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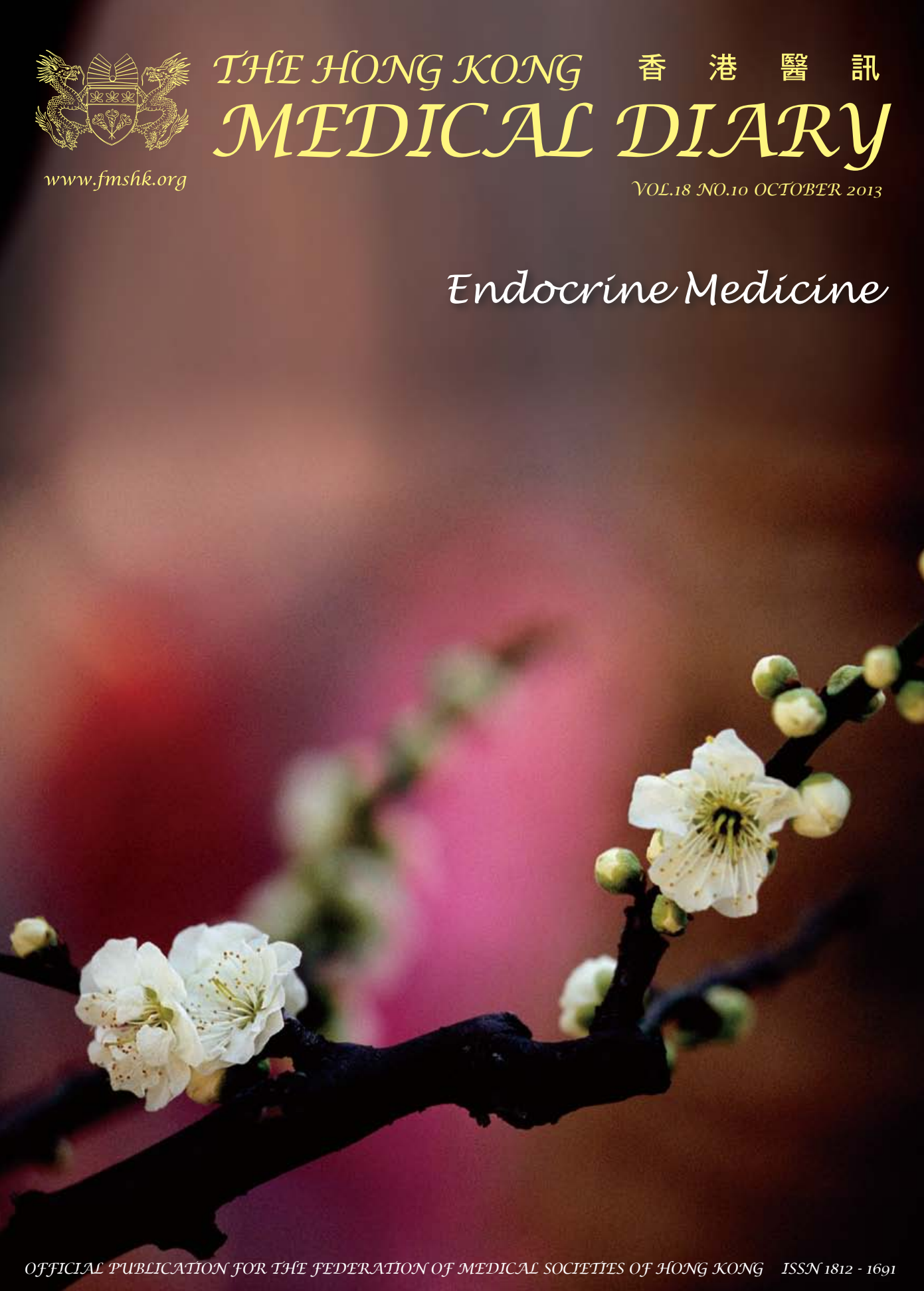

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LIPITOR ABBREVIATED PACKAGE INSERT 1. TRADE NAME: Lipitor® **2. PRESENTATION:** The tablets for oral administration contain atorvastatin calcium equivalent to 10, 20, 40 or 80 mg atorvastatin. **3. INDICATIONS:** Adjunct to diet for the treatment of patients with elevated total cholesterol, LDL cholesterol, apolipoprotein B, and triglycerides and to increase HDL-cholesterol in patients with primary hypercholesterolemia (heterozygous familial and non-familial hypercholesterolemia), combined (mixed) hyperlipidemia (Fredrickson Types IIa and IIb), elevated serum triglyceride levels (Fredrickson Type IV), and for patients with dysbetalipoproteinemia (Fredrickson Type III) who do not respond adequately to diet. For the reduction of total cholesterol and LDL-cholesterol in patients with homozygous familial hypercholesterolemia when response to diet and other non-pharmacological measures are inadequate. Reduce the risk of myocardial infarction, stroke, revascularization procedures and angina in adult patients without clinically evident coronary heart disease, but with multiple risk factors for coronary heart disease such as age, smoking, hypertension, low HDL-C, or a family history of early coronary heart disease. Reduce the risk of myocardial infarction and stroke in patients with type 2 diabetes, and without clinically evident coronary heart disease, but with multiple risk factors for coronary heart disease such as retinopathy, albuminuria, smoking, or hypertension. Reduce the risk of non-fatal myocardial infarction, fatal and non-fatal stroke, revascularization procedures, hospitalization for CHF and angina in patients with clinically evident coronary heart disease. Atorvastatin is also indicated as an adjunct to reduce total-C, LDL-C, and apo B levels in boys and postmenarchal girls, 10 to 17 years of age, with heterozygous familial hypercholesterolemia if after an adequate trial of diet therapy the following findings are present: a. LDL-C remains ≥ 190 mg/dL or b. LDL-C remains ≥ 160 mg/dL and there is a positive family history of premature cardiovascular disease or two or more other CVD risk factors are present in the pediatric patient. **4. DOSAGE:** The recommended starting dose of Lipitor is 10 or 20mg once daily. Patients who require a large reduction in LDL-C (more than 45%) may be started at 40mg once daily. The dosage range is 10 to 80 mg once daily. After initiation and/or upon titration of atorvastatin, lipid levels should be analyzed within 2 to 4 weeks, and dosage adjusted accordingly. **5. CONTRAINDICATIONS:** Hypersensitivity to any component of this medication, active liver disease or unexplained persistent elevations of serum transaminases exceeding three times the upper limit of normal. Pregnant, breast-feeding, or of childbearing potential who are not using adequate contraceptive measures. Atorvastatin should be administered to women of childbearing age only when such patients are highly unlikely to conceive and have been informed of the potential hazards to the fetus. **6. WARNINGS & PRECAUTIONS:** As with other lipid-lowering agents of the same class, moderate (>3 x upper limit of normal [ULN]) elevations of serum transaminases have been reported following therapy with atorvastatin. Liver function tests should be performed before the initiation of treatment and periodically thereafter. Patients who develop any signs or symptoms suggesting liver injury should have liver function tests performed. Patients who develop increased transaminase levels should be monitored until the abnormality(ies) resolve(s). Should an increase in ALT or AST of greater than three times the upper limit of normal persist, reduction of dose or withdrawal of atorvastatin is recommended. Atorvastatin can cause an elevation in transaminases. Atorvastatin should be used with caution in patients who consume substantial quantities of alcohol and/or have a history of liver disease. Myalgia has been reported in atorvastatin-treated patients. **7. INTERACTIONS:** Cyclosporine, fibric acid derivatives, lipid-modifying doses of niacin or cytochrome P450 3A4 inhibitors (e.g. erythromycin, and azole antifungals, clarithromycin, protease inhibitors, diltiazem hydrochloride, itraconazole, grapefruit juice. Inducers of cytochrome P450 3A4 (e.g. efavirenz, rifampin), antacids, colestipol, digoxin, oral contraceptives, fusidic acid **8. PREGNANCY AND LACTATION:** Atorvastatin is contraindicated in pregnancy and while breast-feeding. **9. SIDE EFFECTS:** Nasopharyngitis, hyperglycemia, pharyngolaryngeal pain, epistaxis, nausea, diarrhea, dyspepsia, flatulence, arthralgia, pain in extremity, musculoskeletal pain, muscle spasms, myalgia, joint swelling, liver function test abnormal, blood creatine phosphokinase increased.

Reference: HK PI (SEP2011) Date of preparation: FEB2013 Identifier number: LIP0213

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Contents

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The Cover Shot

A World in a flower, a Buddha in a leaf

Only a close look at the plum blossoms will reveal the infinite wonders of creation.

Prof. Richard YH YU

MD(HK), PhD(Lond), FRCP, Hon FRACP, Hon FHKCP, Hon FPSHK

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According to figures from the International Diabetes Federation, over 371 million people have Diabetes and this figure is rising at an alarming rate.

In this October 2013 Issue on Diabetes, we have the honour of having distinguished Diabetologists from both Universities to share with us the latest development on Diabetes management. The articles cover updates on glucose monitoring, oral hypoglycaemic therapy, injectable treatment for Type 2 Diabetes and how to improve diabetes care through knowledge transfer.

Special thanks to Dr. Jenny LEE for the article on The City Gardener and hope we all can work in an enjoyable office environment.

We are also indebted to Prof. Richard YU for providing us with the magnificent cover photo for this issue.

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Updates on Blood Glucose Monitoring in Patients with Diabetes

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Clinical Assistant Professor, University of Hong Kong

Dr. Elaine HUI

Introduction

Blood glucose monitoring is integral to assessing glycaemic control, which in turn, correlates with risks of diabetic complications. Various methods to monitor blood glucose help to guide clinical decision making in different scenarios, enabling minute-by-minute, day-by-day of up to average 3-monthly analyses of glucose control. HbA1c and fingerstick capillary blood glucose monitoring are the main tools for assessment of average and daily blood glucose levels. Technological advances have improved the accuracy of continuous glucose monitoring and insulin pump devices, becoming a step closer to an 'artificial pancreas' combining real-time glucose sensing, analysis of insulin dose calculation and insulin delivery.

HbA1c as a measure of glucose control

Glycated haemoglobin A1c (HbA1c) is commonly used as a measure of average glucose control over the preceding 2 – 3 months. It reflects the average glycaemic exposure that informs us of the risks of microvascular and macrovascular complications, with approximately 10 - 40% risk reduction for each 1% reduction in mean HbA1c level[1,2].

Limitations of HbA1c

In patients with similar HbA1c values, the diabetic complication rates are significantly lower in patients treated with intensive glucose control, compared to standard therapy, suggesting additional factors, such as glycaemic variations, may play a role in the risk of diabetic complications[3]. HbA1c alone does not reflect day-to-day glycaemic variation and rates of hypo- and hyperglycaemia. Patients could have the same HbA1c, but with frequent episodes of hypo- and hyperglycaemia or with stable glycaemia. HbA1c measurements are also invalid in conditions, such as haemoglobinopathies, that affect red cell survival. Therefore, additional glucose measuring tools are needed to identify aspects of glycaemic dysregulation and guide therapeutic management.

Self-monitoring capillary blood glucose

Checking capillary glucose levels by pricking a fingertip with an automatic lancing device and measuring the blood sample with a glucose meter is routinely used for self-monitoring blood glucose (SMBG). It provides assessment of day-to-day glycaemic variations. As a glucose measuring tool to guide insulin adjustment, SMBG is effective in lowering HbA1c among type 1 and type 2 diabetes patients treated with insulin[4,5]. In type 2 diabetes patients not on insulin, SMBG can still provide feedback on the impact of dietary and lifestyle interventions on blood glucose control, and as a tool for patient education.

Indications for self-monitoring capillary blood glucose[6]:

1) Newly diagnosed diabetes
2) Patients on insulin treatment
3) Patients on oral agents to assess hypoglycaemia
4) During activities, such as driving or intense exercise, to ensure safety
5) During intercurrent illness
6) Diabetes during pregnancy
7) For assessment of glucose control resulting from changes in medications or lifestyle modifications

Timing and frequency of self-monitoring blood glucose:

1) In type 1 diabetes patients and those on intensive insulin regimens (i.e. multiple-dose insulin injections or insulin pump therapy), SMBG should be done at least once before every meal; occasionally at bedtime; when hypoglycaemia is suspected and after hypoglycaemic treatment; and before activities such as driving. Post-prandial blood glucose monitoring (2-hour post-meal) would be helpful in individuals whose pre-meal glucose values are within target, but HbA1c levels are suboptimal[7].
2) In type 2 diabetes, patients on oral agents or less intensive insulin regimens (e.g. once daily injection), the frequency of SMBG will depend upon individual needs and target goals (Table 1).
3) In pregnant women with type 1, type 2 or gestational diabetes, 7-point SMBG profiles (pre-meal, 1 or 2-hour post-meal, and bedtime) have been recommended throughout pregnancy[6].

Advances in blood glucose meters

Blood glucose meters using fingerstick testing have also developed novel ways to tailor specific needs of diabetes patients. For instance, some glucose meters:

- Provide glucose testing as well as blood ketone testing (e.g. Freestyle Optium Xceed) that is useful to ketosis-prone diabetes patients

- Transmit glucose readings wirelessly (e.g. Bayer Contour® Link) to an insulin pump to make insulin dosing easier
- Feature voice commands (e.g. Clever Chek) for the visually-impaired
- Connect glucose readings to mobile phones (e.g. iBGStar®) to keep track of glucose values, carbohydrate intake and insulin dosage

Table 1. Recommended glycaemic targets for adults with diabetes

Measure of glucose control	Type of diabetes	Recommended target	Further considerations
HbA1c	Type 1 or 2	< 7.0%	Higher individualised targets for patients with: - long duration of diabetes - limited life expectancy - elderly - comorbidities - advanced microvascular and macrovascular complications - hypoglycaemic unawareness
	Pre-conception	< 7.0% (ADA)[7] < 6.1% (NICE)[13]	Aim for as close to normal as possible
Capillary blood glucose monitoring	Type 1 or Type 2 on MDI or insulin pump	Before meals: 3.9 – 7.2 mmol/L 2-hr after meals or bedtime: < 10 mmol/L	
	Critically ill in-hospital patients on insulin	Target range: 7.8 – 10.0 mmol[14]	
	Gestational diabetes	5th International workshop conference on GDM[15] Before meals: < 5.3 mmol/L 1-hr after meals: < 7.8 mmol/L 2-hr after meals: < 6.7 mmol/L NICE[13] Before meals: 3.5 – 5.9 mmol/L 1-hr after meals: < 7.8 mmol/L	Aim to achieve target without significant hypoglycaemia

Continuous glucose monitoring

With recent technological advances, continuous glucose monitoring (CGM) devices can detect trends and track patterns in patients with rapidly fluctuating glucose levels, sounding an 'alarm' when glucose rises or drops beyond pre-selected levels. This is particularly helpful in type 1 and type 2 diabetes patients with hypoglycaemic unawareness or nocturnal hypoglycaemia[8]. In a multicentre trial from the Juvenile Diabetes Research Foundation, CGM was effective in lowering HbA1c levels among type 1 diabetes patients who were 25 years or older, but not in younger patients[9]. A meta-analysis has also shown that CGM lowered HbA1c by 0.26% compared to SMBG, without any difference in severe hypoglycaemia[10].

Indications for continuous glucose monitoring:

1) The UK National Institute for Health and Clinical Excellence (NICE) recommends the use of CGM in children or young adults with type 1 diabetes or any adult treated with insulin, who has repeated hypo- and hyperglycaemia, or hypoglycaemic unawareness, unresponsive to conventional insulin dose adjustment[6].

2) In the 2013 Standards of Medical Care in diabetes, the American Diabetes Association (ADA) recommends CGM as a supplemental tool to SMBG in those with hypoglycaemic unawareness and/or frequent hypoglycaemic episodes, in addition to its use to lower HbA1c in selected adults (>25 years of age) with type 1 diabetes on intensive insulin therapies[7].

CGM devices use a small sensor inserted under the skin to detect glucose levels in the interstitial fluid, which then generates glucose readings every 5 minutes, 24 hours a day. Modern sensors can be used for up to 7 days before requiring replacement. A transmitter sends data about glucose levels via radio waves from the sensor to a wireless monitor. There are currently three commercial CGM device manufacturers: Medtronic (Northridge, CA), DexCom (San Diego, CA), and Abbott Diabetes Care (Alameda, CA). Each manufacturer provides softwares to download and analyse the CGM data. A standardised electronic summary has been proposed to include the following statistical and graphical parameters11, allowing clinicians to interpret the CGM data and make purposeful clinical decisions, and to provide instant visual feedback to patients (Figure 1).

Validated parameters to aid CGM data interpretation:

1) Measures of glucose variability:

a) *Standard deviation (SD)* quantifies glucose distribution within 24 hours (as intra-day SD) or between different days (as inter-day SD). It is easy to compare results and is frequently used in CGM analysis reports. However, it assumes a normal glucose distribution, which does not always happen in real-world glucose monitoring.

b) *Coefficient of variation (CV)* equals to (100 x SD)/ means of observations and is a reliable marker for glucose variability, but is limited in clinical use as it is not easily displayed visually.

c) *Interquartile range (IQR)* is not dependent on a normal distribution, and is clinically useful as a measure of glucose variability in relation to the time of day, time of meal or insulin dose.

2) Glucose target ranges

a) *'Within target range'* can be expressed as the % of glucose readings in a pre-set range or hours per day in that specified range

b) *'Above target range'* reflects the % of hyperglycaemic readings

c) *'Below target range'* reflects the % of hypoglycaemic readings

3) Episodes of hypoglycaemia and hyperglycaemia, according to the levels of severity

Although the interstitial fluid glucose values used in CGM are highly comparable to the capillary blood glucose used during fingerstick testing, CGM still requires capillary blood glucose testings at certain time points for sensor calibration. There is a lag time between the interstitial fluid and the capillary blood glucose, which becomes clinically significant when the capillary blood glucose rises/falls sharply. Nonetheless, modern CGM devices have greatly reduced the lag time and improved on sensor accuracy.

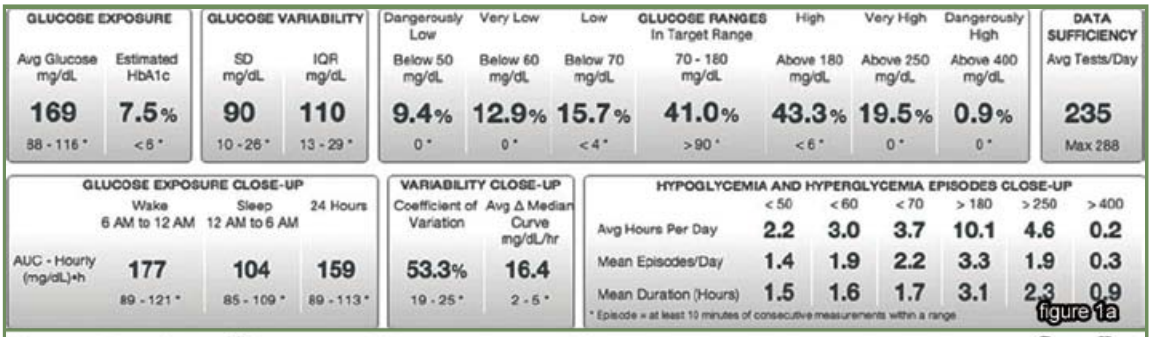

Figure 1. An electronic summary (figure 1 a) and a graphical summary (figure 1b) of a 4-day continuing glucose monitoring data (adapted from Bergenstal et al.[11])

Sensor-augmented insulin pump

Sensor-augmented insulin pump works towards an 'artificial pancreas' model by combining real-time CGM (RT-CGM) with an insulin pump (figure 2). It integrates the use of RT-CGM in the analysis of glucose patterns and calculation of insulin basal rates, insulin duration of action, insulin to carbohydrate ratios and correction factors. In type 1 diabetes patients with baseline HbA1c of 8.3% ± 0.5, patients on sensor-augmented insulin pumps had greater reduction in HbA1c (7.5%), compared to multiple daily insulin injection group (8.1%) (P<0.001), without significant difference in severe hypoglycaemia rates (13.31 cases per 100 person-years vs. 13.48 per 100 person-years, P=0.58)[12]. Limitations to sensor-augmented pump therapy include: constant attachment of 2 subcutaneous devices (sensor and pump); risk of cellulitis at attachment sites; and pump failure, in which reversal to subcutaneous insulin injections is required.

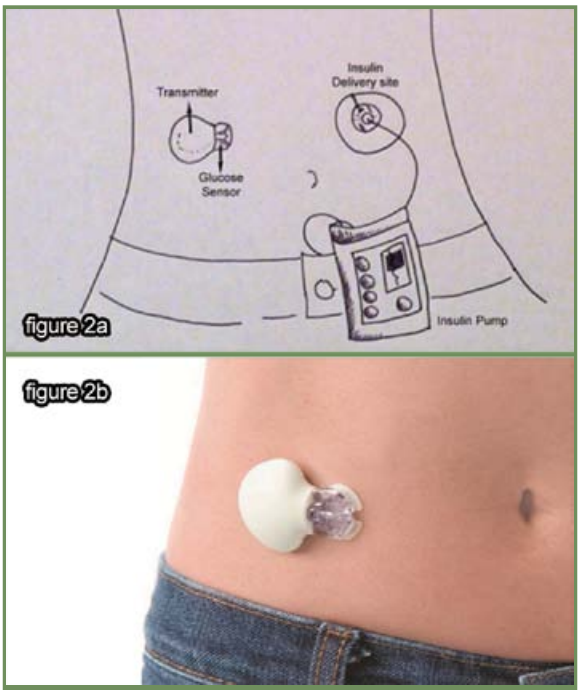

Figure 2. a and b. A sensor-augmented insulin pump system (adapted from Bergenstal et al.[12])

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A Brief Update on Oral Antidiabetic Medications

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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 1 CME credit under the programme upon returning the completed answer sheet to the Federation Secretariat on or before 31 October 2013.

Introduction

Type 2 diabetes mellitus (T2DM), a state of relative insulin insufficiency, was previously usually diagnosed in middle-age adults; however, increasing numbers of young adults/children in high risk populations are being diagnosed[1]. The "ominous octet" (Figure 1) orchestrating the pathophysiology of T2DM, proposed by Ralph DeFronzo in the 2009 American Diabetic Association (ADA) Banting Lecture, formed the basis of pharmacological intervention of T2DM. Insulin resistance is typically present for some time before the diagnosis. Initially, euglycaemia is maintained as long as beta (β)-cells compensate for the resistance by secreting higher amounts of insulin. Overtime, the insulin level declines due to the reduced number of β-cells and their compromised secretory ability[2]. Studies have shown a ~50% or greater decrease in maximal β-cell function at diagnosis of T2DM[3,4].

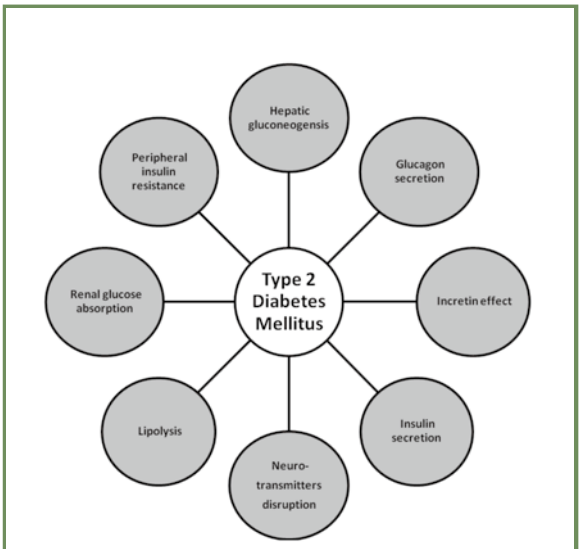

Figure 1. The Ominous Octet depicting the Pathophysiology of Type 2 Diabetes Mellitus

Adapted from Defronzo[5]

The global burden of T2DM is rising, especially in the Asia-Pacific region, and is exerting a significant impact in both public health and socioeconomic aspects. In Hong Kong, 1 in 10 adults will have diabetes[6]. In the China Mainland, the prevalence is predicted to rise from 9.3% in 2011 to 12.1% in 2030, and the adult diabetic population is expected to grow from 90.0 to 129.7 millions[7]. Emerging evidence suggests that for the same degree of body weight, Asians have considerably higher body fat, especially visceral fat compared to Caucasians[8-10], giving rise to the "metabolically obese" phenotype. Asians with T2DM have predispositions for renal complications and strokes as compared to Caucasians[11]. Therefore, physicians in Hong Kong not only need to familiarise themselves with diabetic treatment according to the latest international guidelines, but to strive for the optimal management of the local diabetic populations paying particular attention to how local diabetics differ from those from the rest of the world[12]. This brief update will discuss the profiles of various oral antidiabetic medications, predominantly, for T2DM.

Treatment Target of Type 2 Diabetes Mellitus

The goals of pharmacological therapy for T2DM are to reduce the symptoms of hyperglycaemia and the long term complications. It is well known that glycaemic control reduces the risks for microvascular complications, including neuropathy, retinopathy, and nephropathy[5,13-15]_ENREF_11. Premature mortality from cardiovascular diseases (CVD) is increased in patients with T2DM[16]. However, it remains unclear whether intensive glycaemic control reduces that risk[17]. Glycaemic target put forward by current international guidelines is glycated haemoglobin (HbA1c) ≤6.5-7%. Individualisation has been a key emphasis stating that tighter targets are set for younger and healthier individuals, while looser targets are set for older patients and/or those who have comorbidities or are hypoglycaemia prone[11,18]. Maintenance of long term glycaemic control without deleterious side effects (such as hypoglycaemia, weight gain) has become one of the priority considerations. Evidence for CVD and cancer safety is also prudent as many medications are taken for almost lifelong. Smoking cessation and optimisation of related risk factors such as blood pressure, lipids, and body weight are of equal importance.

Pharmacological Therapy for Type 2 Diabetes Mellitus

Initiation of appropriate pharmacotherapy (multiple many a time), would be interpreted as an adjunct to proactive lifestyle management giving the progressive nature of T2DM. Treatment inertia is commonly observed, particularly in general practice, with undue delay in commencement and escalation of combination of pharmacological therapies. In particular, the β-cell failure which begins earlier and is more severe than previously thought argues for the need for early and aggressive treatment to preserve remaining β-cell function and to limit further disease progression 2. Currently available oral antidiabetic drugs include biguanide, sulfonylurea (SU), meglitinide, thiazolidinedione, alpha(α)-glucosidase inhibitors, and dipeptidyl peptidase-IV (DPP-IV) inhibitors. The most recently developed oral agent is sodium glucose co-transporter 2 (SGLT2) inhibitors. Table 1 summarises the profiles of these oral antidiabetic medications.

Biguanide

Metformin is the only biguanide available. It lowers blood glucose predominantly by suppressing hepatic gluconeogenesis and may also increase glucose uptake and utilisation in skeletal muscle. It does not stimulate appetite and is therefore weight neutral and sometimes, it even promotes a slight weight loss. Metformin does not cause hypoglycaemia if used alone. With its inexpensive cost and evidence of long term safety, metformin has become the first line treatment for many patients diagnosed with T2DM. Unwanted side effects of metformin are dose related gastrointestinal disturbances (eg: anorexia, diarrhoea, nausea), which are usually but not always self-limiting. Lactic acidosis is a rare but potentially fatal complication, and metformin should therefore not be given to patients with advanced renal or hepatic impairment, uncontrolled heart failure, or shock, as these patients are predisposed to lactic acidosis due to reduced drug elimination or reduced tissue oxygenation. Metformin is contraindicated in patients with chronic kidney disease (CKD) stage 3B, 4, or 5, but can be used cautiously with reduced dose in mild to moderate CKD (estimated glomerular filtration rate (eGFR) ≥ 45 ml/min/1.73m2)[11]. Long-term use of metformin may interfere with absorption of vitamin B12 which might contribute to megaloblastic anaemia and the progression of diabetic neuropathy[22]. Although the screening frequency for vitamin B12 level and its cost-effectiveness remain to be elucidated, baseline tests at the initiation of metformin and at intervals of about 1-2 years are recommended as metformin induced vitamin B12 deficiency is treatable with vitamin B12 replacement[23].

Sulfonylurea and Meglitinide

Gliclazide, glipizide, glimepiride, and glibenclamide are the most widely used SUs, while repaglinide and nateglinide are the two meglitinides available. High-affinity receptors for SUs are present on the potassium-adenosine triphosphate (KATP) channels in the β-cell plasma membranes, and these drugs reduce the potassium permeability of β-cells by blocking the KATP channels, causing depolarisation and calcium entry, resulting in insulin secretion. SUs improve glycaemic control and reduce the risk of microvascular complications[5,13-15] at a relatively low drug cost, but this has to be balanced against the risk of weight gain, hypoglycaemia, and the possible adverse effects on the cardiovascular system[17]. Another significant drawback

Table 1. Profiles of Oral Antidiabetic Medications for Glycaemic Control in Patients with Type 2 Diabetes Mellitus.

	Biguanide (Metformin)	Sulfonylurea/ Meglitinide	Thiazolidinedione (Pioglitazone)	α-glucosidase inhibitor	DPP-IV inhibitor	SGLT2 inhibitor
Hypoglycaemia risk	Neutral	Moderate to severe/mild	Neutral	Neutral	Neutral	Neutral
Effect on weight	Neutral/Slight loss	Gain	Gain	Neutral	Neutral	Loss
GI side effects	Moderate	Neutral	Neutral	Moderate	Neutral	Neutral
Bone loss	Neutral	Neutral	Moderate	Neutral	Neutral	No information
CVD risk	Beneficial	?	Neutral	Neutral	Neutral	Neutral
CHF risk	Neutral	Neutral	Moderate	Neutral	Neutral	Neutral
Use in renal impairment	Dosage adjustment required Not to use in eGFR <45 ml/min/1.73m2	Dosage adjustment required Contraindicated in advanced stage	No dose adjustment required	Not to use in eGFR < 25 ml/ min/1.73m2	Dosage adjustment required (except for linagliptin)	Dosage adjustment required Not to use in eGFR <45 ml/min/1.73m^2
Use in hepatic impairment	Contraindicated in advanced stage	Contraindicated in advanced stage	No dose adjustment required	No information	No dose adjustment required for mild to moderate stage Limited information for advanced stage (except for linagliptin)	No dose adjustment required for mild to moderate stage Contraindicated in advanced stage
Drug cost	Low	Low	Relatively high	Relatively high	High	High
HbA1c lowering potency as monotherapy (%) †[20,21]	1.0-2.0	1.0-1.5	0.5-1.4	0.5-0.9	0.5-0.8	0.5-0.7

Data from Garber [19], Ismail-Beigei [20], and Clar [21] et al
DPP-IV denotes dipeptidyl peptidase-IV
SGLT2 denotes sodium glucose co-transporter 2
† In real life practice, the HbA1c lowering potency depends very much on initial HbA1c and whether an appropriate combination is used

of SUs is their exhaustive effects on β-cell function which drive the β-cells to fail earlier[24]. It should also be remembered that the dosage should be reduced in patients with renal and/or hepatic impairment to prevent hypoglycaemia.

Meglitinides, although pharmacologically distinct from the SUs, also stimulate the release of insulin from β-cells[25]. The clinical efficacy of meglitinide monotherapy is similar to that of the SUs[26-28]. In 2010, the Nateglinide And Valsartan in Impaired Glucose Tolerance Outcomes Research (NAVIGATOR) study group reported that among patients with impaired glucose tolerance (IGT) and CVD or CVD risk factors, nateglinide, as compared with placebo, in addition to lifestyle modifications, did not reduce the incidence of diabetes or CVD outcomes. However, nateglinide did not increase adverse CVD effects, although the risk of hypoglycaemia is increased and the mean weight loss was lower as compared to the placebo group[29]. The advantage of the other meglitinide, repaglinide, over SUs is the ability to use it safely in patients with decreased eGFR or renal failure without concern for hypoglycaemia since it has little renal clearance[30].

Thiazolidinedione

Thiazolidinediones increase insulin sensitivity by binding to a nuclear receptor called the perioxisome proliferator-activated receptor-gamma (PPARγ), which occurs mainly in adipose tissue, but also in muscle and the liver. They mediate differentiation of adipocytes, increase lipogenesis, and enhance uptake of fatty acids and glucose. Pioglitazone is now the only thiazolidinedione available in Hong Kong. It is not associated with hypoglycaemia and the additional effects of pioglitazone on the lipid profile (decreases in triglycerides and increases in high density lipoprotein (HDL)) has once made this drug popular[31]. However, in view of an epidemiological study conducted in France which suggested an increased risk of bladder cancer with pioglitazone, the drug was suspended in France and Germany since 2011[32]. After considering further epidemiological evidence, the European Medical Agency (EMA) concluded that there is a small increased risk (relative risk ranging from 1.12 to 1.33) of bladder cancer in diabetic patients treated with pioglitazone, particularly in those treated for the longest durations (more than 2 years) and with the highest cumulative doses (more than 28000mg)[33]. The United States Food and Drug Administration (FDA) also issued a safety communication in 2011 recommending physicians not to use pioglitazone in patients with active bladder cancer and to use it with caution in patients with a prior history of bladder cancer. This unresolved controversy will continue to evolve with more long term data available from various retrospective data base analyses. Rosiglitazone has been discontinued in Hong Kong and Europe since 2010, and is highly restricted in the United States owing to persistent concern about an increased risk of myocardial infarction based on meta-analyses of observational studies[34,35]. Both thiazolidinediones can cause weight gain, fluid retention, and heart failure[36]. Both have been shown to be associated with low-trauma fractures in men and women[37]. In addition, the cost of thiazolidinediones is relatively high.

Alpha-glucosidase inhibitor

Acarbose, an inhibitor of intestinal α-glucosidase, delays carbohydrate absorption, reducing the postprandial increase in blood glucose. Common adverse effects are related to its main action and consist of flatulence, bloating, abdominal pain, and diarrhoea. Like metformin, it does not cause hypoglycaemia and is weight neutral. While postprandial hyperglycaemia is a strong independent predictor for the development of T2DM, a preliminary study has shown that treatment of patients with IGT with acarbose is associated with a significant reduction in insulin resistance with a decrease in postprandial hyperglycaemia and hyperinsulinaemia[38]. Therefore, although acarbose has never been a commonly used antidiabetic medication, it can be used in addition to lifestyle modifications to delay development of T2DM in patients with IGT with up to 25% relative risk reduction[39]. Results from the Acarbose Cardiovascular Evaluation (ACE Trial), a large-scale, double-blind, multicentre trial, would elucidate the cardiovascular effects of acarbose in Chinese subjects with IGT. The cost of this medication is moderate.

Dipeptidyl peptidase-IV inhibitors

The fact that oral glucose has a greater stimulatory effect on insulin secretion than intravenous glucose illustrates the importance of the incretin effect, of which glucagon-like peptide-1 (GLP-1) is one of the several important gastrointestinal peptides involved[40]. Sitagliptin, vildagliptin, saxagliptin, and linagliptin, are the DPP-IV inhibitors available in Hong Kong. They inhibit DPP-IV, an enzyme expressed on the surface of most cell types that deactivates a variety of peptides including GLP-1, thereby potentiating the incretin effect from GLP-1[41]. They are generally well tolerated without the risk of hypoglycaemia when used alone and are weight neutral. DPP-IV inhibitors only produce a modest reduction in HbA1c, but have enhanced synergistic effects when combined with metformin. Recently, DPP-IV inhibitors are suspected to increase the risks of pancreatitis and pancreatic cancer from epidemiological and retrospective database analyses. A causal relationship has not yet been established, but both the EMA and FDA are evaluating its safety[42]. We will have much better insight on these unresolved safety concerns from several ongoing DPP-IV cardiovascular endpoint trials involving a total of >50,000 patients with prospective systematic collection of safety data apart from looking at the adjudicated clinical end points. Dose adjustment is necessary for patients with renal and/or hepatic impairment except for linagliptin, which is primarily excreted un-metabolizsed via the bile and gut[43]. The cost of these DPP-IV inhibitors is high.

Sodium glucose co-transporter 2 inhibitors

The search for new oral treatments for T2DM is ongoing and the latest addition is the SGLT2 inhibitors. Dapagliflozin and canagliflozin are now available in Europe and the United States respectively and are expected to be available in Hong Kong soon. SGLT2 is expressed in the proximal tubule of kidneys and mediates reabsorption of ~90% of the filtered glucose load. SGLT2 inhibitors promote the renal excretion of glucose and thereby lower blood glucose. They are only administered once daily. Another merit with SGLT2

inhibitors is that they can either be used as monotherapy or in combination with any other antidiabetic drugs (oral or injectable) since their mechanism of action is independent from the aetiology of development of diabetes or the mechanisms that protect against hyperglycaemia. The lowering effect of HbA1c is similar to that of DPP-IV inhibitors and is modest (~ 0.8%). The most common side effects are vaginal yeast infection and urinary tract infection[44]. Other beneficial effects from SGLT2 inhibitors include a reduction in body weight (-1.88 to -2.85 Kg), blood pressure (-1.3 to -7.2 mmHg), and a lower risk of hypoglycaemia (3.4% versus 39.7% when using dapagliflozin with metformin as compared to using glipizide with metformin)[21,45]. Long term data on microvascular or cardiovascular outcomes are not yet available. The cost of SGLT2 inhibitors is high.

Management algorithm

With the ever growing list of antidiabetic drugs available on the market, choosing the right drugs for the right patients can be a challenge to everyday practice. The American Association of Clinical Endocrinologists (AACE) has issued a new T2DM management algorithm[11] in May this year with the aim to assist physicians in making the best choice and has been summarised in Figure 2. Lifestyle modifications remain the cornerstone of diabetic management for each and every patient. Although the management of comorbidities of type 2 diabetic patients, including blood pressure, lipids, body weight, albuminuria, psychosocial factors etc… just to name a few, are beyond the scope of this article, it is necessary to remember that successful patient management requires a holistic approach.

Conclusion

Type 2 diabetes mellitus is a chronic, heterogeneous, and progressive disease defined by the presence of hyperglycaemia with insulin resistance and inadequate β-cell function being the major culprits. The burden of T2DM in Hong Kong is staggering. The overall aim of diabetic management is to minimise complications while avoiding hypoglycaemia and weight gain. Oral antidiabetic medications remain the initial therapy for the majority of patients. The choice of drugs would best be made together by the physicians and patients after comprehensive information about the effectiveness and safety of medications is communicated. Last but not least, lifestyle modifications remain the essential foundation in the management of every patient.

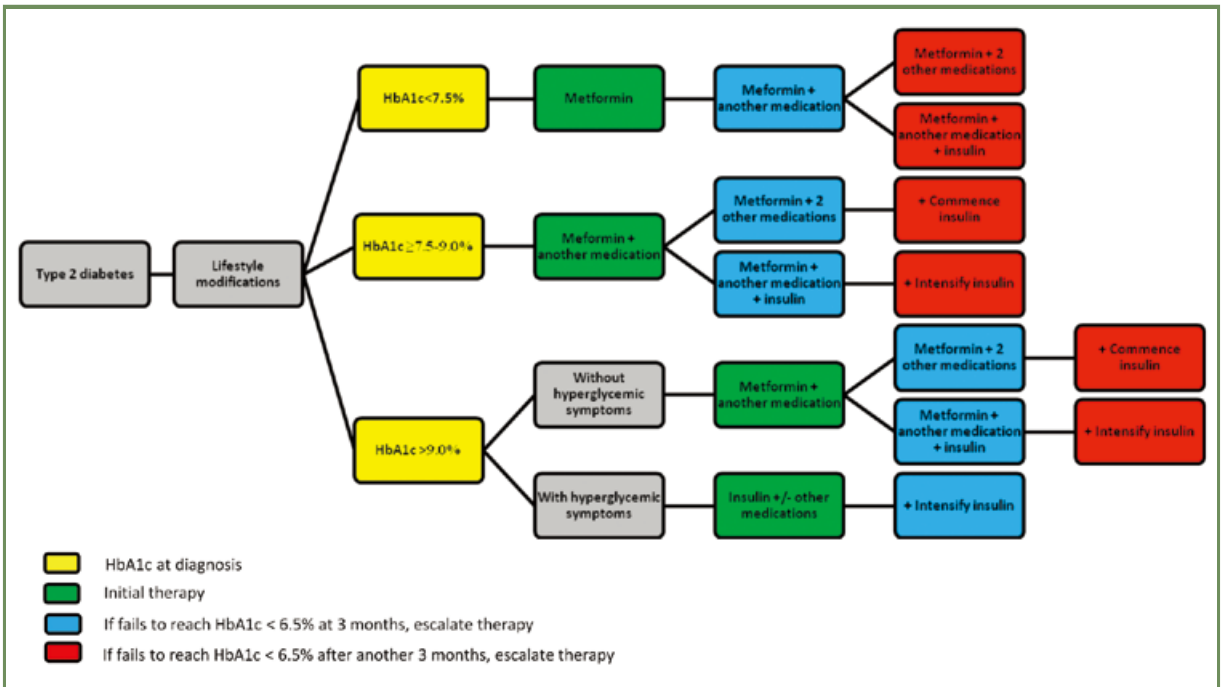

Figure 1. The Ominous Octet depicting the Pathophysiology of Type 2 Diabetes Mellitus

Adapted from Garber _ENREF_18[19]

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MCHK CME Programme Self-assessment Questions

Please read the article entitled "A Brief Update on Oral Antidiabetic Medications" by Dr. Kitty KT CHEUNG and Dr. Francis CC CHOW and complete the following self-assessment questions. Participants in the MCHK CME Programme will be awarded CME credit under the Programme for returning completed answer sheets via fax (2865 0345) or by mail to the Federation Secretariat on or before 31 October 2013. 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. Studies have shown that by the time Type 2 Diabetes is diagnosed, about 50 % or more of beta cell mass is lost.
2. Asians have considerably less body fat, especially visceral fat compared to Caucasians.
3. Metformin can be used cautiously with a reduced dose in mild to moderate chronic kidney disease.
4. The possible side effects of sulfonylurea include the risk of weight gain, hypoglycaemia, and the possible adverse effects on cardiovascular system.
5. There is a small increased risk of colon cancer in diabetic patients treated with pioglitazone, particularly in those treated for long durations and with high cumulative doses.
6. Acarbose can be used in severe renal failure patients.
7. DPP-IV inhibitors are suspected to increase the risk of pancreatitis and pancreatic cancer from epidemiological and retrospective database analyses.
8. SGLT2 inhibitors promote the renal excretion of glucose and thereby lower blood glucose by acting on the distal tubule of the kidney.
9. The most common side effects of SGLT2 are vaginal yeast infection and urinary tract infection.
10. Among currently available oral antidiabetic drugs, sulphonylurea and biguanide have the highest HbA1c lowering potency.

ANSWER SHEET FOR OCTOBER 2013

Please return the completed answer sheet to the Federation Secretariat on or before 31 October 2013 for documentation. 1 CME point will be awarded for answering the MCHK CME programme (for non-specialists) self-assessment questions.

A Brief Update on Oral Antidiabetic Medications

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Answers to September 2013 Issue

Screening for CA Prostate

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

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Presentation: Linagliptin. Film-coated tablet 5 mg. **Indications:** Adjunct to diet and exercise to improve glycaemic control in adults with type 2 diabetes mellitus as monotherapy or as combination therapy with metformin or a sulphonylurea plus metformin. **Dosage:** 5 mg once daily. Can be taken with or without food. Not recommended in paediatric patients. **Contraindications:** Hypersensitivity to linagliptin or to any of the excipients. **Special warnings and precautions:** Should not be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis. When Trajenta is used in combination with a sulphonylurea, a dose reduction of the sulphonylurea may be considered. Should be avoided during pregnancy. Caution while breast-feeding. Caution when driving or operating machines. **Interactions:** Rifampicin. Use in special populations: No dosage adjustment in any degree of renal or hepatic impairment. **Adverse reactions:** Monotherapy – uncommon: nasopharyngitis, cough. Combination with metformin – uncommon: nasopharyngitis, hypersensitivity, cough. Combination with a sulphonylurea plus metformin – very common: hypoglycaemia. **Note:** Before prescribing, please consult full prescribing information.

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Advances in Injection Therapy in Type 2 Diabetes Mellitus

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Introduction

The burden of type 2 diabetes mellitus (T2DM) is increasing rapidly around the world. The prevalence is expected to more than double over the next 20 years, and it is estimated that there will be 440 million people suffering from T2DM by 2030.[1] In China Mainland , the prevalence of diabetes will rise from 4.5% (43.2million) in 2010 to 5.8% (62.6million) in 2030.[1] Type 2 diabetes remains a leading cause of cardiovascular diseases, end-stage renal failure, blindness, amputations, and hospitalisations. The United Kingdom Prospective Study (UKPDS) has demonstrated that intensive glycaemic control effectively reduces microvascular complications by 25% to 76%, although its role in reducing cardiovascular risks remains less certain.[2]

Treatment of diabetes should begin with diet, exercise and weight reduction. In the absence of contraindications, metformin should be initiated together with lifestyle modifications.[3] Oral hypoglycaemic agents become less effective as beta cell function declines. The therapeutic options for patients who have failed lifestyle modifications & metformin include adding (1) a second oral drug, or (2) an injectable agent, including insulin or glucagon-like peptide-1 (GLP-1) analogues. There is no consensus on which is the best treatment to add. However, insulin is preferred when marked hyperglycaemia is present, especially when HbA1c is >8.5%. Many patients eventually require insulin as the beta cell function deteriorates. GLP-1 based therapy, on the other hand, has the advantage of weight reduction and a low risk of hypoglycaemia. This article will focus on insulin and GLP-1 analogues in the management of T2DM.

INSULIN

Insulin therapy has evolved considerably since its discovery in the 1920s. Significant improvements have been made in the purification, production and formulation of insulin. Insulin was initially extracted from the pancreases of cattle and pigs, but since the 1980s, human insulin has been manufactured using recombinant DNA technology.[4] Insulin therapy aims to replicate endogenous basal and stimulated insulin release to suppress hepatic glucose production and minimise post-prandial glucose excursions respectively. Several types of insulin preparations are available. The onset, peak and duration of action of commonly used insulins in Hong Kong are summarised in Table 1. Intermediate-acting and long-acting preparations are used as the basal (fasting) component, and short-acting insulin and rapid-acting insulin analogues are used as the bolus (prandial) component.

Human insulin

(i) Intermediate-acting human insulin: Protaphane HM®, Humulin N®

The only conventional intermediate-acting human insulin currently in clinical use is neutral protamine Hagedorn (NPH) insulin. It is a suspension of crystalline zinc insulin combined with protamine, which allows for a delay in absorption from the subcutaneous tissue resulting in up to 20 hours of action. However, NPH exhibits a pronounced peak 5 – 7 hours after injection, leading to an increased risk of nocturnal hypoglycaemia if injected in the evening (Table 1). There are also wide inter- and intra-individual variabilities in action as NPH must be evenly suspended before administration. NPH is still widely used nowadays due to its low cost, and its ability to be mixed with regular human insulin in a premixed preparation[4].

(ii) Short-acting human insulin: Actrapid HM®, Humulin R®

Regular human insulin has a delayed onset of action (30 – 60 minutes after injection), relatively late peak effect (2 – 4 hours after injection) and longer duration of action (6 – 8 hours) compared with the endogenous insulin secretion that occurs after meal (Table 1). Regular human insulin needs to be administered 30 minutes before meal, which is inconvenient for many patients. It may also lead to early post-prandial hyperglycaemia and late hypoglycaemia.[4]

Human insulin analogues

Insulin analogues are produced by recombinant bioengineering techniques. The human insulin molecule is modified by amino acid substitutions, inversions or additions, so that these analogues can better simulate endogenous insulin secretion. Long-acting insulin analogues have been modified to possess a stronger ability to self-associate, thus resulting in a longer duration of action. On the other hand, rapid-acting insulin analogues have been altered to impede self-aggregation, so that they have a faster onset of action.

(i) Long-acting insulin analogues: Glargine (Lantus®), Detemir (Levemir®)

Glargine and detemir were developed to mimic the physiological profile of basal insulin, aiming at a long and steady action. Both long-acting analogues are relatively peakless, have an onset of action within 1 – 3 hours of injection, and a duration of up to 24 hours. (Table 1) Both glargine and determir demonstrate

less inter-individual variability in absorption when compared with NPH insulin. For patients with T2DM, both glargine (once daily) and detemir (twice daily) were shown to achieve similar HbA1c when compared with NPH insulin, but the risk of hypoglycaemia, in particular nocturnal hypoglycaemia, was lower with glargine & determir.[5-7] A comprehensive review of glargine and detemir found no clinical differences in their efficacy and safety. Detemir was often required as twice daily injections at higher doses, but resulted in less weight gain. Glargine was injected once daily, and resulted in less injection site reactions.[8]

(ii) Ultra long- acting analogues: Insulin degludec (Tresiba®), PEGylated Insulin lispro

Insulin degludec is a novel ultra long-acting basal insulin that forms multihexamers on subcutaneous injection. It has recently been approved by the European Medicines Agency (EMA), but declined by the US Food and Drug Administration (FDA), owing to concerns regarding a potential increase in cardiovascular risks. Degludec has a half-life of longer than 24 hours, and a long duration of action in excess of 40 hours. Degludec has been shown to have lower within-patient variability than glargine.[9] Compared with glargine and determir, degludec has been shown to have comparable efficacy in glycaemic control, but a lower incidence of hypoglycaemia. Degludec also has the ability to be mixed with other insulins, which cannot be done using glargine or determir.[10]

PEGylated Insulin lispro (LY2605541) is another ultra long-acting insulin under development. Phase 2 clinical trials have been completed and a series of phase 3 trials are underway.[11] By embedding insulin lispro in a polyethylene glycol chain, the duration of action of the drug is substantially extended. Steady-state profile data show that it has a flat profile and over 24 hours duration of action.

(iii) Rapid-acting insulin analogues: Lispo (Humalog®), Aspart (Novorapid®), Glulisine (Apidra®)

For many patients with T2DM, basal insulin is often adequate for good glycaemic control, as endogenous insulin secretion will control post-prandial excursions. However, for some patients with longer duration of T2DM or those with difficult control, premeal boluses may be required. Lispro, aspart and glulisine are commercially available as rapid-acting insulin analogues for use as bolus insulins. They have been structurally altered to impede self-aggregation into multimeric complexes. Hence, they have a faster onset of action (10 – 30 minutes after injection), a peak of action (30minutes – 2 hours) and a shorter duration of action (3 – 4 hours) in comparison with regular human insulin. (Table 1) They simulate the physiological meal-stimulated insulin release more accurately, but do not demonstrate significant improvements in glycaemic control in T2DM in terms of HbA1c when compared with regular human insulin in clinical studies.[12] However, from a practical point of view, rapid-acting insulin analogues allow greater convenience and flexibility in the timing of injections. They can be given immediately before meals, as opposed to 30 – 45 minutes before meal for regular human insulin.

Premixed insulin preparations

Most premixed insulin preparations contain an intermediate-acting insulin, together with either a regular human insulin (premixed human insulin), or rapid acting insulin analogue (premixed insulin analogue). (Table 1) Premixed insulin preparations have the obvious advantage of delivering basal and prandial insulin in a single injection, and are more effective in reducing postprandial glucose and HbA1c levels than basal insulin.[13] However, they are less flexible, and are associated with a higher risk of hypoglycaemia.[13] Premixed insulin analogues and premixed human insulin are similar in efficacy in terms of glycaemic control (decreasing fasting glucose and HbA1c) and the incidence of hypoglycaemia, but premixed insulin analogues are superior in controlling postprandial glucose excursions with less intra-subjection variations.[13]

Table 1: Pharmacokinetic parameters of commonly used insulins in Hong Kong

			Action Profile (hours)		
Insulin	**Trade name**	**Manufacturer**	**Onset**	**Peak**	**Duration**
Rapid-acting					
Lispro	Humalog	Eli Lilly	0.2 – 0.5	0.5 – 2	3 – 4
Aspart	Novorapid	Novo Nordisk			
Glulisine	Apidra	Sanofi-Aventis			
Short-acting					
Regular	Humulin R	Eli Lilly	0.5 – 1	2 – 4	6 – 8
	Actrapid HM	Novo Nordisk			
Long Acting					
Glargine	Lantus	Sanofi-Aventis	1 – 3	No peak	Up to 24
Determir	Levemir	Novo Nordisk			
Premixed human insulin: NPH/ regular					
70%/30%	Humulin 70/30	Eli Lilly	0.5 – 1	3 – 12	Up to 24
	Mixtard 70/30	Novo Nordisk			
Premixed insulin analogues					
Neutral protamine lispro/ Lispro					
75%/25%	Humalog mix 75/25	Eli Lilly	0.2 – 0.5	1 – 14	24
50%/50%	Humalog mix 50/50	Eli Lilly			
Insulin aspart protamine/ Aspart					
70%/30%	Novolog Mix 30	Novo Nordisk	0.2 – 0.5	1 – 14	24
50%/50%	Novolog Mix 50	Novo Nordisk			

Adapted from CA Borgono, B Zinman. Insulins: Past, Present and Future. Endocrinol Metab Clin North Am 2012;41:6.[4]

GLUCAGON-LIKE PEPTIDE-1 ANALOGUES

Glucagon-like peptide-1 is secreted from the L-cells of the small intestine following ingestion of a meal. GLP-1 is responsible for the incretin effect, in which oral glucose has a greater stimulatory effect on insulin secretion than intravenous glucose load. The incretin effect is diminished in T2DM. GLP-1 stimulates insulin secretion from the pancreatic beta-cells, and inhibits glucagon secretion from the alpha-cells, both in a glucose-dependent manner. It also slows gastric emptying, and stimulates satiety by binding to its receptor in the hypothalamus. GLP-1 has a short half-life of one to two minutes due to degradation by the enzyme dipeptidyl peptidase 4 (DPP-4).[14] As a glucose-lowering agent, GLP-1 needs to be given as a continuous infusion and therefore has limited therapeutic potential.[14] GLP-1 analogues have been developed so that they are resistant to DPP-4 degradation and can restore the incretin effect in T2DM. GLP-1 analogues have no intrinsic risk of hypoglycaemia as the stimulation of insulin secretion

occurs in a glucose-dependent manner.[15] They are currently approved in combination with metformin and/or sulphonylurea in patients who fail to reach therapeutic goals.[14]

(i) Exenatide (Byetta®)

Exenatide has a half life of 2.4 hours, and is administered subcutaneously as twice-daily injections. It reduces HbA1c by 0.8 – 1.1%, and weight loss of 1.5 – 3.0 kg in 30 weeks. Weight loss is associated with improvement in blood pressure and lipids. Nausea is the most common side effect, and it can be reduced by starting with a small dose first. It is recommended to start at 5 microgram twice daily, and increase to 10 microgram twice daily after 4 weeks. Exenatide is eliminated mainly by the kidneys and should not be used in patients with creatinine clearance of less than 30ml/min. Rare cases of acute pancreatitis have been reported with the use of exenatide and FDA had issued a warning to the label in 2007.[14]

(ii) Liraglutide (Victoza®)

Liraglutide has a longer half-life of 13.5hours, and is administered as an once daily subcutaneous injection. To decrease the gastrointestinal side effects like nausea and vomiting, it should be started at 0.6mg daily for one week, and then stepped up to 1.2mg daily. The dosage can be increased to 1.8mg daily if blood glucose level is still above the goal. In combination with various oral drugs, liraglutide reduces HbA1c by 1.3% – 1.5%. Liraglutide also causes significant weight loss and lowers the systolic blood pressure by 2 – 6mmHg. [14]

(iii) Exenatide once weekly (Bydureon®)

In exenatide once weekly formulations, exenatide is encapsulated in biodegradable polymeric microspheres. After injection of the microspheres, degradation starts resulting in sustained release of exenatide molecules, and subsequent absorption from the subcutaneous tissue. A steady plasma exenatide level is reached after 6 – 7 weeks of treatment. In type 2 diabetic patients treated with metformin, exenatide once weekly produces greater HbA1c reduction of 1.5 – 1.9% than exenatide twice daily (1.0 – 1.5%) and other oral hypoglycaemic agents (0.9 – 1.2%). In addition, exenatide once weekly results in weight loss of 2.3 – 3.6kg, and improvement in blood pressure and lipid profiles. Gastrointestinal side effects, like nausea and vomiting, are reduced by about one-third when compared with twice daily formulations. A direct comparison between liraglutide and exenatide once weekly showed a greater reduction in HbA1c and in weight, but more nausea and/or vomiting with liraglutide.[16] Several other once-weekly long-acting GLP-1 analogues (e.g. taspoglutide, albiglutide, semaglutide) are in development.[17]

Conclusion

Type 2 diabetes mellitus is a chronic disease with progressive decline in pancreatic beta-cell function, eventually leading to insulin deficiency and failure of many patients in achieving satisfactory glycaemic control. Oral insulin secretagogues become less effective as pancreatic beta-cell function declines, and insulin is the preferred second-line medication when patients have marked hyperglycaemia. Patients frequently decline to start insulin due to fear of needles and self-injection. They may also perceive starting insulin therapy as a failure to control their diabetes, and that the disease is becoming more severe. Physicians should spend time and resources to educate patients on the chronic nature of the disease, and that insulin is a very effective mode of treatment. With the help of diabetes nurse educators, patients can usually learn to administer insulin confidently.

Weight gain and fear of hypoglycaemia are also significant barriers in initiation of insulin. GLP-1 analogues, on the other hand, are an attractive option of therapy as they cause weight loss and have no intrinsic risk of hypoglycaemia. They are also simpler to use than insulin as they do not require titration of dosage based on home blood sugar monitoring. The UK National Institute for Health and Clinical Excellence (NICE) guidelines recommend a GLP-1 analogue as an alternative to insulin, especially when obesity is a problem.[18] There are, however, many unanswered questions regarding the long term benefits and risks in the clinical use of GLP-1 analogues in T2DM. Data on cardiovascular safety and pancreatitis risk will become available once ongoing large outcome trials with GLP-1 analogues are completed.[19] A patient-centred approach has been advocated in the latest Position Statement jointly released by the American Diabetes Association and the European Association for the Study of Diabetes. The choice of anti-diabetic agents, including insulin and GLP-1 analogues, has to be individualised for each patient, considering the efficacy, risk of hypoglycaemia, effect on weight, cost and major side effects of each medication. [3]

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- Lightweight[2]

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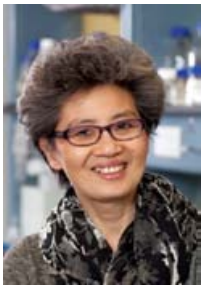
Reorganising Diabetes Care Through Knowledge Transfer



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Burden of diabetes and associated comorbidities

Over 60% of global deaths are due to chronic diseases defined by the World Health Organization such as diabetes, heart disease, respiratory disease and cancer. Amongst these 4 chronic diseases, diabetes plays a causal role in the pathogenesis of cardiovascular-renal diseases and multiple morbidities. In the Emerging Risk Factor Collaborative Study, people with diabetes had 1.3 to 3 fold increased risk of vascular, cancer, non-vascular non-cancer deaths, the latter mainly due to renal failure, sepsis, hepatobiliary and mental diseases[1]. In support of these findings, since 1995, the CUHK-PWH Diabetes Care and Research Team has established a Diabetes Registry which has enrolled more than 10,000 patients with 2-5% of these subjects experiencing one or major events including heart failure, stroke, coronary heart disease, cancer and death on a yearly basis[2].

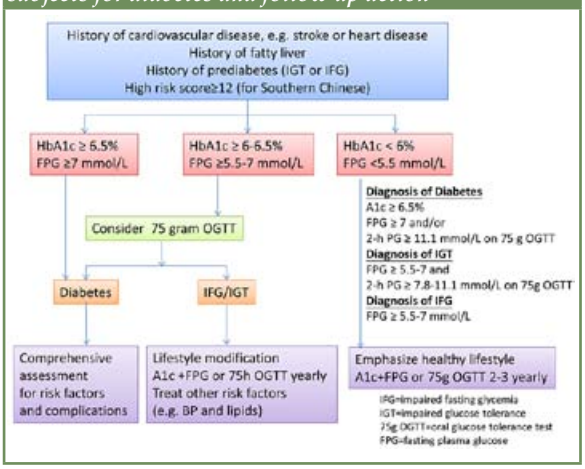
Table 1: A validated risk score to predict diabetes developed in Hong Kong Chinese population (ref 7). Depending on the setting and demographics of the subjects, 10- 50% of subjects with a risk score≥12 had diabetes on 75 gram oral glucose test.

Predictors	Risk score
Age	
≥40-50 versus <40	3
≥50-60 versus <40	6
≥60-70 versus <40	10
≥70 versus <40	12
Body mass index (kg/m2)	
≥23-25 versus <23	2
≥25-30 versus <23	4
≥30-35 versus <23	7
≥35 versus <23	8
Other risk factors	
Hypertension (yes versus no)	3
Dyslipidaemia (yes versus no)	3
Family history of diabetes (yes versus no)	2
Gestational diabetes (yes versus no)	2

Detection of diabetes for early intervention

Despite these devastating consequences, there is a large body of epidemiological and randomised clinical trial data showing that diabetes[3,4] and its associated complications and comorbidities are preventable, treatable and affordable especially if these preventive strategies are implemented during the early stage of disease[5,6]. While population-based screening of diabetes is generally not recommended, targeted screening using known risk factors and simple risk scores[7,8] (Table 1) based on family history, history of cardiovascular disease, hypertension, dyslipidaemia, obesity, gestational diabetes and polycystic ovarian syndrome give a high yield of positive cases who will benefit from early intervention. Furthermore, targeted screening in high risk young subjects (e.g. those with family history) is considered particularly cost-effective due to their high lifetime risk for complications[9].

Figure 1. A proposed flow chart for detection of high risk subjects for diabetes and follow up action



Provided that the assays of glycated haemoglobin (HbA1c) are compatible with international standards, the combined use of fasting plasma glucose and HgA1c can be used effectively to detect people with undiagnosed diabetes[10] (Figure 1). The majority of these subjects with prediabetes or early diabetes will benefit from structured lifestyle modifications including a balanced diet, increased physical activity, reduced consumption of sugar sweetened beverages and snacks, cessation of smoking, stress management, sleep hygiene, avoidance of further gain in body weight and losing 3-5 kg of body weight if overweight/obese[11] (Figure 2). While lifestyle modifications are effective in reducing the risk of diabetes and its complications, it is important to recognise that diabetes is primarily a beta cell disorder and as such, many of these subjects may eventually require some medications for glucose control to preserve the beta cell structure and function[12].

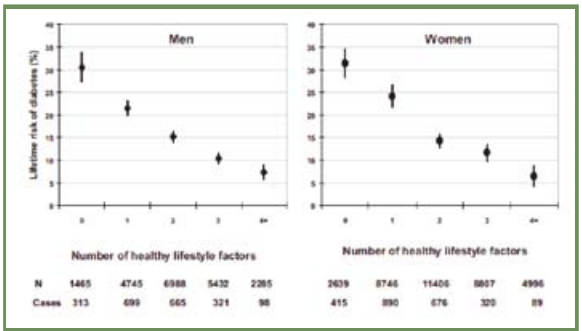


Figure 2. Relationships between baseline lifestyle factors and residual lifetime risk of diabetes at age 45 years in 20,915 men and 36,594 women in the US Physician Health Survey and Women's Health Survey followed up for a mean of 22.6 years. Healthy lifestyle factors included never smoking, moderate alcohol consumption (1 drink per day), regular exercise (2 times per week of vigorous exercise), healthy diet, and normal weight (BMI<25 kg/m2) (Ref 11).

Detection of diabetes and associated risk factors and complications

The biggest challenge in diabetes management is clinical inertia, delayed intervention, frequent default and poor treatment compliance, in part due to the silent and non-urgent nature of the disease[13,14]. These challenges are particularly relevant to young to middle aged people who often have multiple commitments and do not feel the urgency to control these silent conditions resulting in default or delayed intervention[15]. These subjects with young-onset of disease are growing in number and account for 20% of our diabetic populations who are at high risk for complications during their prime of life with enormous impacts on society, individuals and families[16].

Improve diabetes care by reorganising workflow and delegating responsibilities

There are now local and international protocols of diabetes care and recommended treatment targets[17,18]. However to achieve these objectives, changes in the clinic environment and training of paramedical staff are needed to enable the patients to undergo periodic comprehensive assessment for risk stratification. The latter is the first and most important step towards informed decisions and personalised care. From a patient's perspective, regular feedback on individualised risk profiles and trends of treatment targets (notably, HbA1c, blood pressure(BP), LDL-cholesterol, body weight) will raise disease awareness, motivate behavioural changes and reinforce positive changes. From a doctor's perspective, these performance indexes are important in monitoring the effectiveness of intervention and for continuous quality improvement purposes[19,20].

In a recent meta-analysis involving nearly 100,000 patients, quality improvement strategies targeting at the patient and system including patient education, task sharing and case management are associated with the greatest reduction in HbA1c, BP and LDL-cholesterol[21]. These improvements are expected to reduce cardiovascular and renal complications by 20-50% in the long term[22].

Doctor as a mentor, manager and monitor in delivery of diabetes care

Diabetes is common and affects 5-10% of the population in most developed and developing societies[23]. In most surveys, 50% of these affected subjects were undiagnosed[24] and that amongst the diagnosed, only 50% were treated and amongst those treated, less than 10% had attained all 3 ABC treatment goals (A1c<7%, BP<130/80 mmHg and LDL-C<2.6 mmol/l)[25]. In most clinic settings, an average doctor only had 6 minutes of contact time with each of his/her patients[26]. Yet, in patients with diabetes who need to understand the 'what, why and how' of the condition in order to be motivated and learn how to change lifestyle, improve self care, return for regular follow up and often, take long term medications, contact time with regular support, reinforcement and reminders is the key determinant to predict sustained behavioural changes[27].

Thus, despite the amassing body of knowledge regarding the preventable and treatable nature of diabetes, the reality is that changing the behaviour is difficult and remains one of the biggest challenges in translating evidence to practice[28]. Given the growing number of patients and short contact time with doctors, a more affordable and sustainable solution is needed to improve the efficiency and effectiveness of efficacious treatments and strategies, taking incentives and practicality into consideration[29]. In this connection, most of the hospital and primary care systems are not designed to manage the lifelong and pluralistic needs of a middle-aged subject with diabetes over a period of 40 years or more. Amongst these challenges, the systematic collection, integration and communication of health information to both care providers and patients, essential for good clinical practice, is particularly daunting.

During the last two decades, many clinical trials have been conducted to test the efficacy of novel treatments and interventions in controlled settings. While conclusions from some of these studies have been included in treatment guidelines, few experts have highlighted the impact of clinical trial settings on the quality of care. Detailed analysis of these megatrials showed consistent data that patients managed in these controlled settings characterised by the use of a protocol with predefined processes and treatment targets, care coordinator (often a research nurse) and a trial monitor, had the best chances of achieving multiple treatment targets[30].

Leveraging on these observations and with increasing calls by experts to use scientific methods to develop and evaluate multidimensional strategies to improve care in real practice[31], it is indeed feasible for doctors to change their clinic environment and transfer their knowledge to other health care professionals, notably nurses, and use protocols to guide nurses to collect information for doctors to make informed decisions, upon which nurses can be used to reinforce treatment compliance and clarify misconceptions.

Furthermore, it is now recognised that 20-50% of patients with diabetes have negative emotions, including stress, anxiety and depression which may adversely affect treatment compliance and self care. While some of these patients may need pharmacological interventions, many of them will benefit from motivational interviews by nurses and/or empathetic listening and emotional support from their peers[32,33].

Given the complexity of these care protocols (Figure 3) and increasing demands from payers on doctors to report rates of adherence to recommended care processes and attainment of treatment targets within cost affordability[34,35], there is a growing need for doctors to learn how to use management principles and technologies whereby they can leverage the expertise of other co-workers and partners to deliver these care protocols with documentation of intermediate indexes and clinical outcomes.

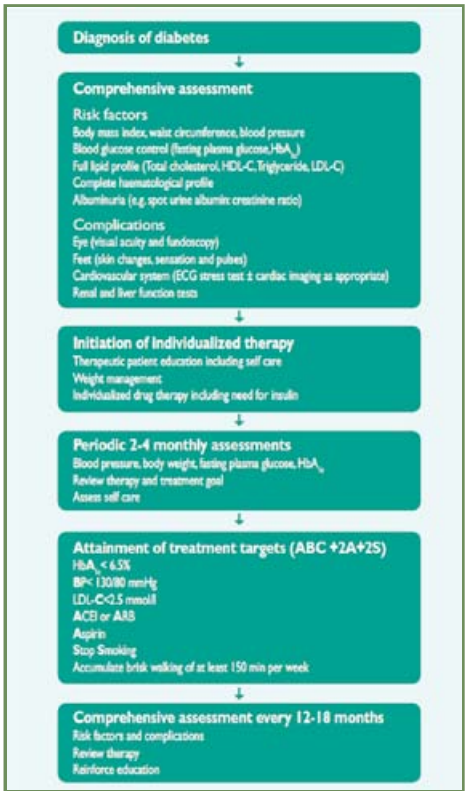


Figure 3. Recommended flow chart in diabetes management by the Western Pacific Declaration on Diabetes (www.wpdd.org).

Using collaborative care and information technology for quality improvement

In 1995, due to limited manpower and large patient volume, the CUHK-PWH Diabetes Care and Research Team developed an integrated care model where we used trained nurses to perform comprehensive assessments including blood and urine tests as well as eye/feet examination, in accordance to international guidelines, for risk stratification every 12-18 months, followed by triage to primary care, non-diabetes specialist and diabetes specialist care[36]. Using this Registry which had enrolled more than 10,000 patients and accrued over 5000 clinical events, we were able to develop and validate a series of risk equations to predict cardiovascular and renal events with 70-90% sensitivity and specificity. In a series of projects, we were also able to use a collaborative approach, augmented by care protocols, to reduce the risk of cardiovascular-renal complications and all-cause deaths in type 2 diabetic patients with or without complications by 50-70%[37,38] (Figure 4).

In 2007, we incorporated these risk equations and care protocols into the web-based disease management programme (Joint Asia Diabetes Evaluation, JADE, Programme) with built in risk engines, care protocols, decisions support and personalised reports to patients and doctors (www.adf.org.hk). Our preliminary analysis showed that 20-40% of patients had significant improvement in ABC targets and psychological well-being after enrolling in the JADE Programme with personalised reports and decision support. Thus, by training a dedicated nurse to collect these information guided by structured templates, who serves as a liaison between doctors and patients, doctors can be relieved of the burden in performing these tasks and concentrate on reviewing the patients' risk profiles, making clinical decisions and supporting co-workers to implement holistic care, in a more efficient and effective manner[39,40] (Figure 5).

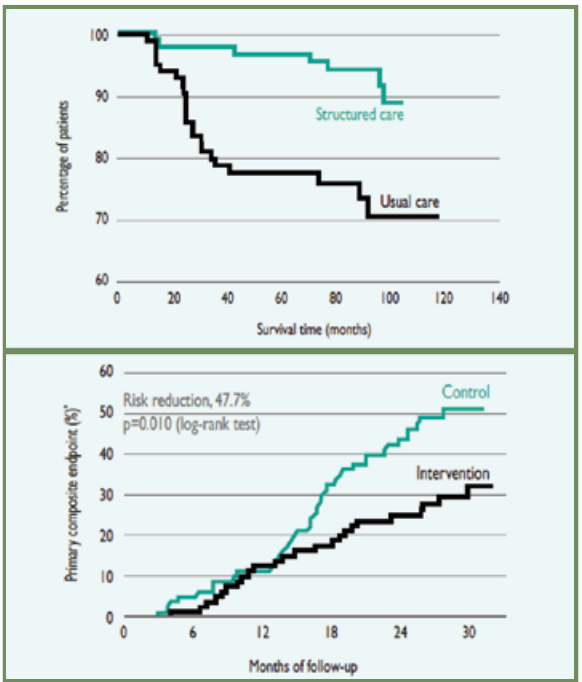


Figure 4. The effects of collaborative care augmented by protocols with predefined processes and treatment targets on clinical outcomes including death and cardiovascular-renal events in Hong Kong Chinese patients 1) with hypertension and type 2 diabetes (Ref 36, upper panel) and 2) with type 2 diabetes and chronic kidney disease (Ref 37, lower panel) (excerpts from www.wpdd.org).

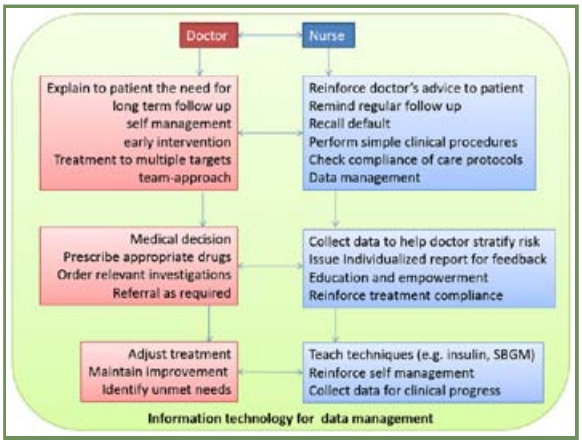


Figure 5. Task sharing between doctors and nurses in quality improvement programme for diabetes care with ongoing monitoring and evaluation.

SBGM-self blood glucose monitoring

Conclusion

Diabetes is a major public health care burden and personal disaster, if not diagnosed, managed or controlled. There are now proven strategies to prevent the onset of diabetes and its complications, which will save life and money in the long term. However due to the non-urgent nature of these silent conditions, these preventive strategies proven to be efficacious in controlled settings are often not implemented in real practice due to reasons such as lack of motivation to change, care fragmentation, lack of mandates and insufficient incentives.

While many parties, including the Government, now recognise the need to use multisectorial strategies including the use of mandates, incentives and audits to create an environment conducive to a healthy lifestyle and practice of preventive medicine[41], doctors are in the prime position to take the first step to empower their subordinates to change the clinic setting, improve the workflow and document these processes and outcomes, which will not only benefit their patients but also bring out the best of their clinical expertise.

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TRADE NAME: AZOREN. PRESENTATION: Azoren 20 mg/5 mg film-coated tablets: White, round, film-coated tablet with "C73" debossed on one side. Azoren 40 mg/5 mg film-coated tablets: Cream, round, film-coated tablet with "C75" debossed on one side. Azoren 40 mg/10 mg film-coated tablets: Brownish-red, round, film-coated tablet with "C77" debossed on one side. INDICATIONS: Treatment of essential hypertension and in patients whose blood pressure is not adequately controlled on olmesartan medoxomil or amlodipine monotherapy. DOSAGE: For adults, the recommended dosage is 1 tablet per day. For more details on dosage & administration, please refer to the full product insert. CONTRAINDICATIONS: Hypersensitivity to the active substances, to dihydropyridine derivatives or to any of the excipients; severe hepatic insufficiency and biliary obstruction; Patients with cardiogenic shock, acute myocardial infarction & unstable angina pectoris. WARNINGS & PRECAUTIONS: Patients with hypovolaemia or sodium depletion; Other conditions with stimulation of the renin-angiotensin-aldosterone system; renovascular hypertension; renal impairment and kidney transplantation; hepatic impairment; hyperkalaemia; concomitant use of lithium; aortic or mitral valve stenosis; obstructive hypertrophic cardiomyopathy; primary aldosteronism; heart failure; ethnic difference possibly because of a higher prevalence of low-renin status in the black hypertensive population. As with any antihypertensive agent, excessive blood pressure decrease in patients with ischaemic heart disease or ischaemic cerebrovascular disease could result in a myocardial infarction or stroke. No studies on the effects on the ability to drive and use machines have been performed. However, it should be borne in mind that dizziness or fatigue may occasionally occur in patients taking antihypertensive therapy. INTERACTIONS: Medicinal products affecting potassium levels; Lithium; NSAIDs; Antacid; CYP3A4 inhibitors; CYP3A4 inducers; Sildenafil. PREGNANCY AND LACTATION: Not recommended during the first trimester of pregnancy and is contraindicated during the second and third trimesters of pregnancy; the use of Azoren during lactation is contraindicated. SIDE EFFECTS: Most commonly observed adverse reactions were: Dizziness; Headaches; Peripheral oedema; Oedema; Pitting oedema; Fatigue; Facial flushing; Abdominal pain. Reference: German SPC (November 2008). LPD Date: 22 October 2009. Date of preparation: MAR2011. Identifier number: AZOR0311.
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The City Gardener

Dr. Jenny LEE

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I like plants in general, but Hong Kong is a city of concrete and construction sites, where any private outdoor space, however tiny, seems to be a luxury. The solution is to create planting space yourself, wherever you may be. True success depends on the type of plants chosen. In Hong Kong, the environment chooses the plants, not us. Let me share with you some of my office plant favourites that look delicate but are in actual fact quite hardy.

African Violet

This is an all-time favourite of many office ladies and there are cheap varieties (down to $10/plant) available in the Flower Market. The trick is to make it flower all year round and that may take some experimenting. I found that they like small pots with just a little amount of soil (about 1/2 cupful), and weekly liquid fertiliser . If given a large pot they tend to spend most of their time expanding roots and refuse to flower. They will flower regularly if given at least 3-4 hours of sunshine each day, but the ambient temperature must be cool, so an air-conditioned room with a south-facing windowsill will be best. Artificial lighting with a small florescent reading light over the plant for most time of the day will be fine too, but less effective. Care must be taken while watering, because any water droplets on the hairy leaves will cause light to refract and burn the leaf. Although I have heard of propagation by seeds, African violets are most conveniently (and without any cost too) propagated by leaf cuttings. Put the stem of a cut leaf into a small bottle of clean water and roots will appear in about 2-3 weeks, followed by tiny green leaves. Transplant this gently into a small pot of soil and it can generate into 3 or 4 new plants, ready to bloom in about 4-5 months' time, from the day of the cutting. I found a special set of plastic pots with a water stand very useful, although a bit plain. They can be bought from an African violet specialty upstairs shop at the Flower Market. All you need now is to find a friend with a nice African violet plant with the kind of flowers you like, and ask for the donation of a leaf.

Purple Clover - 紫花酢醬草 (Oxalis corymbosa)

I bought my purple clover while still in medical school, and that was two decades ago. It is still growing and has propagated (by me) to the homes of many of my friends and colleagues. Because my first plant came with a tag "from Holland", and it already cost over $20 in those days, I thought it should be a very delicate plant. However, it remained weak throughout its first years and often lost all the leaves while placed indoors in an air-conditioned office in a shaded corner. One day it dawned on me that it looked like the wild clover in my backyard except for the size of its leaves and colour. It has flourished since then in a pot and on the ground without much care and fertilisers but with plenty of sun. The ones on my windowsill in the office are also doing well, but it will need at least bright indirect light from the window. The "roots" or underground stems are able to remain dormant for many weeks even without any leaves, so do not throw it away too soon. It prefers soil on the dry side, and requires very little if any fertiliser (it is a wild plant). There are small bell-shaped pink flowers all year long that usually last only one day. I twist off the stems of withered leaves and flowers just to be tidy. This does not harm the plant. With time the underground stems/ roots will multiply and you will have to replant or give them away. The purple leaves that come in different shades and patterns close up at night naturally like an umbrella, so do not worry about that.

Orchids

Orchids are particularly popular around the Chinese New Year. Apart from the traditional peach blossoms they are nearly the only other type of flowering plant I will get in the Flower Market around the CNY. Many of my friends did not know that they are perennial plants and would throw them away after the flowers are gone. Given minimal care and spare, orchids are actually one of the easiest to care for flowering plants I know of. All one needs to do is to cut down the flowering stem after the last flowers have withered, get some new moss (from any plant shop, but try to get the type from New Zealand), cut off the old dried up roots (if you are not sure, skip this step) and replant the orchid in the same pot. For lazy people who do not want to do "ramet" (分株) or spend much time in tidying up an overgrown plant, the best orchids will be the "butterfly orchid". The Butterfly orchid has only a few very stationary big leaves per plant (occasionally wiping to clean the surface for good photosynthesis will be deeply appreciated by your orchid). There may be 2-3 new leaves per year and 1 or 2 old leaves may dry up at the bottom after the flowering, but otherwise they do not change much throughout the year. If kept indoors in a controlled environment, they will require only 1-2 watering per week (try to keep the moss moist on most days). Being flowering plants with very slow metabolism I usually give them very small infrequent "meals" of fertilisers in pellets (mine are grey), about 5-6 dispersed on the moss every 2-3 months. I use inorganic fertilisers because the organic ones will get mouldy and smell in the moist moss. The pellets will release the fertilisers into the moss when being watered. By the end of 9 months there should be 1 to 2 new flowering shoots, ready to bloom again for the CNY. Orchids do best if given 3-4 hours of diffuse sunlight or daylight per day. My DOM in my department took several appalling looking orchids back to her office last Spring. With the minimal care described above she has beautiful blooms this CNY. The leaves will be burned by direct hot sunlight in the summer so please take care. Again orchids are very tough - I have resurrected orchids even at the stage when there was only 1 leaf left, so do not throw them away prematurely.

Hong Kong climate and your plants

Hong Kong has a very hot and humid summer, but both the purple clover and orchids can survive outdoors very well. My clover can survive both the summer sun and rain very well. They may "shrink" a bit in the winter but they will revive in spring. I hang my butterfly orchids under a tree, with some protection from the direct summer sunlight. Although they look delicate they have survived Black rain and typhoon no. 10 with no damage. Check the moss for rotting roots if the rainfall is constant. However, these meaty roots can rot if there is too much moisture around. With all plants, rotate the pot periodically if the light source is always from one side (e.g. a window). Otherwise, you may end up with a "torticollis" plant!

Enjoy!

Dermatological Quiz

Dr. Ka-ho LAU

MBBS(HK), FRCP(Glasg, Edin), FHKCP, FHKAM(Med)

Private dermatologist

Dr. Ka-ho LAU

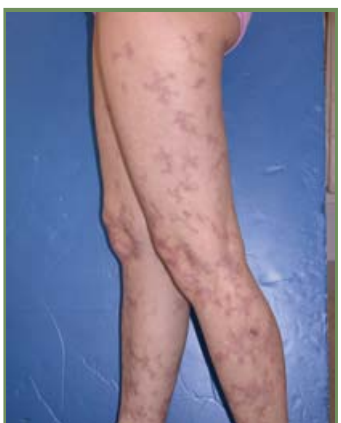

Fig.1: Skin lesions at lower limbs

This 55-year-old man noticed these net-like eruptions at his lower limbs for a few months which were persistent but asymptomatic. On further questioning, he complained of multiple joint pain with active arthritis at his fingers symmetrically.

Questions:

1. What is your clinical diagnosis or differential diagnoses?
2. How will you manage this man?

(See P.36 for answers)

Medical Nutrition Therapy in Type 2 Diabetes

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Type 2 diabetes results from a progressive insulin secretory defect on the background of insulin resistance[1], which is associated with obesity; and Chinese with body mass index ≥ 25 kg/m2 have an increased risk of type 2 diabetes[2]. Medical nutrition therapy (MNT) is commonly known as the groundwork in diabetes management and it has been well documented that MNT can improve glycaemic control, enhance clinical and metabolic outcomes, and reduce the hospitalisation rates[3,4,5,6]. MNT has been shown to reduce glycated haemoglobin (HbAlc) by an average of ~1% to 2%[3, 7].

MNT is effective at any time in the disease process but it appears to have its greatest effect in lowering HbAlc at the initial stage of diagnosis[3]. Outcomes of the MNT interventions are evident by 6 weeks to 3 months and on-going evaluations should be done. Type 2 diabetes is a progressive disease where the β-cell function may deteriorate over time. Therefore, if no clinical improvement in glycaemic control is evident upon follow up, inclusion or adjustment of blood glucose lowering medication(s), including insulin, may be needed in combination with MNT to achieve the goals[3]. Thus, at least one follow-up appointment is recommended annually to diabetic patients to reinforce lifestyle changes, as well as to evaluate and monitor outcomes.

Although following a diet is commonly known as one of the most challenging parts of diabetes management, physicians may not have access to a registered dietitian (RD) at their clinics to provide the necessary support for diabetic patients. Given the importance of MNT in diabetes management, this article aims to provide recommendations for enhancing nutrition care for type 2 diabetic patients.

Maintaining cooperation approach

A consistent and coordinated multidisciplinary approach by the physician, dietitian and nurses can enhance the patient's cooperation and compliance to MNT. Though an appreciation of the dietary management of diabetes by a physician is substantial, detailed instructions of MNT should be delivered by a dietitian. It is strongly recommended by the American Diabetes Association, which stated in the Standards of Medical Care that " individuals who have prediabetes or diabetes should receive individualised MNT as needed to achieve treatment goals, preferably provided by a registered dietitian (RD) familiar with the components of diabetes MNT[1]".

Dietitians are practising in different sectors, including private practices, community services, Department of Health clinics, and hospitals under the Hospital Authority. A list of accredited dietitians in Hong Kong can be found on the website of the Hong Kong Dietitians Association (http://www.hkda.com.hk/). Under normal circumstances, a medical doctor's referral is required for patients to consult dietitians in the Department of Health clinics and HA hospitals.

Dietitians will conduct a detailed nutritional assessment based on the patient's anthropometric measurements, medical history, medications, laboratory results, diet history, and social history. Dietitians will then be able to provide individualised MNT including prescribing meal plans tailored to patients' needs. Patients' progresses and treatment outcomes are documented and reported to the referral sources. Constant reinforcement of dietary advice usually results in enhanced cooperation and better blood sugar control.

Meal Planning

The diet for people with type 2 diabetes is qualitatively the same as that of the non-diabetic counterparts (Figure 1. Food Guide Pyramid). There is no generic way to define a 'diabetic diet' and to prescribe a meal plan fit for all diabetic patients. On the contrary, MNT and meal planning should be individualised by taking into consideration the individual's age, type and duration of diabetes, concurrent medications, treatment goals, personal values, food preferences, culture, lifestyle, economic status, activity levels, abilities, and readiness to change[7].

Figure 1. Food Guide Pyramid [10]

Healthy eating, body weight control and regular physical activities are important objectives in people with type 2 diabetes. Since an estimated 80 to 90% of people with type 2 diabetes are overweight or obese[7], it is vital to encourage any degree of weight loss.

A modest weight loss of 5 to 10% of initial body weight can substantially improve insulin sensitivity and glycaemic control, as well as to relieve hypertension and dyslipidaemia in people with type 2 diabetes[8]. Increased physical activity and overall calorie reduction will decrease body weight. A reduction in total energy intake and/or increased energy expenditure, leading to a total of about 500 calories energy deficit per day should result in a weight loss of 0.5kg per week. Dietitians can help patients to identify and minimise sources of hidden energy intakes, educate them to make healthy food choices, and assist them in meal planning.

Carbohydrates

Carbohydrate foods have a direct impact on the blood glucose levels. Numerous studies have shown that equivalent carbohydrate amounts of sugars and starches produce similar responses in glycaemia[9].

An initial MNT that focuses on carbohydrate control and meal timing consistency may be most important for glucose control. Therefore, control of portion sizes is an important message to convey to patients. It is recommended that carbohydrate foods should contribute to 45-60% of total daily energy intake[7].

A low carbohydrate diet is not ideal for weight loss. Rather, the key issue for weight control is overall caloric reduction. Moreover, restricting carbohydrate intake to less than 130g per day is not recommended as glucose is the primary fuel for the brain and central nervous system [1].

Patients are recommended to eat a controlled amount of carbohydrate foods consistently at main meals and snack times. Thus, dietitian will teach patients about carbohydrate exchanges and how to read food labels. Table 1 shows a variety of carbohydrate foods in different portion sizes that all contain 10g of total carbohydrate.

Table 1. Carbohydrate choices: 10g carbohydrate serving sizes[10]:

	Food	Serving size
Grains, breads, cereals	Rice	1/5 bowl* or 1 heaped table spoon
	Bread	1/2 slice (large) or 1 slice (small)
	Oatmeal	2 level table spoons (raw) or 1/2 bowl* (cooked)
	Cornflakes	1/4 bowl*
	Weetabix	1 piece
Milk or alternatives	Skimmed milk	1 glass (250ml)
	Plain yoghurt	1 cup (150ml)
	High calcium soy milk	1 class (250ml)
Fruits	Apple/ orange/ banana	1/2 pieces
	Grapes	5 pieces (large) or 10 pieces (small)
	Blueberries	1/2 cup

Note: * bowl 300ml volume

Glycaemic Index

The Glycaemic index (GI) classifies carbohydrate foods according to their impact on blood glucose levels (high: GI >70, medium: GI 55-70, low: GI <55). Consuming a low-GI diet was shown to sustain improvements in glycaemic control and HDL-cholesterol compared with a high cereal fibre diet over 6 months[11]. Low GI foods include barley, pasta, chapatti, beans, nuts, lentils, milk, yogurt, and apples[12].

In practice, it is recommended that people with diabetes should have high fibre, low GI carbohydrate food at each meal. However, there are many factors that may affect blood glucose surge, e.g. the ripeness of the food, degree of cooking and processing, and physical form of the food. It is advised to check pre- and post-meal blood glucose levels to assess the impact of particular meals and to determine if choosing lower GI alternatives can improve blood glucose levels.

Dietary Fibre

It is recommended to consume 25-30 g of dietary fibre from a wide variety of foods (14 g fibre per 1000kcal) with special emphasis on soluble fibre (7-13 g)[3] (Table 2. Examples of fibre and soluble fibre content of common food). Evidence suggests that the additional of soluble fibre (e.g. egg plant, okra, oat products, beans, psyllium, and barley) slows gastric emptying and delays the absorption of glucose in the small intestine and thus improves post-meal blood glucose control[13].

Moreover, diets high in total and soluble fibre are shown to further reduce total cholesterol by 2% to 3% and LDL cholesterol up to 7%[14]. Thus, carbohydrate foods which are rich in fibre and have a low energy density are the basis of an optimal dietary plan.

Table 2. Total fibre content and soluble fibre of common food:

Food	Total fibre content (g)	Soluble fibre content (g)
Oatmeal 1/4 cup (35g)	3.5	1.5
Apple (1 small)	2.8	1
Banana (1 small)	2.2	0.6
Orange (1 small)	2.9	1.8
Broccoli (1/2 cup) (cooked)	2.4	1.2
Carrot (1/2 cup) (cooked)	2.0	1.1
Spinach (1/2 cup) (cooked)	1.6	0.5
Kidney beans (1/2 cup) (cooked)	7.9	2.0

Source: Harvard University Health Services. Fibre Content of Foods in Common Portions. May 2004.

Dietary Fat

As people with diabetes have a 2 to 3 times higher risk of having coronary artery disease in comparing to non-diabetics, it is recommended that dietary fat should contribute to 20-30% of total daily energy intake, with total cholesterol less than 200 mg/d, saturated fat <7% of total calories, and minimal trans fat intake[7,15]. This is beneficial for lipid profile control and weight control.

The National Cholesterol Education Program (NCEP) recommends that monounsaturated fats can range up to 20% of total calories intake[15]. It can be found in olive

oil, canola oil, nuts, and avocado. Omega-3 fatty acids like fish oil and flaxseed oil have been shown to lower triglyceride levels and inhibit platelet aggregation. Thus, it is generally recommended to consume at least 2 servings of fatty fish per week.

Patients are advised to avoid full fat dairy products, processed/fatty meat and poultry skin, and limit oil used in cooking. Patients are also recommended to choose lower fat dairy products and ask the butcher for a lean cut and have the skin removed when shopping for meats. Patients will also be educated that there are hidden fats in some carbohydrate-containing foods (e.g. butter in pineapple bun / cake, palm oil in instant noodles, deep-fried foods etc.), and their consumption can lead to unintended weight gain and increased LDL-cholesterol level.

Dietary Protein

Patients with type 2 diabetes with normal renal function are advised to have protein intake contributing to 15-20% of the daily energy intake, which aligns with the recommendation for the general population[3]. Though protein has a very little effect on blood glucose levels and an acute effect on insulin secretion[3], patients are advised to take the fat content and cooking method into consideration when consuming protein-rich foods. A vegetable source of proteins (e.g. beans and pulses, tofu) is very low in fat.

Sugars

Added sucrose, like all carbohydrates, raises the blood glucose. Thus, there is no need to eliminate it completely from the diet, and could be included as part of the meal plan for diabetic patients (up to 10% of total daily energy intakes[7]). However, alternative sweeteners may still have a role in diabetes and body weight management. Suitable sweeteners include aspartame, saccharin, acesulfame potassium, sucralose and Rebaudioside A Erythritol. The inclusion of sugar alcohols e.g. sorbitol, is not recommended as they contribute 2 kcal/g and are commonly found in diabetic chocolate which is high in energy density and offers no advantages in managing weight loss.

Alcohol

Alcohol contributes a significant amount of calories (7 kcal/g) in a diet. Moreover, many people with type 2 diabetes are overweight or obese, hence alcohol intake for diabetic patients should be minimised. The general recommendation for alcohol intake is ≤ 2 units per day for men and ≤ 1 unit per day for women (1 unit: 350 ml beer, 150 ml wine, 45 ml spirits)[10]. Should patients choose to have alcohol, they are advised not to drink on an empty stomach since it may lead to hypoglycaemic effects.

Physical activity

Increasing physical activity improves metabolic control and reduces body weight. Low level aerobic exercises, such as brisk walking for half an hour per day and resistance training, are shown to improve insulin sensitivity, result in weight loss, increase the feeling of well-being, and improve blood pressure and the lipid profiles[1,3]. Patients are generally advised to do more than 150 minutes of moderate intensity physical activity per week (e.g. walking).

Conclusion

Since the outcomes of the MNT interventions are evident, MNT should be an integral component of diabetes prevention, management, and self-management education. For people with type 2 diabetes, increased physical activity and substitution of energy-dense food sources (e.g. foods high in dietary fat and sugar) with carbohydrate foods rich in fibre and low energy density will often lead to better diabetic control.

Dietitian is one of the key health care team members in aiding patients' diabetic control. Patients should receive MNT by dietitians regularly. Consistent reinforcement of dietary advice by dietitians as well as other members of the multidisciplinary team may motivate patients to make sustainable changes.

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A short note about medical nutrition therapy for Type 1 and Gestational Diabetes

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Medical nutrition therapy for Type 1 diabetes

Type 1 diabetes requires a proper dietary management is essential, as well as type 2 diabetes, gestational diabetes and glucose intolerance. The diet should be adjusted in calories to achieve and maintain a desirable body weight and near normal blood glucose levels. Dietary management is also directed at reducing the risks and minimising the complications of diabetes.

The American Diabetes Guideline suggests adequate amount of calories to maintain a growth pattern, and vitamins and minerals for good overall health. Carbohydrate, protein, and fat should be balanced to maintain optimal glucose levels. Spacing meals and snacks should be taken throughout the day to balance the activity of the insulin action of the individual. To avoid hypoglycaemia, usually 6 to 7 feedings a day are needed to control the blood glucose level and meet the nutrient requirements. Carbohydrate needs to be tailored to the patient in order to achieve a good blood glucose control and normal triglycerides. Protein recommendations are 10% to 20% of the total calories, or 0.8g/kg/day for adults according to the Recommended Dietary Allowance (RDA). Fat is ideally less than 30% of the total calories, however, actual intakes are required to be modified, as for some individuals, this may be too low. Polyunsaturated fats are suggested from 6% to 8%, saturated fats are less than 10%, and monounsaturated fats are from 6% to 8%. Cholesterol is recommended to be consumed at no more than 300 mg/day.[1-6]

Medical nutrition therapy for gestational diabetes mellitus (GDM)

The diet for pregnant women with diabetes usually is a healthful, well-balanced eating plan aimed at achieving normoglycaemia and meeting the nutritional needs of the foetus and mother during the pregnancy. Consistency in meal and snack timings as well as consuming a variety of nutrients offered through individualised meal planning should be emphasised, as this can help to promote normal glycaemia in pregnancy and improve maternal and foetal outcomes.

Calorie requirements for GDM

Calorie consumption should be calculated to promote adequate weight gain and foetal-placental growth. The American Diabetes Association (ADA) recommends an intake of 2,000 to 2,500 kcal/day, which is based on 35 kcal/kg of present pregnancy weight, but these recommendations should be adjusted for each patient based on weight gain and blood sugar control.[7]

A few studies showed that the ADA recommendations led to significant weight gain and elevated postprandial blood sugar, which required insulin therapy in about 50% of women. Based on these findings, the researchers recommended calculating energy intake based on 30 kcal/kg of present pregnancy weight for normal-weight women, 24 kcal/kg for overweight women, and 12 kcal/kg for morbidly obese women.[8,9]

A study of obese women with GDM showed that restricting calories to about 1,800/day improved their glycaemic control and still promoted foetal and placental development.[10] However, consuming fewer than 1,800 kcal/day is not recommended because of the risk of ketonaemia and ketonuria, which are associated with childhood neurobehavioural complications.[11]

Macronutrient requirements for GDM

Medical nutrition therapy with an emphasis on controlling carbohydrate intake is considered the first-line therapy and often shows efficacy for normalising blood glucose levels in GDM patients. Besides, a lower carbohydrate loading in the morning and at night is intended to improve blood sugar regulation throughout the day and prevent hyperglycaemia caused by the nocturnal activity of steroid hormones such as cortisol along with other placental hormones that promote insulin resistance.[12,13] The use of protein-rich foods helps to blunt the effects of the carbohydrates on blood glucose. These foods also provide calories without increasing the carbohydrate content of meals. Based on the ADA recommendations, the macronutrients in pregnancy and diabetes are 50% to 60% of daily calories from carbohydrates (complex, high fibre), 10% to 20% from protein, and 25% to 30% from fat (less than 10% saturated).[13]

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Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
		1	* HKMA Shatin Doctors Network - Diabetic Nephropathy Management 123 2	* MPS Workshop – Mastering Shared Decision Making 3	* Blood Pressure Control in Chronic Kidney Disease 4	5
* HKMA Swimming Gala 2013 * HKMA Tennis Tournament 2013 6	* Fournier's Gangrene 7	* HKMA Kowloon West Community Network - Management of Type 2 Diabetic Patients with Comorbidities * FMSHK Officers' Meeting * HKMA Council Meeting 8	* HKMA Central, Western & Southern Community Network - Third Session of the Certificate Course on Dermatology 2013 - Eczema and Beyond * Hong Kong Neurosurgical Society Monthly Academic Meeting –Recent advances in paediatric neuro-oncology 9	* HKMA New Territories West Community Network - Advance Prevention on Measles, Mumps, Rubella and Varicella in the Community * HKMA Hong Kong East Community Network - Update on Treatment of Heavy Menstrual Bleeding * HKMA Structured CME Programme with Hong Kong Sanatorium & Hospital Year 2013 – Update of IBS * MPS Workshop - Mastering Your Risk 10	11	* 15th Beijing/Hong Kong Medical Exchange Conference 12
* 15th Beijing/Hong Kong Medical Exchange Conference * HKMA Tennis Tournament 2013 13	14	* HKMA Tai Po Community Network – ESC/ESH Guidelines: Focus on Vasodilator Beta-blockers 15	* HKMA Central, Western & Southern Community Network - A Modern Understanding in the Management of Acute Pain 16	* MPS Workshop – Mastering Shared Decision Making * FMSHK Executive Committee Meeting 17	18	* HKMA CME – Seminar on Infectious Diseases * HKMA Kowloon East Community Network – Final Session of the CME Course for Health Personnel 2013: Update on Childhood Asthma Management * HKMA CME – Refresher Course for Health Care Providers 2013/2014 19
* HKMA Tennis Tournament 2013 20	21	* HKMA Tai Po Community Network – Primary Prevention of Allergies: When, Who and How? * MPS Workshop – Mastering Adverse Outcomes 22	* HKMA Central, Western & Southern Community Network - Fourth Session of the Certificate Course on Dermatology 2013 - Recent Advance in Cosmetic Dermatology 23	* HKMA Hong Kong East Community Network - Management of Atopic Dermatitis * HKMA Kowloon East Community Network - Management of Atopic Dermatits * MPS Workshop – Mastering Difficult Interactions with Patients * FMSHK Foundation Committee Meeting 24	25	* MPS Workshop – Mastering Your Risk * The 4th GHM Sports Meet 26
* The 4th GHM Sports Meet * HKMA Tennis Tournament 2013 27	28	29	30	* HKMACME-New concept of stroke management 31		

Date / Time	Function	Enquiry / Remarks
2 WED 1:00 pm	**HKMA Shatin Doctors Network - Diabetic Nephropathy Management 123** Organiser: HKMA Shatin Doctors Network, Chairman: Dr. MAK Wing Kin, Speaker: Dr. HO Chung Ping, MH, JP, Venue: Star Seafood Floating Restaurant, 55-57 Tai Chung Kiu Road, Sha Tin, N.T.	Miss Queenie TSANG Tel.: 2964 2966 1 CME point
3 THU 6:30 pm	**MPS Workshop – Mastering Shared Decision Making** Organisers: Hong Kong Medical Association & Medical Protection Society, Speaker: Dr. Fung Shu Yan, Anthony, Venue: HKMA Dr. Li Shu Pui Professional Education Centre, 2/F, Chinese Club Building, 21-22 Connaught Road, Central, Hong Kong	HKMA CME Dept Tel: 2527 8452 2.5 CME points
4 FRI 1:00 pm	**Blood Pressure Control in Chronic Kidney Disease** Organiser: HKMA Kowloon City Community Network, Speaker: Dr. Ho Chung Ping, Venue: Spotlight Recreation Club - Hung Hom	Ms. Candice TONG Tel: 2527 8285 1 CME point
6 SUN 1:00 pm	**HKMA Swimming Gala 2013** Organiser: The Hong Kong Medical Association, Chairman: Dr. IP Man Ho, Venue: HKPU Michael Clinton Swimming Pool	Mr. Andie HO Tel: 2527 8285
8:00 pm	**HKMA Tennis Tournament 2013** Organiser: The Hong Kong Medical Association, Chairman: Dr. CHIN Chu Wah, Venue: Kowloon Tong Club	Ms. Dorothy KWOK Tel: 2527 8285
7 MON 7:30 pm	**Fournier's Gangrene** Organiser: Hong Kong Urological Association, Chairman: Dr. NGAI Ho Yin, Speaker: Dr. Terrilyn PUN, Venue: Multi-disciplinary Simulation and Skills Centre, 4/F, Block F, QEH	Ms. Tammy HUNG Tel: 9609 6064 1 CME point
8 TUE 1:00 pm	**HKMA Kowloon West Community Network - Management of Type 2 Diabetic Patients with Comorbidities** Organiser: HKMA Kowloon West Community Network, Speaker: Dr. CHAN Wing Bun, Venue: Panda Hotel, Tsuen Wan	Miss Hana YEUNG Tel: 2527 8285
8:00 pm	**FMSHK Officers' Meeting** Organiser: The Federation of Medical Societies of Hong Kong, Venue: Gallop, 2/F, Hong Kong Jockey Club Club House, Shan Kwong Road, Happy Valley, Hong Kong	Ms. Nancy CHAN Tel: 2527 8898
8:00 pm	**HKMA Council Meeting** Organiser: The Hong Kong Medical Association, Chairman: Dr. TSE Hung Hing, Venue: HKMA Head Office (5/F, Duke of Windsor Social Service Building, 15 Hennessy Road, Hong Kong)	Ms. Christine WONG Tel: 2527 8285
9 WED 1:00 pm	**HKMA Central, Western & Southern Community Network - Third Session of the Certificate Course on Dermatology 2013 - Eczema and Beyond** Organiser: HKMA Central, Western & Southern Community Network, Speaker: Dr. SHIH Tai Cho, Venue: Central	Miss Hana YEUNG Tel: 2527 8285 1 CME point
7:30 am	**Hong Kong Neurosurgical Society Monthly Academic Meeting –Recent advances in paediatric neuro-oncology** Organiser: Hong Kong Neurosurgical Society, Chairman: Dr. Gilberto Leung, Speaker: Prof. Godfrey CF CHAN, Venue: Seminar Room, Ground Floor, Block A, Queen Elizabeth Hospital	Dr. Gilberto LEUNG Tel: 2255 3368 1.5 CME points
10 THU 1:00 pm	**HKMA New Territories West Community Network - Advance Prevention on Measles, Mumps, Rubella and Varicella in the Community** Organiser: HKMA New Territories West Community Network, Speaker: Dr. SIT Sou Chi, Venue: Maxim's Palace Chinese Restaurant, Tuen Mun	Ms. Vinki CHEUNG Tel.: 3189 8734 1 CME point
1:00 pm	**HKMA Hong Kong East Community Network - Update on Treatment of Heavy Menstrual Bleeding** Organiser: HKMA Hong Kong East Community Network, Chairman: Dr. YIP Yuk Pang, Kenneth, Speaker: Dr. YEO Lee Kung, Evelyn, Venue: HKMA Head Office (5/F., Duke of Windsor Social Service Building, 15 Hennessy Road, Hong Kong)	Ms. Candice TONG Tel: 2527 8285
2:00 pm	**HKMA Structured CME Programme with Hong Kong Sanatorium & Hospital Year 2013 – Update of IBS** Organisers: Hong Kong Medical Association & Hong Kong Sanatorium & Hospital, Speaker: Dr. Chan On On, Annie, Venue: Function Room A, HKMA Dr. Li Shu Pui Professional Education Centre, 2/F, Chinese Club Building, 21-22 Connaught Road Central, Hong Kong	HKMA CME Dept Tel: 2527 8452 1 CME point
6:30 pm	**MPS Workshop - Mastering Your Risk** Organisesr: Hong Kong Medical Association & Medical Protection Society, Speaker: Dr. Hau Kwun Cheung, Venue: HKMA Dr. Li Shu Pui Professional Education Centre, 2/F, Chinese Club Building, 21-22 Connaught Road, Central, Hong Kong	HKMA CME Dept Tel: 2527 8452 2.5 CME points
12 SAT 1:00 pm *(13)*	**15th Beijing/Hong Kong Medical Exchange Conference** Organiser: The Hong Kong Medical Association, Chairman: Dr. TSE Hung Hing, Venue: Changsha, Hunan	Ms. Candy YUEN Tel: 2527 8285 8 CME points
13 SUN 8:00 pm	**HKMA Tennis Tournament 2013** Organiser: The Hong Kong Medical Association, Chairman: Dr. CHIN Chu Wah, Venue: Kowloon Tong Club	Ms. Dorothy KWOK Tel: 2527 8285
15 TUE 1:45 pm	**HKMA Tai Po Community Network – ESC/ESH Guidelines: Focus on Vasodilator Beta-blockers** Organiser: HKMA Tai Po Community Network, Speaker: Dr. KWOK Miu Fong, Jennifer, Venue: Chiu Chow Garden Restaurant, Tai Po	Mr. Andy LAW Tel.: 9133 7281 1 CME point
16 WED 1:00 pm	**HKMA Central, Western & Southern Community Network - A Modern Understanding in the Management of Acute Pain** Organiser: HKMA Central, Western & Southern Community Network, Speaker: Dr. Wong Kar Fai, Richard, Venue: HKMA Central Premises, Dr. Li Shu Pui Professional Education Centre, 2/F, Chinese Club Building, 21-22 Connaught Road Central, Hong Kong	Ms. Hana Tel: 2527 8285 1 CME point
17 THU 6:30 pm	**MPS Workshop – Mastering Shared Decision Making** Organisers: Hong Kong Medical Association & Medical Protection Society, Speaker: Dr. Fung Shu Yan, Anthony, Venue: Eaton Hotel	HKMA CME Dept Tel: 2527 8452 2.5 CME points
8:00 pm	**FMSHK Executive Committee Meeting** Organiser: The Federation of Medical Societies of Hong Kong, Venue: Council Chamber, 4/F, Duke of Windsor Social Service Building, 15 Hennessy Road, Wanchai, Hong Kong	Ms. Nancy CHAN Tel: 2527 8898
19 SAT 1:30 pm	**HKMA CME – Seminar on Infectious Diseases** Organisers: Hong Kong Medical Association, HK Society for Infectious Diseases, Princess Margaret Hospital & Infectious Disease Centre, Speakers: Dr. LUK Chi Kong, David, Dr. KWAN Chi Keung, Dr. LUNG, David Christopher & Dr. SO Man Kit, Thomas, Venue: Lecture theatre, 7/F, Block H, Princess Margaret Hospital, 2-10, Princess Margaret Hospital Road, Lai Chi Kok, Kowloon	HKMA CME Dept Tel: 2527 8452 2.5 CME points
1:30 pm	**HKMA Kowloon East Community Network – Final Session of the CME Course for Health Personnel 2013: Update on Childhood Asthma Management** Organiser: HKMA Kowloon East Community Network, Chairman: Dr. LEUNG Man Fuk, Speaker: Dr. CHIU Wa Keung, Venue: Lecture Theatre, G/F, Block P, United Christian Hospital, 130 Hip Wo Street, Kwun Tong, Kowloon	Ms. Cordy WONG Tel.: 3513 3087 1.5 CME points

Calendar of Events

Date / Time	Function	Enquiry / Remarks
19 SAT 2:15 pm	**HKMA CME – Refresher Course for Health Care Providers 2013/2014** Organisers: The Hong Kong Medical Association, HK College of Family Physicians & Our Lady of Maryknoll Hospital, Speaker: Dr. Cheung Wing I, Veronica, Venue: Training Room II, 1/F, OPD Block, Our Lady of Maryknoll Hospital, 118 Shatin Pass Road, Wong Tai Sin, Kowloon	Ms. Clara TSANG Tel: 2354 2440 2 CME points
20 SUN 8:00 pm	**HKMA Tennis Tournament 2013** Organiser: The Hong Kong Medical Association, Chairman: Dr. CHIN Chu Wah, Venue: Kowloon Tong Club	Ms. Dorothy KWOK Tel: 2527 8285
22 TUE 1:00 pm	**HKMA Tai Po Community Network – Primary Prevention of Allergies: When, Who and How?** Organiser: HKMA Tai Po Community Network, Speaker: Prof. LEUNG Tin Fan, Venue: Chiu Chow Garden Restaurant, Tai Po	Ms. Abi LI Tel.: 8100 6509 1 CME point
6:30 pm	**MPS Workshop – Mastering Adverse Outcomes** Organisers: Hong Kong Medical Association & Medical Protection Society, Speaker: Dr. Leung Kwok Ling, Ares, Venue: HKMA Dr. Li Shu Pui Professional Education Centre, 2/F, Chinese Club Building, 21-22 Connaught Road, Central, Hong Kong	HKMA CME Dept Tel: 2527 8452 2.5 CME points
23 WED 1:00 pm	**HKMA Central, Western & Southern Community Network - Fourth Session of the Certificate Course on Dermatology 2013 - Recent Advance in Cosmetic Dermatology** Organiser: HKMA Central, Western & Southern Community Network, Speaker: Dr. CHAN Hin Lee, Henry, Venue: Central	Miss Hana YEUNG Tel: 2527 8285 1 CME point
24 THU 1:00 pm	**HKMA Hong Kong East Community Network - Management of Atopic Dermatitis** Organiser: HKMA Hong Kong East Community Network, Speaker: Dr. CHAN Tak Yan, Norman, Venue: HKMA Head Office	Ms. Candice TONG Tel: 2527 8285 1 CME point
1:00 pm	**HKMA Kowloon East Community Network - Management of Atopic Dermatits** Organiser: HKMA Kowloon East Community Network, Speaker: Dr. LUK Chi Kong, David, Venue: Lei Garden Restaurant, Kwun Tong	Miss Hana YEUNG Tel: 2527 8285 1 CME point
6:30 pm	**MPS Workshop – Mastering Difficult Interactions with Patients** Organisers: Hong Kong Medical Association & Medical Protection Society, Speaker: Dr. Cheng Ngai Shing, Justin, Venue: Eaton Hotel	HKMA CME Dept Tel: 2527 8452 2.5 CME points
8:00 pm	**FMSHK Foundation Committee Meeting** Organiser: The Federation of Medical Societies of Hong Kong, Venue: Council Chamber, 4/F, Duke of Windsor Social Service Building, 15 Hennessy Road, Wanchai, Hong Kong	Ms. Nancy CHAN Tel: 2527 8898
26 SAT 2:30 pm	**MPS Workshop – Mastering Your Risk** Organisers: Hong Kong Medical Association & Medical Protection Society, Speaker: Dr. Lee Wai Hung, Danny, Venue: Central	HKMA CME Dept Tel: 2527 8452 2.5 CME points
(27)	**The 4th GHM Sports Meet** Organiser: Macau Chinese Medical Association, Chairman: Dr. TSE Hung Hing, Venue: Macau	Miss Nadia HO Tel: 2527 8285
27 SUN 8:00 pm	**HKMA Tennis Tournament 2013** Organiser: The Hong Kong Medical Association, Chairman: Dr. CHIN Chu Wah, Venue: Kowloon Tong Club	Ms. Dorothy KWOK Tel: 2527 8285
31 THU 1:00 pm	**HKMACME-New concept of stroke management** Organiser: Hong Kong Medical Association, Speaker: Dr. PANG Ka Hung, Peter, Venue: HKMA Dr. LI Shu Pui Professional Education Centre, 2/F. Chinese Club Building, 21-22 Connaught Road Central, Hong Kong	HKMA CME Dept Tel: 2527 8452 1 CME point

Federation News

Public talk on Hypertension

On 14 July 2013, a public talk on hypertension was held at the Federation's Lecture Hall attended by over 70 participants. Aligned with the WHO theme, Hypertension, the Foundation is privileged to organise this educational event on the global health issue. The first speaker, Dr. Ben FONG, Specialist in Community Medicine, delivered a talk on the prevention and treatment of hypertension. The second speaker, Dr. Ngai Pang WONG, Specialist in Endocrinology, Diabetes and Metabolism, delivered a talk on the latest update on hypertensive treatment of diabetes mellitus patients.

The participants' attentiveness and active questioning and the informative feedbacks from our speakers helped to complete a very successful & interactive public talk. Meanwhile, we would like to express our sincere gratitude to Takeda for their generosity to sponsor the event.

Answers to Dermatological Quiz

Answers:

1. This middle aged man developed this persistent net-like reticulated mottled erythematous pattern at his lower limbs is compatible with livedo reticularis. It is a common physiological finding resulted from a vasospastic response to cold exposure. Among normal healthy individuals, the predisposition to livedo reticularis varies. If it is persistently present as in our patient, it can also be a reflection of a number of underlying systemic diseases. Differential diagnoses include heat induced erythema ab igne and other reticulated dermatoses such as reticulated erythematous mucinosis and poikilodermatous mycosis fungoides which should have epidermal changes with telangiectasia.

2. Livedo reticularis is a clinical sign and does not require any treatment per se. It is unresponsive to treatments such as vascular laser therapy or vasodilatory medications. Underlying causes require identification and appropriate treatment. In our patient, acquired livedo reticularis with persistent changes is suggestive of underlying diseases. It can be due to vasospasm associated with autoimmune connective diseases (e.g. in our patient with SLE with positive ANA and anti DNA) or Raynaud's disease/ phenomenon. It can be due to reduced intravascular blood flow (e.g. due to thrombocythaemia, polycythaemia rubra vera, presence of cryoglobulinaemia or presence of hypercoagulability state due to antiphospholipid syndrome). It can also be due to vessel wall pathology (e.g. vasculitis as a result of cutaneous polyarteritis nodosa or autoimmune connective tissue disease-associated vasculitis such as rheumatoid arthritis). Vessel obstruction due to embolic events (e.g. cholesterol emboli or septic emboli) rarely presents as livedo reticularis. Relevant investigations, as guided by the relevant clinical presentation, to exclude the above causes should be done to define the underlying diseases so that specific treatment can be given.

Dr. Ka-ho LAU
MBBS(HK), FRCP(Glasg, Edin), FHKCP, FHKAM(Med)
Private dermatologist

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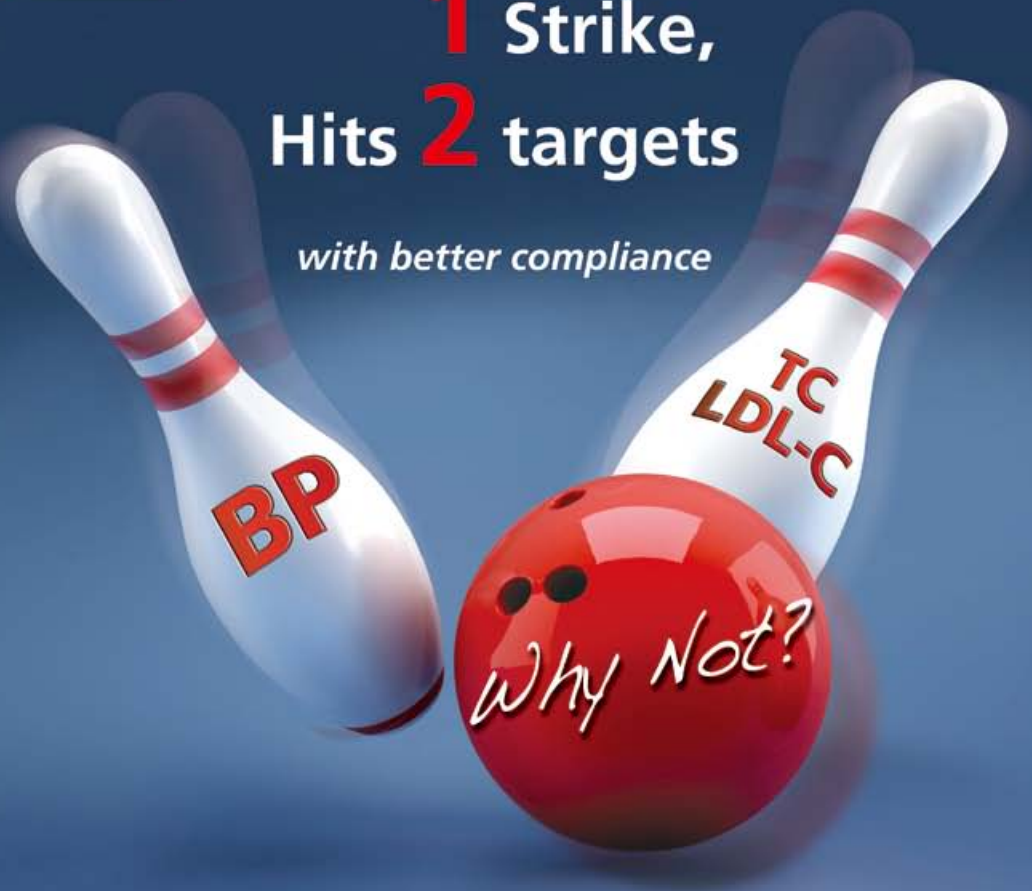

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Reference : 1. Peter Sever et al. Potential synergy between lipid-lowering and blood pressure-lowering in the Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT-LLA 2×2). *European Heart Journal* (2006) 27, 2982-2988

Detailed prescribing information is available on request.

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每日只需一粒，有效減少骨質流失和增加骨質密度[1]
醫學研究証實，更能減低乳房高風險問題超過8成[2]

Takeda

優雅會熱線：2856 1223

武田藥品(香港)有限公司
Takeda Pharmaceuticals (Hong Kong) Ltd.

優雅健乃醫生處方藥物，請依從醫生指示持續服用，不能自行停藥。如有疑問，請向醫生或藥劑師查詢　香港銅鑼灣禮頓道38號東區電訊大廈23及24樓　電話: 2133 9800　傳真: 2856 2728　網頁: www.takeda.com

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