>Statement of Objectives

Upon successful completion of this lesson, you should be able to:

1. Discuss the pathophysiology of Type 2 diabetes and cardiovascular complications.

2. Discuss non-pharmacological interventions and treatments for hyperglycemia, dyslipidemia and hypertension.

3. Discuss reasons for patient non-compliance.

4. Educate patients about the importance of antiplatelet therapy as a primary prevention treatment.

5. Recognize, prevent and treat hypoglycemia.

6. Describe the role of the pharmacist in educating patients and family members about diabetes.

>Instructions

1. After carefully reading this lesson, study each question and select the one answer you believe to be correct. Circle the appropriate letter on the attached reply card.

2. Complete the card and mail, or fax to (416) 764-3937.

3. Your reply card will be marked and you will be advised of your results in a letter from Rogers Publishing.

4. To pass this lesson, a grade of 70% (14 out of 20) is required. If you pass, your CEU(s) will be recorded with the relevant provincial authority(ies). (Note: some provinces require individual pharmacists to notify them.)

2 CEUs

Approved for 2 CE units by the Canadian Council on Continuing Education in Pharmacy.

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ENHANCING PATIENT COMPLIANCE TO REDUCE CARDIOVASCULAR COMPLICATIONS IN PATIENTS WITH TYPE 2 DIABETES

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DIABETES IS A CHRONIC DISEASE THAT IS ON the rise in Canada. Currently, more than 2 million Canadians are diagnosed with diabetes, and by the year 2010, that number is expected to reach 4 million.[1,2] Approximately 90% of those diagnosed have Type 2 diabetes. Cardiovascular complications in patients with Type 2 diabetes account for at least two-thirds of the mortality rate.[3] Therefore, this lesson will focus on enhancing patient compliance to drug therapy and non-pharmacological interventions to reduce cardiovascular complications in patients with Type 2 diabetes. Pharmacists need to understand the pathophysiology of Type 2 diabetes in order to identify patients who are at risk of insulin resistance, and raise their awareness of cardiovascular complications. Personal clinical experience has shown that patients who understand the rationale behind the drug treatments for hyperglycemia, hyperlipidemia, hypertension and hypercoagulation are more willing to adhere to their medication regimes. Non-pharmacological interventions, such as exercise, healthy weight loss, smoking cessation and moderate alcohol consumption are part of the treatment plan and need to be reinforced to patients. Patients on insulin or oral antihyperglycemic agents, need to be told how to recognize, prevent and manage hypoglycemic reactions. And finally, patients requiring insulin will need moral support and patience. Pharmacists can deliver all of these services to patients and caregivers to achieve the common goals of reducing mortality and morbidity secondary to diabetes.

PATHOPHYSIOLOGY

TYPE 2 DIABETES MELLITUS IS ONE OF THE most common chronic diseases in the world. The major cause of death in individuals with Type 2 diabetes is the result of macrovascular disease (stroke, peripheral vascular and coronary artery disease (CAD). The United Kingdom Prospective Diabetes Study (UKPDS) demonstrated that the risk of microvascular complications (retinopathy, nephropathy and neuropathy) is strongly associated with previous hyperglycemia.[6] The study also showed a weak association with macrovascular complications.

The pathophysiology for Type 2 diabetes has become clearer in the past decade. The underlying cause of diabetes is still unknown, but there is a better understanding of the development and consequences of the disease. Hyperglycemia is no longer the only focus. In most cases of Type 2 diabetes, hyperglycemia is just one of the many defects associated with a basic metabolic disorder, the insulin resistance syndrome.[6-8] Patients with this syndrome will manifest hyperglycemia, dyslipidemia, hypertension and a hypercoagula-

ble state.[4,8,9,10] All of these factors combine to increase the risk for a cardiovascular event.
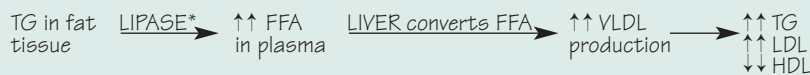
Hyperglycemia

It is becoming increasingly clear that hyperglycemia is the result of insulin resistance and ß-cell dysfunction.[4,11] It is suggested that in the beginning, there is a progressive deterioration of tissue sensitivity to insulin (insulin resistance). The ß-cells in the pancreas must increase insulin production in order to compensate for the reduction in insulin sensitivity. Eventually, the ß-cells become "exhausted" and are no longer able to compensate for increases in insulin resistance.[4,11] At this point, glucose intolerance and overt Type 2 diabetes develop. It is important to note that insulin resistance may precede the clinical diagnosis of diabetes by years or decades.[12]

Dyslipidemia

Dyslipidemia is a common consequence of the insulin resistant state. The most common lipid abnormalities of Type 2 diabetes are high triglycerides, high low-density lipoprotein (LDL) cholesterol, and low high-density lipoprotein (HDL) cholesterol. These abnormalities may be present during the "asymptomatic phase" of diabetes, when blood glucose control is good.[12]

Free fatty acids (FFAs) are a major source of fuel for the liver, kidney, skeletal muscle and heart muscle. FFAs are the alternative energy source to glucose, preserving glucose for cerebral requirements and proteins which serve as substrates for gluconeogenesis.[3] FFAs are stored in the form of triglycerides (TGs), located in the adipose tissue. TGs can be converted back into FFAs by the process of lipolysis, utilizing an enzyme called lipase. Insulin is a potent hormone for inhibiting lipase. In individuals with insulin resistance, the

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TABLE 1   **Insulin Resistance in Fat Tissue**

TG in fat tissue → LIPASE* → ↑↑ FFA in plasma → LIVER converts FFA → ↑↑ VLDL production → ↑↑ TG ↑↑ LDL ↓↓ HDL

*LIPASE: This enzyme is normally inhibited by insulin to prevent the breakdown of triglycerides in fatty tissue. In individuals with insulin resistance, lipase continues to break down triglycerides, thus increasing FFA in the plasma.

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insensitivity of the adipocytes to insulin will cause the cells to undergo a greater breakdown of stored TG. Consequently, increased FFAs in the plasma leads to increased FFA uptake by the liver. The liver then converts the FFA to very low-density lipoprotein (VLDL) cholesterol. The imbalance of VLDL production (increased) and its metabolism (decreased) results in high TGs, high LDL cholesterol, and low HDL cholesterol. With this dyslipidemia profile, atherosclerotic plaques are more likely to form around the arteries of patients with diabetes, thus increasing their risk for a cardiovascular event.[4,9]

It is important to note that lipolysis is occurring in adipocytes, but NOT hepatocytes in people with insulin resistance. Therefore, they are generally not at risk for ketoacidosis compared to people with Type 1 diabetes, despite the fact that lipolysis is occurring. In order for ketoacidosis to occur, there has to be an absolute or relative insulin deficiency in the liver to induce lipolysis in hepatocytes, and FFAs are further metabolized to hydroxybutyrate, acetoacetic acid and acetone. Although patients with Type 2 diabetes have increased insulin resistance, the hepatocytes are still sensitive to the presence of insulin to prevent this unwanted effect.

Hypertension

Approximately 50% of hypertensive patients have insulin resistance.[13] It is suggested that hyperinsulinemia may be responsible for the frequent co-existence of diabetes and hypertension.[13-16] Evidence indicates that insulin stimulates the sympathetic nervous system, resulting in increased plasma norepinephrine concentrations. In addition, insulin resistance may impair normal vasodilatory mechanisms and increase the responsiveness of the body to angiotensin, while increasing the total exchangeable body sodium and causing volume overload.[13,14] The coexistence of diabetes and hypertension magnify the risk of cardiovascular and microvascular complications in diabetes.[1,17,18]

Hypercoagulable state

Patients with diabetes have increased platelet aggregation, clotting factors, fibrinogen and plasminogen activator inhibitors.[1,5,7,10,19] In addition, they are susceptible to plaque formations in the arteries as a result of the dyslipidemia profile. These plaques can disrupt at any time due to the increased sympathetic tone secondary to autonomic neuropathy.[10] Consequently, these patients are at high risk for thrombosis, leading to a potentially catastrophic event.

TREATMENTS

Non-pharmacological interventions

Modifiable risk factors have been identified and individuals with diabetes are encouraged to follow these interventions to reduce their risk of insulin resistance[5] and cardiovascular complications. The following non-pharmacological interventions are recommended:

FACULTY   Enhancing Patient Compliance to Reduce Cardiovascular Complications in Patients with Type 2 Diabetes

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REVIEWERS
All lessons are reviewed by pharmacists for accuracy, currency and relevance to current pharmacy practice.

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1. Proper nutrition.
2. Regular exercise.
3. Healthy weight loss.
4. Smoking cessation.
5. Moderate alcohol consumption.

Proper Nutrition

Pharmacists can help patients contact available resources in the community for appropriate support. This may include a dietitian, diabetes nurse educator or a pharmacist who is a Certified Diabetes Educator to achieve these goals. In addition, pharmacists need to know the process required to refer a patient to the local diabetes clinic, by contacting the nearest local hospital or health unit. All patients should be informed of the difference between a "nutritionist" and "dietitian." A nutritionist may or may not have training from an accredited institution, whereas a dietitian is regulated through a licensing body. A referral can be obtained by contacting the Dietitians of Canada at their Web site: www.dietitians.ca.

Promote Regular Exercise

It is a well known fact that physical activity can have positive impact on diabetes. When patients lose weight, insulin sensitivity is heightened, and blood pressure and lipoprotein profile are improved.[5] Many people equate achieving physical fitness with jogging, aerobics or joining a fitness club. To clear up these misconceptions, pharmacists can suggest a 10-minute walk to start, gradually increasing that activity to 60 minutes a day, 3-5 times a week.[20] If they cannot tolerate a continuous 60-minute walk due to other medical conditions, divide the activity into six 10-minute walks per day. Encouraging patients to join a fitness club is also sound advice. Many fitness clubs offer programs or personal trainers to tailor exercise to the patient's physical abilities. Unfortunately, not all patients can afford the membership fee. Pharmacists can help by suggesting alternative physical activity for these patients, or refer them to a nurse educator when possible.

The major challenge for many patients is selecting an activity that they are able to participate in, while enjoying it enough to incorporate it into a daily routine. Many patients may become discouraged if the activity causes significant

pain or is perceived as a chore. It is critical for all patients to obtain physician approval before beginning any exercise program, because an ECG or a stress test may be necessary. Pharmacists can assess the patient's tolerance to activity by obtaining adequate medical history from the patient and offering advice on an appropriate physical exercise. Assessment should include any pain the patient may encounter with activity, cardiovascular health and pulmonary function.[20] Patients who have pain with activity, particularly those patients with neuropathy in their feet or arthritis, may not be able to tolerate walking, but may do well with aqua aerobics or swimming. For individuals with limited mobility, such as congestive heart failure, chronic obstructive pulmonary disease or arthritis, armchair exercises, yoga or tai chi are appropriate exercise alternatives. A number of videos can be ordered from www.Armchair Fitness.com. Similar exercise videos may be available at local diabetes clinics or libraries for patients to borrow if affordability is a problem. Patients with hypertension, angina, a history of myocardial infarct, congestive heart failure, proliferative retinopathy and atherosclerosis, must understand that they should avoid activities involving heavy lifting or exercises that may cause significant increases in blood pressure. If possible, try to encourage the patient and family members to participate in a routine exercise that they can do together. Family members should also understand that exercise is an important part of the treatment plan and that they can offer constant encouragement to the patient.

Patients should also be reminded to increase their physical activity gradually. Patients with CHF, angina and COPD are at high risk for an adverse event due to exercise. These individuals should be closely supervised by a family member, friend or personal trainer in the initial stages of an exercise program. Exercise will affect a patient's need for insulin and/or antihyperglycemic agent(s) and they should be reminded of this factor.

Healthy Weight Loss

Approximately 80% of individuals with Type 2 diabetes are overweight, with a body mass index (BMI) defined as >25 kg/m². [5,20]

The BMI is the index often used to assess body weight by using the equation: weight (kg)/height (m)², while a BMI <18.5 kg/m² would be considered underweight. A healthy weight reduction is recommended at a rate of 0.25-1.0 kg (0.5-2.0 lbs) per week.[20] However, some patients experience weight gain occurring with improved glycemic control, especially at the beginning of intensive diabetes treatment. Antidiabetic drugs such as insulin, sulfonylureas and repaglinide are all implicated in causing weight gain.[7,11] It is important at this point to rule out that weight gain is not due to the patient eating more to prevent hypoglycemia. If this is the case, dosage adjustment is required. Patients who gain weight, despite good glycemic control and no significant change in their diets, need to understand that the increased weight gain can occur because improved glycemic control improves energy utilization,[20] and can lead to weight gain. The goal for weight loss should be re-evaluated and new goals set to prevent further weight gain. A dietitian should be consulted to re-evaluate the patient's overall diet, and the pharmacist can look at alternative medications such as metformin or thiazolidinedione. *(Note: The thiazolidinedione class can increase weight. However, it is often secondary to fluid retention.[21])*

In obese patients with a BMI >28 kg/m² and other risks for cardiovascular disease (DM, hypertension, high cholesterol), weight loss is critical for reducing cardiovascular risk. If a patient is still not able to lose excess weight despite being on an appropriate diet and exercising for a month, the anti-obesity drug orlistat may be considered to help reduce weight.[22] Discuss the option with patients and their physicians to add this therapy when necessary.

Smoking Cessation and Moderate Alcohol Consumption

Both cigarette smoking and alcohol consumption are independent risks for increasing microvascular and macrovascular diseases.[3,5,20] Patients need to be encouraged to gradually stop smoking and consume alcohol moderately. Frequently, smoking cessation is the most challenging goal for the patient, and the last lifestyle issue to be addressed.

Smoking is a major, independent risk factor for cardiovascular disease. Smokers have a 70% greater level of cardiovascular risk than non-smokers, and those who smoke at least 2 packs a day have a two to three times greater risk for cardiovascular disease.[23] In a large prospective study (MRFIT), individuals with diabetes who smoked and had high cholesterol and high blood pressure, were shown to have a 2.6 times higher risk for a heart attack compared to those who did not have diabetes but had the same risk factors.[24] Patients need to understand that smoking cessation is a preventable cause of death.[24]

All patients with diabetes should be asked whether or not they smoke. If the patient does smoke, setting a goal for quitting soon after a diagnosis of diabetes will add to the stress and frustration the patient may be undergoing. Pharmacists should be aware of their patients' emotions. They can include anger, fear, denial and depression.[20] Patients find it stressful when accepting a diagnosis of diabetes, dealing with changes in dietary habits and physical activity, and frequently checking their blood glucose to achieve euglycemia. Smoking may be perceived as the only factor that helps them deal with stress at this stage.

Weight gain is another problem associated with smoking cessation. However, these problems can be overcome once a solid professional relationship has been established with the patient. The two key questions, "Do you smoke?" and "Do you want to quit?" should be revisited at appropriate intervals. This may take weeks or months before the goal of smoking cessation is set.

Once the patient is willing to try to quit smoking, pharmacists can play a critical role in informing patients of available pharmacological therapies to manage the symptoms of nicotine withdrawal. Nicotine replacement therapy and bupropion are first-line treatments that reliably increase long-term smoking cessation.[25] Nicotine patches and gum are generally well-tolerated by patients. Bupropion should be used with caution in patients with a history of seizures. Higher doses should be avoided (>450 mg/d). Bupropion needs to be started 7 to 10 days before the set date for quitting smoking. Support from family and friends should be encouraged. Patients will require strategies to help cope with cravings. Strategies include focusing on the reasons why they want to quit, chewing sugar-free gum, eating low-calorie snacks (i.e. celery), learning relaxation techniques and exercise. Patients should also be encouraged to join a smoking-cessation support group through a smoking cessation clinic, diabetes clinic or The Lung Association.

PHARMACOLOGICAL INTERVENTIONS
Hyperglycemia
The diagnosis of diabetes must be based on venous blood test results conducted by a laboratory.[1] Confirmation of the diagnosis depends on repeated values done on another day, unless unequivocal hyperglycemia and metabolic decompensation are present.

The strongest evidence for optimal glucose control comes from United Kingdom Prospective Diabetes Study (UKPDS) in Type 2 diabetes.[6] It demonstrated that long-term intensive treatment with normal glycemia could significantly reduce the severity and frequency of microvascular complications and, to some extent, reduce macrovascular complications. The stepwise treatment approach to Type 2 diabetes is currently being revised by the Canadian Diabetes Association (CDA) Expert Committee. (The new guideline will not be available until December 2003). The following recommendations, published in the Fall of 2002, are from the Britain's NICE (National Institute for Clinical Excellence) guideline on the management of Type 2 diabetes. These recommendations are based on evidence-based medicine and are graded accordingly. It is important to note that drug intervention should only occur after 1 to 3 months of lifestyle modification.[1,22] These guidelines specifically promote the use of metformin as first-line therapy for patients who are obese (BMI >25 kg/m^{2}), and identifies the place of therapy for the use of thiazolidinedione (see Table 4). The 1998 Canadian Diabetes Management Guidelines only stated that thiazolidinedione be used in combination with insulin for patients with poor glucose control, despite being on insulin. This combination therapy is considered a contraindication in the NICE guideline due to the increased risk of edema.

Because patient compliance to antihyperglycemic medication(s) is important for optimal glycemic control, pharmacists should be aware of the reasons why some patients are non-compliant in order to help resolve the problem. Common problems include inability to cope with changes in their lives, misunderstanding the disease, unfavourable drug side-effects or fear of side-effects, inability to afford the drug, complicated drug regimen, and physical or mental limitation.

Patients who are overwhelmed with the added changes to their lives, have a family history of poor outcomes with diabetes or are misinformed about diabetes will not start or follow through with treatment. Women, in particular, who may be caring for children, spouses or elderly parents, often neglect to take their diabetes medication due to the demands on their time and the effort required to regiment their medications(s) and meals. Patients with a family history of poor outcomes with diabetes may feel hopelessness and despair. They may be in denial and refuse to begin treatment. Finally, patients may be misinformed about the disease, believing it's not a serious disease until they are required take insulin. Typically, these patients don't monitor their blood glucose and skip their oral medication(s) because it interferes with their daily activity. If these patients are identified, they can be educated about diabetes. Refer them to a

TABLE 2	Diagnosis of Diabetes and Target Blood Glucose[1]	
Diagnosis of Diabetes Mellitus[1]	Fasting Plasma Glucose >7.0 mmol/L	Plasma Glucose 2 hours after 75 g of glucose load >11.0 mmol/L
Optimal Target Goals[1]	Fasting Blood Glucose 4 - 7 mmol/L	1 -2 hours Post-meal Blood Glucose 5 - 11 mmol/L
1998 Canadian Diabetes Management Guidelines		

diabetes clinic and their physicians for extra educational support and help in dealing with their emotional and social issues. It must be emphasized that well-controlled diabetes can reduce morbidity and mortality.

Pharmacists should encourage patients with diabetes to include family members in their diabetes care.[20] Diabetes treatment and targeted goals should be explained thoroughly to patients and family members. Having a family member in attendance during these informative sessions will help reinforce any information that the patient may have missed, and provide family members with a better understanding of diabetes to help them provide the caring and supportive environment required by the patient.

Unfavourable effects of drugs are problematic for patients. Some patients stop taking their drugs without consulting with any health care professional. Some patients are afraid of hypoglycemic reaction causing death because it happened to a family member or friend. They often eat more, which defeats the effect of the drug. Non-compliance to medication can be easily identified when refilling prescriptions. Ask patients about their glucose control. As discussed earlier, if a patient gains weight while on medications, he or she may stop taking it. Look for alternative treatments or refer the patient to a dietitian when necessary. If medications are adjusted, the patient will need to know when to expect the peak action of the medication and duration of action so as not to overeat to compensate for hypoglycemia. This is especially important for patients on insulin or sulfonylureas or repaglinide. Gastrointestinal side-effects are common and can also cause patients to discontinue treatment (mainly nausea and/or diarrhea) associated with metformin. For many patients, this side-effect may be dose related. It can be overcome by starting with a lower dose (i.e. 250 mg bid), increasing slowly.[7] If the side-effect persists, thiazolidinedione can be offered. However, affordability of the drug should be considered.

Mental and physical limitations such as forgetfulness, poor vision and hand dexterity can be challenging compliance issues, especially for older patients. By asking about blood glucose readings and looking

TABLE 3 — Available Needles

Novofine (For Novolin Pen)	Ultra-fine III (For HumaPen)	Ultra-fine Original (For HumaPen)
30 G x 6 mm 30 G x 8 mm	30 G x 8 mm 30 G x 12 mm 31 G x 5 mm	29 G x 12.7 mm

Note: Novolin and HumaPen needles are NOT interchangeable because the delivery of insulin is not guaranteed.

TABLE 4 — Britain's NICE Guideline for Treatment of Hyperglycemia[21]

Drug Class/Drug	Recommendations	Grade*
Biguanide (Metformin)	First-line drug treatment for overweight people (BMI >25kg/m^2), and whose blood glucose is not controlled with lifestyle modifications. OR	A
	First-line drug treatment or combination treatment for people who are NOT overweight.	A
Insulin Secretagogues (Sulphonylureas and Repaglinide)	First-line treatment for non-obese people or when metformin is contraindicated (renal, liver, cardiac, or respiratory insufficiency). OR	A
	Use in combination with metformin in overweight people when blood glucose is not adequately controlled.	A
Thiazolidinediones (Rosiglitazone, Pioglitazone)	Treatment for people who are unable to take metformin and insulin secretagogues combination therapy. OR	A
	Hemoglobin A1C (HbA$_{1C}$) target level cannot be reached despite adequate trial of combination therapy with metformin and insulin secretagogues.	A
	Combination therapy with insulin is contraindicated. (N.B.: People at the greatest risk from adverse effects of edema and congestive heart failure (CHF) due to this combination are elderly, patients with longstanding diabetes, people on high doses of insulin and/or thiazolindinedione.)[21,22,23]	A
Alpha-glucosidase inhibitors	An alternative oral medication for people who cannot use other oral drugs.	A
Insulin	Insulin therapy is to be initiated when blood glucose control is inadequate with optimal oral agents.	A
	Continue with metformin when insulin is added.	B
	Continue with sulphonylurea when insulin is added.	D

Refer to Table 10 for interpretation of grade level.
See also Nov. 2001 Pharmacy Practice CE for a summary of oral antidiabetic agents.[11]

at refill history, pharmacists can identify patients whose blood glucose control is erratic. For a patient on multiple medications with a tendency to forget to take them, pharmacists can suggest a dosette, with a day's or week's worth of medications in the box. Suggest to patients that they keep the dosette in a room that's used the most, such as the kitchen or bedroom. Patients should try to schedule their med-

ications around mealtime and bedtime. If possible, alternative drugs that allow once-a-day dosing rather than multiple daily dosing may be explored. It may be helpful to have a family member or friend remind the patient to take medications. However, if that is not possible, patients can set an alarm clock to remind them to take medications.

Patients with diabetes often have

impaired vision, leading to the challenge of accurately reading their blood glucose meter. A potentially serious consequence is when one of these patients inadvertently administers the wrong dose. Having a family member help with blood glucose monitoring and administering is ideal, but may not be possible, especially for someone who lives alone. Suggest a magnifying glass to help patients read the numbers on the glucose meter and the insulin pen. Patients can be taught to listen to the "click" sound dialed on an insulin pen. Each "click" can be counted as one unit. Another possibility is to suggest prefilled syringes, which the pharmacy can prepare on a weekly basis. However, the potential for error is greater if the patient requires two or more different doses a day. Further, the patient cannot adjust the insulin dosage when necessary.

For patients with poor hand dexterity (tremulous or arthritic), ensure they have a blood glucose device and insulin pen that they can manipulate. If necessary, these patients can be referred to a diabetes clinic to try different products and receive the appropriate education for the selected devices.

Finally, some patients resist starting insulin because they fear needles or a poor outcome. Diabetes education is essential for these patients. Pharmacists can help patients cope with this new therapy by discussing why insulin is needed. Patients need to be reassured that starting insulin therapy does not mean that he or she is a failure. Insulin therapy can be described as a hormone replacement therapy,[7] and the patient informed whether oral medication needs to be continued. If the patient is started on an insulin pen, appropriate needles can be selected to optimize insulin delivery and provide patient comfort. For example, use the longer length of needle (i.e. 12 mm) for obese patients (BMI >27 kg/m²).[20,27] For patients who are fairly thin, use a shorter needle (5 - 6 mm) to prevent it from entering the muscle. If short needles are used, patients should be reminded that they do not need to pinch the skin when injecting.

Target goals for blood glucose control should be discussed with patients individually. Patients need to keep a daily record of blood glucose readings to provide the

feedback tool necessary for diet, exercise and medication compliance. In addition, the daily record is helpful for the diabetes nurse educator, pharmacist and physician when adjusting medications to achieve optimal glycemic control.

Dyslipidemia
Individuals with Type 2 diabetes who are over 30 years of age are now classified as

TABLE 5	Canadian Standard for Lipid Targets[30]		
TG		LDL Cholesterol	Total Cholesterol: HDL cholesterol ratio
<2.0 mmol/L		<2.5 mmol/L	<4.0 mmol/L

TABLE 6	Britain's NICE Guideline for Treatment of Dyslipidemia[22]	
Recommendations		**Grade***
When a person is diagnosed with Type 2 diabetes, obtain fasting total cholesterol (TC), triglyceride (TG), low-density lipoprotein (LDL), and high-density lipoprotein (HDL).		A
Rule out adverse lipid profile secondary to: 1. alcohol consumption 2. hypothyroidism 3. liver disease 4. renal disease		C
FOR PRIMARY PREVENTION AND SECONDARY PREVENTION***		
NO DRUG THERAPY		
if TC <5 mmol/L (or LDL <3.0 mmol/L) OR TG <2.3 mmol/L Discuss the rise of coronary artery disease with patients and consider treatment when level of cholesterol OR triglycerides is higher.		D
Monitor lipid profile and cardiovascular disease risk annually.		D
START A STATIN if TC ≥5 mmol/L (or LDL ≥3.0 mmol/L) OR 2.3 mmol/L ≥ TG ≤10 mmol/L		B
ADD A FIBRATE After 6 months treatment with a statin, if TG is still ≥2.3 mmol/L		D
START A STATIN OR FIBRATE if TC ≤5 mmol/L (or LDL ≤3.0 mmol/L) AND 2.3 mmol/L ≥ TG ≤10 mmol/L.		B (for statin) C (for fibrate)
START A FIBRATE when TG >10 mmol/L. Refer patient to a specialist.		C
Upon initiation of any therapy, follow up in 3 months and adjust dosage as necessary.		D
Monitor therapy annually.		D

Refer to Table 10 for interpretation of grade level.
**Primary Prevention (To prevent CAD in people without cardiovascular disease and adverse lipid profile).*
***Secondary Prevention (To prevent CAD in people with cardiovascular disease and adverse lipid profile).*
Note: The targets set by Canadian standards for LDL and TG is lower than targets recommended by NICE guidelines when initiating drug therapy. Drug therapy should be initiated to reach the Canadian standard. However, NICE guidelines may be considered for patients who cannot afford or tolerate the drug.

very high risk (>30%) for symptomatic coronary artery disease within 10 years.[30] Lipid lowering is critical for patients with diabetes to reduce the risk of mortality, and morbidity.[1,4,5,7,20] The goals and treatments have not changed since 2000.[30] NICE guidelines recommend appropriate lipid screening for any patient diagnosed with Type 2 diabetes. They also have recommendations for the initiation and selection of drug therapy as a primary prevention and secondary prevention against CAD in patients with diabetes. The recommendations are based on evidence-based medicine. Diet and regular exercise are integral parts of treatment to attain the targeted goals.[5,7,20,30]

Inform the patient of his or her target goals before drug treatment begins. Weight reduction, proper diet, moderate alcohol consumption and smoking cessation are all important aspects of treatment.[1,5,20]

Most patients tolerate antidyslipidemic agents very well. However, gastrointestinal side-effects (nausea, abdominal pain, flatulence and diarrhea) and lack of symptoms associated with dyslipidemia often lead patients to question the benefit of the therapy and discontinue treatment. For patients with gastrointestinal side-effects, symptom management can be offered and an alternative drug can be tried. Reinforce the beneficial effects and target goals.

Dyslipidemia does not cause any symptoms and cholesterol results are not readily available every day, unlike blood glucose readings, so some patients stop taking the drug. This is especially common in patients who are trying to cut back on the cost of their medications. Again, reinforcement of the benefit of treatment is very important. Suggest to the patient to keep a record of target goals and all subsequent results. This record is an excellent tool for enhancing compliance to drug therapy, exercise and diet and provides quantifiable feedback for the patient.

Hypertension

Cardiovascular disease is a major cause of mortality and morbidity in people with diabetes.[1,7,9,31-36] Improved cardiovascular outcomes, as a result of pharmacological therapy, appear to be associated with consequent reduction in blood pressure (BP)

(level Ia evidence).[24] In addition, numerous studies have shown that reducing blood pressure (BP) in diabetic patients will reduce the risk of cardiovascular events.[16,32,35-38] Therefore, managing high blood pressure in people with Type 2 diabetes is critical to reduce the risk of death and complications from diabetes.[22]

Currently, the target BP is 130/80 mm Hg for all patients with diabetes in Canada.[5] NICE guidelines suggest a different BP target for diabetic patients, depending on the presence or absence of microalbuminuria. They are ≤135/75 mm Hg and ≤140/80 mm Hg respectively.

For many of these patients, more than one medication is necessary to reach these targets.[17] Pharmacists need to clearly explain the importance of compliance to medication, and the reason for combination therapy when it is initiated. As well, weight reduction, proper diet, moderate alcohol consumption and smoking cessation are all important components of treatment.[1,5,20] Note that thiazide is considered a first-line drug therapy in the NICE guideline. The 1998 Canadian Diabetes Management Guidelines, on the other hand, do not mention its use. Further, the recent results of the ALL-HAT study supports the use of thiazide as first-line treatment for hypertension because it is well tolerated and cost-effective in lowering blood pressure and preventing heart attack.[39] Therefore, this change may be seen in our new guidelines as more studies support its efficacy and safety for this population.

The question yet to be answered is whether angiotensin-converting enzyme inhibitor (ACE-I) can reduce cardiovascular events, beyond their blood lowering effects. The Heart Outcomes Prevention Evaluation (HOPE) trial seems to suggest that ACE-I may have this cardioprotective effect, and may be offered to patients with diabetes as preventative therapy.[36] However, the Staessen et al (2001) study concluded that the blood pressure lowering effect of ACE-I is the main difference in outcome.[32] This topic is continually being debated.

The main compliance issues with antihypertensive drugs relate to side-effects and affordability of the drug. Cough and sexual dysfunction are the most troublesome side-effects leading to discontinua-

tion of treatment. Cough is the main side-effect for patients taking an ACE-I. Alternative treatment may be considered such as angiotensin receptor blocker (ARB)[22] for patients with or without microalbuminuria. However, if cost is an issue, the less costly drug that the patient can afford should be considered and discussed with patients and physicians.

Approximately 60% of patients with neuropathy secondary to diabetes have sexual dysfunction.[40] These patients may not be compliant with ß-blockers and thiazides because they are implicated in the cause of sexual dysfunction.[41] These drugs may magnify the problem they are already experiencing. The high degree of sensitivity of this matter often discourages patients from discussing it with a health care professional. Any patient with diabetes who has neuropathy should be aware of these drugs' side-effects. If the patient's refills of any of these drugs are late, the pharmacist should raise the issue. Provide a private area for this sensitive discussion to allow the patient to speak openly. Spouses should be involved in the discussion, when possible, to help them better understand the problem.

Antiplatelet Therapy

Haffner and colleagues showed that patients with diabetes (without previous myocardial infarction) were at the same high risk of coronary events as were nondiabetic patients with previous myocardial infarction.[44] As discussed earlier, patients with Type 2 diabetes are in a hypercoagulable state. For this reason, antiplatelet therapy is now considered safe and beneficial for patients with diabetes as a primary therapy for prevention of cardiovascular events.[1,5,22] NICE guidelines recommend ASA 75 mg for patients with diabetes who have >15% 10-year risk of a coronary event (Grade A recommendation). *(Note: Only a low dose of ASA is required. 80 mg or 81 mg doses are available in Canada.)* The 1998 Canadian guideline also recommends ASA for high-risk patients with diabetes who are over 30 years of age, without specifically defining "high risk."

The calculation to predict coronary risk is based on Framingham data. The tables can be found in Fedor et al. (2000).[30] This calculation does not factor

TABLE 7 Britain's NICE Guideline for Treatment of Hypertension[24]	
Recommendations	**Grade***
First-line treatment for patients without microalbuminuria, use angiotensin-converting enzyme inhibitor (ACE-I), angiotensin II blocker (ARB), ß-blocker or thiazide diuretic. Note: Thiazide diruretics may have a modest adverse effect on metabolic control. However, the overall cardiovascular risk reduction offered outweighs this. (Level II)	A
First-line treatment for patients with microalbuminuria, use ACE-I.	B
If ACE-I is contraindicated in people with microalbuminuria, then use ARB as the alternative first-line treatment.[42,43]	B
Combination therapy with ACE-I or ARB include B-blockers, calcium-channel blockers or thiazide diuretic.	B
Calcium-channel blockers should be prescribed as second-line treatment or as part of combination treatment.	B
DO NOT use any short-acting calcium- channel blocker.	D
BP target ≤135/75 mm Hg (with microalbuminuria). BP target ≤140/80 mm Hg (without microalbuminuria). Note: The Canadian BP target of <130/80 mm Hg must be the aim for all patients. However, consider NICE guidelines for patients who have difficulty attaining that goal.	B B

* Refer to Table 10 for interpretation of grade level.
Use ACE-I with caution in patients with peripheral vascular disease, renovascular disease, or those with elevated serum creatinine (Cr).
Monitor Cr and electrolytes q3-7d after ACE-I is initiated or when dose is increased.

in diabetes. Alternatively, the Cardiac Risk Calculator from New Zealand can be downloaded from the following Web site: http://www.nzgg.org.nz/library/gl_complete/bloodpressure/appendix.cfm. Diabetes is factored into this calculation. The Risk Calculator will instantly give the estimated risk of a cardiovascular event over 2 to 10 years, as soon as the figures for gender, age, systolic blood pressure, smoking, total cholesterol and diabetes are completed. The Meade and Brennan study showed that ASA has no benefit when systolic pressure is greater than 145 mm Hg.[45] NICE guidelines recommend that ASA therapy be initiated only when systolic blood pressure (SBP) is 145 mm Hg or lower. SBP should be maintained while on ASA therapy (Grade B). This precaution is not found in the Canadian guidelines. Clopidogrel is just as effective as ASA, however it is more costly.[46] It is an alternative therapy for those who are allergic to ASA. The cost-effectiveness of clopidogrel should be discussed with patients so they can make an informed decision.

Patients must understand that antiplatelet therapy can prevent a stroke or heart attack by minimizing the damage should a clot occur. Healthy lifestyle alterations and compliance to medications to achieve target goals must not be neglected as they are the key factors in preventing the initial clot formation. When antiplatelet treatment is presented to patients, compare taking antiplatelet therapy to having home insurance. A plaque in the artery can disrupt at any time, and there is no way of predicting when. Similarly, one never knows if your house is going to burn down. Antiplatelets will help slow the clotting process and reduce the number of clots formed, minimizing the damage. Like home insurance, if the house burns down, it will cover the cost to minimize the damages.

MANAGEMENT OF HYPOGLYCEMIA

SINCE THE PUBLICATION OF TWO SIGNIFICANT trials show that tight blood glucose control can reduce the risk of microvascular complications,[6,47] more patients are adhering to tight blood glucose control. As a result, the risk for hypoglycemia is increasing. It is estimated that 20% of patients who use antihyperglycemic agents are hypoglycemic.[48,49] Patients and their family members need to recognize the symptoms of hypoglycemia. These symptoms include nervousness, shaking, cool clammy skin, physical weakness, excessive hunger, headache, blurred vision, confusion, drowsiness and poor co-ordination. In the Fall of 2002, the Canadian Diabetes Association published the guidelines for the prevention and management of hypoglycemia.[48] The following are the highlights of their recommendations. Some recommendations are new and did not appear in the 1998 Canadian Clinical Practice Guidelines for Management of Diabetes.

Preventions

1. The risk of hypoglycemia increases exponentially in elderly patients, using sulfonylureas. The dose used should be half of that used for younger people. Gliclazide may be preferred over glyburide.

2. (New) Patients who are currently taking insulin, or starting an intensive insulin regime, should be counselled about the risks and prevention of hypoglycemia. They must be informed how changes in their diet and physical activity can alter their need for insulin.

3. (New) To reduce the risk of asymptomatic nocturnal hypoglycemia, patients should be advised to:

a) Periodically monitor overnight blood sugar.

b) If bedtime blood sugar is 7 mmol/L or less, patients will require a snack of at least 15 g of carbohydrate and protein. (See Table 8.)

4. Using rapid-acting insulin analogue (Humalog or NovoRapid) instead of regular insulin at suppertime may prevent the delayed nighttime effect of regular insulin and reduce the risk of nocturnal hypoglycemia.

5. (New) All patients currently taking insulin, or starting therapy with insulin or oral hypoglycemic agents, should be told how to recognize and prevent drug-induced hypoglycemia.

Management of Hypoglycemia

1. For mild to moderate hypoglycemia (patient's blood sugar (BG) is 4.0 mmol/L or less, but patient is still conscious and able to treat him or herself) treat with 15 g of carbohydrate that can be easily absorbed. (See Table 8.) Patient must wait for 15 minutes, then check BG. If BG reading is less than 4 mmol/L, then repeat

TABLE 8   Carbohydrates

Examples of quick-acting carbohydrates (15 g)

6 Lifesavers candies (patient must chew)
3 Dextrose tablets (patient must chew)
3 teaspoonfuls of sugar diluted in water
¾ cup of regular pop drink
¾ cup of orange juice
¾ cup of apple juice

Examples of quick-acting carbohydrates (20 g)

8 Lifesaver candies
4 Dextrose tablets
4 teaspoonfuls of sugar diluted in water
1 cup of regular pop drink
1 cup of orange juice
1 cup of apple juice

Examples of 15 g carbohydrate snacks

1 slice of bread (with peanut butter)
6 soda crackers (or read package)
2 Aeroroot cookies
1 handful of nuts
½ cup of hot or cold cereal

TABLE 9   Summary of the Canadian Standard Target Goals

BG control[1]	Fasting: 4-7 mmol/L	Postmeal: 5-11 mmol/L	HbA$_{1C}$: ≤0.074
Lipid[30]	TG <2.0 mmol/L	LDL <2.5 mmol/L	TC: HDL* <4 mmol/L
BP[5,7]		<130/80 mm Hg	

*TC: HDL= Total cholesterol to HDL ratio

TABLE 10   Britain's NICE Guidelines

Classification of Evidence

Evidence Level	Description
Ia:	evidence from meta-analysis of randomized controlled trials
Ib:	evidence from at least one randomized trial
IIa:	evidence from at least one controlled study without randomization
IIb:	evidence from at least one other type of quasi-experimental study
III:	evidence from non-experimental descriptive studies, such as comparative studies, correlation studies and case-control studies
IV:	evidence from expert committee reports or opinions and/or clinical experience of respected authorities

Adapted from Agency for Health Care Policy and Research (1992). Acute Pain Management: Operative or Medical Procedures and Trauma Agency for Health Care and Research/U.S. Department of Health and Human Resources, Public Health Service, Rockville, MD.

Grading of Recommendations

Evidence Level	Description
A	directly based on category I evidence
B	directly based on category II evidence, or extrapolated recommendation from category I evidence
C	directly based on category III evidence, or extrapolated recommendation from category I or II evidence
D	directly based on category IV evidence, or extrapolated recommendation from category I, II or III evidence

Adapted from Eccles M. et al. North of England Evidence Based Guidelines Development Project: Guidelines for angiotensin converting enzyme inhibitors in primary care management of adults with symptomatic heart failure. BMJ, 1998; 316:1369.

with another 15 g of carbohydrate.

2. For severe hypoglycemia (an event that may require a third party to help) in a conscious person, treat with oral ingestion of 20 g of quick-absorbing carbohydrate. (See Table 8.)

Note: GLUCOSE GEL IS NOT RECOMMENDED to be administered buccally, because absorption through mucosa is minimal.[44] It must be swallowed to have significant effect.

3. For severe hypoglycemia in an unconscious person in the home situation, it is recommended that the caregiver use glucagon 1 mg subcutaneously or intramuscularly (if drug is available), and call for emergency services.

4. For severe hypoglycemia in an unconscious person in a hospital setting, or other institutional setting where an intravenous line can be started, administer intravenous glucose 10 - 25 g (20 - 50 ml of D50W) over 1 to 3 minutes.

5. Glucagon PRN order is recommended for any patient in a hospital setting, or other institutional setting, who is at risk of severe hypoglycemia, and intravenous access is not readily available.

6. Sulfonylurea-induced, severe hypoglycemia can be long-lasting. A treatment of 50% dextrose IV bolus followed by an infusion of 10% dextrose for several hours may be needed. Recurrent hypoglycemia may require a second bolus of 50% dextrose plus octreotide 50 mcg subcutaneously. Glucagon is not recommended for hypoglycemia induced by sulfonylureas.

7. Recommend a snack of 1 starch and 1 protein (i.e. 1 slice of bread with peanut butter) for any patient who has just experienced a hypoglycemic episode, and the scheduled meal is more than 1 hour away. Emphasize "TREAT, BUT DO NOT OVERTREAT."

ROLE OF THE PHARMACIST

THE INCIDENCE OF DIABETES WILL CONTINUE TO rise, and treatments are becoming more complicated as we learn more about the disease. Pharmacists need to take an active role in diabetes care.

1. Be aware of new treatment guidelines.

2. Identify patients at high risk of car-

diovascular complications.

3. Help patients on insulin pen to select needles that provide comfort and optimize insulin absorption.

4. Educate patients and their caregivers about the importance of medication compliance.

5. Recognize patients who are non-compliant to treatment, identify the reason for non-compliance, and find a solution to the problem.

6. Reinforce that non-drug interventions are equally as important as medications.

7. Discuss recognizing, preventing and managing hypoglycemia with patients.

8. Inform patients of their target goals in the treatment of hyperglycemia, hypertension, dyslipidemia.

9. Find the available resources within the community to support patients with diabetes and their family members.

REFERENCES

1. Meltzer S, Leiter L, Daneman D, et al. 1998 clinical practice guidelines for the management of diabetes in Canada. CMAJ, 1998;159: S1-29.

2. Diabetes in Canada. Minister of Public Works and Government Services of Canada 1999.

3. Geiss LS, Herman H, Smith PJ. Mortality in non-insulin-dependent diabetes. In: National Diabetes Data Group. Diabetes in America, ed. 2. Bethesda, MD: National Institute of Health and National Institute of Diabetes and Digestive Kidney Diseases, 1995, pp 233-257.

4. Donnelly R, Garber A. Diabetes, obesity and metabolism. Journal of Pharmacology and Therapeutics, 2001;3(1):S1-43.

5. Insulin resistance and the pharmacist. Pharmacy Practice, 2002; April CE Lesson.

6. United Kingdom Prospective Diabetes Study Group. Intensive blood glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with Type 2 diabetes (UKPDS 33). Lancet, 1998;352:837-53.

7. Practical diabetes management. Clinical support for primary care physicians. IntraMedical Services 2000.

8. Bonora E, Kiechl S, Willeit J, et al. Prevalence of insulin resistance in metabolic disorders. Diabetes, 1998;47:1643-50.

9. Ginsberg H. Diabetic dyslipidemia and arthrosclerosis. Lipids Online 2000. www.lipidsonline.org/slides.

10. Nesto R. Clinical evaluation and non-lipid treatment of CAD in diabetes patient. Lipids Online 2000. www.lipidsonline.org/slides.

11. Cornish B. Treatment of hyperglycemia in Type 2 diabetes. Pharmacy Practice, 2001; November CE Lesson.

12. Folsom AR et al. A prospective study of coronary artery disease in relation to fasting insulin glucose and diabetes. The artherosclerosis risk in communities (ARIC) study. Diabetes Care, 1997;20:935-42.

13. Grandberry MC, Fonseca VA. Insulin resistance syndrome: Options for treatment. South Med J, 1999: 92(1);2-14.

14. Opara JU, Levine JH. The deadly quartet:The insulin resistance syndrome. South Med J, 1997; 90(12):1162-68.

15. The National High Blood Pressure Education Program Working Group. National high blood pressure education program working group report on hypertension in diabetes. Hypertension, 1994;23(2):145-58.

16. Makrilakas K, Bakris G. Diabetic hypertensive patients: Improving their prognosis. J Cardiovasc Pharmacol, 1998;31(2):S34-40.

17. United Kingdom Prospective Diabetes Study Group. Tight blood pressure control and risk of macrovascular and microvascular complications in Type 2 diabetes (UKPDS 38). BMJ, 1998;317:703-13.

18. Adler A, Stratton I, Neil HAW, et al. Association of systolic blood pressure with macrovascular and microvascular complications of Type 2 diabetes (UKPDS 36): Prospective and observational study. BMJ, 2000;321:412-19.

19. Sanmuganathan PS, Ghahramani P, Jackson PR, et al. ASA for primary prevention of coronary heart disease: Safety and absolute benefit related to coronary risk derived from meta-analysis of randomized trials. Heart, 2001;85:265-71.

20. Building competency in diabetes education: The essentials. Canadian Diabetes Association 2001.

21. Rosiglitazone (Avandia) and pioglitazone (Actos). Drug Programs Branch Bulletin 2002;2(1);1-4.

22. National Clinical Guidelines for Type 2 diabetes. National Institute for Clinical Excellence (NICE); October 2002. www.nice.org.uk.

23. Hahn AR, Heath Wg, Chang MH. Cardiovascular disease risk factors and preventive practices among adults - United States: A behavioural risk factor atlas. Morbidity and Mortality Weekly Report, 1998;47(S-5);35-69.

24. Neaton JD, Wentworth D. Multiple risk factor intervention trial research group. Serum Cholesterol, blood pressure, cigarette smoking and death from coronary heart disease. Arch of Int Med, 1992;152:56-60.

25. American Diabetes Association. Smoking and diabetes: Position statement. Diabetes Care, 2002;25(1):S80-1.

26. Bailey WC, Fiore MC, Stuart JC, et al. Treatment tobacco use and dependence. October 2000. www.surgeongeneral.gov/tobacco/tobaqug.htm .

27. Framework for diabetes education for health professionals: Specialty modules. Canadian Diabetes Association, 1999.

28. Management of blood glucose. Inherited Clinical Guideline G. National Institute for Clinical Excellence (NICE); September 2002. www.nice.org.uk.

29. Important safety information regarding Actos. Eli Lilly, November 2001.

30. Fedor JG, Jiri JF, Genest JGJ, et al. Recommendations for the management and treatment of dyslipidemia. CMAJ, 2000;162(10); 1441-7.

31. Estacio RO, Jeffers BW, Gifford N, et al. Effect of blood pressure control on diabetic microvascular complications in patients with hypertension and Type 2 diabetes. Diabetes Care, 2000;23:B54-64.

32. Hansson L, Zanchetti A, Carruthers SG, et al. Effects of angiotensin-converting- enzyme inhibition compared with conventional therapy on cardiovascular morbidity and mortality in hypertension: The Captopril Prevention Project (CAPP) randomized trial. Lancet, 1998;353:611-16.

33. Staesen JA, Want JG, Thijs L. Cardiovascular protection and blood pressure reduction: A meta-analysis. Lancet, 2001;358: 1305-15.

34. Kannel WB, Wilson PW, Zhang TJ. The epidemiology of impaired glucose tolerance and hypertension. Am Heart J, 1991;121:1268-73.

35. Hansson L, Zanchetti A, Carruthers SG, et al. Effects of intensive blood pressure lowering and low-dose aspirin in patients with hypertension: Principal results of the Hypertension Optimal Treatment (HOT) randomized trial. Lancet,1998;351:1755-62.

36. Heart Outcomes Prevention Eveealuation (HOPE) Study Investigators. Effects of ramipril on cardiovascular and microvascular outcomes in people with diabetes mellitus: Results of the HOPE study and MICRO-HOPE substudy. Lancet,2000;355:253-9.

37. Bakris G, Boone J. Patients with hypertension and diabetes need tight blood pressure control. American College of Cardiology Conference 2000.

38. Blood Pressure Lowering Treatment Trialists' Collaboration. Effects of ACE inhibitors, calcium-channel antagonist, and other blood-pressure-lowering drugs: Results of prospectively designed overviews of randomized trials. Lancet, 2000;356:1955-64.

39. ALLHAT (Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial) Officers and Coordinators. Major outcomes in high-risk hypertensive patients randomized to angiotensin-converting enzyme inhibitor or calcium-channel blocker vs diuretic. JAMA, 2002;288(23):2981-97.

40. Elliot S. Symposium lecture: Update of physiology and sexuality. Diabetes Conference 2001, Edmonton, AB.

41. Koda-Kimble MA, Young YL, Applied therapeutics: The clinical use of drugs, ed. 7. Lippincott Williams & Wilkins, 2001, pp 99-6.

42. Parving HH, Hehnert H, Brochener-Mortensen J, et al. The effect of irbesartan on the development of diabetic nephropathy in patients with Type 2 diabetes. N Engl J Med, 2001,345:870-8.

43. Brenner BM, Cooper ME, de Zeeuw D, et al. Effects of losartan on renal and cardiovascular

outcomes in patients with Type 2 diabetes and nephropathy. N Engl J Med, 2001;345:861-9.

44. Haffner SM, Lehto S, Ronnemaa T, et al. Mortality from coronary heart disease in subjects with Type 2 diabetes and nondiabetic subjects with and without prior myocardial infarction. N Engl J Med, 1998;339:229-34.

45. Meade TW, Brennan PJ. Determination of who may derive most benefit from aspirin in primary prevention: Subgroup results from a randomized controlled trial. BMJ, 2000;321:13-7.

46. Beeker CR, Fintel JD, Green D. Antithrombotic therapy, ed. 2. West Islip: Professional Communications, 2001, pp 63-76.

47. Diabetes Control and Complications Trial Research Group. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. N Engl J Med, 1993;329:977-86.

48. Ellen LT, Pacaud D. Hypoglycemia: Understanding the enemy. Canadian Diabetes Association, 2002;15(3):1-7.

49. Yale JF, Begg I, Gerstein H, et al. Canadian Diabetes Association clinical practice guidelines for the prevention and management of hypoglycemia in diabetes. Can J Diabetes, 2002;26:22-35.

QUESTIONS

1. Which of the following is NOT a macrovascular complication of diabetes?
a) Stroke
b) Neuropathy
c) Peripheral vascular disease
d) Coronary artery disease

2. What causes the highest mortality for patients with diabetes?
a) Renal failure
b) Infections secondary to neuropathy
c) Claudication
d) Cardiovascular disease

3. Which of the following statements is TRUE with regard to the pathophysiology of Type 2 diabetes?
a) The cause of Type 2 diabetes is high cholesterol.
b) Initially, ß-cells reduce insulin production while adipocytes down-regulate insulin receptors to cope with insulin resistance.
c) Hyperglycemia is always the only manifestation of insulin resistance.
d) Many people may already have insulin resistance, but they don't know it.

4. What is the most common dyslipidemia profile seen in patients with insulin resistance?
a) High HDL, high LDL, low TG
b) Low TG, low LDL, high HDL
c) High TG, low HDL, high LDL
d) High LDL, low TG, low HDL

5. All of the following statements are TRUE, EXCEPT:
a) Hypercoagulable state in patients with diabetes is the result of increasing platelet aggregation, clotting factors and plasminogen inhibitor-1.
b) There is no correlation between hyperglycemia and macrovascular complications.
c) The coexistence of diabetes and high blood pressure increase cardiovascular risks significantly.
d) In patients with insulin resistance, abnormal lipid profile may exist when hyperglycemia is not present.

CASE STUDY #1

Mrs. D.A. is a 42-year-old woman who has been recently diagnosed with Type 2 diabetes. She is a new patient who has come into your pharmacy to fill a prescription. The following information is gathered from Mrs. D.A.

Ht: 160 cm
Wt: 72 kg
BMI: 28 kg/m² {(72 kg ÷ (1.6m)²}
RX: Metformin 500 mg p.o. t.i.d.
Mrs. D.A. walks up to 20 minutes a day.
Smokes 2 packages of cigarettes a day.
Drinks alcohol occasionally.
Recently separated from her husband.
She has a 4-year-old son.
She will be laid off in a month.
Her mother had Type 2 diabetes and died at age 55.

6. What other critical information do you need to obtain from Mrs. D.A.?
a) Has she had her cholesterol tested?
b) Has she been in contact with a diabetes clinic?
c) What have her blood glucose readings been in the past?
d) All of the above.

7. What is NOT a priority on your list of things to discuss with Mrs. D.A. today?
a) How often she will need to monitor her blood glucose.
b) When to expect the medication to work.
c) Pharmacological options to stop smoking.
d) When you will call her to follow up.

8. Three days later, Mrs. D.A. experiences diarrhea with metformin. She has decided to stop the medication. What is the most viable option for her?
a) Reduce metformin dose to 250 mg bid, and slowly increase it q3d.
b) Stop metformin and use rosiglitazone or pioglitazone.
c) Stop metformin and use glyburide.
d) Start insulin.

9. Mrs. D.A. is on a nicotine patch for smoking cessation. Which statement will NOT help her achieve her goal?
a) She is advised to have low-calorie snacks (celery sticks, carrots) or sugarless gum when she craves a cigarette.
b) She should take bupropion sustained-release on the day she has decided to quit smoking.
c) Help her make a list to remind herself why she wants to quit smoking.
d) Encourage her to join a smoke-free support group.

10. What is a healthy weight-loss goal for Mrs. D.A.?
a) 0.25 - 1.0 kg or 0.5 -2 lbs a day
b) 0.25 - 1.0 kg or 0.5 - 2 lbs a month
c) 0.25 - 1.0 kg or 0.5 - 2 lbs a week
d) None of the above.

11. Mrs D.A. has brought in her cholesterol results for you to explain for her. You calculated her 10-year risk for a cardiovascular event as 38%. She has no allergy to ASA and no history

QUESTIONS (continued)

of gastrointestinal bleeding. You recommend that she start low-dose ASA. To help her comply with this treatment, she needs to understand how this therapy works. Which statement is TRUE?
a) ASA will stop a heart attack from occurring.
b) ASA will thin her blood to improve circulation and prevent the development of neuropathy.
c) ASA will thin her blood to make it easier for the heart to pump blood to the rest of her body, preventing her from having a heart attack.
d) She is at high risk for a cardiovascular event and ASA will help minimize the damage if she has a clot.

CASE STUDY #2
Mrs. I.D. is a 68-year-old woman with Type 2 diabetes. She has just started on insulin. Her doctor calls and asks you to teach her how to use a Novolin Pen. Her new prescription is for Novolin 30/70 10 U every morning and 6 U at supper. Mrs. I.D. is 160 cm tall, weighs 45 kg and has a BMI of 18.7 kg/m².

12. Which needle is ideal for Mrs. I.D.?
a) Novolin 30 G x 6 mm
b) Novolin 30 G x 8 mm
c) Ultra-fine III 30 G x 12 mm
d) None of the above

13. In order for Mrs. I.D. to be compliant, you need to discuss the following with her, EXCEPT:
a) Review the signs and symptoms of hypoglycemia
b) Remind her to take her blood glucose reading at least 4 times a day (before meals and at bedtime).
c) Exercise will increase the effect of insulin.
d) Drink a full glass of orange juice and eat a couple of cookies when she experiences a hypoglycemic reaction.
e) When insulin will reach its peak of action and be sustained in the body after injection.

14. Mrs. I.D.'s insulin dosage has been increased. Her insulin dose is now

22 U every morning and 12 U at supper. Her blood glucose readings are consistently low at bedtime (2.2 - 3.1 mmol/L) and her morning fasting blood glucose readings are high (12.1 - 15.6). When asked, she tells you that she eats at night because her blood glucose is low. She is afraid of dying in her sleep because that's what happened to her husband when his blood glucose levels were low. What can you do to help her overcome this fear, and help her achieve target blood glucose?
a) Draw a diagram and discuss again when insulin is expected work.
b) Suggest to her doctor that her supper insulin dosage be reduced.
c) Give her a handout and discuss again how much food to eat when she experiences hypoglycemia and when to recheck her blood glucose.
d) All of the above.

CASE STUDY #3
Mr. O.B. is an overweight 53-year-old, self-employed businessman. He has Type 2 diabetes and is on metformin and insulin. His blood pressure reads 160/94 mm Hg. When he sees you at the pharmacy, he tells you he is under a lot of stress. He has no problems with his kidneys. He has stopped taking ramipril because he can't afford it anymore due to business slowdown, and his blood pressure is on the rise.

15. What can you do for Mr. O.B.?
a) Discuss a less costly drug that he can afford as an alternative treatment and call his doctor to inform him of the situation.
b) Refer Mr. O.B. to a diabetes clinic to provide extra social support.
c) Ask Mr. O.B. about his physical activity and blood glucose.
d) All of the above

16. If Mr. O.B. has sexual dysfunction secondary to diabetes, which of the following class of drug(s) can potentiate the problem?
a) A thiazide or a calcium-channel blocker
b) Only a thiazide

c) Only a B-blocker
d) A thiazide or a B-blocker

17. Mr. O.B. tells you that the doctor wants him to exercise. He wants to join a fitness club, but he can't afford it right now. He has no other medical problem. The following advice may be useful in initiating his physical activity, EXCEPT:
a) He can start walking 10 minutes a day, increasing the time gradually as tolerated.
b) He must do a cardiovascular exercise to increase his heart rate to 120 beats/minute for 5 minutes, and increase the time gradually.
c) He can bicycle for 10 minutes, slowing increasing the time.
d) There are exercise videos that he can rent or borrow from the library or diabetes clinic to do at home.

18. What is Mr. O.B.'s blood pressure target?
a) <140/85 mm Hg
b) <140/80 mm Hg
c) <130/80 mm Hg
d) <135/75 mm Hg

19. When should glucagon 1 mg s.c/i.m be used?
a) For a conscious hypoglycemic patient.
b) For any unconscious hypoglycemic patient.
c) For an unconscious patient who has poor veins and intravenous line cannot be started.
d) For a person with hyperglycemia.

20. Which of the following statements is TRUE with regard to hypoglycemia treatment?
a) Administer Glucose Gel bucally to an unconscious hypoglycemic patient.
b) Administer 20 to 50 mL of D50W intravenously over 1 to 3 minutes to an unconscious hypoglycemic patient if patient's vein is accessible.
c) Give 12 Lifesaver candies to a patient if s/he is conscious and experiencing hypoglycemia.
d) Repeat blood glucose monitoring 5 minutes after receiving treatment.

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1. a b c d   6. a b c d   11. a b c d   16. a b c d
2. a b c d   7. a b c d   12. a b c d   17. a b c d
3. a b c d   8. a b c d   13. a b c d e   18. a b c d
4. a b c d   9. a b c d   14. a b c d   19. a b c d
5. a b c d   10. a b c d   15. a b c d   20. a b c d

_____   _____
Last Name   First Name

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Licensing Prov.   Licence #   Licensing Prov.   Licence #

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Email address

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Address (❏ Home ❏ Business)   City   Province

_____
Postal Code   Telephone

Type of practice

❏ Retail (chain)   ❏ Owner
❏ Retail (independent)   ❏ Full-time employee
❏ Grocery   ❏ Part-time employee
❏ Other (specify)

_____   Year Graduated _____

Feedback on this CE lesson
1. Do you now feel better able to provide pharmaceutical care for
   patients with Type 2 diabetes?   ❏ Yes   ❏ No
2. Was the information in this lesson relevant to your practice?   ❏ Yes   ❏ No
3. Will you be able to incorporate the information from this lesson
   into your practice?   ❏ Yes   ❏ No
4. Was the information in this lesson... ❏ Too basic   ❏ Appropriate   ❏ Too Difficult
5. Do you feel this lesson met its stated learning objectives?   ❏ Yes   ❏ No
6. What topic would you like to see covered in a future issue? _____

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