suitable for all beginners and first-timers 適合未有網球基礎之人士
Intermediate 中班	Suitable for players with basic tennis skills & wishing to improve their overall level of tennis, or for those who have completed the Elementary Stage & recommended by the coach. 適合有基本技術而欲繼續進修之人士或已經完成初班及經教練推薦之人士
Advanced I 進階班	Suitable for players with basic tennis skills & wishing to improve their overall level of tennis, or for those who have completed the Intermediate Stage & recommended by the coach. 適合有基本技術而欲繼續進修之人士或已經完成中班及經教練推薦之人士
Advanced II 高級班	Suitable for players with basic tennis skills & wishing to improve their overall level of tennis, or for those who have completed the Advanced I Stage & recommended by the coach. 適合有基本技術而欲繼續進修之人士或已經完成進階班及經教練推薦之人士

上課地點 ： 維多利亞公園
日期 ： 5 月份 (逢星期日)
上課時間 ： 2 小時，共 4 節 (早上 10:00 – 12:00 或 下午 1:00 – 3:00)
名額 ： 20 人 (每班人數: 2-6 人)
費用 ： $1440
參加資格 ： 香港醫學組織聯會會員暨家屬
裝備 ： 請自備網球拍
報名辦法 ： 請填妥報名表格，傳真至 2865 0345 或郵寄至以下地址:
(郵寄地址: 香港醫學組織聯會 香港灣仔軒尼詩道十五號溫莎公爵社會服務大廈四樓)

表格可於以下網址 www.fmshk.org 下載

****可代查詢及報考教練專業試**

4/F, Duke of Windsor Social Service Building, 15 Hennessy Road, Wanchai, Hong Kong
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- More effective glycaemic control than NPH insulin[2,3,5,6]
- No undesirable weight gain[2-8]

References: 1. Heise T, Nosek L, Ronn BB *et al.* Lower within-subject variability of insulin detemir in comparison to NPH insulin and insulin glargine in people with type 1 diabetes. *Diabetes* 2004; 53(6): 1614-1620. **2.** Russell-Jones D, Bolinder J, Simpson R. Lower and more predictable fasting blood glucose and reduced risk of nocturnal hypoglycaemia with once daily insulin versus NPH in subjects with type 1 diabetes. *Diabetologia* 2002; 45(Suppl 2): A51. **3.** Hemansen K, Fontaine P, Kukolja KK *et al.* Insulin analogues (insulin detemir and insulin aspart) versus traditional human insulins (NPH insulin and regular human insulin) in basal-bolus therapy for patients with type 1 diabetes. *Diabetologia* 2004; 47(4): 622-629. **4.** De Leeuw I, Vague P, Selam JL *et al.* Insulin detemir used in basal-bolus therapy in people with type 1 diabetes is associated with a lower risk of nocturnal hypoglycaemia and less weight gain over 12 months in comparison to NPH insulin. *Diabetes Obes Metab* 2004; in press. **5.** Home P, Bartley P, Russell-Jones D *et al.* Insulin detemir offers improved glycemic control compared with NPH insulin in people with type 1 diabetes: a randomized clinical trial. *Diabetes Care* 2004; 27(5): 1081-1087. **6.** Pieber T, Grill V, Kristensen A *et al.* Treatment with insulin detemir allows flexible timing of administration in subjects with type 1 diabetes. *Diabetes* 2003; 52(Suppl 1): A130. **7.** Haak T, Tiengo A, Waldhäusl W *et al.* Lower within-subject variability of fasting blood glucose and reduced weight gain with insulin detemir compared to NPH insulin in patients with type 2 diabetes. *Diabetes Obes Metab* 2004; *in press.* **8.** Levemir® Abbreviated SPC, June 2004.

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