PRACTICAL DIABETES CARE

For Canadian Health Care Professionals

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ELSEVIER

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Canadian Diabetes Association

CONTENTS

INTRODUCTION

I have been a practising endocrinologist for more than 20 years. As with most endocrinologists, approximately 75% of my practice has involved the long-term care of people with diabetes. I have thoroughly enjoyed every minute and look forward to doing this for many years to come. As a full-time faculty member at the University of Manitoba, I have also spent considerable time teaching medical students, physicians in post-graduate training programs, family physicians in practice, and allied health care professionals, including diabetes educators, nurses, dietitians, pharmacists, and social workers. Over my years of teaching, I have discovered that I have a particular talent for successfully translating evidence-based clinical practice guidelines into the reality of daily clinical practice in diabetes.

After 20 years, I want to share my approach to the management of diabetes. This practical guide is targeted toward all health care professionals involved in diabetes care. These groups are, for the most part, involved with the care of people with type 2 diabetes. Accordingly, I am limiting this handbook to a discussion of type 2 diabetes.

Recognizing the rapidly increasing prevalence of type 2 diabetes across Canada and around the world, and mindful of the burden of disease that it brings to so many people, it is my goal to translate evidence-based guidelines into daily practice.

Remember, diabetes care involves the management of a chronic, lifelong disease. It is multifaceted, affecting a person's daily life, family, and workplace. Beyond the usual health impact, diabetes may also carry a significant psychological burden. Successful care means whole [person] care. That can be daunting for an individual health care provider. Team care — such as a diabetes health care team — can make a huge difference. Teams can be on-site, off-site, virtual, fluid in their composition, and changing as the needs of the person with diabetes change. Teams provide support not only for the person but for the team as a whole. It is an approach that is gaining acceptance as the population with diabetes grows and the need for care increases.

By way of disclaimer, I represent the physician member of the health care team. I do not claim to possess the expert skills of a diabetes educator, nurse, or dietitian. Therefore, the views expressed in this handbook derive from the physician's perspective; they do not include the invaluable knowledge and expertise that these other members offer as an integral part of the diabetes health care team. So, seek out the diabetes team members in your area.

I hope you will find this handbook to be useful in your everyday clinical practice as you manage your patients with type 2 diabetes.

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DIABETES CARE IN THE OFFICE

Introduction

Diabetes care comprises a significant amount of routine office practice for family physicians. As with all chronic diseases, diabetes takes time. As well, recognizing the associated complications of diabetes, it is no longer sufficient to simply review blood glucose levels with patients. The complete assessment of people with diabetes must include a review of diabetes medications, blood glucose levels, nutritional intake, physical activity, and stress. Also important is a review of possible micro- and macrovascular complications. All of these components play a role in successful diabetes management.

Awareness of diabetes and its growing impact is the first step in practice. With the prevalence of diabetes increasing at astounding rates, it would be difficult not to identify risk factors in the average primary care practice.

Risk factors for type 2 diabetes include:

- Age ≥40 years
- First-degree relative with type 2 diabetes
- Member of a high-risk ethnic group: Aboriginal, Hispanic, Asian, South Asian, or African descent
- Associated conditions of insulin resistance, including impaired glucose tolerance (IGT), polycystic ovarian syndrome, gestational diabetes mellitus, acanthosis nigricans, metabolic syndrome with IGT or impaired fasting glucose (IFG), hypertension, and dyslipidemia
- The presence of cardiovascular risk factors, such as hypertension, abdominal obesity, or obstructive sleep apnea
- The presence of psychiatric disorders, including schizophrenia, bipolar disease, depression and/or the use of atypical antipsychotic medications
- The use of medications known to be associated with diabetes, e.g. glucocorticoids and highly active antiretroviral therapy

Diagnosis of Diabetes

The diagnosis of diabetes is straightforward and there are a number of ways to diagnose the disease.

- **Random plasma glucose ≥11.1 mmol/L** (with or without typical symptoms of hyperglycemia, including excessive thirst (polydipsia), increased urination (polyuria), blurred vision, extreme fatigue, or unintended weight loss).
- **Fasting plasma glucose (FPG) ≥7.0 mmol/L** (fasting means no caloric intake for at least 8 hours).
- **Glycated hemoglobin (A1C) ≥ 6.5%** is another valid diagnostic test for diabetes. It is important to remember, however, that some factors — e.g. iron deficiency — may affect A1C values.
- The gold-standard test remains **the 2-hour ≥11.1 mmol/L in a 75-g oral glucose tolerance test (OGTT)**.

Normally, the diagnostic test for diabetes should be confirmed on another day, but a delay of treatment should not occur in those persons who are symptomatic or who are suspected to have type 1 diabetes.

Table 1 summarizes the diagnostic criteria for diabetes.

TABLE 1

Diagnosis of diabetes

FPG ≥7.0 mmol/L
or
A1C ≥6.5% (in adults)
or
2hPG in a 75 g OGTT ≥11.1 mmol/L
or
Random PG ≥11.1 mmol/L

2hPG, 2-hour plasma glucose; A1C, glycated hemoglobin; FPG, fasting plasma glucose; OGTT, oral glucose tolerance test

Diagnosis of Prediabetes

Prediabetes defines an earlier stage of glucose intolerance, identified as either impaired glucose intolerance (IGT) or impaired fasting glucose (IFG). Recently, A1C values of 6.0–6.4% have been recommended as diagnostic values for prediabetes. However, it has also been recognized that some individuals with lower blood glucose levels may still be at increased risk for diabetes. Accordingly, any patient with an FPG of 6.1–6.9 mmol/L and/or an A1C of 5.5–5.9%, in the presence of diabetes risk factors, should be screened with a 75-g OGTT. Besides being at greater risk from converting to type 2 diabetes, prediabetes — particularly IGT — confers a separate risk for the development of cardiovascular disease (CVD). Thus, there is value in recognizing prediabetes.

Table 2 summarizes the diagnostic criteria for prediabetes.

TABLE 2

Diagnosis of prediabetes

Test	Result	Prediabetes category
FPG (mmol/L)	6.1–6.9	IFG
2hPG in a 75 g OGTT (mmol/L)	7.8–11.0	IGT
A1C (%)	6.0–6.4	Prediabetes

2hPG, 2-hour plasma glucose; A1C, glycated hemoglobin; FPG, fasting plasma glucose; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; OGTT, oral glucose tolerance test

Management of Prediabetes

What is the best approach to the management of prediabetes? Research has demonstrated overwhelmingly that lifestyle changes (i.e. nutritional intake, physical activity) can reduce the risk of prediabetes evolving into type 2 diabetes. The challenge is that these changes must be consistent and maintained over time. Some physicians may consider initiating pharmacologic therapy for these patients, e.g. an insulin sensitizer such as metformin. However, it may be difficult for patients to commit to long-

term pharmacologic therapy for a condition that they do not necessarily consider a medical state or disease. Working diligently with a nonpharmacologic approach is generally deemed to be the most acceptable choice for patients. As prediabetes confers a separate risk for CVD, it is important to screen for any other modifiable CVD risk factors, including hypertension and dyslipidemia.

Diagnosis of Metabolic Syndrome of Insulin Resistance

Metabolic syndrome refers to a constellation of conditions that confer a high risk of CVD in an individual. These conditions include prediabetes, diabetes, hypertension, dyslipidemia, and abdominal obesity, all of which can and should be modified. Table 3 lists the clinical characteristics for diagnosing metabolic syndrome.

TABLE 3

Clinical characteristics for diagnosing metabolic syndrome

Risk factor	Threshold value	
	Men	Women
Elevated waist circumference		
Canada, United States	≥102 cm	≥88 cm
Europid, Middle Eastern, sub-Saharan African, Mediterranean	≥94 cm	≥80 cm
Asian, Japanese, South and Central American	≥90 cm	≥80 cm
TG	≥1.7 mmol/L	
HDL-C		
Men	<1.0 mmol/L	
Women	<1.3 mmol/L	
BP	≥130/85 mm Hg	
FPG	≥5.6 mmol/L	

BP, blood pressure; FPG, fasting plasma glucose; HDL-C, high-density lipoprotein cholesterol; TG, triglycerides

Organization of Diabetes Care: The Diabetes Health Care Team

Diabetes is primarily a self-managed disease. People with diabetes must commit themselves to a daily balance of lifestyle choices with respect to nutritional intake and physical activity, often in association with medications (i.e. oral agents, insulin or both). These demands of daily life may be difficult to accomplish alone — both for the person with diabetes, trying to cope, and for the physician who is trying to help him/her manage the disease.

That's why successful diabetes management "shares" the care with the diabetes health care team. Central to this team is the person with diabetes and his/her family. Pivotal team members also include the family physician, diabetes educators, and possibly an endocrinologist. When necessary, the diabetes health care team expands to include other health care and community service specialists and providers. Endocrinologists may take on roles beyond the customary consultant role; indeed, they may act as mentors, educators, and facilitators of shared care/case-management approaches with a primary care provider.

Most local health care jurisdictions have community-based diabetes education resources that can provide patient education and counselling regarding nutrition, physical activity self-monitoring of blood glucose (SMBG), and insulin administration. Advanced diabetes education teams can provide additional support with respect to managing complex diabetes medication regimens, specific diabetes problem-solving, and, oftentimes, help diabetes patients cope with the day-to-day stress of juggling nutritional intake, physical activity and medications.

Clinical organizational practices that have been shown to improve the care of people with diabetes include reminder and recall systems for both physician and patient; these systems render the regular monitoring of diabetes and its complications an automatic function. Depending on the individual clinic situation, reminder and recall systems are increasingly centralized through an electronic scheduling system. Such systems can be used for specific diabetes case management and or specific problem-solving by various health care team members.

For primary care providers who are not using electronic systems, various paper tools can still prove useful. Diabetes care plans, flow sheets, and other similar charts and forms can be used to maintain updated patient profiles and chronicle any complications by tracking clinical and laboratory data.

Type 2 Diabetes: Clinical Assessment

For the person who is newly diagnosed with diabetes, a complete clinical assessment is necessary. This should include assessment of acute complications (i.e. symptoms of hyperglycemia), as well as chronic microvascular complications (retinopathy, neuropathy, nephropathy) and chronic macrovascular complications (CVD, or peripheral or cerebral vascular disease).

It is particularly important to assess for the presence of chronic complications at the time of diagnosis, as the time of true onset of diabetes often predates the time of diagnosis; thus, chronic complications may already be present.

For the person with known diabetes, initial evaluation should include the above, as well as information-gathering regarding past and current diabetes medications, previous diabetes education experience, and assessment of diabetes knowledge.

Checklist for Diabetes Assessment

- **Current status**
  - Symptoms of hyperglycemia:
    - Thirst
    - Urinary frequency
    - Blurred vision
    - Skin, vaginal or urinary tract infections
    - Unexpected weight loss

- **Diabetes assessment**
  - Current diabetes medications
  - Previous diabetes education knowledge and skills, including: blood glucose monitoring, insulin administration, and dosage adjustment
  - Any episodes of hypoglycemia

- Nutritional intake, including meal and snack patterns, food choices, and weight history
- Physical activity
- Family history of diabetes
- Health determinants, including family or caregiver supports, financial issues, and health beliefs

- **General assessment**
  - Other health problems, including depression
  - Other medications, including nonprescription medications
  - Allergies
  - Smoking and alcohol history

- **Diabetes complication assessment**
  - Retinopathy:
    - Date of last retinal assessment
    - Blurred vision
  - Neuropathy:
    - Peripheral numbness or paraesthesia
    - Foot ulcers
    - Erectile dysfunction
    - Gastroparesis, with early satiety after meals and/or bloating
    - Significant diarrhea and/or constipation
    - Hypoglycemia unawareness
  - Nephropathy:
    - Hypertension
  - CVD, peripheral or cerebral disease:
    - Dyslipidemia
    - Angina
    - Myocardial infarction
    - Transient ischemic attack, cerebral vascular accident
    - Claudication

- **Physical examination**
  - General:
    - Weight, body mass index, and waist circumference
    - Blood pressure (BP)
  - Systems: Assessing for complications
    - Eye
      - Cataracts
      - Fundoscopic exam (does not replace retinal assessment through dilated pupils by an experienced examiner)
    - Oral: teeth and gums
    - Thyroid (thyroid disorders are common; however, there is no specific relationship to type 2 diabetes)
    - Foot examination
      - Screening for vascular integrity:
        - Colour
        - Skin and nail condition
        - Peripheral pulses
      - Screening for peripheral neuropathy:
        - Semmes-Weinstein 10-g monofilament
        - Presence of vibration sense or proprioception
        - Presence of infection or ulceration
        - Presence of ankle reflexes

- **Investigations**
  - Glycemic control:
    - Glycated hemoglobin (A1C)
    - Review of self-monitoring of blood glucose (SMBG) records
  - Complication assessment:
    - CBC
    - Electrolytes
    - Liver function
    - Renal function:
      - Urine albumin/creatinine ratio
      - Serum creatinine
      - Estimated glomerular filtration rate (eGFR)
    - Lipid profile

- TSH
- Retinal exam through dilated pupils by an experienced examiner
- Baseline EKG for adults aged >40 years, or aged >30 years and the presence of diabetes >15 years, identified micro/macrovascular complications or other cardiac risk factors
- Stress test/exercise EKG, if indicated by the presence of typical or atypical cardiac symptoms, the presence of associated vascular disease, or baseline EKG abnormalities (e.g. Q waves)

Management Algorithms for Type 2 Diabetes

Lifestyle

Lifestyle changes remain the foundation upon which diabetes management is built. This is where diabetes management starts, and the issue should be revisited regularly. By way of a disclaimer, I am not a diabetes educator, dietitian, or nurse. What I describe throughout this book with respect to lifestyle changes by no means replaces the expert advice delivered by a team of dedicated diabetes educators. However, I hope to provide strategies that can be used in office situations to fill the gap until the diabetes health care team can become involved.

Fundamental, practical approaches can be made in the physician's office, with reinforcement made through community-based diabetes education programs. Simple office strategies include the following:

Nutritional intake

- Review the person's nutritional intake by reviewing what they ate over the past 24 hours. This can be done quickly and is often more revealing because you are asking "What did you actually eat?" rather than "What do you usually eat?"
- Review quantities and sources of junk and fast foods, as well as sugar (regular soft drinks, unsweetened fruit juices and even excessive quantities of milk contain significant amounts of sugar).
- Review portion size. Easy tools include the "plate method" and the "handy portion guide" (also known as the "hand jive") to provide people with helpful reference points for portion size.

- Review habits regarding dining away from home (e.g. How often do they eat fast food, or visit restaurants and buffets?).

Physical activity

- Establish if a person is active outside of his/her normal daily activities (being busy at work doesn't count!).
- Walking is the simplest and least expensive way to start a physical activity regimen. Does the person have adequate running/walking shoes and somewhere safe to walk, especially in winter?
- Start small; walking for 10 to 15 minutes twice daily seems more manageable if a person hasn't walked in years. Can they ultimately aim for 30 to 60 minutes each day?
- What are the barriers to physical activity, and can they be overcome? Often, the person's state of mind or readiness to change presents the greatest challenge.

Self-monitoring of blood glucose (SMBG)

SMBG provides useful educational feedback to people with diabetes. Understanding target blood glucose levels (Table 4) can help them assess the effect of their diabetes medication regimen and motivate them to change their nutritional intake and physical activity regimen to improve blood glucose control. Moreover, SMBG can motivate a person to think about his or her diabetes in order to continue meeting the daily challenges that the disease presents.

For patients taking oral medication that has the potential to trigger hypoglycemia, it is crucial that they perform SMBG. Naturally, the use of any insulin regimen necessitates the use of monitoring to evaluate the effect of the insulin regimen on glucose control, as well as assess for risk of hypoglycemia.

SMBG frequency is truly at each patient's discretion. One practical regimen is to check once or twice per day, but at different times over the course of a given week (either before meals or 2 hours after meals). That way, over time, a person will be able to evaluate his or her diabetes control

fairly well and recognize any patterns of high or low blood glucose levels and take steps to correct them.

Glycated hemoglobin (A1C)

A1C is an effective and objective retrospective marker of blood glucose control for the previous 3 months. While the recommended A1C target is ≤7.0%, this target can be individualized. Indeed, there will be circumstances where this target is too stringent, as trying to achieve it may result in recurrent episodes of hypoglycemia. This must be considered in those individuals who would be vulnerable to hypoglycemia. In those circumstances, the target A1C can be relaxed to >7.5% or even higher (up to 8.5%) depending on individual circumstances (e.g. significant comorbidities, dependence on external caregivers).

When to Add Medications

The decision regarding whether and when to initiate or add medications should be based on glycemic control. If glycemic control is poor (generally deemed to be A1C ≥8.5%), medication (singly or in combination) should be started at the time that lifestyle changes are initiated. Timely reassessment will help determine the need to start or add medications, as indicated. The following table lists A1C and blood glucose targets.

TABLE 4

Target blood glucose and A1C levels for adults

	A1C (%)	FPG/ preprandial PG (mmol/L)	2h postprandial PG (mmol/L)
Target for most patients	≤7	4–7	5–8/10
Normal range	≤6	4–7	5–8

2h postprandial PG, 2 hour postprandial plasma glucose; A1C, glycated hemoglobin; FPG, fasting plasma glucose; PG, plasma glucose

Management Algorithms for Type 2 Diabetes: Oral Agents

The choice of oral agent(s) should be determined on an individual basis. A basic knowledge of the mechanism of action for the various oral agent categories is necessary. The general approach is to evaluate oral agents, singly or in combination, on the basis of their ability to decrease and maintain A1C levels in the context of their safety, tolerability, ease of use, and cost.

Most often, an insulin sensitizer (i.e. metformin) is the first-line agent. Combinations of oral agents in submaximal dosages can result in more rapid and improved glycemic control and have proven to be a very useful approach. Oral agents may be used effectively in combination with insulin, often basal insulin (intermediate or long-acting) once or twice daily.

The current evidence shows that lower blood glucose levels at the time of initiation of therapy have been found to be associated with lower A1C levels over time and decreased long-term complications. With this in mind, a patient will have better long-term control of diabetes if the diagnosis and treatment intervention is initiated early, when the metabolic abnormalities of diabetes are usually less severe.

Table 5 summarizes the oral agents currently available in Canada, their general mechanism of action, dosage and dosing strategies, and common adverse effects.

TABLE 5

Oral antihyperglycemic agents

Agent	Mechanism	Dosage	Action time	Benefits	Disadvantages
Biguanide (insulin sensitizer)					
Metformin Glucophage	• Insulin sensitizer • Reduces hepatic glucose output	• Start 250–500 mg bid ac meals • Start with low dose and increase slowly • Maximum dose 2550 mg/day in divided doses	8 hrs	• Does not promote weight gain • Rarely causes hypoglycemia • Can be used in combination with daytime insulin	• GI: nausea; bloating; diarrhea • Slow increase in dose decreases these side effects • Contraindicated with renal or hepatic impairment, or CHF
Sulfonylureas (insulin secretagogues)					
Glyburide Diabeta	• Stimulates pancreatic secretion of insulin	• Start 2.5–5 mg od or bid ac meals • Maximum dose 10 mg bid	16–24 hrs		• May cause weight gain • May cause hypoglycemia
Gliclazide Diamicron	• As above	• Start 80 mg od • Maximum dose 160 mg bid	8–16 hrs	• Causes less hypoglycemia than glyburide	• May cause weight gain
Diamicron MR	• As above	• Start 30 mg od • Maximum dose 120 mg od	24 hrs		
Glimepiride Amaryl	• As above	• Start 1–2 mg od • Dosage range: 1–8 mg od	24 hrs	• May be used in combination with daytime insulin • May cause less hypoglycemia than glyburide	• May cause weight gain

Agent	Mechanism	Dosage	Action time	Benefits	Disadvantages
Alpha-glucosidase inhibitor					
Acarbose Prandase Glucobay	• Inhibits glucosidase enzymes in carbohydrate digestion • Decreases • Postprandial glucose rise	• Start 25 mg with first bite of food • Titrate weekly to Usual dose of 50–100 mg/meal	Best effect seen postprandially	• No hypoglycemia if used alone	• GI: bloating, flatus • Start with low dose and increase slowly to decrease GI side effects • Beano counteracts GI effects • When treating hypoglycemia, use dextrose tablets, milk or honey
Meglitinide (insulin secretagogue)					
Repaglinide GlucoNorm	• Stimulates pancreatic insulin secretion • Different mechanism than sulfonylureas	• Start 0.5 mg taken 0–30 minutes before each meal • Or, titrate according to carbohydrate intake (1 mg/15 g carbohydrate) • Available in 0.5,1 and 2 mg dosages	Short-acting; stimulates insulin secretion in response to glucose rise at mealtime	• Controls postprandial glucose rise • Provides flexibility to fit varied mealtimes	• May cause hypoglycemia
Thiazolidinediones (insulin sensitizers)					
Rosiglitazone Avandia*	• Insulin sensitizer • Insulin action improved in liver, muscle and adipose tissue	• 2–8 mg daily as a bid dosage	Effect seen after 6 weeks	• May increase TG, decrease HDL	• Rosiglitazone is associated with a risk of CVD • Pioglitazone is associated with a risk of bladder cancer • Both may cause weight gain, peripheral edema, macular edema or CHF • Associated with an increased fracture risk in women
Pioglitazone Actos	• Insulin sensitizer • Insulin action improved in liver, muscle and adipose tissue	• 15–45 mg daily			

Agent	Mechanism	Dosage	Action time	Benefits	Disadvantages
					• Both contraindicated in CHF, hepatic impairment (monitor liver functions regularly)
Rosiglitazone/ metformin combination Avandamet*	• As per rosiglitazone and metformin	• R(1–4 mg)/ M(500–1000 mg)			• As per rosiglitazone • Should not be used- in combination with daytime insulin
Incretins (augment insulin action)					
Sitagliptin Januvia	• Augments endogenous insulin • Blocks glucagon action in liver (sensitizer and secretagogue effect	• 100 mg daily • 50 mg daily with eGFR 30-49 mL/min • 25 mg daily with eGFR <30 mL/min	4–6 weeks	• Weight neutral • Low risk for hypoglycemia	• Rare risk of pancreatitis
Sitagliptin/ metformin combination Janumet	• As per sitagliptin and metformin	• S (50 mg) • M (500–1000 mg)	As per sitagliptin and metformin	• As per sitagliptin and metformin	• As per sitagliptin and metformin
Saxagliptin Onglyza	• Augments endogenous insulin • Blocks glucagon action in liver (sensitizer and secretagogue effect	• 5 mg daily • 2.5 mg daily with eGFR 15-50 mL/min	4–6 weeks	• Weight neutral	• Requires dosage reduction in the presence of chronic kidney disease • Rare risk of pancreatitis
Saxagliptin/ metformin combination Kombiglyze	• As per saxagliptin and metformin	• S (2.5 ,5mg) • M (500, 1000 mg)	As per saxagliptin and metformin	• As per saxagliptin and metformin	• As per saxagliptin and metformin
Linagliptin Trajenta	• Augments endogenous insulin • Blocks glucagon	• 5 mg daily	4-6 weeks	• Does not require dosage adjustment in the presence of chronic kidney disease	• Rare risk of pancreatitis

Agent	Mechanism	Dosage	Action time	Benefits	Disadvantages
	action in liver (sensitizer and secretagogue effect				
Linagliptin/ metformin Jentadueto	• Augments endogenous insulin • Blocks glucagon action in liver (sensitizer and secretagogue effect	• L (2.5 mg) • M (500, 850, 1000 mg)		• Does not require dosage adjustment in the presence of chronic kidney disease	• Rare risk of pancreatitis
GLP 1 analogue (augments endogenous insulin)					
Liraglutide Victoza **Exenatide** Byetta	• Blocks glucagon action in liver	• 0.6–1.8 mg daily • 5-10 mcg bid	4–6 weeks	• Weight neutral • May lead to weight loss • Liraglutide now approved for use in combination with basal insulin (see insulin section)	• May cause nausea • Rare risk of pancreatitis • Contraindicated in those with past history or family history of medullary thyroid cancer/multiple endocrine neoplasia
Weight loss agent					
Orlistat Xenical	• inhibits fat absorption	• 100 mg with each meal			• Adverse GI effects
Novel agents					
Sodium-glucose co-transporter inhibitors					
Canagliflozin Invokana **Dapagliflozin** Forxiga **Remogliflozin** **Sergliflozin**	• Inhibit renal reabsorption of glucose	• 100–300 mg daily • 10 mg daily • 1000 mg od/bid • 500-1000 mg tid			• Glycosuria may increase risk of UTI
Dopamine agonist					
Bromocriptine-QR Cycloset**	• 0.8 mg daily, titrated weekly to 1.6–4.8 mg				• Nausea • Postural dizziness

*Difficult to prescribe, requiring physician and patient waivers **Novel use for diabetes

General Approaches to Diabetes Management

To reiterate, all people with diabetes will benefit from diabetes education, specifically with respect to nutritional intake and physical activity. Although behaviour changes take time, even small changes may improve clinical outcomes.

However, in the presence of significant hyperglycemia, it is important to start medications at the same time that lifestyle changes are being addressed.

What is significant hyperglycemia? By consensus, A1C 8.5% represents the cut-off. Accordingly:

- For A1C <8.5%, lifestyle ± one oral agent can be initiated. Metformin is the recommended first choice of oral agents.
- Renal function must be assessed before recommending metformin. In the presence of reduced renal function (defined as serum creatinine >130 µmol/L or eGFR <60 mL/min), metformin should be kept to a maximum dose of 500 mg bid. In the presence of worsening renal function with a serum creatinine >160 µmol/L or eGFR <30 mL/min, metformin should not be administered.
- For an A1C ≥8.5%: Combination therapy using 2 agents should be considered. The following options are recommended:

Metformin plus one of the following agents:

- Secretagogue:
  - Glyburide
  - Gliclazide/Gliclazide MR
  - Glimepiride
- Incretin agent:
  - DPP-4 inhibitor:
    - Sitagliptin
    - Saxagliptin
    - Linagliptin
  - GLP-1 analogue:
    - Liraglutide
    - Exenatide

The incretin class — GLP-1 agonists and DPP-4 inhibitors — appear to be useful in the older population. However, concerns about the relationship between incretins and pancreatic inflammation or possible malignant changes (pancreatic and medullary carcinoma of the thyroid) render a thorough medical review important before initiating therapy. It is important to remember that, to date, no significant warnings have been reported for this medication class.

- Meglitinide (target is postprandial hyperglycemia only)
- Alpha 1 glucosidase inhibitor (target is postprandial hyperglycemia only)
- Thiazolidinediones (TZDs) may play a limited role in diabetes. While TZDs were used extensively in the past, the evidence linking the TZD roziglitazone, in particular, to cardiac events has decreased their usage. There still may be a role for pioglitazone in the management of pre-diabetes or early, mild diabetes in people with no history or risk factor profile for cardiac disease. Remember that rosiglitazone cannot be prescribed without both a physician and patient waiver.

Remember, reassess in a timely manner — i.e. within 4-6 weeks — if glycemic control is not within or approaching target. Then reassess lifestyle factors and consider adding another agent and/or basal insulin. Aggressive combination therapy from the onset of newly diagnosed diabetes, including the use of basal insulin, has been shown to be effective.

Management of Type 2 Diabetes: Insulin ± Oral Agents

Table 6 lists the currently available types of insulin by their time action profiles.

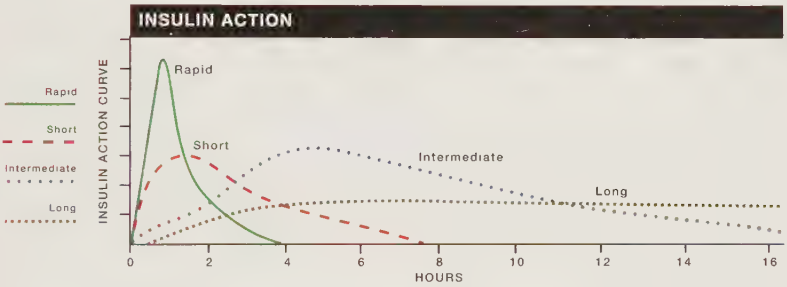
TABLE 6

Insulin types

Type	Trade name	Onset	Peak (h)	Duration (h)
Rapid-acting (Bolus)				
Lispro Aspart Glulisine	Humalog NovoRapid Apidra	10–15 min	1.0–1.5 hrs	3–5 hrs
Short-acting				
Regular R	Humulin R Novolin ge Toronto	0.5–1 hr	2–4 hrs	6–8 hrs
Intermediate-acting (Basal)				
NPH	Humulin N	1–3 hrs	4–8 hrs	12–18 hrs
Long-acting (Basal)				
Glargine Detemir	Lantus Levemir	90 min	No peak	24 hrs
Premixed (short- and intermediate-acting, R/NPH)				
10/90	Humulin (*premix available)	0.5 hr	2–12 hrs	12–18 hrs
30/70*	Novolin ge			
40/60			2-3 hrs	
50/50			1 hr	
Premixed insulin (rapid- and intermediate-acting)				
25% rapid-acting/75% intermediate-acting	Humalog Mix25	15 min	1 hr	10-14 hrs
30% rapid-acting/70% intermediate-acting	NovoMix 30			

FIGURE I

Time action profiles of insulin available in Canada



Insulin/Oral Agent Combinations

The insulin regimens outlined below are listed in the order in which they are commonly administered in type 2 diabetes. However, any regimen may be chosen, depending on individual circumstances.

Bedtime insulin and oral agents

This is a relatively simple method to introduce insulin into a combination regimen most, if not all, oral agents. Here, basal insulin (either intermediate or long-acting) is added at bedtime to help counteract hepatic glucose output during the night and thus lower FPG in the morning. Starting the day with a lower FPG level will allow the oral agents taken during the day to be more effective.

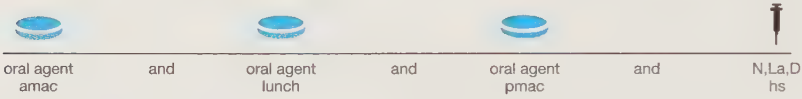
Legend for all figures to follow

A = Apidra; amac = before breakfast; bid = twice daily; D = detemir insulin; H = lispro insulin; hs = bedtime; La = glargine insulin; N = NPH insulin; NR = insulin aspart; pmac = before supper; qid = 4 times daily; R = regular insulin; TDD = total daily dosage; tid = 3 times daily

BEDTIME INSULIN AND ORAL AGENTS

N (or La or D) at hs and oral agents during the day.

Indications: Type 2 diabetes, to lower fasting glucose levels and to allow oral agents to have optimal effect.



Notes:

- Start with ≤5 units hs if the person is lean; ≤10 units hs if the person is not lean
- Alternatively, calculate the starting dosage by 0.2–0.3 units/kg
- Titrate the dosage according to the first morning SMBG by 1–2 units every 3 days until the FPG is at target
- Rapid insulin correction factor (CF): 1–2 units for every 3.0 mmol/L >7.0 mmol/L can be used at meals, along with oral agents

Daytime insulin and oral agents

Once- or twice-daily basal insulin can be used with most oral agents during the day in effective combinations. Generally, thiazolidinediones should not be used in combination with daytime insulin.

DAYTIME INSULIN AND ORAL AGENTS

Insulin twice daily amac and pmac with oral agents (except TZDs).

Indications: Type 2 diabetes.

Notes:

- Long-acting analogue or intermediate-acting insulin; the second dose may be given at bedtime, rather than at supper
- Initial dosage: ≤5 units bid if person is lean; ≤10 units bid if person is not lean
- Alternatively, calculate the starting dosage by 0.2–0.3 units/kg
- Titrate the dosage according to SMBG, FPG and pre-supper blood glucose by 1–2 units every 3 days until blood glucose is at target

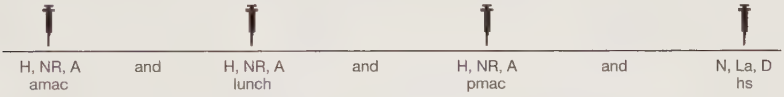
Basal/Bolus: qid

I prefer the term "basal/bolus" for this regimen, as I believe it is a functional term that describes precisely the insulin regimen. It also more closely patterns physiological insulin secretion. Basal insulin refers to either intermediate or long-acting insulin. Bolus refers only to rapid-acting insulin.

BASAL/BOLUS: QID

Indications: Either type 1 or 2 diabetes for optional control. This regimen requires close contact with the DHC team.

Dosage: 40 to 50% of TDD (N, La,D) at hs. Balance given as premeal H, NR, A based on insulin/CHO ratio.



Notes:

- TDD should be calculated as indicated below for basal and bolus insulin
- Alternatively, TDD can be calculated as 0.2–0.3 units/kg to start

Basal Insulin

- If starting as a new regimen, initial dosage: ≤5 units bid if person is lean; ≤10 units bid if person is not lean
- Alternatively, calculate the starting dosage by using 50% of calculated TDD
- Titrate the dosage of basal insulin according to the FPG by 1–2 units every 3 days until the FPG is at target

Rapid Insulin

- Rapid insulin dosage may be determined by the insulin to carbohydrate, starting with 1 unit rapid insulin/15 g carbohydrate
- Alternatively, rapid insulin dosage may be determined as a "flat dosage" for each meal, based on an average carbohydrate intake for each meal, calculating 1 unit/15 g carbohydrate to begin
- CF for rapid insulin: 1–2 units for every 3.0 mmol/L >7.0 mmol/L at meals only. A correction dose is not recommended at night if the person is using a long-acting analogue, as this increases the risk for nocturnal hypoglycemia

Basal/Bolus Insulin: tid

This is an alternative regimen that may help patients who have difficulty fitting in the lunchtime bolus insulin dose.

BASAL/BOLUS: TID

N amac and hs and H, NR, A (or R) amac and pmac.

Indications: Either type 1 or type 2 diabetes; may provide optimal control.

Dosage: 50 to 70% of TDD (2/3 N and 1/3 H, NR, A) amac and 15% to 25% of TDD (H, NR, A) pmac and 15 to 25% of TDD (N) at hs.

Notes:

- This option is meant for patients using NPH as their basal insulin rather than a long-acting insulin analogue
- TDD may be calculated as 0.2–0.3 units/kg to start

Basal Insulin

- If starting as a new regimen, initial dosage: ≤5units bid if the person is lean; ≤10 units bid if the person is not lean
- Alternatively, calculate the starting dosage as 50% TDD
- Titrate the dosage of basal insulin according to the FPG and pre-supper blood glucose by 1–2 units every 3 days until the blood glucose is at target

Rapid Insulin

- Rapid insulin dosage may be determined by the insulin/carbohydrate ratio for breakfast and supper only in this regimen
- Alternatively, rapid insulin dosage may be determined as a "flat dosage" for each meal, based on average carbohydrate intake for each meal calculating at 1 unit/15 g carbohydrate to begin
- CF for rapid insulin: 1–2 units for every 3.0 mmol/L > 7.0 mmol/L at meals only, and not at night if person is using a long-acting analogue

Premixed bid

The use of premixed insulin is considered when optimal glycemic control is not sought and a more complex insulin regimen is not practical.

PREMIX: BID

Indications: Type 2 diabetes, when optimal control is not desired. The disadvantage is that specificity in dosage adjustment is lost and a change in dose affects both insulins.

Dosage: 50 to 70% of TDD amac and 30 to 50% of TDD pmac.

Hypoglycemia Management

Current evidence suggests that 15 g of glucose is required to produce an increase in blood glucose of 2.0 mmol/L within 20 minutes, with adequate symptom relief for most people.

Examples of 15 g of carbohydrate for the treatment of mild-to-moderate hypoglycemia (>2.8 mmol/L) include:

- 15 g of glucose in the form of glucose tablets
  (1 tablet = 5 g carbohydrate)
  15 mL (3 teaspoons) or 3 packets of table sugar dissolved in water
- 175 mL (3/4 cup) of juice or regular soft drink
- 6 Life Savers™ (1 = 2.5 g of carbohydrate)
- 15 mL (1 tablespoon) of honey

A snack containing carbohydrate and protein should be consumed after the hypoglycemia has resolved, if mealtime is more than an hour away. The cause of the hypoglycemia should be assessed and strategies for avoiding hypoglycemia in the future need to be developed.

Retinopathy screening

People with type 2 diabetes should have their eyes examined at diagnosis. Screening for retinopathy should be performed by an experienced eye-care professional, either in person or through the interpretation of photographs.

The follow-up interval for individuals with minimal or no retinopathy is every 1 to 2 years. Table 7 outlines screening guidelines for retinopathy.

TABLE 7

Screening for retinopathy

When to initiate screening
In all individuals at diagnosis of type 2 diabetes
Screening methods
• 7 standard field, stereoscopic-colour fundus photography with interpretation by a trained reader (gold standard)
• Direct ophthalmoscopy or indirect slit-lamp fundoscopy through dilated pupil
• Digital fundus photography
If retinopathy is present
• Establish appropriate monitoring intervals (1 year or less) with an eye-care specialist
• Maintain glycemic, BP, and lipid targets
• Screen for other diabetes complications
If retinopathy is not present
• Rescreen every 1–2 years
• Maintain glycemic, BP, and lipid targets
• Screen for other diabetes complications

BP, blood pressure

Chronic kidney disease: nephropathy and hypertension

Screen for chronic kidney disease at the time of diagnosis of type 2 diabetes and annually thereafter. Screening for chronic kidney disease consists of a random urine albumin to creatinine ratio (uACR), as well as estimated glomerular filtration rate (eGFR). These are now simple "tick-off" tests on biochemistry requisitions.

The criteria for diagnosis of chronic kidney disease in diabetes is as follows:

- **Random uACR ≥2.0 mg/mmol and/or eGFR ≤60 mL/min confirmed by uACR ≥2.0 mg/mmol in 2 to 3 tests or repeat eGFR ≤60 mL/min within 3 months**

Some laboratories will quantify the ACR as microalbuminuria vs. macroalbuminuria. Those patients with macroalbuminuria can be considered to have nephropathy/chronic kidney disease, unless another cause of macroalbuminuria can be identified.

Interventions for microalbuminuria and nephropathy are outlined in Table 8, while follow-up therapies are outlined in Table 9.

TABLE 8

Interventions for nephropathy

Management of hypertension: This is the most important aspect of the intervention for nephropathy	• Hypertension in adults with diabetesshould be treated to achieve a target BP <130/80 mm Hg
ACE inhibitor or ARB for kidney protective effect	
Optimal glycemic control nutritional intake and SMBG	• Reinforce physical activity, appropriate • Initiate or adjust medication, as necessary
Smoking cessation and hypertension	• Smoking affects renal vasculature
Assess lipids	• Microalbuminuria can be a marker for dyslipidemia
Antiplatelet therapy (enteric-coated acetylsalicylic acid)	• 81–325 mg/day is recommended for adults with additional CVD risk factors or for secondary prevention in those with CVD

ACE, angiotensin converting enzyme; ARB, angiotensin II receptor antagonist; CVD, cardiovascular disease

TABLE 9

Follow-up nephropathy

1. Treat hypertension	• Target BP <130/80 mm Hg
2. Monitor renal function by eGFR or CrCl	• eGFR can be determined by the MDRD formula* (or by lab assay in certain jurisdictions) • Creatinine clearance can be determined by the Cockcroft-Gault equation
3. Monitor ACE/ARB therapy	• Serum creatinine may rise to as much as 30% above baseline, stabilizing within 2–4 weeks • No upper limit of creatinine re: contraindication, but caution when creatinine clearance <30mL/min • Serum potassium • ACR: after 3 months, and annually, looking for reduction
4. Indications for referral	• ACR persistently >60 mg/mmol • eGFR <30 mL/min • Serum creatinine >30% above baseline within 3 months of ACE or ARB therapy • Inability to achieve target BP

* Available at: www.nephron.com/cgi-bin/MDRD_GFR.cgi

ACE, angiotensin converting enzyme; ACR, albumin to creatinine ratio; ARB, angiotensin II receptor antagonist; BP, blood pressure; CrCl, creatinine clearance; eGFR, estimated glomerular filtration rate; MDRD, Modification of Diet in Renal Disease

Hypertension

Hypertension in adults with diabetes should be treated to achieve a target BP <130/80 mm Hg. Treatment includes lifestyle intervention, as well as the initiation of antihypertensive therapies (listed in order of choice). Combination therapy is often required.

- Angiotensin Converting Enzyme Inhibitor (ACE)
- Angiotensin Receptor Blocker (ARB)
- Dihydropyridine calcium channel blocker
- Thiazide diuretic
- Cardioselective beta blocker

Neuropathy

Diabetic neuropathy can affect the sensory, motor or autonomic nervous system. Classifications and descriptions of diabetic neuropathy are noted in Table 10.

TABLE 10

Classifications and descriptions of diabetic neuropathy

Classification	Description	Interventions
Diffuse symmetrical polyneuropathy	• Common presentation is peripheral "numbness and tingling," involving hands and feet • Severe presentations have variable types of pain disrupting sleep. Neuropathic pain must be distinguished from intermittent claudication	**Anticonvulsants*** • Gabapentin • Pregabalin • Valproate **Antidepressants*** • Amitriptyline • Duloxetine • Venlafaxine • Opioid analgesics • Capsaicin cream • Topical nitrate spray
Focal mononeuropathies		
Cranial	• e.g. third nerve palsy with ptosis	• Usually resolve spontaneously
Peripheral	• e.g. carpal tunnel syndrome • Foot drop	
Radiculopathy	• Pain in truncal spinal nerve distribution	
Diabetic amyotrophy	• Proximal neuropathy manifested by pain, proximal muscle weakness, and muscle atrophy	• May respond to treatment for peripheral neuropathy
Autonomic neuropathy		
Gastrointestinal dysfunction	• Gastroparesis with vomiting, abdominal bloating, and pain	• Gastrointestinal motility pharmaco-therapy, e.g. domperidone • Frequent small meals

		• Consider basal/bolus insulin regimen with rapid-acting insulin after meals, as blood glucose starts to rise
	• Diarrhea	• Antidiarrheal medications
	• Constipation	• Increase water and dietary fibre intake
Genitourinary dysfunction	• Difficulty with micturition • Incontinence or incomplete emptying (neurogenic bladder) • Erectile dysfunction • Retrograde ejaculation	• Options for erectile dysfunction include phospho-diesterase type 5 inhibitors, vacuum pump, intrapenile prostaglandins, injections or prosthesis • Urology referral
Cardiovascular dysfunction	• Postural hypotension	• Elastic stockings • Mineral-ocorticoid medication
	• Atypical angina	• High index of suspicion
Other	• Hypoglycemia unawareness	• Frequent SMBG
	• Anhydrosis, resulting in dry, cracked feet	• Use moisturizers

*Allow 6–8 weeks for effect

SMBG, self-monitoring of blood glucose

Use of a monofilament to detect neuropathy

The 10-g Semmes-Weinstein monofilament consists of a nylon filament mounted on a handle that has been standardized to deliver a 10-g force when applied properly. Screening with a monofilament is a validated method of assessing for the presence of peripheral neuropathy; it also helps the clinician to determine the risk of foot ulceration.

The monofilament should be applied to the plantar surface of the great toe, and the first and fifth metatarsal heads. The duration of time with which the monofilament should be in contact with the skin should be 2 seconds. Ideally, the application should occur twice at the same site. Avoid applying the monofilament to ulcer sites, calluses, scars, or necrotic tissue.

Photo: American Diabetes Association

To perform a monofilament examination, ask the patient to indicate when and where they can feel the monofilament touching his/her foot. Protective sensation is deemed to be present if the patient correctly answers more than 75% of the time.

Table 11 identifies risk categories and interventions using the Semmes-Weinstein monofilament. Table 12 shows classifications and interventions for diabetic foot ulcers.

TABLE 11

Risk categories and interventions using the Semmes-Weinstein monofilament

Category	Classification	Intervention
0	• Intact protective sensation	• Low to no risk of foot complications • Education to be provided • Specialized footwear not necessary at this time • Examine feet at each visit, at least every 4–6 months
1	• Absent protective sensation • Normal foot morphology • No history of ulceration	• Examine feet at each visit, or at least four times per year • Appropriately fitted footwear with a soft insole • Education to be provided
2	• Absent protective sensation • Foot deformity present • Plantar ulceration absent	• Examine feet at each visit, or at least four times per year • Appropriately fitted footwear with a suitable insole • Education to be provided
3	• Absent protective sensation • History of plantar ulcer	• Examine feet at each visit, or at least four times per year • Appropriately fitted footwear with a suitable insole (may need custom footwear) • Education to be provided

TABLE 12

Classification and intervention for diabetic foot ulcers

Wagner's grade	Criteria	Intervention
0	• Skin intact • No open lesions • May be non-blanching erythema	• Pare callous; appropriate footwear to protect feet and reduce pressure over pressure points
1	• Superficial skin ulceration (may be seen under area of high pressure)	• Pare callous to expose ulcer base; obtain specimen for culture, if evidence of infection (redness, heat, pus) is present • A hydroactive gel covered by clean gauze is the simplest approach • Saline wet to dry dressings are an alternative, if necrotic debris is present at the base of the wound • Pressure relief is critical for healing and can be accomplished with appropriate footwear, crutches, wheelchairs, and casting • Infected ulcers require antibiotics
2	• Deeper ulceration, associated with infection/cellulitis • Does not extend to bone	• X-ray to determine if bone is involved • Manage the same as Grade 1 ulcer; use antibiotics
3	• Ulcer has extended to deeper tissue layers such as bone	• X-ray to determine if bone is involved

	• Has abscess formation or osteomyelitis	• Surgical debridement of infected bone • Appropriate antibiotics administered • Use noninvasive assessment of peripheral circulation (ankle brachial index); vascular surgical referral may be indicated
4	• Localized gangrene of toes, forefoot, heel	• Manage as for Grade 3 ulcer • Urgent noninvasive assessment of peripheral circulation; vascular surgical referral may be indicated
5	• Gangrene of entire foot	• Urgent assessment as for grade 4 lesions • Vascular surgical referral

Antibiotic therapy for foot infections

Although the first-line therapy for many foot infections is an agent such as cloxacillin, cephalexin, clindamycin or amoxicillin clavulinic acid, the increasing prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA) in Canada renders the consideration of an agent such as trimethoprim sulfamethoxazole an option in situations where the risk of MRSA-related infections is high. In patients who require intravenous antibiotic therapy, vancomycin IV is an appropriate first-line therapy for the management of infections caused by MRSA.

Although the antibiotic choices above are suggested as empiric therapy, the ideal approach is to obtain a specimen for culture, initiate empiric therapy, and modify the therapy according to the results of the culture.

TABLE 13

Interventions for foot complications

Complication	Intervention
• Non-blanching erythema over pressure points	• Reduce pressure with appropriate foot wear
• Calluses and corns	• Reduce pressure with appropriate footwear • Pare carefully • Use pumice stone
• Cutaneous fungal infections • Intertrigo	• Clotrimazole cream 1% or tolnaftate cream 1% or powder applied twice daily • May require antibiotics for superimposed bacterial infection • Keep affected skin areas dry • Use antifungal cream
• Toenail abnormalities	• May be hypertrophic (thick and horn-like) • Cut nails every 3–6 weeks straight across to prevent formation of sharp edges
• Paronychia (nail bed infections)	• Twice daily saline solution soaks and adequate nail care • Systemic antibiotics may be necessary
• Cellulitis	• Requires antibiotics; the route of administration (oral vs. parenteral) will depend on the severity of the infection
• Claw foot	• Appropriate footwear and orthotic devices
• Charcot foot	• For acute Charcot foot, reduce deformity by removing pressure with immobilizing foot in cast

	• For established Charcot foot, appropriate insoles and shoes are required
• Intermittent claudication	• Regular foot care and as much walking as possible to build collateral blood flow
• Ischemia	• A painful, cold and white extremity is a surgical emergency (may indicate acute occlusion) • Referral to a vascular surgeon

Dyslipidemia

Diabetes is associated with a high risk of vascular disease (2- to 4-fold greater than that of people without diabetes). Indeed, CVD is the primary cause of death among people with diabetes. Thus, aggressive management of all cardiovascular risk factors — especially dyslipidemia — is very important. Table 14 identifies target lipids values for people with diabetes; Table 15 addresses the treatment of dyslipidemia.

The lipid profile should be determined by a fasting test and repeated annually if no abnormalities are identified, or repeated every 3–6 months to check the effect of therapy. For those individuals in whom a prolonged fast is not feasible due to concerns regarding hypoglycemia stemming from their diabetes regimen, it is acceptable to conduct an 8-hour fast or measure non-fasting apolipoprotein B (apo B) or non-High Density Cholesterol (non-HDL C) which is calculated as Total Cholesterol,TC, minus HDL-C.

TABLE 14

Target lipid value based on level of risk

Risk level	LDL-C (mmol/L)
High (most patients with diabetes)	≤2.0*

Low Density Lipoprotein Cholesterol, LDL-C

*For individuals at high risk who also have established CVD, consider a target LDL-C <1.8 mmol/L. An alternative target is non-fasting apo B ≤0.8 g/L or non-HDL cholesterol (TC minus HDL-C) <2.6mmol/L

TABLE 15

Treatment of dyslipidemia

Lipid status	Therapy
LDL-C above target	Lifestyle modification plus statin*

*If a statin does not achieve target LDL-C, a second-line agent (e.g. cholesterol absorption inhibitor [ezetimibe], bile acid sequestrant [cholestyramine, colesevelam or colestipol HCl], fibrate or nicotinic acid] may be added

If triglycerides >10.0 mmol/L, a fibrate may be used to reduce the risk of pancreatitis

Vascular protection

In addition to management of dyslipidemia, there are a number of other strategies to employ to confer general vascular protection in people with diabetes. A simple mantra of the ABC's of vascular protection includes:

A – A1C — optimal glycemic control
B – Blood pressure — optimal blood pressure control
C – Cholesterol — optimal LDL-cholesterol levels
D – Drugs — appropriate use of vascular protective medications (statin, ACE-inhibitor or ARB, ASA)
E – Exercise/Eating — appropriate lifestyle changes
S – Smoking cessation

A, B and C have been discussed already. In terms of D, drugs, statins, ACE inhibitors or ARBs, should be used to reduce cardiovascular risk in adults with diabetes as follows:

For statins:

Statin therapy should be used to reduce cardiovascular risk in adults with diabetes with any of the following features:

1. Clinical macrovascular disease
2. Age ≥40 years
3. Age <40 years and 1 of the following:
    - Diabetes duration >15 years and age >30 years
    - Microvascular complications
    - Warrants therapy based on the presence of other risk factors according to the 2012 Canadian Cardiovascular Society Guidelines for the Diagnosis and Treatment of Dyslipidemia

For ACE inhibitor or ARB:

1. Clinical macrovascular disease
2. Age ≥55 years, for those with additional risk factors or end organ damage
3. Age <55 years and microvascular complications
4. ASA should not be routinely used for the primary prevention of cardiovascular disease in people with diabetes, but should be used in the presence of additional cardiovascular risk factors

Essentially, in the presence of micro/macrovascular disease or if the patient is ≥55 years, use a combination of statin and ACE/ARB. Add ASA for macrovascular disease. If the patient is >30 years and has had diabetes for >15 years and/or has dyslipidemia, use a statin.

DIABETES IN THE OFFICE – CLINICAL CASES

CASE STUDY – Marilyn

Marilyn is a 54-year-old woman who is new to your practice. This is her first visit, and she requests a complete assessment as her sister was recentlydiagnosed with type 2 diabetes. Marilyn describes herself as "relatively healthy"; however, she would like to lose the 9 kg that she has gained over the years. She has no significant past history. Aside from her sister's recent diabetes diagnosis, Marilyn relates that her brother underwent coronary bypass surgery 4 years ago and is "doing quite well." She doesn't smoke. Briefly, on exam, she is overweight with a BMI of 30.0 kg/m^2. Her blood pressure, sitting, is 140/88 mm Hg.

Marilyn has several risk factors to screen her for diabetes: age, current BMI, and history of diabetes and coronary artery disease (CVD) in a first-degree relative. Marilyn can be screened in a number of ways. As she does not complain of any classic symptoms of diabetes, i.e. polydipsia, polyuria, blurred vision or unexplained weight loss, performing a random blood glucose test to check for a level >11.1 mmol/L is not indicated. Conventionally, she can undergo a fasting plasma glucose (FPG) test looking for an FPG >7.0 mmol/L, or a more involved 75-g oral glucose tolerance test (OGTT) looking for a 2-hour value >11.1 mmol/L. Marilyn could also undergo a non-fasting A1C looking for A1C ≥6.5%.

It would also be reasonable for Marilyn to have a fasting lipid profile done, in light of her brother's history of CVD. This would be easy for her, if she opts for one of the fasting diabetes screens. Marilyn opts to have an FPG test, and wants a lipid profile, as well.

Scenario 1: Marilyn's FPG is 6.9 mmol/L

Marilyn's result of 6.9 mmol/L indicates impaired fasting glucose, a condition of prediabetes. With prediabetes, not only is Marilyn at risk for type 2 diabetes; she is also at risk for cardiovascular disease (CVD). With respect to her prediabetes, lifestyle changes are certainly the first

strategy. A full assessment of Marilyn's nutritional intake and physical activity patterns should be done, and referral to a diabetes health care team for in-depth counseling would certainly help. In the meantime, simple suggestions such as cutting out junk food and fast food, decreasing portion sizes and walking at least 30 minutes per day can help her get started. Using easy "office tools" such as the plate method or handy portion guide to determine appropriate portion size can be used. Also helpful would be a discussion regarding the practicalities of exercise, i.e. does she have a treadmill or exercise bike that is collecting dust? Can she put it somewhere she'll use it, such as in front of the TV? Would she prefer to walk outside? Does she have somewhere secure to walk outside? Does she have a pair of properly fitted walking shoes?

The question of medication may come up. Insulin sensitizers such as metformin could be used; however, greater emphasis should be placed on helping Marilyn make lifestyle changes that she can sustain over the long term. Lifestyle changes may also help with respect to her lipid levels. If her low-density lipoprotein cholesterol (LDL-C) is >2.0 mmol/L, then serious consideration should be given to starting a statin if lifestyle changes do not bring the LDL-C into target.

Scenario 2: Marilyn's FPG result is 7.8 mmol/L

By the diagnostic criteria, Marilyn has diabetes. It would be prudent to confirm the diagnosis by repeating the test on another day or by conducting an alternative test. This confirmation may be needed to assure Marilyn of the diagnosis.

All that has been said above, regarding lifestyle changes, applies here. In this scenario, Marilyn may want to consider adding medication to her lifestyle regimen. The choice would be either metformin or possibly a DDP-4 inhibitor. Other options, such as acarbose, may only address postprandial glucose rise; as well, the adverse gastrointestinal effects associated with acarbose may preclude sustainability. Pioglitazone may be another option; however, choosing the TZD class would mean giving serious consideration to any CVD risks. As well, pioglitazone has now been associated with an increased risk of bladder cancer. In the presence of

Marilyn's CVD risk profile — with her brother's known CVD and waiting for her own lipid profile — the TZD class would not be the first choice.

Marilyn may decide against taking any medication at this time and work on effecting lifestyle changes. This should be reassessed in a timely manner, likely after 2–3 months.

Scenario 3: Marilyn's result is 10.2 mmol/L

Not only does Marilyn have type 2 diabetes; her FPG is high enough to have a serious discussion regarding starting an insulin sensitizer. Of course, confirmation of the diagnosis is required. Her lifestyle changes need to be initiated now. If it is uncovered that Marilyn has a major lifestyle issue that is significant and can be addressed directly (e.g. drinking 2 litres of regular soft drinks every day), then medication can be forestalled for a brief time to assess the effect of major lifestyle changes.

Scenario 4: Marilyn's result is 14.8 mmol/L

This may be surprising, as Marilyn has no diabetes symptoms; however, it is still quite possible. With this result, confirmation of the diagnosis is required only if it can be determined that Marilyn will not suffer any metabolic deterioration in the meantime. However, with this degree of hyperglycemia, no delay in management should occur. Again, obvious lifestyle issues need to be addressed and medication initiated in an timely fashion. Here, consideration should be given to combination therapy from the beginning, in a more aggressive approach to her diabetes. Combinations could include metformin and a DDP-4 inhibitor, or metformin and a sulfonylurea. Serious consideration could also include metformin and a GLP-1 agonist. Insulin (likely basal insulin) could also be added, along with metformin ± a sulfonylurea. With this degree of hyperglycemia, initial aggressive therapy can always be modified as improvement occurs. Naturally, a thorough assessment for any possible diabetes-related complications must also be done.

CASE STUDY – Raymond

Ray is a 62-year-old man who has had type 2 diabetes for 10 years. He had been on metformin 1000 mg bid during this time, with good control; his A1C ranged from 7.0–7.5%. However, over the past year, his A1C has increased steadily, and is now 8.5%. Ray does not report any significant changes in his lifestyle; his nutritional intake and physical activity habits have remained the same. Of note, Ray has an allergy to sulfa drugs.

A number of strategies can be employed in this situation. Certainly, despite Ray saying that nothing has changed, his eating and activity habits should be reviewed, as new information may be discovered. With respect to medication, there is little to be gained from increasing his metformin beyond 1000 mg bid. Ray requires a second agent. Usually a secretagogue would be the second-line choice; but he is allergic to sulfa drugs and all sulfonylureas would be precluded. Ray could add an incretin agent, probably a DPP-4 inhibitor, which is a once-daily oral agent. If that is not sufficient, then changing the DDP-4 to a GLP-1 agonist might be more potent; however, GLP-1 agents are injectable. If Ray prefers an oral agent over an injectable agent, there are further options. He could consider pioglitazone, but a comprehensive review of his cardiac risk profile beyond his diabetes should be completed before choosing this agent. The TZD class (in particular, rosiglitazone) has been shown to be associated with an increased risk of significant CVD outcomes; as well, adverse effects such as weight gain, edema, and increased risk of congestive heart failure exist for the entire TZD class. Pioglitazone has recently been shown to increase the risk of bladder cancer. Choosing this agent would require a thoughtful discussion with Ray.

Other oral agents may improve postprandial blood glucose levels. These classes include alpha-1 glucosidase inhibitors and the short-acting secretagogues or meglitinides. Serious consideration should also be given to adding basal insulin (e.g. NPH, glargine, or detemir) at bedtime to lower his FPG levels.

In fact, Ray decides on the latter option and adds NPH insulin at bedtime. His blood glucose control improves and he is educated about titrating his dose according to his morning FPG levels. This regimen works well for the following year; however, his A1C begins to rise once again. Ray also notes that his blood glucose levels are between 6.0 and 9.0 mmol/L in the morning, rising to 10.0 to12.0 mmol/L by suppertime.

A number of strategies may be employed. Ray could consider adding an incretin agent, either a DPP-4 or a GLP-1. Adding an alpha-1 glucosidase inhibitor and a short-acting meglitinide secretagogue may also work. Perhaps, the simplest strategy would be to add basal insulin in the morning. As Ray is taking NPH at bedtime, this is easy to do. If he was taking a long-acting analogue — such as glargine or detemir — adding a dose of detemir in the morning might work. Adding a morning dose of glargine may not work, as it has a longer time profile; thus, consideration of adding a rapid-acting bolus insulin at meals would be a better option.

CASE STUDY – Beverly

Beverly is a 59-year-old woman who is complaining of an unexplained weight loss of 4.5 kg within the last 3 weeks. She has also noticed increased urination, particularly at night, and a "dry mouth." Beverly has a past history of hypertension, which is well-controlled with a thiazide diuretic. She has a family history of diabetes (her brother). In the office, a capillary blood glucose is measured at 22.0 mmol/L.

Beverly most decidedly has diabetes, despite the relatively short onset of marked symptoms. While Beverly needs a confirmatory diagnostic test, her management should not be delayed due to the severity of her symptoms and the possibility that her metabolic condition could deteriorate before the second test is done.

With the degree of hyperglycemia, initial management should be fairly intensive. Beverly should likely be started on combination therapy of metformin as an insulin sensitizer and an insulin secretagogue, likely gliclazide, to decrease the risk of hypoglycemia. The metformin will be started at a low dose, with instructions to Beverly to slowly titrate up the dose; gliclazide can be started at a higher dose — even the maximum dosage — to be more effective. She chooses gliclazide MR because of its once-daily dosing. Her marked hyperglycemia with weight loss signals catabolic metabolism in the absence of sufficient insulin. Therefore, serious consideration should be given to adding at least basal insulin to her oral regimen.

Beverly requires a priority referral to a diabetes health care (DHC) team. In the meantime, some survival skills can be imparted: She can be taught self-monitoring of blood glucose (either in the office, by the DHC team, or at a pharmacy). As well, simple lifestyle changes with respect to nutritional intake can be also taught in the office while waiting for more formal education; simply, Beverly should avoid any sugar-containing food or beverages, such as fruit juice, regular soft drinks, sugary desserts, and snacks. She should also avoid milk and fruit in large quantities.

Beverly is started on metformin and taught how to titrate up the dose. She is currently taking 1000 mg bid without any adverse effects. She is also taking gliclazide MR 120 mg od, which is the maximal dose. Beverly has also been seen by the DHC team on a priority basis and she is trying her best with the suggested lifestyle changes. As she declined the addition of insulin at this time, a timely return appointment is made 2 weeks after her diagnosis. She is frustrated because her SMBG results indicate that her blood glucose levels remain well above target, with pre-meal levels ranging from 10.0–14.0 mmol/L, and 12.0–18.0 mmol/L before lunch and supper.

Beverly obviously requires more aggressive management, which would mean insulin at this point. It is explained to Beverly that insulin is not a choice of last resort. Rather, she requires insulin to reverse the ongoing catabolic metabolism. Beverly is started on basal NPH bid because her blood glucose levels remain elevated throughout the day. At the same time, the concept of basal/bolus insulin with the addition of rapid-acting insulin at meals is explained, as this may be the eventual course of management.

Beverly asks if there are any other oral options. With her degree of hyperglycemia, adding other oral agents is unlikely to be successful. With the addition of insulin, it still would be possible to add a DDP-4 inhibitor or a GLP-1 agonist to provide further benefit. This addition may reduce the dosage of insulin required.

DIABETES IN THE ELDERLY

The main issue to remember in approaching diabetes in the elderly is to treat the whole person, not just his or her blood glucose. Often, this may be overlooked in a zealous attempt to achieve the "perfect" target blood glucose level. Optimal diabetes management in the elderly must take into account an individual's overall health, level of independence, and ability to manage multiple medications (for diabetes and co-existing conditions), as well as possible multiple insulin injections, self-monitoring of blood glucose (SMBG), and management of hypoglycemia. Social circumstances may be of great importance for the elderly, i.e. what degree of support is required for the person to manage his/her diabetes? Often, the risk benefit ratio may favour "safer" blood glucose control over "target" blood glucose control.

Approaching diabetes in the elderly requires some functional definitions. There are those who are the *well elderly* and those who are the *frail elderly*. Age is not the defining factor that distinguishes these 2 groups; rather, the definition is predicated upon the presence of comorbidities, which include microvascular complications (retinopathy, neuropathy, nephropathy) and macrovascular complications (cardiovascular, cerebrovascular, and peripheral vascular disease) of diabetes. Comorbidities also include illnesses unrelated to diabetes, which can contribute to an individual's frail state.

In the well elderly, glycemic targets should be no different than in other age groups. While the risk of hypoglycemia exists for many people who strive to maintain target blood glucose levels, this risk may have greater consequences in the elderly. Older people may be quite vulnerable to hypoglycemia and suffer from confusion, exacerbation of comorbid conditions (e.g. shortness of breath, angina) and falls. Thus, the presence of comorbid conditions, as well as living circumstances, must be considered when determining appropriate glycemic targets in the elderly. Recommended target blood glucose levels in the elderly are outlined in Table 1.

TABLE 1

Recommended target blood glucose levels in the elderly

	A1C (%)	Preprandial blood glucose (mmol/L)	2-hour post-meal blood glucose (mmol/L)
Well elderly	≤7	4–7	5-8/10
Frail elderly	<8.5	5–12	7–12

A1C, glycated hemoglobin

In elderly patients, clinical judgment should be used, and blood glycemic targets may be relaxed. The clinician should set a "safe" glucose range, one that will reduce the risk of hypoglycemia. However, there remains a need to prevent the occurrence of acute complications of hyperglycemia, namely the increased risk of sepsis and hyperosmolar states. As well, there is a need to prevent the development and progression of any long-term complications.

Other considerations include the practicalities of administering diabetes medications (particularly insulin regimens), especially in elderly patients who rely on external caregivers. In these situations, there may be limitations regarding when medications can be given, as well as issues with respect to access to food and ready assistance by a caregiver.

The Diabetes Health Care Team

Oftentimes, the elderly require more support services to manage their diabetes. In these circumstances, the diabetes health care team expands to include a variety of allied health care professionals, including home care nurses, home care workers and family members, who often play major caregiver roles.

Antihyperglycemic Agents in the Elderly

Essentially, the general recommendations and precautions identified for the general diabetes population (see Tables 5 and 6 in Chapter 1, Diabetes Care in the Office) extend to the elderly population. However, there are some specific considerations for the elderly.

Metformin, an insulin sensitizer, remains a first-line oral agent; however, the clinician must remain aware of the relative and absolute contraindications regarding metformin, as adverse effects may be more prevalent in the elderly.

Renal function must be assessed before recommending metformin. In the presence of reduced renal function (defined as serum creatinine >130 µmol/L or estimated glomerular filtration rate (eGFR) <60 mL/min), metformin should be kept to a maximum dose of 500 mg bid. In the presence of worsening renal function with a serum creatinine >160 µmol/L or eGFR <30 mL/min, metformin should not be administered.

Sulfonylureas are still used commonly in the elder population. However, glyburide may be associated with significant hypoglycemia. Thus, priority should be given to gliclazide as it carries less risk for hypoglycemia; as well, gliclazide is available in a mono-release formulation, which aids in medication administration. Glimepiride is a long-lasting secretagogue that appears to have a lower risk of hypoglycemia than glyburide; it is also administered once daily.

Thiazolidinediones (TZDs) may play a limited role in diabetes in the older person. While TZDs were used extensively in the past, the evidence linking the TZD rosiglitazone, in particular, to cardiac events has decreased their usage. There may be a role for pioglitazone in the management of prediabetes or early, mild diabetes in people with no history or risk factor profile for cardiac disease. Also, pioglitazone has been recently linked to a risk of bladder cancer.

Newer oral medications of the incretin class — *GLP-1 agonists* and *DPP-4 inhibitors* — appear to be useful in the older population. However, concerns about the relationship between incretins and pancreatic

inflammation or possible malignant changes (pancreatic and medullary carcinoma of the thyroid) render a thorough medical review important before initiating therapy. It is also important to remember that, to date, no significant warnings have been reported for this medication class.

People with decreased renal function, as indicated by eGFR <50 mL/min), should be prescribed sitagliptin and saxagliptin at a dose that is reduced by 50%. At an eGFR <30 mL/min, the dose of sitagliptin and saxaglipin should be further reduced to 25%. However, linagliptin does not require a dosage reduction in patients with decreased renal function. Those using GLP-1 agonists, liraglutide or exenatide, should also be prescribed the lowest dose.

Other drug classes, including *meglitinides* (short-acting insulin secretagogues) and *alpha-1 glucosidase inhibitors*, have been used successfully in the elderly population. No specific concerns regarding these agents have been reported, to date, aside from the usual concern for hypoglycemia and gastrointestinal tolerance, in the case of alpha-1 glucosidase inhibitors.

Oral Agent Combinations in the Elderly

Similar to younger people with diabetes, common effective combinations include an insulin sensitizer (metformin) plus an insulin secretagogue. Considering the reduced risk of hypoglycemia with gliclazide and — to a somewhat lesser extent — glimepiride, these agents would be the preferred secretagogues for use in elderly patients.

Many older people use weekly pill dispensers that they or their caregivers fill and maintain. Pharmacies commonly dispense oral medications in blister or bubble packs, which can be very helpful in maintaining medication adherence.

Insulin Use in the Elderly

Insulin can be very useful in managing diabetes in the elderly person. An approach similar to the younger adult population is used, i.e. combinations of longer-acting (basal) insulins with oral agents, and progression to rapid (bolus)- and long-acting insulin regimens as indicated.

What follows is a practical guide to oral agents and/or insulin regimens. The regimens considered to be most practical in the older person include the following:

- Addition of a basal insulin at bedtime, while continuing the oral medication regimen during the day.
- Using basal insulin twice daily, while continuing the oral medication regimen during the day.

The long-acting insulin analogues glargine and detemir have a lower risk of hypoglycemia than NPH insulin:

- Use of a pre-mixed insulin regimen can be helpful particularly for the elderly person who is reliant on external caregivers.
- Often, rapid insulin can be used as a "correction" dosage at mealtimes when blood glucose levels are out of target.

Some older people prefer and manage a more complex basal/bolus insulin regimen without any problems. Where external caregivers are required, a more practical approach is needed. A fixed dosage of rapid insulin can be given at each meal with a plus/minus rapid insulin correction factor (CF) algorithm added for either high or, more importantly, low pre-meal glucose levels, along with basal insulin at bedtime.

Following is a short description of some insulin regimens that can be easily adapted to the older person with diabetes. If the situation calls for a more complicated basal/bolus insulin regimen, a practical approach or compromise can usually be found; usually, this would consist of a predetermined "flat dose" of rapid insulin with meals, as opposed to carbohydrate counting, to calculate the dose of rapid insulin each time.

Insulin/Oral Agent Combinations

The insulin regimens outlined below are listed in the order in which they are commonly administered in type 2 diabetes, with particular reference to the elderly. However, any regimen may be chosen, depending on individual circumstances.

Legend for all figures below

A = Apidra; amac = before breakfast; bid = twice daily; D = detemir insulin; H = lispro insulin; hs = bedtime; La = glargine insulin; N = NPH insulin; NR = insulin aspart; pmac = before supper; qid = 4 times daily; R = regular insulin; TDD = total daily dosage; tid = 3 times daily

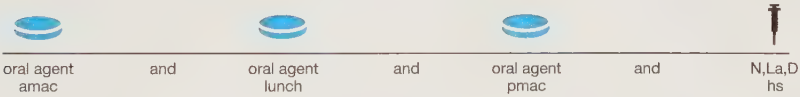
Bedtime Insulin and Oral Agents

This is a relatively simple method to introduce insulin into a combination regimen with oral agents. Here, basal insulin is added at bedtime to help counteract hepatic glucose output during the night and thus lower fasting blood glucose in the morning. Starting the day with a lower fasting blood glucose level will allow the oral agents taken during the day to be more effective. Commonly, NPH is started as the bedtime basal insulin. However, the long-acting insulin analogues glargine or detemir may also be used.

BEDTIME INSULIN AND ORAL AGENTS

N (or La or D) at hs and oral agents during the day.

Indications: Type 2 diabetes, to lower fasting glucose levels and to allow oral agents to have optimal effect.



Notes:

- Start with ≤5units hs, if the person is lean; ≤10 units hs, if the person is not lean
- Alternatively, calculate the starting dosage by 0.2–0.3 units/kg
- Titrate the dosage according to the first morning SMBG by 1–2 units every 3 days until the fasting plasma glucose is at target
- Rapid insulin correction factor (CF): 1–2 units for every 3.0 mmol/L >7.0 mmol/L can be used at meals, along with oral agents. The target of 7.0 can be relaxed depending on the individual

Daytime Insulin and Oral Agents

Once- or twice-daily basal insulin can be used with most oral agents during the day in effective combinations. Generally, TZDs should not be used in combination with daytime insulin. NPH is usually tried first in this regimen.

Glargine is primarily used once/day, and detemir can often be used twice/day. Sometimes, a mixed insulin regimen — including basal and rapid — can be used instead of basal insulin alone. In this case, the oral agent would be metformin, glimepiride (which has an indication for use with daytime insulin) or possibly one of the incretin class of agents.

DAYTIME INSULIN AND ORAL AGENTS

Insulin twice daily amac and pmac with oral agents (except TZDs).

Indications: Type 2 diabetes.

Notes:

- Long-acting analogue or intermediate-acting insulin
- Initial dosage: ≤5 units bid if person is lean; ≤10 units bid if person is not lean
- Alternatively, calculate the starting dosage by 0.2–0.3 units/kg
- Titrate the dosage according to SMBG, FPG, and pre-supper by 1–2 units every 3 days until SMBG is at target

Premixed Insulin bid

PREMIX: BID

Indications: Type 2 diabetes, when optimal control is not desired and for those with difficulty differentiating insulins. The disadvantage is that specificity in dosage adjustment is lost and a change in dose affects both insulins.

Dosage: 50 to 70% of TDD amac and 30 to 50% of TDD pmac.

Notes:

- This regimen is intended for situations where a realistic compromise between optimal and safe blood glucose targets is required. The nature of premixed insulins renders it impossible to adjust one insulin in the mix without the other. This regimen may also offer a practical solution to a person who requires an external caregiver to administer the insulin.

- When choosing a premixed insulin, it may be preferable to choose one of the rapid/basal premixes. The rapid insulin component matches the timing of food digestion and may result in smoother blood glucose control with a lower risk of hypoglycemia a number of hours after insulin and the meal.

Basal/Bolus qid

The following regimens are designed for the well elderly. I prefer the term "basal/bolus" for this regimen, as I believe it is a functional term that describes precisely the insulin regimen. It also more closely patterns physiological insulin secretion.

BASAL/BOLUS: QID

Indications: Either type 1 or 2 diabetes for optional control. This regimen requires close contact with the DHC team.

Dosage: 40 to 50% of TDD (N, La,D) at hs. Balance given as premeal H, NR, A based on insulin/CHO ratio.

Notes:

- TDD should be calculated as indicated below for basal and bolus insulin
- Alternatively, TDD can be calculated as 0.2–0.3 units/kg to start
- Lastly, this regimen may be a step-wise progression from a previous insulin regimen, whereby previous insulin dosages can be adapted

Basal Insulin

- If starting as a new regimen, initial dosage: ≤5units bid, if person is lean; ≤10 units bid, if person is not lean
- Alternatively, calculate the starting dosage by using 50% of calculated TDD
- Titrate the dosage of basal insulin according to the FPG by 1–2 units every 3 days until the FPG is at target

Rapid Insulin

- Rapid (bolus) insulin dosage may be determined by the insulin to carbohydrate ratio, starting with 1 unit rapid insulin/15 g carbohydrate.
- Alternatively, rapid insulin dosage may be determined as a "flat dosage" for each meal, based on an average carbohydrate intake for each meal, calculating 1 unit/15 g carbohydrate to begin, or the remaining 50% TDD may be distributed among the daily meals.
- Rapid insulin CF: 1–2 units for every 3.0 mmol/L > 7.0 mmol/L at meals only. A correction dose is not recommended at night if the person is using a long-acting analogue, as this increases the risk for nocturnal hypoglycemia.

Basal/Bolus tid

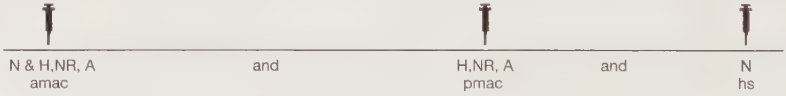
This is an alternative regimen that may help patients who have difficulty fitting in the lunchtime bolus insulin dose. It works better with NPH insulin, to provide insulin coverage through lunchtime.

BASAL/BOLUS: TID

N amac and hs and H, NR, A (or R) amac and pmac.

Indications: Either type 1 or type 2 diabetes; may provide optimal control.

Dosage: 50 to 70% of TDD (2/3 N and 1/3 H, NR, A) amac and 15% to 25% of TDD (H, NR, A) pmac and 15 to 25% of TDD (N) at hs.



Notes:

- This option is meant for patients using NPH as their basal insulin rather than a long-acting insulin analogue
- TDD may be calculated as 0.2–0.3 units/kg to start

Basal Insulin

- If starting as a new regimen, then for the basal insulin, initial dosage: ≤5units bid, if the person is lean; ≤10 units bid, if the person is not lean
- Alternatively, calculate the starting dosage as 50% TDD
- Titrate the dosage of basal insulin according to the FPG and pre-supper blood glucose by 1–2 units every 3 days until the blood glucose is at target

Rapid Insulin

- Rapid insulin dosage may be determined by the insulin/carbohydrate ratio for breakfast and supper only in this regimen
- Rapid insulin dosage may be determined as a "flat dosage" for each meal, based on average carbohydrate intake for each meal calculating at 1 unit/15 g carbohydrate to begin. Or, the remaining 50% TDD can be distributed among the daily meals
- Rapid insulin CF: 1–2 units for every 3.0 mmol/L > 7.0 mmol/L at meals only, and not at night if person is using a long-acting analogue

Hypoglycemia Management

Current evidence suggests that 15 g of glucose is required to produce an increase in blood glucose of 2.0 mmol/L within 20 minutes, with adequate symptom relief for most people.

Examples of 15 g of carbohydrate for the treatment of mild to moderate hypoglycemia (>2.8 mmol/L) include:

- 15 g of glucose in the form of glucose tablets (1 tablet = 5 g carbohydrate)
- 15 mL (3 teaspoons) or 3 packets of table sugar dissolved in water
- 175 mL (3/4 cup) of juice or regular soft drink
- 6 Life Savers™ (1 = 2.5 g of carbohydrate)
- 15 mL (1 tablespoon) of honey

A snack containing carbohydrate and protein should be consumed after the hypoglycemia has resolved, if mealtime is more than an hour away.

The cause of the hypoglycemia should be assessed and strategies for avoiding hypoglycemia in the future need to be developed.

Diabetes Complications in the Elderly

The basic approach to screening and intervention for both micro- and macrovascular complications is no different in the older person than in the general diabetes population. However, there are some specific issues that should be considered.

Retinopathy

Older people may already have vision issues (e.g. cataracts, glaucoma, macular degeneration). In the presence of any of these eye conditions, monitoring for diabetic retinopathy on a regular basis by an experienced eye-care professional takes on renewed importance, as visual deterioration from any cause presents a barrier to independent living.

Nephropathy

Hypertension, usually seen with nephropathy, can be challenging to manage in the elderly. While the choice of medications is no different than in younger people with diabetes (i.e. ACE inhibitors, or ARBs), there may be an increased risk of adverse effects such as postural hypotension leading to dizziness, difficulty in coping, and falls. Older people may also have an increased prevalence of underlying chronic kidney disease from another etiology, which can render the management of hypertension difficult and may exacerbate decreased renal function.

Older people with marked chronic kidney disease face many challenges with respect to dialysis. Indeed, much supportive care will be required for patients, whether they are undergoing hemodialysis or peritoneal dialysis.

Neuropathy, peripheral vascular disease and foot care

Foot care presents a major issue in the elderly population with diabetes. Regular foot assessment and care — including nail trimming — often requires support from external caregivers. If a person's foot becomes compromised by infection or ulceration, the necessary immobility required for healing can lead to further health problems.

Cardiovascular and cerebrovascular disease

Cardiovascular disease and cerebrovascular disease are serious complications that require a complex management plan, including vascular assessment, and such interventions as angiography, angioplasty, or surgery. Recovery can be slow in the presence of comorbidities related to age and/or diabetes. Blood glucose control is of significant concern, and requires close monitoring and medication adjustment. Often, in the acute situation, insulin presents the better choice for glycemic control; in the event that insulin is initiated, it is crucial that the diabetes health care team and caregivers monitor frequently for hypoglycemia and hyperglycemia.

Quality of Life

Last, and certainly not least, it is important to remember the issue of quality of life. Blood glucose control should never be ignored; however, there is a need to revisit blood glucose targets regularly. The elderly, in particular the frail elderly, should have safe glycemic targets, i.e. targets that ensure maintained good health without diminishing the quality of life.

CASE STUDY – Eileen

This case vignette is offered here to highlight many of the issues facing the elderly person with diabetes, with the intent of increasing health care professionals' awareness regarding these issues and how they can be managed.

Eileen is an 86-year-old female who was diagnosed with type 2 diabetes 25 years ago. For many years, her diabetes was controlled with the use of an oral medication, glyburide 10 mg bid. She had her diabetes regularly assessed by her family doctor and she was told the disease was stable, with A1C ranging from 7.8–8.3%. Eileen is very conscientious about her diabetes: she monitors her blood glucose 2 or 3 times/day, usually before meals, and is very concerned if it exceeds 8.0–9.0 mmol/L.

However, Eileen has vascular disease, a complication of her diabetes, and she was hospitalized recently for vascular surgery. Unfortunately, the surgery was unsuccessful and she underwent a below-knee amputation to her left leg. This has changed her life dramatically. Prior to the amputation, she was independent; currently, she is confined to a wheelchair. Once she is released from hospital, she must move into an assisted-living facility where meals are provided.

During her hospitalization, Eileen's blood glucose levels have risen, and and they are no longer controlled by her oral medications. This was to be expected, given her inactivity during hospitalization and the counter-regulatory stress rise postoperatively. Her blood glucose levels range between 12.0 and 18.0 mmol/L before meals. This distresses Eileen, which has made her blood glucose levels increase even further. Rapid insulin has been administered before meals, using a "sliding scale" approach. Now Eileen is ready for discharge; so the insulin is stopped and she is placed back on glyburide 10 mg bid.

Prior to her hospitalization and surgery, Eileen was diligent in the management of her diabetes, eating balanced meals and monitoring her blood glucose levels frequently. Now, however, she feels that

she has lost control of her life. She is no longer mobile and independent, and in the assisted-living facility she will have little choice in her meals.

The loss of control regarding her diabetes has only served to increase her anxiety and stress levels, which has resulted in the unwanted effect of further increased blood glucose levels. Indeed, Eileen has noticed that her blood glucose levels regularly range between 12.0 and 22.0 mmol/L before meals. Her anxiety about her blood glucose is escalating, and the staff find Eileen becoming increasingly anxious. She refuses to eat because she is afraid of elevating her blood glucose levels; as a result, she has begun experiences low blood glucose levels, as her glyburide continues. Both Eileen and her caregivers are becoming increasingly frustrated. Eileen wants good blood glucose control again and the staff can't understand why her blood glucose levels are "swinging" from high to low.

How could this situation have been addressed to improve the outcome? Eileen's concern about her diabetes control needs to be acknowledged. However, she must also be aware that, for her situation, blood glucose control can be relaxed from the standard target of 4.0–7.0 mmol/L before meals. A pre-meal range of 5.0–8.0 mmol/L and/or a post-meal range 8.0–10.0 mmol/L, closer to the frail elderly targets, will protect Eileen from the acute complications of hyperglycemia.

The maximum dose of glyburide is clearly no longer adequate. Indeed, with her blood glucose levels so high, the addition of other oral medications will be unlikely to help the situation. Eileen needs insulin; but how, in her new situation?

There are a few strategies that might work. First, a new target blood glucose range of 5.0–8.0 mmol/L before meals and/or 8.0–10.0 mmol/L after meals is an important point to establish with Eileen and the staff caring for her. Adding basal insulin, NPH bid or glargine or detemir od along with an oral agent during the day may work. Changing her oral agent to gliclazide — which carries less risk for hypoglycemia — will also help.

If this strategy still does not reduce Eileen's blood glucose levels to the new target range, then premixed insulin should be considered. Choosing a premix of rapid and longer-acting would make more sense

than a regular/longer-acting premix to better time the rapid-insulin peak to the post-meal glucose peak. Using with basal or a premix bid would also help the staff, if they will be administering the insulin, should Eileen be incapable of doing so.

The choice of an insulin/oral agent combination or regularly scheduled insulin alone is a more proactive approach that will result in smoother blood glucose control, rather than simply adding on an insulin sliding scale.

Considerations

1. Eileen's past experience of independent management of her diabetes and her continuing desire to remain independent in this practice.
2. Deteriorating health problems that necessitate hospitalization, her diabetes control worsens and many changes are made to her diabetes management.
3. Eileen's increased anxiety and stress will only increase her blood glucose levels. Increased frustration on the part her health care providers will also have the same effect.
4. The staff would benefit from understanding that every time Eileen refuses to eat as a method of controlling her blood glucose levels, her blood glucose level will drop too much because the glyburide is continued. This drop results in rebound hyperglycemia, and thus the cycle of hyperglycemia/hypoglycemia continues.
5. Understanding on the part of staff can lessen Eileen's anxiety and help normalize her blood glucose control.

DIABETES IN PREGNANCY: GESTATIONAL DIABETES MELLITUS

As with type 2 diabetes, the incidence of gestational diabetes mellitus (GDM) is increasing. It is important to recognize and appropriately manage GDM, as it is now understood that GDM not only increases the risk of the development of type 2 diabetes in the mother, but also the risk of early childhood obesity and possible early-onset type 2 diabetes in the child.

GDM is defined as glucose intolerance with first onset or recognition during pregnancy. Risk factors for GDM include the following:

- Maternal age ≥35 years
- Family history of diabetes
- Member of a high-risk ethnic group, including Aboriginal, Hispanic, Asian, South Asian, and African
- Pre-pregnancy obesity
- Polycystic ovary syndrome
- Acanthosis nigricans
- Excess weight gain in current pregnancy
- Previous delivery of a large infant (>4.0 kg)
- Previous GDM
- Corticosteroid use

Screening for GDM: 2-Step Screening

All pregnant women should be screened for GDM at 24–28 weeks' gestation. If a risk factor — as described above — is identified during pregnancy, screening should be performed at that time. If the screen is negative but the risk factor persists, screening should be repeated in the remaining trimesters.

The preferred screening test is a 50-g oral glucose load, administered at any time of day, followed by a plasma glucose test at 1 hour:

- If the 1-hour value is ≥7.8 mmol/L, proceed to the OGTT
- If the 1-hour value is ≥11.1 mmol/L, a diagnosis of GDM can be made

Diagnosis of GDM

Table 1 depicts OGTT (2-hour 75-g) threshold values for diagnosis. If ≥1 value is met or exceeded, the diagnosis is GDM.

TABLE 1

OGTT (2-hour 75-g) threshold values for diagnosis

Parameter	Blood glucose (mmol/L)
Fasting	≥5.3
1-hour	≥10.6
2-hour	≥9.0

Screening for GDM: 1-Step Screening

An alternative diagnostic test, known as the 1-step test, precludes the 1-hour, post 50-g screen; rather, it utilizes a 2-hour 75-g OGTT but has lower recommended threshold values. Table 2 outlines the parameters and blood glucose levels regarding the 1-step test. Again, one or more abnormal values are needed for diagnosis.

TABLE 2

1-step test

Parameter	Blood glucose (mmol/L)
Fasting	≥5.1
1-hour	≥10.0
2-hour	≥8.5

Management of GDM

Nutritional therapy is the primary treatment for GDM. A woman diagnosed with GDM should be assessed and followed as required by a registered dietitian (as part of the diabetes health care team) to ensure that her nutritional intake is appropriate to achieve recommended glycemic control,

appropriate weight gain, and adequate nutritional intake for both her and her baby.

As a disclaimer, I am not a dietitian but I can offer some practical tips that a patient can heed before she has an opportunity to meet with a dietitian. Often, the distribution of carbohydrate throughout the day can make a real difference: use the 24-hour recall to determine where and how much carbohydrate is being consumed. Is breakfast all carbohydrate, with cereal, toast, milk and/or juice being consumed? Does the patient snack on carbohydrate-rich foods (such as bagels, fruit or fruit juice, milk and cookies) to excess? Does she eat white rice at all meals and in large quantities? Having her eat a balance of all food groups at each meal — utilizing either the "plate method" or the "handy portion guide" (also known as the hand jive) to ensure proper portion size — is a good start.

Physical activity should be encouraged, with individualized targets set regarding frequency, type, duration, and intensity. A simple way to start is to ascertain if there is any pregnancy barrier to gentle walking, especially after meals, to reduce postprandial glucose rise. Target blood glucose levels for pregnant women with GDM are listed in Table 3.

TABLE 3

Target blood glucose levels for women with GDM

Parameter	Blood glucose (mmol/L)
Fasting	<5.3
1-hour postprandial	<7.8
2-hour postprandial	<6.7

If the woman with GDM does not achieve glycemic targets within 1–2 weeks of initiating nutritional therapy, insulin should be started. Strong consideration should be given to using a basal/bolus insulin regimen, as it addresses most effectively the postprandial glucose rise typically seen in GDM.

Basal insulin use includes NPH insulin. The rapid-acting analogues lispro and aspart may be used in pregnancy; the long-acting insulin analogues detemir and glargine may also be used.

Often, small doses of rapid insulin pre-meal are sufficient to lower glucose levels to target. Glucose levels should be reassessed in a timely fashion, as the window of opportunity is small in pregnancy. It is generally recommended that glucose control should be reassessed every 1–2 weeks. If pre-meal rapid insulin is insufficient to maintain target blood glucose levels (particularly fasting levels), then the addition of small doses of bedtime basal insulin should be considered.

Postpartum Follow-up

Upon delivery, insulin may be discontinued. Postpartum (between 6 weeks and 6 months), the 75-g 2-hour OGTT should be performed to assess for possible development of type 2 diabetes.

CASE STUDY – Karen

Karen is a 36-year-old woman who is pregnant with her third child; she is currently at 26 weeks' gestation. She undergoes the standard 1-hour, 50-g glucose screen and her blood glucose is 8.3 mmol/L. Since this is considered a positive screen, Karen undergoes a 75-g 2-hour OGTT in a timely fashion. The results indicate 1 abnormal value.

Thus, Karen can be diagnosed definitively with GDM. She has at least 1 recognized risk factor, i.e. her age. She may also have other risk factors, including a family history of type 2 diabetes, previous history of GDM, and overweight in pre-pregnancy. Karen wants to understand how this will affect her pregnancy.

Karen should be told that GDM is a form of insulin resistance in later pregnancy that can often be modified by changes in nutritional intake and incorporation of moderate physical activity into her daily routine.

Karen's GDM changes the status of her pregnancy into a higher-risk category. She will benefit from some straightforward nutritional education. She will learn to identify the carbohydrate component of her diet and find out how to distribute carbohydrate intake evenly throughout the day (ingestion of a large amount of carbohydrate at any single time can result in hyperglycemia). Moderate physical activity, such as walking after meals, can also reduce postprandial glucose levels. If glucose targets are not being met within a timely fashion (1–2 weeks), pre-meal rapid insulin will be introduced and, possibly, intermediate insulin at bedtime, if fasting blood glucose levels remain above target.

If Karen does require insulin during her pregnancy, she can discontinue it immediately postpartum, as the placental source of insulin resistance will be gone. However, Karen still carries a long-term risk of developing type 2 diabetes so she should undergo a nonpregnancy 75-g 2-hour OGTT within 6 months postpartum. She can also be counselled about healthy eating and physical activity, in order to reduce any future risk of GDM or type 2 diabetes.

PRE-EXISTING DIABETES AND PREGNANCY

Ideally, women with pre-existing diabetes will undergo preconception planning with their diabetes health care team. Such planning will optimize glycemic control and assess for the presence of any maternal long-term complications of diabetes.

Women with type 2 diabetes should optimize glycemic control to attain A1C ≤7.0% in order to decrease the risks of congenital malformation, first trimester spontaneous abortion, pre-eclampsia, and progression of retinopathy and/or nephropathy.

Preconception Planning

As part of preconception planning in the presence of diabetes:

- Women should discontinue any oral antihyperglycemic agents and begin insulin to attain glycemic targets.
- Women should be screened for microalbuminuria and nephropathy. If positive for either, women should attain optimal glycemic and blood pressure control. Women with nephropathy should be followed carefully, as nephropathy may progress during pregnancy.
- Women using angiotensin-converting enzyme inhibitors or angiotensin receptor blockers should switch to other antihypertensive agents considered safe in pregnancy.
- Women on statin therapy should have it discontinued prior to conception.
- Women should undergo a retinal assessment; repeat retinal assessment should occur as needed during pregnancy and postpartum.
- Women with pre-existing diabetes are at increased risk of delivering a baby with a neural tube defect. Therefore, it is recommended that these women take a 5-mg folic acid supplement (available by prescription) from preconception through the first 12 weeks of pregnancy.

Management with Insulin

Similar to insulin use in the presence of GDM, a variety of insulin regimens can be used, including qid and tid basal/bolus, and bid split/mixed regimens. Premixed insulins are not recommended. As with GDM, strong consideration should be given to using a basal/bolus insulin regimen.

The rapid-acting insulin analogues lispro and aspart may be used in pregnancy. NPH insulin has also long been used in pregnancy. Now, however, the long-acting insulin analogues detemir and glargine may also be used.

Target blood glucose levels for pregnant women with pre-existing diabetes are outlined in Table 4.

TABLE 4

Target blood glucose levels for pregnant women with pre-existing diabetes*

Parameter	Blood glucose (mmol/L)
Fasting	<5.3
1-hour postprandial	<7.8
2-hour postprandial	<6.7

*There may be a need to adjust targets in the first trimester, due to the risk of hypoglycemia

First trimester

Insulin sensitivity may increase and insulin requirements may actually decrease.

Second and third trimesters

Insulin resistance develops, likely through the action of placental hormones, and insulin requirements can generally be expected to rise.

Postpartum follow-up

With delivery, insulin requirements drop significantly. Often, women may require less than their pre-pregnancy insulin dosage for a period of time immediately postpartum.

CASE STUDY – Lana

Lana is a 28-year-old woman who was diagnosed with type 1 diabetes 2 years ago. She is using a basal/bolus insulin regimen of glargine and glulisine. She comes to your office for a routine assessment. At 7.5%, her A1C is slightly above optimal. She tells you that she and her husband are hoping to start trying to conceive and she wonders what she needs to do.

Because preconception planning is very important in helping to reduce risks in a pregnancy complicated by diabetes, it is helpful to address this issue with women long before they consider pregnancy. Elevated A1C at the time of conception increases the risk of congenital anomalies, so one of the first tasks is to work with Lana to determine where her blood glucose levels are above target and how can she improve them. Ideally, Lana should wait until her A1C is optimal before trying to conceive.

As pregnancy can affect any underlying diabetic retinopathy, Lana should have a retinal assessment performed if it has been more than 1–2 years since her last assessment. If there was previous evidence of diabetic retinopathy, a complete assessment by a retinal specialist at this time would be in order. As well, she should have a renal screen to determine the presence of diabetic nephropathy; this screen should include an albumin-to-creatinine ratio or other microalbuminuria screen. Blood pressure levels should also be assessed.

Lastly, you'll inform Lana that she should start folic acid supplementation preconception at a dose of 5 mg od, which should be continued until 12 weeks' gestation. At that point, the folic acid dosage can be reduced to that contained in regularly available prenatal supplements.

Lana wants to know what to expect through the course of her pregnancy. It should be explained that she may be at risk of hypoglycemia during the first trimester because of increased insulin sensitivity; thus, she may need to decrease her insulin dosages during this time. Later, toward the end of the second trimester and onwards, insulin resistance

arising from placental hormones will occur and she can expect to increase her insulin requirements significantly.

Target glucose levels are tighter in pregnancy (see Table 4). Thus, Lana will be asked to self-monitor her blood glucose more frequently than she may be accustomed to doing.

With pre-existing diabetes, the pregnancy is considered higher risk, so Lana will need a referral for delivery by an obstetrician. As well, she should undergo regular fetal assessment through the third trimester. In women with pre-existing diabetes, there is a small risk of a third trimester sudden intrauterine death, so Lana can expect to deliver before her due date, usually sometime after 36 weeks' gestation.

As soon as Lana delivers her baby, her insulin requirements will return to her pre-pregnancy levels (or even lower) for a short time after the placental source of insulin resistance is no longer present. Thus, Lana will need to monitor her blood glucose levels carefully and readjust her insulin dosages as necessary.

DIABETES CARE IN HOSPITAL

In my 20 years' experience managing diabetes in both hospital and outpatient settings, I have witnessed diabetes management that has ranged from the good, to the bad, to the ugly, to the "it's so complex that no one can understand what to do!" Unfortunately, it is the patients with diabetes who suffer the most, as they are buffeted by swinging blood glucose levels while trying to recover from illness or surgery.

I believe that hospital management of diabetes doesn't have to result in such poor experiences for patients, nor does it have to be complicated for medical staff to manage. Over the years, I have developed a logical and straightforward approach to diabetes hospital management; it is an approach I share here, in the hope that it can help medical staff improve the hospital experience for patients with diabetes.

With this in mind, this chapter is intended for use by the following health care professionals working on hospital wards:

- Attending physicians
- Residents and other medical trainees
- Nurse practitioners
- Physician assistants
- Nurses
- Clinical assistants
- Dietitians
- Allied health professionals/providers

Since the prevalence of diabetes is increasing throughout the world, it stands to reason that more patients who are admitted to hospital have diabetes. If it is considered by either the patient or the medical staff to be a minor medical problem and placed at the bottom of the usual long list of medical issues, then be warned! Diabetes can easily rise to the top of that list, causing complications that may significantly worsen and prolong the patient's stay in hospital. Poorly controlled diabetes in one hospital admission can, unfortunately, be the cause of subsequent and perhaps more complicated admissions. With consistent attention to the basic principles of diabetes management and some exercise of logic and

common sense, diabetes-related complications, particularly iatrogenic complications, can be significantly reduced.

It is important to understand that the best advocate for optimal diabetes management is your patient! Persons with diabetes best understand their diabetes. They have been well-educated in the curriculum of diabetes self-management, and have been "in charge of" and directing the management of their diabetes for years. So, now, imagine such an individual entering hospital and losing that control. It is bad enough to lose control over one's health — whether the person is now ill with pneumonia, a heart attack or a broken leg — now the person has also lost control of his or her diabetes management, medication or insulin regimen, eating habits and exercise routine. Worse yet, people in such a situation feel that they are at the mercy of someone they would rightfully consider far less knowledgeable in managing their diabetes in hospital.

All people admitted to hospital are stressed. By its broadest definition, stress encompasses such factors as the anxiety and stress of illness, disruptive sleep and wake cycles, inflammatory response, shortness of breath, pain, and fear. The medical implications of stress include the increase of the stress hormones, catecholamines, cortisol, growth hormone, and glucagon. These hormones all share the property of increasing blood glucose levels. Add to that stress-induced hyperglycemia, bed rest with inactivity, glucose-containing intravenous solutions, the use of tube feeds or total parenteral nutrition or the use of drugs know to increase blood glucose levels (e.g., corticosteroids), and the makings of a hyperglycemia "perfect storm" are present.

Further complicating diabetes management in hospital is the fact that the most common acute complication in people with diabetes who are hospitalized is hypoglycemia (not hyperglycemia). Consider the reasons for this: by nature, the hospital diet is strict in calories but often wanting in taste, due to the necessary requirements for salt and fat restrictions. Furthermore, an institutional kitchen is simply not equipped to produce restaurant-quality meals. As well, many patients simply do not have an appetite while they are ill.

Added to this setting is the innate desire of health care professionals to "fix" what appears to be "broken:" illness, infection, chest pain, coronary arteries, broken leg, and, of course, blood glucose levels. It has been well-recognized that optimal diabetes control is the target and that means blood glucose levels of between 4.0 and 7.0 mmol/L. If a patient's blood glucose level is high, the overwhelming desire is to lower it. Insulin is dispensed quite freely, usually in aliquots of 5 units, which somehow conveys the false message of appropriate diabetes management. At the very least, it keeps the number of calls from the ward staff to a minimum.

Finally, there is the scenario that is most inappropriate for someone with diabetes: the attempt to establish "good" glucose control in hospital. There are probably still instances where a patient is admitted to control their diabetes. For all the reasons stated above, however, it is virtually impossible to establish good diabetes control in hospital. To attempt to do so is usually an exercise in futility for patient and staff alike.

So, why bother attempting to optimize blood glucose control in hospital? There is more than sufficient evidence to show the harm that hyperglycemia can cause in a hospitalized patient. The presence of hyperglycemia in a septic patient will both prolong and decrease healing, and may be the root cause of septic complications in both surgical and nonsurgical patients. However, the use of insulin to control hyperglycemia without a logical approach will inevitably result in hypoglycemia, the most common complication affecting people with diabetes in hospital. Often, the result is blood glucose levels that swing between high and lows. Unfortunately, as the blood glucose swings, so does the patient. The added ill effects and symptoms of highs and lows, and all the swinging in between, have now been added to their illness.

The first principle in managing diabetes in hospital is to determine target blood glucose levels; for most patients, that translates to a range of 5.0/6.0–10.0/12.0 mmol/L. This range will maintain good white blood cell function against infection, while avoiding acute complications of hypo- or hyperglycemia. For more critically ill patients, this target can be adjusted to 5.0/6.0-8.0/10.0 mmol/L, depending upon the availability of nursing staff to monitor blood glucose levels.

The advent of rapid-acting insulins — which start working within 15 minutes, peak at 90–120 minutes and are virtually cleared from the body after 2–3 hours — has heralded a new era of much easier blood glucose control. Rapid-acting insulins reduce the risk of hypoglycemia, as they have a shorter duration of action than regular insulin and, accordingly, are usually given with meals.

Rapid-acting insulins are also effective for use as a corrective measure to maintain optimal blood glucose targets for patients in hospital. This approach replaces the commonly used (and, in my opinion, misused) insulin sliding scale. Sliding scales represent a reactive — rather than proactive — approach to blood glucose control. They deliver variable amounts of insulin at variable times, generally resulting in those swinging blood glucose levels mentioned earlier. The use of a rapid-acting insulin corrective algorithm or correction factor (CF) instead will result in much smoother blood glucose control. The application of this principle will be explained for each hospital setting.

Table 1 offers a review of diabetes oral medications and insulin. It is important to recognize the mechanism of action of the available oral medications.

TABLE 5

Oral antihyperglycemic agents

Agent	Mechanism	Dosage	Action time	Benefits	Disadvantages
Biguanide (insulin sensitizer)					
Metformin Glucophage	• Insulin sensitizer • Reduces hepatic glucose output	• Start 250–500 mg bid ac meals • Start with low dose and increase slowly • Maximum dose 2550 mg/day in divided doses	8 hrs	• Does not promote weight gain • Rarely causes hypoglycemia • Can be used in combination with daytime insulin	• GI: nausea; bloating; diarrhea • Slow increase in dose decreases these side effects • Contraindicated with renal or hepatic impairment, or CHF
Sulfonylureas (insulin secretagogues)					
Glyburide Diabeta	• Stimulates pancreatic secretion of insulin	• Start 2.5–5 mg od or bid ac meals • Maximum dose 10 mg bid	16–24 hrs		• May cause weight gain • May cause hypoglycemia
Gliclazide Diamicron	• As above	• Start 80 mg od • Maximum dose 160 mg bid	8–16 hrs	• Causes less hypoglycemia than glyburide	• May cause weight gain
Diamicron MR	• As above	• Start 30 mg od • Maximum dose 120 mg od	24 hrs		
Glimepiride Amaryl	• As above	• Start 1–2 mg od • Dosage range: 1–8 mg od	24 hrs	• May be used in combination with daytime insulin • May cause less hypoglycemia than glyburide	• May cause weight gain

Agent	Mechanism	Dosage	Action time	Benefits	Disadvantages
Alpha-glucosidase inhibitor					
Acarbose Prandase Glucobay	• Inhibits glucosidase enzymes in carbohydrate digestion • Decreases • Postprandial glucose rise	• Start 25 mg with first bite of food • Titrate weekly to Usual dose of 50–100 mg/meal	Best effect seen postprandially	• No hypoglycemia if used alone	• GI: bloating, flatus • Start with low dose and increase slowly to decrease GI side effects • Beano counteracts GI effects • When treating hypoglycemia, use dextrose tablets, milk or honey
Meglitinide (insulin secretagogue)					
Repaglinide GlucoNorm	• Stimulates pancreatic insulin secretion • Different mechanism than sulfonylureas	• Start 0.5 mg taken 0–30 minutes before each meal • Or, titrate according to carbohydrate intake (1 mg/15 g carbohydrate) • Available in 0.5,1 and 2 mg dosages	Short-acting; stimulates insulin secretion in response to glucose rise at mealtime	• Controls postprandial glucose rise • Provides flexibility to fit varied mealtimes	• May cause hypoglycemia
Thiazolidinediones (insulin sensitizers)					
Rosiglitazone Avandia*	• Insulin sensitizer • Insulin action improved in liver, muscle and adipose tissue	• 2–8 mg daily as a bid dosage	Effect seen after 6 weeks	• May increase TG, decrease HDL	• Rosiglitazone is associated with a risk of CVD • Pioglitazone is associated with a risk of bladder cancer • Both may cause weight gain, peripheral edema, macular edema or CHF • Associated with an increased fracture risk in women
Pioglitazone Actos	• Insulin sensitizer • Insulin action improved in liver, muscle and adipose tissue	• 15–45 mg daily			

Agent	Mechanism	Dosage	Action time	Benefits	Disadvantages
					• Both contraindicated in CHF, hepatic impairment (monitor liver functions regularly)
Rosiglitazone/ metformin combination Avandamet*	• As per rosiglitazone and metformin	• R(1–4 mg)/ M(500–1000 mg)			• As per rosiglitazone • Should not be used- in combination with daytime insulin
Incretins (augment insulin action)					
Sitagliptin Januvia	• Augments endogenous insulin • Blocks glucagon action in liver (sensitizer and secretagogue effect	• 100 mg daily • 50 mg daily with eGFR 30-49 mL/min • 25 mg daily with eGFR <30 mL/min	4–6 weeks	• Weight neutral • Low risk for hypoglycemia	• Rare risk of pancreatitis
Sitagliptin/ metformin combination Janumet	• As per sitagliptin and metformin	• S (50 mg) • M (500–1000 mg)	As per sitagliptin and metformin	• As per sitagliptin and metformin	• As per sitagliptin and metformin
Saxagliptin Onglyza	• Augments endogenous insulin • Blocks glucagon action in liver (sensitizer and secretagogue effect	• 5 mg daily • 2.5 mg daily with eGFR 15-50 mL/min	4–6 weeks	• Weight neutral	• Requires dosage reduction in the presence of chronic kidney disease • Rare risk of pancreatitis
Saxagliptin/ metformin combination Kombiglyze	• As per saxagliptin and metformin	• S (2.5 ,5mg) • M (500, 1000 mg)	As per saxagliptin and metformin	• As per saxagliptin and metformin	• As per saxagliptin and metformin
Linagliptin Trajenta	• Augments endogenous insulin • Blocks glucagon	• 5 mg daily	4-6 weeks	• Does not require dosage adjustment in the presence of chronic kidney disease	• Rare risk of pancreatitis

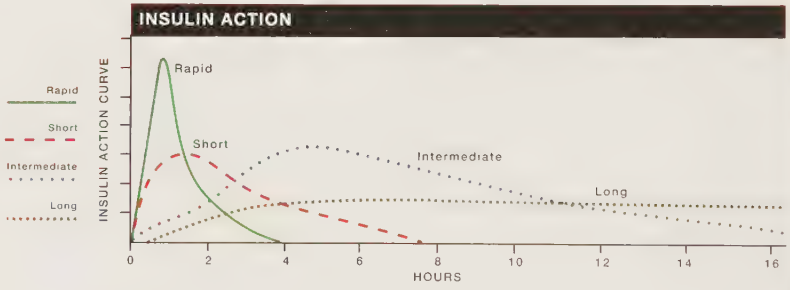
Agent	Mechanism	Dosage	Action time	Benefits	Disadvantages
	action in liver (sensitizer and secretagogue effect				
Linagliptin/ metformin Jentadueto	• Augments endogenous insulin • Blocks glucagon action in liver (sensitizer and secretagogue effect	• L (2.5 mg) • M (500, 850, 1000 mg)		• Does not require dosage adjustment in the presence of chronic kidney disease	• Rare risk of pancreatitis
GLP 1 analogue (augments endogenous insulin)					
Liraglutide Victoza	• Blocks glucagon action in liver	• 0.6–1.8 mg daily	4–6 weeks	• Weight neutral • May lead to weight loss • Liraglutide now approved for use in combination with basal insulin (see insulin section)	• May cause nausea • Rare risk of pancreatitis • Contraindicated in those with past history or family history of medullary thyroid cancer/multiple endocrine neoplasia
Exenatide Byetta		• 5-10 mcg bid			
Weight loss agent					
Orlistat Xenical	• inhibits fat absorption	• 100 mg with each meal			• Adverse GI effects
Novel agents					
Sodium-glucose co-transporter inhibitors					
Canagliflozin Invokana	• Inhibit renal reabsorption of glucose	• 100–300 mg daily			• Glycosuria may increase risk of UTI
Dapagliflozin Forxiga		• 10 mg daily			
Remogliflozin		• 1000 mg od/bid			
Sergliflozin		• 500-1000 mg tid			
Dopamine agonist					
Bromocriptine-QR Cycloset**	• 0.8 mg daily, titrated weekly to 1.6–4.8 mg				• Nausea • Postural dizziness

*Difficult to prescribe, requiring physician and patient waivers **Novel use for diabetes

Table 2 identifies the various insulin types available and Figure I depicts insulin time action profiles. It is important to realize that there is a significant difference between rapid- and short-acting insulin with respect to time to onset and duration of action. (See Table 2 on page 85.)

FIGURE I

Time action profiles of insulins available in Canada



The following is a set of assumptions or understandings regarding hospital management of patients with diabetes:

- Acute illness generally results in hyperglycemia.
  More stable conditions may result in hypoglycemia when the pre-admission diabetes medications and dosages are continued in the presence of the "calorie/carbohydrate-controlled" hospital diabetes diet.
- It is important to individualize safe target blood glucose ranges for hospitalized patients.
- Hospital is not the setting to establish optimal good blood glucose control.
- Above all else, remember that hypoglycemia causes more harm in hospital than does hyperglycemia.

TABLE 2

Insulin types

Type	Trade name	Onset	Peak (h)	Duration (h)
Rapid-acting (Bolus)				
Lispro Aspart Glulisine	Humalog NovoRapid Apidra	10–15 min	1.0–1.5 hrs	3–5 hrs
Short-acting				
Regular R	Humulin R Novolin ge Toronto	0.5–1 hr	2–4 hrs	6–8 hrs
Intermediate-acting (Basal)				
NPH	Humulin N	1–3 hrs	4–8 hrs	12–18 hrs
Long-acting (Basal)				
Glargine Detemir	Lantus Levemir	90 min	No peak	24 hrs
Premixed (short- and intermediate-acting, R/NPH)				
10/90 30/70* 40/60 50/50	Humulin (*premix available) Novolin ge	0.5 hr	2–12 hrs 2-3 hrs 1 hr	12–18 hrs
Premixed insulin (rapid- and intermediate acting)				
25% rapid-acting/75% intermediate-acting 30% rapid-acting/70% intermediate-acting	Humalog Mix25 NovoMix 30	15 min	1 hr	10-14 hrs

DIABETES IN THE EMERGENCY ROOM

Please note that this chapter does not address the management of the acute complications of diabetic ketoacidosis or hyperglycemic hyperosmolar states. Rather, it is meant to identify and help avoid the pitfalls that can complicate the situation of people with diabetes who are admitted to the emergency room (ER) for other reasons.

People with diabetes are at greater risk for a variety of acute medical events, including sepsis, cardiovascular disease, acute myocardial infarction, and renal disease. Thus, diabetes will be on the problem list of many ER patients. However, in the chaos that typifies the ER, patients' diabetes — or more, importantly, their blood glucose status — may be temporarily neglected as their more emergent issues are dealt with. Diabetes, if left poorly controlled, can complicate almost any medical condition and lead to the development of further medical problems, particularly sepsis.

A quick survey of every patient, asking whether they have diabetes, would be useful. For those with diabetes, a quick further inquiry regarding their medication regimen (oral agents or insulin) and — perhaps more importantly — when they last took their medication, does not take much time and can provide much information to prevent further acute diabetes complications.

Here is a sample of a useful quick survey regarding a patient's diabetes:

- Do you know if you have type 1 or type 2 diabetes? (Remember, the use of insulin does not differentiate type 1 from type 2.)
- What medications — pills and/or insulin — do you take for your diabetes? What diabetes medications did you take today? At what time did you take them?
- When was your last blood glucose reading? What was the reading?
- Have you been able to eat? When did you last eat?

If people with type 2 diabetes are without their diabetes medications, they will only become increasingly hyperglycemic and open to the risk of metabolic derangements and sepsis. Thus, there is a need for increased

advocacy for the patient with diabetes in the ER. This may come from the patient, his/her family or health care staff. It is of benefit to all to listen and pay attention to the patient's diabetes status. Simple maintenance of an appropriate blood glucose range will decrease the risk of a more complicated hospital stay.

A Practical Approach for Blood Glucose Control in the ER

- Set a target blood glucose range that is appropriate for the situation: 5.0/6.0-10.0/12.0 mmol/L
- For stable patients who can eat, continue their diabetes medication regimen and use glucose monitoring to maintain the target glucose range
- Use the following rapid insulin correction factor (CF) every 4–6 hours to maintain target blood glucose: Give 1 unit of rapid insulin for every 3.0 mmol/L blood glucose level greater than 12.0 mmol/L
- Patients must have a source of food/glucose, either oral or intravenous (IV)
- For patients with significantly acute illness and who cannot eat, use the rapid insulin CF or consider establishing an insulin infusion:
  - Start with regular/rapid insulin at 1 unit/hour with a simultaneous glucose infusion
  - Titrate the insulin ± 1unit/hour to maintain the target blood glucose range. (See further details in the following section, Diabetes on the Medical Ward)

CASE STUDY – Evelyn

Evelyn is a 65-year-old woman with longstanding type 2 diabetes. She takes gliclazide MR 90 mg od and metformin 850 mg tid. She presents in the evening with sepsis, which may be caused by a urinary tract infection. She is vomiting and not eating. She did not take her diabetes medications today and her blood glucose level is 18.0 mmol/L. She is being started on IV fluids, 5% dextrose and water/1/2 normal saline (D5W/1/2 NS) at 100 cc/hour and IV antibiotics. She is to be reassessed tomorrow.

The concerns here are the risk of continued hyperglycemia complicating her sepsis, her inability to keep food down, and medication. Don't forget, metformin must be re-evaluated in the presence of possible dehydration, causing a rise in serum creatinine.

A logical approach would be either of the following:

- Discontinue all oral diabetes medications
- Perform regular blood glucose monitoring every 2 hours
- Use the rapid insulin CF every 4 hours

or

- Start an insulin infusion until Evelyn is able to tolerate oral fluids and medications once again

DIABETES ON THE MEDICAL WARD

Clinical experience has shown that blood glucose levels swing, often quite widely, on the internal medicine ward. Unfortunately, these swings are often iatrogenic in nature. Fortunately, however, iatrogenic causes can be fixed through the understanding of the basic reason for blood glucose variability on the hospital ward and the application of a few general principles.

In the acute phase of illness and hospitalization, blood glucose levels tend to rise; in the longer, more stable, hospitalization blood glucose levels tend to drop in response to the strict hospital diet. Usual sleep/wake cycles are disrupted, thereby increasing both stress and blood glucose levels. Inactivity can also increase blood glucose levels. The timing of meals and snacks will vary from the patient's home routine. Often, it's the lack of appreciation for the seemingly small details that can result in major problems. For example, on most wards, supper is served at 6:00 p.m. and that may be the last food a patient eats until morning. If they receive insulin secretagogue oral agents or long-acting insulin at supper or bedtime, there is now a real possibility of nocturnal hypoglycemia occurring. In fact, hypoglycemia is a more serious problem on hospital wards than is hyperglycemia. Yet, it seems that it is hyperglycemia that is chased with variable amounts of insulin around the clock resulting in those infamous blood glucose swings.

In order to achieve stable diabetes control on the ward, consider the key understanding noted above: It is important to determine a safe target blood glucose range for the individual hospitalized patient. An appropriate target range that will avoid the acute problems of hyper- or hypoglycemia is 5.0/6.0–10.0/12.0 mmol/L. This target range will decrease the risk of hyperglycemia contributing to a risk of sepsis, and avoid the risks of hypoglycemia.

A Practical Approach to Blood Glucose Control on the Medical Ward

For stable, less acutely ill patients, utilize the patient's usual diabetes regimen with dosage adjustments as required. Some patients will need an increase in their dosage of approximately 10–15% to accommodate the initial stress of hospitalization. Remember, however, that once the situation has stabilized, there will likely be a need to reduce dosage by at least 15–20% to account for the strictly controlled hospital diet.

Use the rapid insulin CF at mealtimes to maintain the target blood glucose range as follows:

- Give 1–2 units for every 3.0 mmol/L greater than 10.0/12.0 mmol/L (the upper target range). This correction algorithm can be used with any existing diabetes regimen.
- Avoid giving rapid insulin CF at bedtime, as that will increase the risk of hypoglycemia.

Insulin Sliding Scales and Why the Author Hates Them!

Insulin sliding scales deliver variable dosages of insulin at variable times, as determined solely by a blood glucose reading. Overall, it is reactive to the last blood glucose value rather than being proactive toward the next glucose value. No other variables are taken into consideration (e.g., time of day). Thus, a dose of insulin may be given at night when the patient will have no food intake until morning. Or, another dose of insulin may be administered on top of a previously ordered dose of oral agent or insulin. So, in effect, the patient may have an oral agent or insulin peaking on top of the sliding scale dose. Thus, sliding scales contain all the ingredients for a perfect storm, resulting in wildly swinging glucose levels.

The rapid insulin correction is preferred because it is a proactive, rather than reactive, approach. It builds on an already established diabetes regimen and works to keep the patient's blood glucose in the designated target range.

Insulin Infusions

Acutely ill patients who are unable to eat are best controlled by insulin infusion:

- Start with regular/rapid insulin at 1 unit/hour IV simultaneously running with 5% D5W at 75 cc/hour (the D5W provides some carbohydrate substrate for the insulin and provides a safety measure to avoid insulin left running unopposed by any glucose). Titrate the insulin infusion ± 1 unit/hour at a time until the target blood glucose is met through hourly/ 2 hourly bedside glucose monitoring.
- Once the target is met, check again 1–2 hours later as sometimes the target range can be overshot.
- Once the patient is eating again, he/she returns to the previous regimen, utilizing the rapid insulin correction to adjust for blood glucose over the target range.

Transferring from an Insulin Infusion to an Oral Agent Regimen

It is important to remember the basic classification of oral agents and, more importantly, the contraindications for each of them. Combination therapy that utilizes oral agents ± insulin is a very useful diabetes regimen. This regimen can be initiated in hospital; however, it should be noted that reassessment and adjustment will require outpatient follow-up.

When returning to the previous oral agent regimen, it is important to remember basic pharmacokinetics. There will be some delay in the action of oral agents in lowering blood glucose once they have been started. So, some overlap with insulin is best: for example, the insulin infusion should continue until the oral agents have begun to work (a few hours after the first oral dose). Alternatively, the insulin infusion could be stopped at the same time the oral agent is started. The rapid insulin CF could be used to maintain target blood glucose levels until the oral

agents have taken effect. Its logical (and safer) to begin the change in the regimen first thing in the morning to coincide with breakfast service and to allow assessment during the day when more staff is available.

When returning to the previous insulin regimen, the same approach applies. Remember to start with 15–20% less of the "home dosage" to protect against hypoglycemia. The rapid insulin CF will maintain target blood glucose levels and will also provide a gauge for adjusting the total daily dose (TDD). This TDD can be distributed as best fits the patient's current situation twice, three or four times daily (bid, tid, qid).

When transferring to a new insulin regimen, the 24-hour insulin requirements can be determined from the infusion and used as the starting TDD. Again, the TDD can be distributed as best fits the situation. The approach currently being used is a basal/bolus insulin regimen. Basal insulin refers to either intermediate (NPH) or long-acting (glargine or detemir) insulin given as the "background" insulin od or bid. Bolus insulin refers to rapid-acting (lispro, aspart, or glulisine) insulin given with meals. Further use of the rapid insulin CF will provide the feedback for dosage adjustments. Remember, the hospital is not the venue to establish a stable insulin dosage as there are too many variables. The logical approach is to adjust the insulin dosage to maintain the safe target blood glucose range (5.0/6.0–10.0/12.0 mmol/L). Detailed dosage adjustment is best done through post-discharge follow-up with a diabetes health care team.

Key Points for the Medical Ward

- Set a safe target blood glucose range. 5.0/6.0–10.0/12.0 mmol/L will be appropriate for most patients.
- Establish a set diabetes regimen, whether oral medication and/or insulin. Base it on the home regimen. In more stable patients, the TDD will be reduced by 15–20% for safety to start. In less stable patients, the blood glucose levels may be higher; in that case the TDD will be increased by 15–20% to start.
- Avoid insulin sliding scales; avoid bolus insulin dosages in response to high blood glucose levels.
- Use the rapid insulin CF, in addition to the set diabetes regimen.

Special Considerations

Any guide to diabetes management on the hospital ward would not be complete without specific mention of corticosteroids. Whether given orally, parenterally, in pulse or constant regimens, steroids elevate blood glucose levels tremendously. Only aggressive use of insulin can address these elevations. In the person with known diabetes, aggressive augmentation of the pre-existing insulin regimen is required. Steroid use may "uncover" a diabetes predisposition and result in secondary diabetes. These people will need insulin de novo, as oral agents will rarely be sufficient.

CASE STUDY – Henry

Henry is a 61-year-old man admitted with a non-ST elevation myocardial infarction (NSTEMI). He is found to have new-onset type 2 diabetes, with a random blood glucose of 20 mmol/L at the time of admission. He is being kept NPO, pending a coronary angiogram, with IV dextrose 50 cc/hr.

The primary objective is to achieve and maintain a safe target blood glucose range of 5.0/6.0–10.0/12.0 mmol/L. The logical approach is to start an insulin infusion until he starts eating. He can then be transitioned to either continuing with a basal/bolus insulin regimen or a combination of oral medication and basal insulin.

CASE STUDY – Gwen

Gwen is a 50-year-old woman who is newly diagnosed with lymphoma and will be starting chemotherapy in hospital. High-dose corticosteroids are part of her chemotherapy protocol. She has type 2 diabetes, which was previously controlled with glyburide 5 mg bid. After day 1 of her chemotherapy, her blood glucose level is 25 mmol/L.

The primary concern here is that high blood glucose levels will increase her risk of infection, along with the expected low white blood cell count she will experience from the chemotherapy. The sustained elevated

blood glucose levels secondary to corticosteroids will respond only to insulin. There may be a pattern to the blood glucose levels. If the steroid is given once daily in the morning, the effect on blood glucose will be seen through the day and will taper off over 12 hours.

Accordingly, a logical approach is to give a combination of rapid and basal (long-acting) insulin in the morning to provide continuous insulin coverage throughout the day. Further set dosages of rapid insulin may be needed at mealtimes to bolster the sustained effect of the basal insulin. Adding the rapid insulin correction at mealtimes will also help to maintain target blood glucose levels.

CASE STUDY – Richard

Richard is a 73-year-old man with longstanding type 2 diabetes for which he took metformin 1000 mg bid, glyburide 10 mg bid and NPH insulin 20 units at HS. He is admitted with pneumonia and dehydration. His serum creatinine is rising, as are his blood glucose levels, which are currently 18 mmol/L.

The issue with Richard is not just maintaining a target blood glucose level; rather, the rising serum creatinine and impending renal failure are of primary concern. Metformin should be decreased by 50% once the glomerular filtration rate reaches 60 mL/min, and stopped once it reaches 30 mL/min. Clearance of other medications may also be affected; so the dosage of glyburide may also need to be reduced.

The logical approach here would be to stop metformin and add basal insulin in the morning to supplement the bedtime dose. Adding the rapid insulin correction will help at meals. If he is not eating, then consideration should be given to using an insulin infusion instead.

DIABETES ON THE SURGERY WARD

All information regarding the medical ward also applies to the surgery ward. Here, however, the differences are likely to lie in an increased need for insulin infusions to carry the patient through the perioperative period when they are not eating. Maintaining target blood glucose levels is

key to reducing the risk of perioperative sepsis. Therefore, the use of the rapid insulin correction algorithm can be very useful.

One major consideration on surgery wards is the common use of nutritional support, either through tube feeds or total parenteral nutrition (TPN). The basic component of these two nutritional supports is glucose. Accordingly, blood glucose levels remain high in these patients. The only way to maintain target blood glucose levels is through the aggressive use of insulin. Insulin infusion is the most effective route; however, where such a regimen is not possible, multiple injections of basal insulin (bid) along with rapid insulin every 4-6 hours should work.

The challenge comes when a tube feeding regimen (less often, TPN) is changed from 24 hours to a modified time frame, in order to encourage feeding. Those modifications — such as overnight feeds or bolus feeds throughout the day — usually respond best to the use of rapid insulin boluses with the feeds supplemented by intermediate/long-acting insulin once daily (OD) or twice daily (BID).

A Practical Approach to Blood Glucose Control on the Surgery Ward

For stable, less acutely ill patients, utilize the patient's usual diabetes regimen with adjustments in the dosage as required. Some patients will need an increase in their dosage of approximately 10–15% to accommodate the initial stress of the hospitalization. But remember, once that initial situation has stabilized, there will likely be a need to reduce dosage by at least 15–20% to account for the strictly controlled hospital diet.

Use a the rapid insulin CF at mealtimes to maintain the target blood glucose range as follows: give 1–2 units for every 3.0 mmol/L greater than 10/12 mmol/L. This CF can be used alongside any existing diabetes regimen.

Acutely ill patients who are unable or not allowed to eat and perioperative patients who are still not eating are best controlled by an insulin infusion.

- Start with regular/rapid insulin at 1 unit/hour intravenously (IV) simultaneously running with 5% dextrose and water (D5W) at 75 cc/hour (the D5W provides some carbohydrate substrate for the insulin).
- Titrate the insulin infusion ± 1 unit/hour at a time until the target blood

glucose is met through hourly/2 hourly bedside glucose monitoring.

- Once target is met, check again 1–2 hours later as sometimes the target range can be overshot.
- Once the patient is eating again, he/she can be transferred back to the previous regimen, utilizing the rapid insulin correction algorithm to adjust for blood glucose over the target range.

Key Points

1. Set a safe target blood glucose range: 5.0/6.0–10.0/12.0 mmol/L will be appropriate for most patients.
2. Establish a regular diabetes regimen, whether oral medications and/or insulin, that is based upon the home regimen. In more stable patients, the TDD should be reduced by 15–20% for safety to start. In less stable patients, whose blood glucose levels may be higher, the TDD should be increased by 15–20% to start.
3. Avoid insulin sliding scales and bolus insulin dosages in response to high blood glucose levels.
4. Use the rapid insulin CF instead, in addition to the set diabetes regimen.
5. Remember: tube feeds and TPN are significant sources of glucose. Insulin will be required to maintain adequate control.

CASE STUDY – Stan

Stan is a 55-year-old man with longstanding type 2 diabetes for which he takes glyburide 10 mg bid. He has been admitted with an infected diabetic foot ulcer. He requires a number of surgical débridement procedures in the operating room (OR), as well as an aortogram to assess the possibility of an aorta-femoral bypass. Currently he is NPO on standby. His blood glucose level is 15.0 mmol/L.

The issue here is maintaining the target blood glucose level of 6.0–12.0 mmol/L while he is on standby throughout the day. The logical approach is to start an insulin infusion. Then, as often happens, Stan is bumped from the emergency slate and allowed to eat, but he will be NPO after midnight for standby for the OR tomorrow. The logical approach is to still use insulin.

There are two options: (1) he could continue with the insulin infusion utilizing a square-wave bolus for his supper (i.e., increase the insulin infusion rate by 2 units for 2 hours over the mealtime), or (2) the insulin could be stopped but he would need a rapid insulin dose for supper. This dose could be calculated as an extrapolation from his hourly requirements throughout the day, such as if he is requiring 2 units /hour, 48 units/day. This calculation results in 24 units basal and 24 units bolus divided among the 3 meals or 8 units for a meal. Adding the corrective rapid insulin algorithm will help to maintain target blood glucose.

DISCHARGE PLANNING

Utilizing the strategies elucidated in this chapter, blood glucose levels can usually be maintained in hospital. The potential for problems occurs after discharge. Deterioration of blood glucose control can happen quite easily once a patient is home. Usually, hyperglycemia occurs related to a combination of inactivity and a change in nutritional intake. Hyperglycemia increases the risk of sepsis and introduces the real possibility of readmission to hospital; this risk applies to medical and surgical patients alike; however, the risk may be greater for the surgical patient with a healing incision. Follow-up assessment in a timely fashion can reduce this risk.

The need to arrange post-discharge assessment cannot be overstated. This assessment may occur in a variety of ways: through a primary care provider, a hospital or community-based diabetes health care team and/or designated diabetes case manager. The key is to provide support to adjust oral agents and insulin dosages to maintain the target blood glucose range. While the optimal target blood glucose range is 4.0–7.0 mmol/L pre-meal and 5.0–8.0 mmol/L 2 hours post-meal, these targets may vary depending on the situation. Post-discharge blood glucose control should be tighter for those recovering from surgery and/or sepsis, to decrease any further risk of sepsis.

Newly diagnosed individuals will require basic diabetes survival skills before leaving hospital, including SMBG, insulin injection, and recognition and treatment of hypoglycemia. Most importantly, they need to be connected to community-based follow-up for their diabetes.

Diabetes is a serious condition with potentially devastating complications that affects people of all age groups worldwide. In 2009, more than 2.4 million Canadians were thought to have diabetes, a 240% increase over the previous decade. By 2019 that number is expected to rise to 3.7 million.

A multi-faceted approach utilizing an inter-professional team has been shown to effectively lower the development and progression of complications in diabetes. Integrating the latest *2013 Canadian Diabetes Association Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada*, this practical book helps translate research and evidence-based recommendations into everyday clinical practice, with the goal of helping all members of the health care team more effectively manage their diabetic patients.

Dr. Sora Ludwig *has been a practising endocrinologist for more than 20 years, specializing in the long-term care of people with type 2 diabetes. She has been actively involved in the development of the Canadian Diabetes Association's* Clinical Practice Guidelines *since 1998.*

An Associate Professor at the University of Manitoba, Dr. Ludwig has taught medical students, physicians in post-graduate training programs, family physicians in practice, and allied health care professionals, including diabetes educators, nurses, dietitians, pharmacists, and social workers.

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