
CHAPTER 10 – HEMATOLOGY, METABOLISM AND ENDOCRINOLOGY

First Nations and Inuit Health Branch (FNIHB) Clinical Practice Guidelines for Nurses in Primary Care.
The content of this chapter was revised June 2010.

Table of Contents

COMMON HEMATOLOGIC PROBLEMS.....	10–1
Anemia	10–1
Iron Deficiency Anemia	10–4
Megaloblastic Anemia	10–6
Specific Anemias and Additional Diagnostic Tests	10–9
Anemia of Chronic Disease	10–9
Lead Poisoning–Related Anemia	10–9
Hemolytic Anemia	10–9
COMMON ENDOCRINE AND METABOLIC PROBLEMS	10–10
Diabetes Mellitus.....	10–10
Hyperthyroidism	10–21
Hypothyroidism	10–25
Metabolic Syndrome	10–28
Osteoporosis.....	10–31
METABOLIC EMERGENCIES	10–34
Diabetic Ketoacidosis and Hyperosmolar Hyperglycemic State	10–34
Hypoglycemia	10–37
SOURCES.....	10–39
APPENDIX A	10–43
APPENDIX B.....	10–44
APPENDIX C	10–45
APPENDIX D	10–46
APPENDIX E.....	10–48

Hematologic, metabolic and endocrine disorders often manifest signs and symptoms in more than one body system. This chapter will not discuss the history and examination of all body systems.

Other related chapters include:

- integumentary (*see the chapter “Skin”*)
- eyes (*see the chapter “Eyes”*)
- ears, nose, throat (*see the chapter “Ears, Nose, Throat and Mouth”*)
- cardiovascular (*see the chapter “Cardiovascular System”*)
- respiratory (*see the chapter “Respiratory System”*)
- gastrointestinal (*see the chapter “Gastrointestinal System”*)
- neurologic (*see the chapter “Central Nervous System”*)

For each hematologic, endocrine or metabolic problem, the expected physical findings are noted by body system with references to the corresponding section of the guidelines. See example excerpt below:

HYPERTHYROIDISM

PHYSICAL FINDINGS

- Integumentary: inspect and palpate skin, noting pigmentation pattern, moistness and turgor (usually warm, moist skin with sweaty palms); inspect hair for texture and thickness (usually thin and silky); inspect nails for ridges, discoloration or splitting (*see “Assessment of the Integumentary System” in the chapter “Skin”*)

See individual sections for information on history and physical examination relevant to each of these systems.

COMMON HEMATOLOGIC PROBLEMS

ANEMIA

Anemia can be generally defined as a reduction in hemoglobin level or as a decrease in circulating red blood cell (RBC) mass to below age-specific and gender-specific limits. Anemia can be a single entity or, most commonly, one symptom of a more complicated or chronic disease.¹

In determining the seriousness of the anemia, the level of hemoglobin is less important than the underlying cause. However, there are more than 200 types of anemia, which makes determining the cause difficult.

TYPES OF ANEMIAS

Anemias can generally be divided into three types according to the size of the RBCs as measured in the mean corpuscular volume (MCV). *See Table 1, “Anemia Classification.”*

Table 1 – Anemia Classification²

RBC Classification	Laboratory Tests	Findings	Differential Diagnosis
Normocytic, Normochromic Anemia	<ul style="list-style-type: none"> • Normal MCV = 80–100 fL • Normal mean corpuscular hemoglobin concentration [MCHC] • Reticulocyte count 	Blood loss, hemolysis	<ul style="list-style-type: none"> • Anemia of acute hemorrhage
		No blood loss	<ul style="list-style-type: none"> • Anemia of chronic disease • Mixed deficiency anemia • Hemolytic anemias • Sickle cell anemia³ • Endocrine disorder • Hemoglobinopathy • Aplastic anemia
Microcytic, Hypochromic Anemia	<ul style="list-style-type: none"> • Low MCV (< 80 fL) • Low MCHC • Serum ferritin (preferred over serum iron) • TIBC • RBC distribution width (RDW) 	Ferritin < 20 µg/L	<ul style="list-style-type: none"> • Iron deficiency anemia
		Ferritin > 20 µg/L	<ul style="list-style-type: none"> • Thalassemias • Anemia of chronic disease • Hemoglobinopathy • Lead overload
Macrocytic, Normochromic Anemia (also called megaloblastic anemia)	<ul style="list-style-type: none"> • High MCV (> 100 fL) • Normal MCHC • Reticulocyte count • Vitamin B₁₂ level • Folate level 	Blood loss	<ul style="list-style-type: none"> • Vitamin B₁₂ deficiency • Folate deficiency • Alcoholism or liver disease • Hemolytic anemia • Myelodysplasia
		No blood loss	

Reprinted with permission from Medication Use and Management Services (MUMS) *Anemia Review Panel. Anemia guidelines for family medicine*. 2nd ed. Toronto, ON: MUMS Guideline Clearinghouse; 2008. p. 3.

UNCOMMON ANEMIAS⁴

- Aplastic anemias (characterized by lack of production of RBC from the marrow)
- Sideroblastic anemias (characterized by increased iron absorption)
- Secondary to hemostatic disorders (for example, hemophilia, von Willebrand disease)

CLINICAL SIGNS AND SYMPTOMS

The severity of clinical symptoms is related more to the period of time over which the condition develops and not the absolute value of the hemoglobin. An acute hemorrhagic condition may produce life-threatening symptoms (for example, tachycardia, lightheadedness, shortness of breath, postural hypotension, syncope)⁵ with loss of as little as 20%

of the total blood volume (or 20% of the total red cell mass). Conversely, anemias developing over periods long enough to allow compensatory mechanisms to operate will be associated with much greater loss of red cell mass before symptoms are manifested.

Angina pectoris, intermittent claudication and nighttime muscle cramps are some of the effects of anemia on already-compromised perfusion.

The signs and symptoms of anemia occur when the oxygen-carrying capacity of the blood is unable to meet the oxygen requirements of body tissues. Most body systems are affected as shown in Table 2, “*Signs and Symptoms of Anemia*.”

Table 2 – Signs and Symptoms and Anemia⁶

Body System	Sign/Symptom
Cardiovascular system	<ul style="list-style-type: none"> • Chest pain • Tachycardia, palpitations • Cardiac hypertrophy • Increased pulse pressure, systolic ejection murmur
Central nervous system	<ul style="list-style-type: none"> • Debilitating fatigue • Depression, irritability • Impaired cognitive function • Dizziness, vertigo, syncope • Headache
Gastrointestinal system	<ul style="list-style-type: none"> • Anorexia, nausea • Diarrhea • Indigestion • Melena, blood in stools
Genitourinary system	<ul style="list-style-type: none"> • Menstrual problems • Loss of libido
Immune system	<ul style="list-style-type: none"> • Impaired T-cell and macrophage function
Peripheral nervous system	<ul style="list-style-type: none"> • Numbness, tingling of extremities • Decreased vibrational sense • Positive Romberg's sign • Exaggerated or absent deep tendon reflexes
Peripheral vascular system	<ul style="list-style-type: none"> • Low skin temperature, cold intolerance • Pallor of skin, mucous membranes and conjunctivae
Respiratory system	<ul style="list-style-type: none"> • Dyspnea, shortness of breath

Adapted from Harding, SR. Common anemias. In: Gray J (Editor). *Therapeutic Choices*. 5th ed. Ottawa, ON: Canadian Pharmacists Association; 2007. p. 1114-1130.

HISTORY

Inquire about the following:⁷

- Signs or symptoms as noted in Table 2, “*Signs and Symptoms of Anemia*”
- Chronic illness (for example, impaired cardiac/ kidney/liver/thyroid function and chronic inflammation)
- Alcohol use
- Diet
- Medications
- Surgeries
- Family history

PHYSICAL FINDINGS

Assess all body systems for the signs of anemia as noted in Table 2, “*Signs and Symptoms of Anemia*.” See a specific anemia below for details on the physical findings for that particular anemia.

DIAGNOSTIC TESTS

- CBC, which includes:
 - Hemoglobin
 - Hematocrit
 - Complete white blood cell (WBC) count
 - Differential WBC count
 - Platelet count
 - MCV
 - RDW-(RBC distribution width)
- Reticulocyte count
- Serum ferritin⁵
- Peripheral blood smear

Subsequent investigations should be based on these values.

Normal hemoglobin ranges from 120–160 g/L in women and 130–180 g/L in men. These levels may vary slightly with geographic location; people living near the coast will have lower levels and those living at higher altitudes will have higher levels of hemoglobin.

Keep in mind that if anemia develops through rapid bleeding, the hematocrit and hemoglobin will be normal for the first several hours (because in acute hemorrhage the loss of RBCs and plasma is equal). Therefore, interpretation of the clinical signs will be of more value in diagnosing the amount of blood loss than will the results of laboratory tests.

IRON DEFICIENCY ANEMIA

Microcytic anemia with low serum ferritin due to depletion of iron stores. Iron deficiency anemia is not a disease, but a sign of an underlying disorder causing iron deficiency (for example, gastrointestinal tract blood loss).

Iron deficiency anemia (IDA) is the most common type of microcytic, hypochromic anemia.⁸

In Inuit women of childbearing age (18–49 years), serum iron deficiency is present in 40% of women, with two-thirds of the iron deficient women having IDA.⁹

CAUSES⁸

- Inadequate dietary intake of iron (common in strict vegetarians and vegans, children, adolescents and elderly people)

RISK FACTORS

- Increased requirements for iron without concomitant increase in intake (during growth spurts in infants, young children, adolescents and pregnant women)
- Blood loss due to excessive menstruation, disease of the gastrointestinal tract (for example, peptic ulcer, hiatus hernia), malignant gastrointestinal disease, angiodysplasia or previous acute blood loss (for example, trauma, surgery)
- Family or personal history of hematological disorders (for example, thalassemia), telangiectasia (for example, Osler-Weber-Rendu disease) or bleeding disorders (for example, von Willebrand disease)
- First Nations ethnicity
- Impaired absorption of iron because of partial gastrectomy, malabsorption syndromes (for example, Crohn's disease, ulcerative colitis, celiac disease)
- Chronic renal failure

HISTORY

- Symptoms vary according to severity of the anemia, underlying cause, rapidity with which the underlying condition developed and presence of pre-existing heart and lung disease

Mild Condition¹⁰

- Often asymptomatic
- Fatigue, weakness
- Dyspnea, shortness of breath
- Palpitations after exertion

Moderate or Severe Condition^{8,11}

- Symptomatic at rest
- Exercise intolerance, lack of strength or endurance with reduced ability to perform activities of daily living
- Symptoms of heart failure, syncope may be present
- Palpitations, chest pain
- Dizziness, headache, tinnitus
- Irritability, insomnia, inability to concentrate
- Hypersensitivity to cold and malaise
- Menstrual disturbances

Other Pertinent History

- Medications such as:
 - Anticoagulants
 - ASA and nonsteroidal anti-inflammatories (NSAIDs)
 - Clopidogrel
 - Anticonvulsants (for example, phenytoin [Dilantin], primidone)
 - Sulfamethoxazole/trimethoprim (Septra; long-term use only)
 - Oral contraceptives (which reduce the incidence of anemia)
 - HIV medications (for example, zidovudine [AZT])
 - Hepatitis C virus medications (for example, ribavirin)
 - Antineoplastic drugs (for chemotherapy)
 - Methotrexate, azathioprine
- Alcohol intake
- Comorbidities such as chronic inflammatory disease (for example, rheumatoid arthritis, SLE, Crohn's disease), malignant disease, diminished renal, hepatic or thyroid function, cardiac disease
- Surgeries
- Family history of anemias
- Dietary history (for example, strict vegetarianism)

PHYSICAL FINDINGS

- Review general appearance, paying particular attention to apparent skin pallor, fatigue and lethargy
- Vital signs: resting pulse (increased), respiration rate (increased), oxygen saturation, temperature, blood pressure (orthostatic hypotension, including orthostatic pulse from lying to standing) and weight (recent loss)
- Integumentary: inspect and palpate skin, note pallor (palms), dryness and temperature (cool); test capillary refill; inspect nails (usually thin, brittle, and coarsely ridged or concave [koilonychia]); inspect hair (dry, brittle) (*see “Assessment of the Integumentary System” in the chapter “Skin”*)
- Head and Neck: assess eyes for pallor of conjunctiva; observe cracks at corners of mouth and glossitis (*see “Assessment of the Eyes” in the chapter “Eyes”*)
- Respiratory: auscultate lungs (clear unless congestive heart failure present) (*see “Assessment of the Respiratory System” in the chapter “Respiratory System”*)
- Cardiovascular: auscultate the heart, noting murmurs and rate/rhythm; point of maximal impulse (PMI) displaced if enlargement has occurred (*see “Assessment of the Cardiovascular System” in the chapter “Cardiovascular System”*)
- Gastrointestinal: auscultate bowel sounds; assess the abdomen for hepatomegaly and splenomegaly; perform digital rectal exam (assess for hemorrhoids and melena/blood in stools) (*see “Assessment of the Gastrointestinal System” in the chapter “Gastrointestinal System”*)
- Neurologic: assess muscle strength and sensation; perform mental status examination (particularly for elderly clients) (*see “Assessment of the Central Nervous System” in the chapter “Central Nervous System”*)

DIFFERENTIAL DIAGNOSIS⁸

- Anemia of chronic disease
- Thalassemia minor
- Rule out other causes of anemia (*see “Anemia”*)

COMPLICATIONS

- Decompensation of pre-existing medical problems
- Heart failure, myocardial infarction

DIAGNOSTIC TESTS^{12,13}

- Complete blood count
- Reticulocyte count
- Serum iron level (test of choice as it is the first parameter to decrease)
- Total iron-binding capacity (TIBC)
- Serum ferritin level
- Peripheral blood smear
- Test three separate samples of stool for occult blood
- Upper GI endoscopy if no overt blood loss or obvious cause for IDA
- Colonoscopy or barium enema if no causal findings on upper GI endoscopy

Diagnostic Test Findings

- MCV = low
- Hemoglobin = low
- Hematocrit = low
- Serum ferritin = low to normal (note that ferritin can increase with any illness)
- Total iron binding capacity (TIBC) = high (in anemia of chronic disease TIBC is low)
- Serum iron = low

MANAGEMENT**Goals of Treatment¹⁴**

- Identify and address underlying cause of the iron deficiency
- Alleviate signs and symptoms of anemia
- Restore to normal or adequate hemoglobin level
- Replenish body stores of iron

Appropriate Consultation

Consult a physician immediately if hemoglobin < 90 g/L, stool is positive for occult blood or client appears acutely ill.

Nonpharmacologic Interventions

Client Education

- Explain nature, course and prognosis of anemia; this is a symptom related to lifestyle and/or a chronic condition that can be cured or managed
- Counsel client about appropriate use of medications (dose, frequency, side effects, importance of compliance, avoidance of abrupt discontinuation)
- Suggest dietary modifications to increase intake of iron (for example, organ meats, egg yolk, prunes, grapes, raisins, nuts, cereals, dark green vegetables). Keep in mind that iron in meat and poultry (heme iron) is more readily absorbed than iron contained in egg yolks and plants (non-heme iron).¹⁶ Recommend frequent periods of rest to reduce fatigue
- Recommend avoidance of alcohol
- Reassess use of ASA and NSAIDs or ensure proper gastric protection (for example, proton pump inhibitor use)
- Counsel client about prevention of constipation due to iron (for example, encourage a high-fibre diet)

Pharmacologic Interventions

Oral iron therapy:

The usual target dose for patients with iron deficiency anemia is 105 to 200 mg of elemental iron daily in two or three divided doses.¹⁷

Preparations containing iron salts differ in their elemental iron content:

- Ferrous gluconate (35 mg elemental iron/300 mg tablet)
- Ferrous sulfate (60 mg elemental iron/300 mg tablet)
- Ferrous fumarate (100 mg elemental iron/300 mg capsule)

Polysaccharide-iron complex is a non-ionic preparation that contains 150 mg elemental iron/capsule.

There is no evidence that one preparation is better than another. Administration of lower doses of elemental iron is likely to be better tolerated, but may require a longer period to correct the anemia and normalize hemoglobin levels.¹⁶

Use a graduated approach to dosing to minimize GI side effects and improve compliance.¹⁵ Initiate therapy with a single tablet taken after a meal. As tolerance permits increase the dose at weekly intervals until the patient is taking one tablet with each meal. If well tolerated, shift the time of administration to before meals to maximize iron absorption.

Avoid concurrent administration with drugs that reduce iron absorption: antacids, calcium preparations, cholestyramine, histamine H₂ antagonists (for example, ranitidine), levodopa, proton pump inhibitors (for example, omeprazole), quinolone antibiotics (for example, ciprofloxacin), tetracycline antibiotics. Separate administration by 2 or more hours.¹⁶

Vitamin C increases iron absorption. However, avoid concurrent administration with coffee, tea and milk, which impair absorption of iron.¹⁶

Monitoring and Follow-Up¹⁸

Clients receiving pharmacologic therapy for IDA should have:

- Initial follow-up 1 month after initiating therapy
- Re-test hemoglobin (should rise about 20 g/L in 1 month)
- Subsequent follow-up visit after 3–6 months to assess restoration of iron stores. Test reticulocyte count if concerns regarding response to therapy

Referral

Arrange follow-up with a physician to determine cause of iron deficiency anemia or:

- If, during initial treatment phase, there is no response after 1 month of oral therapy
- Whenever symptoms are not controlled by therapy
- If there is evidence of complications

MEGALOBLASTIC ANEMIA¹⁵

Macrocytic, normochromic anemias that arise due to deficiencies in cobalamin (vitamin B₁₂) or folic acid (folate) with the production of abnormally large, oval RBCs with an elevated MCV.

Vitamin B₁₂ deficiency can result in nerve demyelination and degeneration of the spinal cord resulting in neurologic symptoms (even without a diagnosis of anemia).

CAUSES^{19,20}

Vitamin B₁₂ deficiency (pernicious anemia), may result from:

- Longstanding inadequate dietary intake of meat and dairy products (for example, strict vegetarianism)
- Impaired absorption

Risk Factors for Vitamin B₁₂ Deficiency

- Gastrectomy or surgery to the ileum, Crohn's disease, inflammatory bowel disease
- Increased requirements (for example, in pregnancy)
- Long-term use of acid-suppressive drugs (for example, proton pump inhibitors)
- Hashimoto's thyroiditis
- Vitiligo
- Raw fish intake (fish tapeworm)

Folic acid deficiency may result from:

- Inadequate intake of green leafy vegetables, legumes and liver (for example, in elderly, alcoholic and chronically ill clients)
- Alcoholism
- Impaired absorption (for example, after gastrectomy or surgery to the ileum, Crohn's disease, pancreatic insufficiency, inflammatory bowel disease)
- Renal dialysis
- Increased demand (for example, in pregnancy, terminal illness, chronic inflammatory disorders)
- Use of drugs that are folate antagonists such as methotrexate, phenytoin (Dilantin), sulfa-related drugs sulfamethoxazole/trimethoprim (Septra)
- HIV disease (and associated drug therapy)
- Other chemotherapy agents

HISTORY^{19,21}

- Insidious onset
- Frequently occurs in the fifth to sixth decades of life
- Fatigue, lethargy
- Shortness of breath
- Indigestion, anorexia, constipation or diarrhea
- Glossitis

Due to the nerve demyelination, clients with severe vitamin B₁₂ deficiency also experience the following signs and symptoms which may not be reversible:

- Neurologic symptoms: numbness and tingling of extremities, paresthesia and other symptoms of peripheral neuropathy, muscle atrophy, decreased vibration sense, positive Romberg's, scissor-type gait, exaggerated or absent deep tendon reflexes
- Neuropsychiatric symptoms: dementia, depression, memory loss

PHYSICAL FINDINGS

- Review general appearance, paying particular attention to apparent fatigue and lethargy
- Vital signs: resting pulse (increased), respiration rate (increased), oxygen saturation, temperature, blood pressure (orthostatic hypotension) and weight (recent loss)
- Integumentary: inspect and palpate skin, note moisture and temperature; test capillary refill; inspect nails; inspect hair (*see "Assessment of the Integumentary System" in the chapter "Skin"*)
- Head and Neck: observe oral cavity, looking for red, smooth, shiny (atrophic glossitis) tongue
- Respiratory: auscultate lungs (clear unless pleural effusion present) (*see "Assessment of the Respiratory System" in the chapter "Respiratory System"*)
- Cardiovascular: auscultate the heart (*see "Assessment of the Cardiovascular System" in the chapter "Cardiovascular System"*)
- Gastrointestinal: auscultate bowel sounds; assess the abdomen for tenderness, hepatomegaly or splenomegaly; perform digital rectal exam (assess for hemorrhoids and melena/blood in stools) (*see "Assessment of the Gastrointestinal System" in the chapter "Gastrointestinal System"*)
- Musculoskeletal: assess muscle mass for atrophy (*see "Assessment of the Musculoskeletal System" in the chapter "Musculoskeletal System"*)
- Neurologic: assess muscle strength, gait (scissor type), deep tendon reflexes (exaggerated or absent), Romberg's test (positive), vibration sense (decreased) and sensation; perform mental status examination (particularly for elderly clients) (*see "Assessment of the Central Nervous System" in the chapter "Central Nervous System"*)

DIFFERENTIAL DIAGNOSIS

Other types of anemia (*see "Anemia"*).

COMPLICATIONS

- Falls or other trauma (related to neurologic symptoms of Vitamin B₁₂ deficiency anemia)
- Heart failure

DIAGNOSTIC TESTS

- Complete blood count
- Reticulocyte count
- Serum iron level
- Total iron-binding capacity (TIBC)
- Serum ferritin level
- Peripheral blood smear
- Vitamin B₁₂ level
- Serum level of RBC folate (is more reliable, but is a very expensive test; often serum folate is done instead; this should be discussed with a physician or nurse practitioner)

Diagnostic Test Findings

- MCV = low
- Hemoglobin = low
- Hematocrit = low
- Serum ferritin = high
- Total iron binding capacity (TIBC) = normal
- Serum iron = high
- Serum Vitamin B₁₂ = low (vitamin B₁₂ deficiency anemia) OR = normal (folate deficiency anemia)
- Serum RBC folate (or serum folate) = low (folate deficiency anemia) OR = normal (vitamin B₁₂ deficiency anemia)

MANAGEMENT**Goals of Treatment**

- Alleviate signs and symptoms of anemia
- Restore normal or adequate hemoglobin level
- Identify and address underlying cause of anemia
- Replace identified deficiencies

Appropriate Consultation

Consult a physician immediately if the symptoms of anemia are significant or if complications or neurologic and/or neuropsychotic symptoms are present.

Nonpharmacologic Interventions**Client Education**

- Explain nature, course and prognosis of anemia; this is a symptom related to lifestyle and/or a chronic condition that can be cured or managed
- Counsel client about appropriate use of vitamins and/or medications (dose, frequency, side effects, importance of compliance and avoidance of abrupt discontinuation if applicable)¹⁵
- Provide dietary counselling on foods rich in folic acid: green, leafy vegetables, grains, wheat bran, liver
- Stress abstinence from alcohol if this a factor in disease process
- Stress importance of returning for follow-up

Pharmacologic Interventions

For vitamin B₁₂ deficiency (pernicious) anemia:

vitamin B₁₂, 800–1,000 µg IM/SC daily for 1–2 weeks (to saturate vitamin B₁₂ stores),
then 100–1,000 µg IM/SC weekly (until hemoglobin and hematocrit are normal),

then 100–1,000 µg IM/SC monthly for life

or

vitamin B₁₂ 1,000–2,000 µg PO daily for life

For folic acid deficiency anemia:

folic acid, 1 mg PO daily until hematologic recovery occurs²²

In patients with malabsorption, a dosage of folic acid 1 mg to 5 mg daily for 1–4 months is recommended (1 mg/day is usually sufficient).²²

If pregnant woman, then folic acid 1 mg PO daily for 2–3 weeks then 0.4 mg PO daily.

If drug-induced folate deficiency anemia, then folic acid 0.5 mg PO daily.

Ongoing supplements may be needed depending on underlying cause of deficiency.

Monitoring and Follow-Up

- Follow up 2 weeks after treatment is started to determine response to therapy including increased sense of well-being, increased appetite and diminution of neurologic signs and symptoms (for vitamin B₁₂ deficiency anemia)

- Recheck hemoglobin and hematocrit, as with both types of deficiency anemias there is usually a rapid response: within 1 week, hematocrit levels begin to rise
- Continue to follow up monthly and repeat blood work until stabilized

For clients with megaloblastic anemia:²³

Serum potassium level should be monitored closely in clients receiving treatment for megaloblastic anemia and supplementary potassium administered as needed. Older patients taking diuretics for heart failure are at particular risk of hypokalemia. Consult a physician.

As hemoglobin rises in response to vitamin B₁₂ administration, the MCV gradually decreases and the client may become microcytic, with the hemoglobin plateauing at a level below normal. If this occurs, oral iron therapy should be added to achieve maximum hemoglobin response.

Referral

Arrange follow-up with a physician as required:

- During initial treatment phase if there is no response after 1 month of therapy
- Whenever symptoms are not controlled by therapy
- If there is evidence of complications

SPECIFIC ANEMIAS AND ADDITIONAL DIAGNOSTIC TESTS

ANEMIA OF CHRONIC DISEASE

Anemia of chronic disease (ACD) begins as a normocytic, normochromic anemia but can evolve to microcytic, hypochromic anemia. ACD is the result of decreased RBC lifespan, ineffective bone marrow response to erythropoietin due to decreased RBC lifespan and impaired ability to use stored iron (altered iron metabolism).^{24,25}

Chronic diseases often involved include chronic inflammatory conditions (for example, rheumatoid arthritis), infections, neoplasms, systemic diseases (for example, systemic lupus erythematosus) and clients with decreased renal, hepatic or endocrine function.^{25,26}

ACD is often mild and asymptomatic with nonspecific symptoms.

DIAGNOSTIC TESTS^{27,28}

- Complete blood count
- Serum iron level
- Total iron-binding capacity (TIBC)
- Serum ferritin level
- Consider measuring blood urea nitrogen (BUN), antinuclear antibody (ANA) and thyroid-stimulating hormone (TSH), liver function tests and performing serum protein electrophoresis (SPE) related to underlying chronic condition

Diagnostic Test Findings

- MCV = normal or low (mimicking iron deficiency anemia)
- Hemoglobin = low
- Hematocrit = low
- Serum ferritin = high or normal
- Total iron binding capacity (TIBC) = low or normal
- Serum iron = low

LEAD POISONING–RELATED ANEMIA

Lead poisoning results in a microcytic, hypochromic anemia related² to microcytosis because lead interferes with the production of heme, which results in poorly hemoglobinized cells and has the significant manifestation of hemolysis.²⁹

Ask about possible sources of lead exposure³⁰:

- Lead gunshot
- Leaded paints
- Batteries (leaching into ground at dumpsite)

DIAGNOSTIC TESTS

- Serum lead level
- Peripheral blood smear (stippling on basophils are seen)

HEMOLYTIC ANEMIA³¹

Premature, accelerated destruction of RBCs, either episodically or continuously. There are hereditary forms where structural defects and enzyme deficiencies are present and acquired forms that are related to immune-mediated hemolysis (transfusion reaction), infections, drug/toxic sources and physical causes (for example, burns). Reticulocytes are usually increased, indicating bleeding or RBC destruction.³²

DIAGNOSTIC TESTS

- Direct antiglobulin test (Coombs' test)
- Measure cold agglutinins and G6PD (glucose-6-phosphate dehydrogenase) to check for extravascular hemolysis

COMMON ENDOCRINE AND METABOLIC PROBLEMS

DIABETES MELLITUS³³

Diabetes mellitus is a metabolic disorder characterized by hyperglycemia, which is due to defective insulin secretion, defective insulin action or both.

- In 2005–2006, approximately 1.9 million Canadian men and women had been diagnosed with diabetes³⁴
- About 10% of people with diabetes have type 1 diabetes; the remaining 90% have type 2 diabetes³⁵
- The incidence and prevalence of diabetes is 4 times higher in First Nations women and 2.5 times higher in First Nations men than non-First Nations people of the same sex
- The highest incidence is in First Nations people aged 40–49 years old, whereas it is 70 years and older in non-First Nations people
- From 1980 to 2005 the prevalence of diabetes went from 9.5% to 20.3% in First Nations women and from 4.9% to 16% in First Nations men. These are among the highest rates in the world
- In 2005 over 40% of First Nations individuals aged 60 and older had diabetes whereas less than 25% of non-First Nations individuals aged 80 and older had it³⁶

For more information on diabetes see also the 2008 *Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada* (available at: <http://www.diabetes.ca/files/cpg2008/cpg-2008.pdf>).

CLASSIFICATION

Type 1³⁷

Type 1 diabetes mellitus is caused by autoimmune or idiopathic destruction of pancreatic β -cells, which leads to absolute insulin deficiency and tendency to ketoacidosis. Onset is usually at younger age (< 30 years). Type 1 diabetes is rare among Aboriginal people.

Type 2

Type 2 diabetes mellitus results from defective insulin secretion and/or an insulin resistance. Age at onset is more commonly middle age or older people, but it has been diagnosed in Aboriginal children younger than age 10. People with type 2 diabetes are much less prone to ketoacidosis.

Gestational Diabetes

Gestational diabetes mellitus (GDM) is hyperglycemia with onset or first recognition during pregnancy. The prevalence of gestational diabetes in non-Aboriginal women is 3.7% compared to its prevalence in Aboriginal women of 11.5%.³⁸ Women with gestational diabetes often go on to have type 2 diabetes later in life. Offspring of mothers with GDM are at increased risk of obesity and type 2 diabetes mellitus. Diagnosis and management of gestational diabetes is described in the Obstetrics section of the guidelines (*see "Gestational Diabetes" in the chapter "Obstetrics"*). Gestational diabetes mellitus should be differentiated from a woman with pre-existing type 2 diabetes mellitus who is pregnant, as the management issues are very different.

Prediabetes³⁹

Prediabetes refers to impaired fasting glucose (IFG) and impaired glucose tolerance (IGT), both of which predispose individuals to diabetes and its complications. IFG is diagnosed based on an elevated fasting blood glucose levels. IGT is diagnosed based on an elevated 2-hour-post 75 gram oral glucose tolerance test (GTT). *See Table 3, "Diagnostic Plasma Glucose Levels for Diabetes and Prediabetes"* for specific diagnostic criteria.

Prevention of diabetes through interventions involving lifestyle changes (for example, nutrition and exercise) as well as annual screening for diabetes should be a priority for these people.

CAUSES^{40,41}

- Genetic predisposition
- Infectious diseases (for example, cytomegalovirus, mumps, rubella, Epstein-Barr viruses)
- Autoimmune (for type 1 only)
- Drug or chemical-induced
- After pancreatitis

Risk Factors for Type 2 Diabetes³⁸

- Age ≥ 40 years
- Family history (1st degree relative with type 2 diabetes)
- Member of high-risk population (for example, Aboriginal)
- History of IFG or IGT*
- Metabolic syndrome
- History of gestational diabetes
- History of delivery of a macrosomic infant (large babies [> 4.5 kg at delivery])
- Hypertension*
- Dyslipidemia*
- Abdominal obesity*
- Overweight*
- Vascular disease (coronary, cerebrovascular or peripheral)*
- Presence of complications of diabetes
- Polycystic ovarian syndrome*
- Schizophrenia[†]
- Acanthosis nigricans (darkened patches on the skin)*

* Associated with insulin resistance

[†] The incidence of type 2 diabetes is at least 3 times higher in people with schizophrenia

HISTORY^{42,43}**Type 1 Diabetes**

- Acute onset of:
 - Polyuria, polydipsia, polyphagia
 - Weight loss
 - Blurred vision
- Frequent or recurring infections (for example, vaginal [yeast] infections, urinary tract infections, skin infections of feet)
- Ketoacidosis

Type 2 Diabetes

Gradual onset and slow progression of symptoms. Often people are asymptomatic for several years and present with complications of diabetes when they are diagnosed.

- Polyuria, polydipsia, polyphagia
- Nocturia
- Weight loss
- Fatigue, irritability, lack of energy
- Blurred vision, changes in vision, frequent changes in optical prescription
- Nausea and vomiting
- Cuts, wounds or bruises that are slow to heal
- Frequent or recurring infections (for example, vaginal [yeast] infections, urinary tract infections, skin infections of feet)
- Paresthesia of hands/fingers or feet/toes
- Erectile dysfunction

Family History

- Diabetes mellitus and other endocrine problems
- Dyslipidemia
- Hypertension
- Vascular disease (coronary, cerebrovascular or peripheral)
- Renal disease
- Infertility
- Hirsutism
- Autoimmune diseases
- Pancreatitis
- Blindness

Past History and Current Health⁴⁴

For all patients, review/discuss the following:

- Risk factors for diabetes (see above)
- Eating habits (food choices, meal patterns, cultural influences concerning food)
- Physical activity level (frequency and intensity of activity), factors limiting physical activity
- Medications
- Allergies
- Smoking habits
- Alcohol use (quantity, frequency)
- Contraceptive, reproductive and sexual history
- Weight history
- Social factors (family dynamics, education, employment, lifestyle, coping skills, economic factors)

When considering a diagnosis of diabetes, include the following in your history:

- Symptoms (as above) and complications associated with diabetes
- For adult females: gestational history (including weight of baby and delivery details)

For patients already diagnosed with diabetes, include the following in your history:

- Frequency, severity and cause of episodes of hypoglycemia or episodes of ketoacidosis
- Symptoms and management of complications: eye, kidney, genitourinary (including sexual), bladder, gastrointestinal, heart, cerebrovascular, peripheral vascular and foot
- Previous and current diabetes management (for example, medications)
- Patterns and results of glycemic control (for example, home blood glucose monitoring, laboratory tests, eye exams)

PHYSICAL FINDINGS¹³

A complete review and examination of all body systems must be done at diagnosis of diabetes then at least annually to detect the presence of complications secondary to the diabetes. Follow-up visits may not include a thorough respiratory, thyroid or musculoskeletal assessment.

- General appearance
- Measure height, weight, waist circumference, calculate body mass index (BMI)
- Vital signs: pulse, respiration rate, BP (including orthostatic BP to detect autonomic neuropathy)
- Integumentary: inspect skin for infection (for example, feet or nails), colour, temperature, bruising, wounds, hyperpigmented patches of acanthosis nigricans, sites of insulin injection (if applicable) (*see “Assessment of the Integumentary System” in the chapter “Skin”*)
- Head and Neck: (*see “Assessment of the Ears, Nose and Throat” in the chapter “Ears, Nose and Throat”*)
 - Eyes: assess for fundoscopic signs of retinopathy (*see “Assessment of the Eyes” in the chapter “Eyes”*)
 - Oral cavity: perform a thorough oral health exam (poor dental health puts the client at risk for infection)
 - Neck: perform a thyroid assessment

- Respiratory: perform a routine respiratory exam (*see “Assessment of the Respiratory System” in the chapter “Respiratory System”*)
- Cardiovascular: perform a complete cardiac exam (including signs of heart failure, bruits), palpate and auscultate peripheral pulses (*see “Assessment of the Cardiovascular System” in the chapter “Cardiovascular System”*)
- Gastrointestinal: perform abdominal exam; check for enlargement of organs (for example, liver) (*see “Assessment of the Gastrointestinal System” in the chapter “Gastrointestinal System”*)
- Musculoskeletal: assess for signs of limited joint mobility, arthropathy of hands, edema of limbs (*see “Assessment of the Musculoskeletal System” in the chapter “Musculoskeletal System”*)
- Neurologic: perform complete neurologic exam; assess feet for changes in vibrational sense, proprioception, response to light touch (with 10 g monofilament), reflexes (*see “Assessment of the Central Nervous System” in the chapter “Central Nervous System”*)

DIFFERENTIAL DIAGNOSIS⁴⁵

- Impaired fasting glucose (IFG)
- Impaired glucose tolerance (IGT)
- Nondiabetic glycosuria (benign renal glycosuria or renal tubular disease)
- Drug side effects (for example, antipsychotics, oral contraceptives (especially progestin-only pills in breastfeeding women with a history of gestational diabetes⁴⁶), corticosteroids, thiazide diuretics)
- Diabetes insipidus (polyuria, polydipsia and nocturia but not hyperglycemia)
- Pheochromocytoma (tumour in adrenal medula)
- Cushing’s syndrome
- Transient hyperglycemia secondary to severe stress, burns or infections

COMPLICATIONS^{14,47}

- Diabetic ketoacidosis (DKA) (common in type 1 diabetes) (*see “Diabetic Ketoacidosis” in the section “Metabolic Emergencies”*)
- Hyperosmolar hyperglycemic state (HHS) (*see “Hyperosmolar Hyperglycemic State” in the section “Metabolic Emergencies,”*)
- Macrovascular complications:
 - Coronary artery disease
 - Stroke
 - Peripheral vascular disease

- Microvascular complications:
 - Nephropathy, end-stage renal disease
 - Retinopathy, cataracts (early onset), blindness
- Peripheral neuropathy
- Recurrent infections (for example, urinary, vaginal [yeast], skin)
- Premature death from complications

DIAGNOSTIC TESTS⁴⁸

One of:

- Fasting plasma glucose (FPG)
- Random plasma glucose
- Plasma glucose level 2 hours after oral GTT (with 75 g load)

Table 3 – Diagnostic Plasma Glucose Levels for Diabetes and Prediabetes

	Fasting plasma glucose	2-hour plasma glucose after oral GTT (with 75 g load)	Random plasma glucose
IFG	6.1–6.9	not applicable	not applicable
IFG (isolated)	6.1–6.9 and	< 7.8	not applicable
IGT (isolated)	< 6.1 and	7.8–11	not applicable
IFG and IGT	6.1–6.9 and	7.8–11	not applicable
Diabetes	≥ 7 or	≥ 11.1 or	≥ 11.1 mmol/L in the presence of symptoms of diabetes (for example, polydipsia, polyuria)

NOTE: A confirmatory glucose test (any of the above) must be done on another day in all cases prior to making a diagnosis. The only exception is that a diagnosis of diabetes can be made when a client presents with hyperglycemia at the levels described above and also has diabetic ketoacidosis.

Other Tests at Diagnosis^{16,49}

- Hemoglobin A1C (Hb_{A1C})
- Fasting lipid levels (total cholesterol [TC], high-density lipoprotein cholesterol [HDL-C], triglycerides [TG] and calculated low-density lipoprotein cholesterol [LDL-C])
- Serum creatinine for estimating glomerular filtration rate (eGFR)
- Thyroid stimulating hormone (TSH)
- Obtain random urine sample for:
 - Albumin to creatinine ratio (microalbumin)
 - Dipstick test for glucose, ketones, protein, blood
 - Microscopy if dipstick abnormal for blood
 - Electrocardiogram (ECG) (for a baseline measurement)

See “*Monitoring and Follow-Up*” for diagnostic tests after initial diagnosis.

MANAGEMENT

The management and prevention of diabetes mellitus and associated complications should be a high priority in health planning and healthcare delivery in Aboriginal communities. Many studies have noted that culturally appropriate care for diabetes is essential and requires a focus on the geographical, linguistic, educational and social differences among Aboriginal

peoples.⁵⁰ There is no evidence at present that therapeutic strategies should differ from those used in the general population.

Goals of Treatment

- Attain optimum glycemic control for type 1 or type 2. Target FPG 4–7 mmol/L; 2-hour postprandial 5–10 mmol/L; Hb_{A1C} ≤ 7%⁵¹
- Educate the client for self-care
- Prevent complications
- Attain optimum control of concomitant hypertension, dyslipidemia and other cardiovascular risk factors
- Stop smoking

Appropriate Consultation

Consult a physician immediately for further management if diabetes mellitus is suspected or diagnosed. All pharmacologic therapy for clients with diabetes is initiated by a physician.

Nonpharmacologic Interventions

The content of self-management education sessions must be individualized according to the client’s type of diabetes, current state of metabolic stability, treatment plan, readiness for change, learning style, abilities, motivation and the resources available.

Psychological stress:

- Discuss fears, concerns about the diagnosis of diabetes
- Assess support, other stressors in the patient's life
- Assess readiness for change
- Review importance of learning about diabetes and understanding diabetes so they can help themselves

Diet and nutrition:⁵²

Nutrition therapy can reduce HbA1C by 1% to 2% and, when used with other nonpharmacologic interventions, can further improve clinical and metabolic outcomes.

- Consultation with a dietitian is recommended initially (if available)
- Nutrition education is equally effective in a small group or one-to-one
- Clients with type 1 diabetes should be taught to match insulin doses to carbohydrate intake
- Clients with type 2 diabetes should be encouraged to be consistent in timing and spacing of meals
- After initial diagnosis of diabetes, clients should be encouraged to keep a dietary intake journal which can be reviewed during health care visits. A 3-day dietary intake recall can be used for assessment purposes
- Refer to *Appendix A* for a summary of specific nutritional considerations

Physical activity:⁵³

Physical activity can help achieve improved cardiorespiratory fitness, improved glycemic control, decreased insulin resistance, improved lipid profile and maintenance of weight loss.

- All clients with diabetes should be encouraged to do aerobic exercise and resistance exercise
- Refer to *Appendix B* for definitions, frequencies, intensities and examples of aerobic and resistance exercises recommended

Weight reduction:⁵⁴

A modest weight loss of 5% to 10% of initial body weight can substantially improve insulin sensitivity, glycemic control, BP and lipid control.

Home blood glucose monitoring (HBGM):⁵⁵

The goal of HBGM is to facilitate learning about diabetes. Close follow-up to review results of HBGM is required to help patients understand and learn from their HBGM.

- Provide hands-on training of HBGM with client's own HBGM device
- HBGM should include both pre- and postprandial measurements and results should be recorded in a diary or downloaded using appropriate software
- Clients should perform HBGM when having symptoms of hypoglycemia
- For clients with type 2 diabetes on once-daily insulin, with or without oral antidiabetes medications, HBGM should be individualized, suggesting at least once a day at variable times, with a maximum average weekly frequency of 14 tests for most clients. For clients using multiple daily dosing insulin, HBGM should be individualized⁵⁶
- For most patients treated with type 2 diabetes on oral antihyperglycemic medications or lifestyle changes alone, self-monitoring of HBGM should be individualized depending on glycemic control and type of therapy. Recent evidence by the Canadian Agency for Drugs and Technologies in Health does not recommend HBGM on a routine basis (> 7 times per week) due to the costs exceeding the benefits²⁴
- For women with gestational diabetes not using antidiabetes drugs, the optimal daily frequency of HMBG should be individualized²⁴
- Quality control tests should be done annually by comparing laboratory and HBGM device results when done within 15 min of each other, to ensure accuracy of the HBGM device
- Clients with type 1 diabetes should be instructed to perform urine ketone testing during acute illness when HBGM is > 14 mmol/L or if symptoms of diabetic ketoacidosis are apparent (*see "History" in the section "Metabolic Emergencies," "Diabetic Ketoacidosis"*)

Foot care:⁵⁷

Basic foot care education should include:

- Awareness of the client's personal risk factors
- Importance of at least an annual inspection and assessment of the feet by a health care professional
- Daily self inspection of feet
- Proper nail and skin care

- Injury prevention
- Knowing when to seek help or specialized referral

Refer to *Appendix C* for DOs and DON'Ts for foot care.²⁵

Other client education:⁵⁸

- Explain the nature, course and prognosis of diabetes and long-term complications; emphasize that complications can be prevented or delayed when glucose is well controlled²¹
- Explain the signs and symptoms of hyperglycemia and hypoglycemia and what steps should be taken if these conditions occur
- Review and discuss the goals of treatment (as outlined above) and the client's beliefs, motivations, attitudes, knowledge, psychomotor skills and coping skills
- Review and discuss healthy self-management behaviours (including diet, HBGM, medications, physical activity and smoking cessation)
- Provide hands-on training of insulin self-administration
- Explain how to manage diabetes when the client is ill
- Review nonpharmacologic and pharmacologic interventions (*see "Pharmacologic Interventions"*)
- Review laboratory monitoring and screening strategies (*see "Monitoring and Follow-Up" and "Screening Strategies"*)
- Set short-term goals (including glycemic control, BP and lipid control, weight reduction, quality of life and attendance at health care appointments)
- Set long-term goals (for example, preventing complications, weight maintenance and prevention of weight regain)⁵⁹
- Encourage smoking cessation (if applicable)
- With women of childbearing age, discuss contraception and emphasize the importance of glycemic control before conception and during pregnancy⁶⁰
- If possible, involve the entire family in the client's self-management education to enlist their support for the client

Pharmacologic Interventions

Type 1 diabetes:⁶¹

Insulin therapy as prescribed by a physician.

Include further client self-management education regarding:

- Different types of insulin and the onset, peak and duration of action

- Timing of injections
- Location of injections and rotation of injection sites
- Risk, prevention and treatment of insulin-induced hypoglycemia
- Acute effects of exercise, which lowers plasma glucose levels
- How to match insulin to carbohydrate intake or encourage to maintain a consistent carbohydrate intake
- Storage of insulin

Type 2 diabetes:⁶²

If glycemic targets are not achieved within 2–3 months with lifestyle changes, then antihyperglycemic pharmacotherapy should be initiated. Pharmacotherapy should be initiated without waiting to see the benefit of lifestyle changes in patients with an HbA_{1C} \geq 9%.⁶³ Adjustments and additions of medications should be made to attain the target HbA_{1C} (7%) within 6–12 months.

Physician-initiated drug therapy:

Step 1: Initial therapy:

Metformin is the preferred first-line therapy for clients with type 2 diabetes mellitus and an HbA_{1C} < 9%.⁶³ It improves HbA_{1C} levels but does not induce weight gain, is very rarely associated with hypoglycemia and reduces the incidence of diabetic complications and all-cause mortality.

For patients presenting with an HbA_{1C} \geq 9% consider initiating therapy with either a combination of metformin plus an agent from another drug class, or initiate insulin therapy.⁶³

Step 2: Combinations of antihyperglycemic agents:

If glycemic targets are not met, then combine metformin with other classes of antihyperglycemic agents including insulin. Selection of additional agents should be individualized taking into consideration the degree of hyperglycemia and the properties of the antihyperglycemic agents, including: effectiveness in lowering blood glucose, durability of glycemic control, side effects, contraindications, risk of hypoglycemia, presence of diabetes complications and comorbidities and patient preferences. A comparative overview of medications for type 2 diabetes is shown in Table 4.⁶⁴ The product monographs should be consulted for complete and up-to-date information on dosing and side effects.

Table 4 – Type 2 Diabetes Medications

Drug class/Drug	Specific agent(s)	Risk of hypoglycemia	Comments
Alpha-glucosidase inhibitor	acarbose (Glucobay)	Negligible risk as monotherapy	<ul style="list-style-type: none"> • Weight-neutral • Must be taken with the first bite of a meal • GI intolerance is common
Dipeptidyl-peptidase IV inhibitor	sitagliptin (Januvia)	Negligible risk as monotherapy	<ul style="list-style-type: none"> • Weight-neutral • Improves postprandial blood glucose control
Insulin			
Sulfonylureas	gliclazide (Diamicon), glimepiride (Amaryl), glyburide (DiaBeta)	May be significant. Greatest risk with glyburide, less with glimepiride and lowest with gliclazide	<ul style="list-style-type: none"> • Promote weight gain • The short-acting meglitinides are used for postprandial blood glucose control
Meglitinides	nateglinide (Starlix), repaglinide (GlucosNorm)	Minimal to moderate risk	
Biguanide	metformin (Glucophage, Glumetza)	Negligible as monotherapy	<ul style="list-style-type: none"> • Weight-neutral • Improves cardiovascular outcomes in overweight patients • Diarrhea is a prominent side effect
Thiazolidinediones	pioglitazone (Actos), rosiglitazone (Avandia)	Negligible as monotherapy	<ul style="list-style-type: none"> • Promote weight gain • May induce edema and heart failure (avoid in patients with heart failure) • Increased incidence of macular edema and fractures in women
Insulin			
Rapid-acting analogues	Aspart (NovoRapid), glulisine (Apidra), lispro (Humalog)		
Short-acting	Regular (Humulin-R, Novolin ge Toronto)		
Intermediate-acting	NPH (Humulin-N, Novolin ge NPH)		
Long-acting basal analogues	Detemir (Levemir), glargine (Lantus)	Significant	<ul style="list-style-type: none"> • Promote weight gain • Greatest potential effect on HbA1C
Premixed	Regular-NPH (Humulin 30/70, Novolin ge 30/70, 40/60, 50/50); Biphasic insulin aspart (Novomix 30); Insulin lispro/lispro protamine (Humalog Mix25, Mix50)		

Vascular protection in clients with diabetes:⁶⁵

Low-dose (81–325 mg/day) acetylsalicylic acid (ASA) therapy may be considered as a primary preventive therapy in clients with diabetes mellitus and as a secondary preventive therapy in people with diabetes mellitus and cardiovascular disease. The decision to prescribe ASA for primary prevention

should be based on clinical judgment given the lack of evidence for benefit and the side effects associated with long term use (for example, ASA therapy confers less benefit in patients with diabetes than in those without diabetes).

Coronary Artery Disease Risk Assessment⁶⁶**The following clients with diabetes are considered at high risk for a cardiovascular event:**

- Men aged ≥ 45 years, women aged ≥ 50 years
- Men < 45 years and women < 50 years with 1 of the following:
 - Microvascular disease (especially nephropathy or retinopathy)
 - Multiple additional risk factors, especially with a family history of premature coronary or cerebrovascular disease in a first-degree relative
 - Extreme level of a single risk factor (for example, LDL-C > 5 mmol/L, systolic BP > 180 mm Hg)
 - Duration of diabetes > 15 years with age > 30 years

Adapted with permission from Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Canadian Diabetes Association 2008 clinical practice guidelines for the prevention and management of diabetes in Canada. *Can J Diabetes* 2008;32(suppl 1):S102.

In diabetic individuals with a high cardiovascular risk, treatment with an angiotensin-converting enzyme inhibitor or angiotensin II receptor antagonist is associated with better outcomes. Lipid lowering medications (mainly statins) should also be considered.

Prevention and treatment of comorbidities:⁶⁷

Clients with diabetes have a 2- to 4-fold greater risk of cardiovascular disease as the primary cause of death than those clients without diabetes. Thus, any risk factors for coronary artery disease such as hypertension and dyslipidemia should be aggressively treated.

Monitoring and Follow-Up⁶⁸

Note that follow-up testing may be required more frequently than the guidelines stated below, depending on the client, their medications, their diagnostic test results and their other medical conditions. Consult with a physician for guidance about a specific client.

Refer to *Appendix D – Sample Flow Sheet for Adults with Diabetes*.

Initial follow-up after diagnosis:

- There are many self-management education topics to be covered following diagnosis (diet, physical activity, HBGM, foot care, medications). Therefore, follow-up should focus on enabling the client to be able to self-manage their diabetes and may occur every 4–6 weeks initially or more often as needed. Be careful not to overload the client with too much information

- All clients (and their families) should be screened for symptoms of psychological distress
- All clients should be considered for a pneumococcal immunization and annual influenza vaccine

Every 3 months:

- Measure BP, weight (calculate BMI), waist circumference
- Measure Hb_{A1C}
- Review compliance with drug therapy
- Review HBGM diary
- Review compliance with nonpharmacologic interventions (for example, diet and nutrition, physical activity, weight reduction) (may be done every 6 months or every year when patient is stable)
- Discuss incidents of hypoglycemia and hyperglycemia
- Review smoking status and encourage smoking cessation
- Perform foot examination

Every 6 months:

- If chronic kidney disease present (eGFR < 60 mL/min) at diagnosis in person with type 2 diabetes, perform random urine for albumin:creatinine ratio (ACR) and serum creatinine for estimated glomerular filtration rate (eGFR)

Every 1 year:

- Perform quality control of HBGM device; compare venous fasting blood glucose with HBGM device reading (should both be done < 15 minutes apart)
- Measure fasting lipid levels (TC, HDL-C, TG and LDL-C)
- If the type 2 diabetic does not have chronic kidney disease, perform random urine for albumin:creatinine ratio (ACR) and serum creatinine for estimated glomerular filtration rate (eGFR); see the section “*Coronary Artery Disease Risk Assessment*”
- Provide influenza vaccine annually
- Perform screening for peripheral neuropathy using 10 g monofilament testing

- Screen men for erectile dysfunction with a sexual function history (*see 2008 Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada*, page S147, available at: <http://www.diabetes.ca/files/cpg2008/cpg-2008.pdf>)
- Schedule client to see a physician and an optometrist or ophthalmologist for screening and evaluation for diabetic retinopathy

Every 2 years:

- Perform an electrocardiogram (ECG)

As needed:

- Measure fasting blood glucose
- Perform urine dipstick

Referral

- Refer all newly diagnosed clients to a physician as soon as possible for complete evaluation
- Refer client to a dietitian for initial assessment and dietary counselling if possible
- Arrange follow-up with a physician or nurse practitioner every 6–12 months if stable or more frequently as necessary

PREVENTION

Primary Prevention, Type 1 Diabetes Mellitus

There are no known proven strategies to prevent type 1 diabetes mellitus.

Primary Prevention, Type 2 Diabetes Mellitus

- The major focus of any diabetes strategy should be primary prevention
- Programs should be targeted to school children and their parents (to prevent diabetes in future generations) and to individuals who are at increased risk
- Primary prevention is aimed at weight control through a program of diet and exercise

Secondary and Tertiary Prevention

Secondary prevention efforts are aimed at screening for the disease and providing strategies for risk reduction. As an example, a 5% reduction from initial body weight can reduce progression from impaired glucose tolerance (IGT) to type 2 diabetes by almost 60%.⁶⁹ Tertiary prevention involves metabolic control, follow-up and management of complications for individuals with diabetes.

SCREENING STRATEGIES

Screening for Diabetes Mellitus⁷⁰

High-risk groups require aggressive screening for diabetes.

The 2008 Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada (Canadian Diabetes Association) recommend the following screening principles (available at: <http://www.diabetes.ca/files/cpg2008/cpg-2008.pdf>).

People ≥ 40 years of age with no other risk factors should be screened using fasting blood glucose tests every 3 years. Screening should be annual and starting from a younger age for anyone with any two of the following risk factors:

- Family history (1st degree relative with type 2 diabetes)
- Member of high-risk population (for example, Aboriginal)
- History of impaired fasting glucose (IFG) or impaired glucose tolerance (IGT)
- Metabolic syndrome
- History of gestational diabetes
- Maternal history of GDM or maternal type 2 DM in pregnancy (screen offspring from age 10 if obese)
- History of delivery of a macrosomic infant
- Hypertension
- Dyslipidemia
- Abdominal obesity (waist circumference [WC] > 102 cm in men and > 88 cm in women)
- Overweight (body mass index [BMI] > 25 kg/m²)
- Vascular disease (coronary, cerebrovascular or peripheral)
- Presence of complications of diabetes
- Polycystic ovarian disease
- Schizophrenia
- Acanthosis nigricans (darkened patches on the skin)

Screening for Complications

People with type 1 and 2 diabetes mellitus require aggressive screening for retinopathy, nephropathy, neuropathy, cardiovascular disease, foot ulcers and erectile dysfunction.

Evidence shows that the risk of microvascular complications such as retinopathy, neuropathy and nephropathy can be reduced in both type 1 and type 2 diabetes.⁷¹ The risk of macrovascular complications can be reduced by improved glucose control, but requires longer follow-up to show a benefit.⁷²

Aggressive control of multiple risk factors (for example, hyperglycemia, hypertension, dyslipidemia and microalbuminuria) through behaviour modification and drug therapy can significantly decrease cardiovascular and microvascular events in clients with type 2 diabetes.⁷³

The 2008 *Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada* (available at: <http://www.diabetes.ca/files/cpg2008/cpg-2008.pdf>) recommends the following screening guidelines:⁷⁴

Retinopathy

There are an estimated 2 million individuals in Canada who have some form of diabetic retinopathy, which is almost the total number of people diagnosed with diabetes.⁷⁵ Diabetic retinopathy remains the leading cause of visual impairment in people < 65 years old.⁷⁶

- Type 1 diabetes:
 - Screening and evaluation for retinopathy by an eye care specialist should be performed annually, starting 5 years after the onset of diabetes for those ≥ 15 years of age with type 1 diabetes
 - Interval for follow-up is based on severity of retinopathy, or annually if no retinopathy
- Type 2 diabetes:
 - Screening and evaluation for retinopathy by an eye care specialist should be performed at the time of diagnosis of type 2 diabetes
 - In clients with type 2 diabetes who have no or minimal retinopathy, the recommended interval for follow-up is every 1–2 years
- Women who are pregnant or are considering becoming pregnant should have more frequent ophthalmologic assessments
- Retinopathy findings necessitate referral to an ophthalmologist
- Development and progression of retinopathy may be prevented by achieving optimal metabolic control

Nephropathy

- Diabetic nephropathy is the primary cause of end-stage renal disease (ESRD) in Canada where 34.4% of people with ESRD have diabetes⁷⁷
- Development and progression of nephropathy may be prevented by achieving optimal control of blood glucose and blood pressure

- Elevated, persistent microalbuminuria is the earliest and most reliable clinical sign of diabetic nephropathy in both type 1 and type 2 diabetes
- Screening for adults with type 1 diabetes should begin 5 years after onset of diabetes, then annually if no chronic kidney disease
- Screening for those with type 2 diabetes should begin at the time of diagnosis and annually thereafter if no chronic kidney disease
- Recommended screening test is a random urine collection for albumin:creatinine ratio (ACR) and serum creatinine for estimated glomerular filtration rate (eGFR)
 - If $eGFR \leq 60$ mL/min or ACR is abnormal, then order serum creatinine for eGFR within 3 months and repeat random urine ACRs with urine analysis twice in 3 months. If abnormal ACR, rule out other causes of false positive ACR (for example, acute illness, urine infection, CHF, menstruation, fever or engaging in strenuous activity). If $eGFR \leq 60$ mL/min or 2 of 3 ACRs abnormal, then nephropathy (chronic kidney disease) is diagnosed. If $eGFR > 60$ mL/min and ACR normal, then rescreen in 1 year
 - If $eGFR > 60$ mL/min and ACR normal, then rescreen in 1 year
- 24-hour urine collection is recommended when the accuracy of the eGFR is questioned; otherwise, it is not useful as it is typically not collected correctly
- Once nephropathy is diagnosed, follow-up monitoring (at least twice yearly) should include a random urine ACR and serum creatinine (converted to eGFR) in order to monitor progression of nephropathy
- All clients with nephropathy are considered to be at high risk for cardiovascular (CV) events and should be treated to reduce this risk including optimization of BP, dyslipidemia
- Treatment with angiotensin converting enzyme (ACE) inhibitors or angiotensin II receptor blockers (ARB) slows the progression of diabetic nephropathy, and should be considered in patients with persistent microalbuminuria (> 2 mg/mmol in men, > 2.8 mg/mmol in women), even in the absence of hypertension.⁷⁸ Women must avoid becoming pregnant when taking one of these agents

Neuropathy

- Detectable neuropathy will develop within 10 years of onset of diabetes in 40% to 50% of patients with either type of diabetes mellitus
- Annual screening for peripheral neuropathy for clients with type 1 diabetes should begin 5 years after onset of diabetes. Screening for those with type 2 diabetes should begin at the time of diagnosis and then annually
- Neuropathy can be detected by assessing decrease in or loss of ability to sense vibration and/or loss of sensitivity to a 10 g monofilament at the base of the great toe

Cardiovascular Disease

- The majority of people with diabetes (65% to 80%) will die from cardiovascular (CV) disease. A large proportion will have no symptoms before a myocardial infarction (either fatal or nonfatal), thus screening for clients at high risk for vascular events (coronary artery disease [CAD]) is essential
- Clients should achieve and maintain healthy eating habits and a desirable weight, should engage in regular physical activity and should stop smoking
- Complete a coronary artery disease risk assessment as above to understand whether the client is at high risk for a CV event (*see “Coronary Artery Disease Risk Assessment”*). See also the 2008 Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada, page S95 (available at: <http://www.diabetes.ca/professionals/resources/2008-cpg/>)
- A baseline, resting electrocardiogram (ECG) should be performed in clients:
 - > 40 years old
 - having diabetes > 15 years
 - with hypertension, proteinuria, reduced pulses or vascular bruits
- A repeat, resting ECG should be performed every 2 years for clients considered high risk for CV events. Clients with abnormal resting ECGs should have further investigations (for example, ECG stress test)
- A fasting lipid profile (TC, HDL-C, TG and LDL-C) should be carried out in diabetic adults at the time of diagnosis and every 1–3 years as clinically indicated
- Pharmacotherapy for dyslipidemia should be instituted by a physician for primary and secondary prevention of CAD

- Most clients with diabetes will develop hypertension (blood pressure > 130/80 mm Hg) which is a treatable CV risk factor. BP should be measured at each health care visit. Lifestyle modifications (including sodium reduction and increased physical activity) should be initiated along with pharmacotherapy (initiated by a physician)
- The United Kingdom Prospective Diabetes Study Group (1998) showed that tight blood pressure control (target blood pressure < 130/80 mm Hg), even more than tight glucose control, can dramatically reduce the risk of death and diabetic complications from cardiovascular events such as myocardial infarction and stroke
- Most clients require 2–3 medications to control their BP. It is important to warn patients in advance that they will likely require several medications for BP control

Foot Ulcers

- Foot problems are a major cause of morbidity and mortality in people with diabetes
- Foot examinations by the clients and health care professional are an integral component of diabetes management to decrease the risk of foot lesions and amputations. Professionals should examine the client's feet annually or more frequently in those at high risk (for example, Aborigines)
- The essentials of management of diabetic foot ulcers include:⁷⁹
 - Assess underlying cause(s): neuropathy and/or ischemia
 - Determine cause of pressure at the origin of the ulcer
 - Ulcers can be gently probed with a blunt-tipped instrument or sterile cotton-tip to detect sinus tracts or palpable bone suggestive of deep infections
 - Plantar-surface ulcers require pressure relief. Clients with plantar-surface foot ulcers should be non-weight-bearing as much as possible and utilize off-loading footwear or appliances
 - Clinically noninfected ulcers do not routinely require cultures or antibiotics
 - More serious infections in chronic foot ulcers tend to be polymicrobial and require empiric use of broad spectrum systemic antibiotics and should be tailored according to culture and sensitivity results. Consult a physician or nurse practitioner

- Wound bed preparation involves debridement of necrotic tissue (neuropathic and noncritical ischemic wounds only). Autolytic debridement should be considered before chemical, mechanical or surgical debridement. Debridement of poorly vascularized extremities should be performed with caution. Maintenance of an adequate moist wound environment with appropriate wound dressings will also be required
- Comorbidities need to be managed (for example, hyperglycemia)
- Refer to a specialized wound clinic, enterostomal nurse or chiropodist where available
- The Registered Nurses Association of Ontario's Best Practice Guideline on *The Assessment and Management of Foot Ulcers for Peoples with Diabetes*⁸⁰ offers an evidence-based nursing approach (available at: <http://www.rnao.org/Page.asp?PageID=924&ContentID=719>). It has very useful appendices, including Appendix:
 - C – Risk Factors for Ulceration
 - D – Risk Factors for Amputation
 - E – Wound Classification
 - F – Patient Handout
 - G – Diagnostic texts to Determine Vascular Supply
 - J – Use of Semmes-Weinstein Monofilament
 - K – Suggestions for Assessing and Selecting Shoes and Socks
 - L – Factors Affecting Wound Healing
 - M – Topical Antimicrobial Agents
 - N – Guide to Dressing Foot Wounds

Erectile Dysfunction

- Erectile dysfunction (ED) affects 34–45% of men with diabetes and has a negative impact on quality of life
- All adult men with diabetes should be regularly screened for ED with a sexual function history beginning at diagnosis
- Treatment with a phosphodiesterase type 5 (PDE5) inhibitor can be considered in men with diabetes and ED. A physician consultation will be needed

HYPERTHYROIDISM

A syndrome related to excessive thyroid hormone production and its effects. Thyrotoxic crisis is a life-threatening syndrome occurring with decompensated hyperthyroidism.

Prevalence of overt hyperthyroidism is < 1.9% but increases to 2.7% when “subclinical” hyperthyroidism is included. The annual incidence of overt hyperthyroidism is estimated to be 2 to 3 per 1000 women.⁸¹

CAUSES

- Graves' disease (most common)
- Toxic multinodular goitre (which develops in response to some bodily need, for example, pregnancy)
- Subacute thyroiditis
- Thyroid cancer
- Postpartum thyroiditis (onset 2–6 months postpartum) is a mild, short-term form
- Iodine-containing drugs (amiodarone⁸¹), lithium and contrast media (dye)⁸²

Risk Factors⁸³

- Surgery affecting the thyroid gland
- Vitiligo
- Pernicious anemia
- Leukotrichia (premature gray hair)
- Autoimmune diseases (for example, type 1 diabetes)
- *For Graves' disease*: positive family history, female 20–40 years of age, other autoimmune disorders
- *For toxic multinodular goitre*: older age; long-standing simple goitre; conditions such as puberty or pregnancy; immunologic, viral or genetic disorders
- *For subacute thyroiditis*: female usually 40–50 years of age

HISTORY

- Usually female between 20 and 40 years of age
- Symptoms (as listed below) variable in severity
- Fatigue, weakness
- Insomnia
- Weight loss with no change in diet or appetite
- Heat intolerance
- Excessive sweating
- Alterations in bowel habits (for example, diarrhea, constipation)
- Menstrual changes (for example, decreased menses)
- Restlessness, nervousness, irritability, anxiety

- Inability to concentrate
- Mood swings (from depression to extreme euphoria)
- Visual changes (for example, diplopia, photophobia, eye irritation, bulging eyes, decreased blinking)
- Difficulty swallowing, hoarse voice
- Palpitations
- Exertional dyspnea, fatigue, chest pain
- Edema (for example, periorbital, pretibial, in feet)
- Loss of hair, change in hair texture (hair becomes fine and silky)

Special considerations in the **elderly** client:

- Classic presentation may be absent
- Usually only three clinical signs: fatigue, weight loss, tachycardia
- Goitre is much less common in this age group
- New onset atrial fibrillation/flutter may be how it presents

Special considerations in the **pregnant** client:

- Thyrotoxicosis may improve during pregnancy but will relapse in the postpartum period

PHYSICAL FINDINGS⁸⁴

A complete review of systems is required as symptoms may be subtle and involve every body system.

- Review general appearance, paying particular attention to signs of nervousness or hyperactivity
- Vital signs: resting pulse (may be increased or irregular), temperature, BP (systolic hypertension) and weight (decreased)
- Integumentary: inspect and palpate skin, noting pigmentation pattern, moistness and turgor (usually warm, moist skin with sweaty palms); inspect hair for texture and thickness (usually thin and silky); inspect nails for ridges, discolouration or splitting (*see “Assessment of the Integumentary System” in the chapter “Skin”*)
- Head and Neck: (*see “Assessment of the Ears, Nose and Throat” in the chapter “Ears, Nose and Throat”*)
 - Eyes: assess for exophthalmos (prominent or protruding eye balls), lid lag and/or extraocular movements; test visual acuity (*see “Assessment of the Eyes” in the chapter “Eyes”*)
 - Neck: palpate for lymphadenopathy, perform thyroid assessment including inspection (noting that diffuse enlargement is found in only 50% of clients), palpation (noting thrills, nodules, firmness and tenderness) and auscultation (noting bruits); measure size

- Respiratory: auscultate lungs (clear unless heart failure present) (*see “Assessment of the Respiratory System” in the chapter “Respiratory System”*)
- Cardiovascular: auscultate the heart, noting murmurs and rate/rhythm; point of maximal impulse (PMI) displaced if enlargement has occurred (*see “Assessment of the Cardiovascular System” in the chapter “Cardiovascular System”*)
- Gastrointestinal: assess the abdomen for hepatomegaly and splenomegaly (*see “Assessment of the Gastrointestinal System” in the chapter “Gastrointestinal System”*)
- Musculoskeletal: test muscular strength, focusing on signs of proximal muscle weakness; examine fingers and toes for thickening; assess lower extremities, noting pretibial myxedema (nonpitting edema) (*see “Assessment of the Musculoskeletal System” in the chapter “Musculoskeletal System”*)
- Neurologic: perform complete neurologic exam, noting fast relaxation of tendon reflexes; evaluate for tremor (place piece of paper in client’s hand and observe movement for tremors) (*see “Assessment of the Central Nervous System” in the chapter “Central Nervous System”*)

THYROTOXIC CRISIS (“THYROID STORM”)

- Stressful event precipitates episode (trauma, infection, withdrawal of thyroid medication⁸⁵)
- Nausea, vomiting and abdominal pain may precede the storm
- Tachycardia and tachyarrhythmias (atrial fibrillation)
- Agitation, confusion, delirium, psychosis or coma with high fever and diaphoresis may occur

DIFFERENTIAL DIAGNOSIS⁸⁶

- Transient thyroiditis
- Thyroid cancer
- Pheochromocytoma (rare tumour in the adrenal gland)
- Menopause
- Anxiety, panic disorder or depression
- Tremors, such as essential, physiological, cerebellar and senile
- Congestive heart failure and atrial fibrillation
- Medication use related TSH and T4 changes (for example, glucocorticoids [prednisone or equivalent > 20 mg/day⁸⁷], amiodarone, lithium)

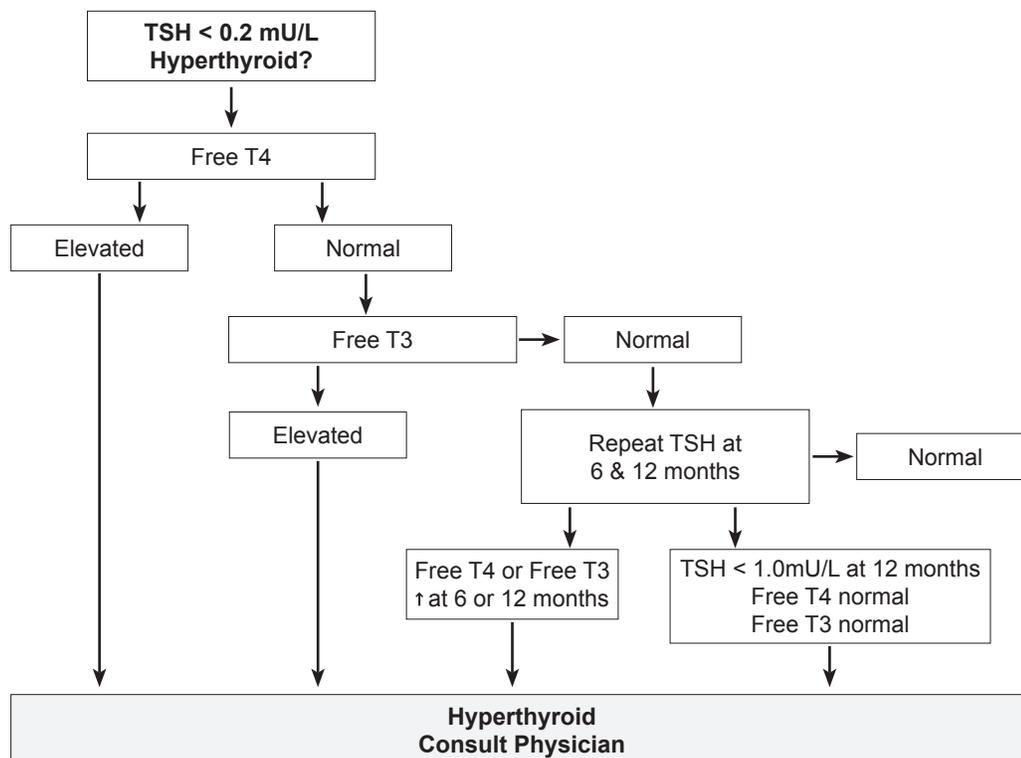
COMPLICATIONS

- Exophthalmos
- Loss of vision
- Corneal abrasions
- Atrial fibrillation
- Angina
- Heart failure

- Hypertension
- Thyrotoxic crisis (“thyroid storm”) (rare)
- Osteoporosis (in elderly women)
- Hypothyroidism (following treatment)

DIAGNOSTIC TESTS

- Measure TSH (will be decreased)
- Measure free T4 and free T3 (per chart below)

Diagnostic Tests for Suspected Hyperthyroidism

Adapted with permission from Toward Optimized Practice Clinical Practice Guideline Working Group. (2008). *Clinical Practice Guideline: Investigation and Management of Primary Thyroid Dysfunction*⁸⁶

Subclinical hyperthyroidism is a low TSH level with normal free T4 and T3 levels.

Depending on client presentation, the physician may consider ordering the following additional tests:⁸⁶

- Calcium
- Alkaline phosphatase, liver function tests (LFTs)
- Complete blood count (CBC)
- Urine pregnancy test (female clients)
- Electrocardiogram (ECG) for elderly clients or those with cardiac arrhythmias

MANAGEMENT**Goals of Treatment**

- Identify complications (for example, cardiac, ophthalmological)
- Relieve symptoms
- Return to euthyroid state
- Prevent complications

Appropriate Consultation

Consult a physician if hyperthyroidism is suspected or diagnosed. All pharmacologic therapy for clients with hyperthyroidism is initiated by a physician.

Nonpharmacologic Interventions

Short term while awaiting response to pharmacologic intervention:

- Dietary modifications: high-calorie diet, frequent nutritious snacks, caffeine restriction
- Frequent rest periods to avoid fatigue
- Protection of the eyes to prevent irritation and abrasions: sunglasses, patches at night, use of artificial tears to prevent drying; sleep with the head of bed elevated⁸⁹

Client Education

- Explain nature, course and prognosis of disease
- Counsel client about appropriate use of medications (dose, frequency, side effects, avoidance of abrupt discontinuation)

Pharmacologic Interventions^{90,91}

Options for definitive treatment include surgery (rarely considered due to complications of hypoparathyroidism and vocal cord paralysis), radioactive iodine therapy and antithyroid drug therapy.

Beta-blockers (for example, propranolol, atenolol) are often initiated before or in conjunction with other therapies to ameliorate some of the symptoms of hyperthyroidism. They can usually be tapered and stopped once a response to medication has been achieved.

Radioactive Iodine Therapy

- Radioactive iodine therapy is the treatment of choice (contraindicated in pregnancy)
- One dose is usually sufficient. Permanent hypothyroidism requiring life-long thyroid hormone replacement therapy is the notable complication

Antithyroid Drug Therapy

- Antithyroid drugs (propylthiouracil and methimazole) block synthesis of thyroid hormone and are preferred for clients with mild hyperthyroidism or small goitres. Also used as “pretreatment” before radioactive iodine therapy. Methimazole is preferred in adults and children except during the first trimester of pregnancy and in patients with life-threatening thyrotoxicosis⁹²

- Propylthiouracil is preferred over methimazole when an antithyroid drug is to be started during the first trimester of pregnancy (concerns regarding the teratogenic potential of methimazole during the first trimester take precedence over those regarding the hepatotoxic potential of propylthiouracil)⁹²
- Euthyroid state achieved in 4–6 weeks for clients taking methimazole and in 6–12 weeks for propylthiouracil. Clients usually remain on drugs for 1–2 years
- Agranulocytosis is a rare side effect of both drugs. Assess client for severe sore mouth, sore throat, fever. Monitor white blood count (WBC) before initiating therapy then periodically during the first 3 months of treatment
- Consider supplemental multivitamin, calcium and vitamin D

Subclinical hyperthyroidism:^{85,93}

- There is insufficient evidence supporting treatment of clients with subclinical hyperthyroidism except those in high risk groups as follows:
 - Frail and/or elderly
 - Clients with previous radioactive iodine therapy, thyroid surgery, type 1 diabetes mellitus, autoimmune disease, family history of thyroid disease or atrial fibrillation
 - Symptoms of hyperthyroidism
 - Other risk factors for atrial fibrillation

Monitoring and Follow-Up⁹⁴

- Clients not treated with pharmacologic therapy should be followed periodically based on their clinical presentation (for example, every 3–12 months)
- Clients on beta-blockers should be initially followed every 1–3 months, then periodically depending on symptoms
- Successful treatment of hyperthyroidism may be followed by a serious depression; advise the client and family of this potential risk and frequently monitor the client’s mental health
- Elderly women with hyperthyroidism are at increased risk for accelerated bone loss; consider monitoring bone density annually in these clients

Radioactive Iodine Therapy:

- Monitor free T4 levels every 4–8 weeks until client becomes euthyroid or hypothyroid and thyroid hormone replacement is needed
- Once stable, assess client at 3 months, then at 6 months, then annually

Antithyroid Drug Therapy:

- Monitor free T4 level 1 month after treatment and every 2–3 months thereafter
- Order WBC after several weeks of therapy and after dose changes
- Order liver enzymes every 3–6 months when patient is stable

Referral

Thyrotoxic crisis (“thyroid storm”) is a medical emergency; consult physician and medivac client. Arrange follow-up with a physician as required:

- During initial treatment phase
- Whenever symptoms are not controlled by therapy
- If there is evidence of complications
- Once yearly when client is stable (this may also be done with a nurse practitioner)
- Clients with eye involvement need referral to an ophthalmologist

HYPOTHYROIDISM

A clinical state resulting from decreased secretion of thyroid hormones or from resistance to hormone action; this leads to a progressive slowing of all body functions.

Prevalence of hypothyroidism is three times higher among women than men. Estimated prevalence rates for overt hypothyroidism in geriatric populations is 0.2% to 3%. The prevalence of “subclinical” hypothyroidism is estimated between 4% and 8.5% of the adult US population where up to 20% of women over 60 years are estimated to have “subclinical” hypothyroidism.⁸⁸

CAUSES**Primary Hypothyroidism⁹⁵**

The most common form is a defect in the thyroid gland causing it to produce insufficient thyroid hormone.

- Idiopathic decrease in production of hormone
- Autoimmune thyroiditis (Hashimoto’s disease)
- Endemic iodine deficiency
- Congenital defects
- Radioactive iodine therapy
- Thyroidectomy
- Subacute thyroiditis (after a viral illness)
- Acute bacterial thyroiditis (rare)

- Postpartum, subacute granulomatous thyroiditis
- Insufficient dose of thyroid replacement therapy
- Medications (for example, lithium, amiodarone)

Secondary Hypothyroidism⁹⁵

- Insufficient stimulation from the pituitary or hypothalamus axis (pituitary or adrenal disease)

Risk Factors

- Woman > 40 years of age (at highest risk)
- Presence of another autoimmune disorder (for example, type 1 diabetes, Addison’s disease)
- Recent acute viral or bacterial infection
- Treatment with radioactive iodine
- Thyroidectomy
- Evidence of pituitary or hypothalamic disease
- Women in postpartum period

HISTORY⁹⁵

Symptoms may be subtle, insidious.

Early Symptoms

- Weakness
- Fatigue
- Cold intolerance
- Lethargy
- Dry, flaky skin
- Nail changes
- Headache
- Menorrhagia
- Anorexia
- Constipation

Late Symptoms

- Slowing of intellectual activity (for example, memory, decreased concentration, slowed speech)
- Slowing of motor activity (reflex delay)
- Absence of sweating
- Yellow skin
- Coarseness or loss of hair (often lateral eyebrows)
- Modest weight gain
- Periorbital and peripheral edema (myxedema)
- Hoarseness, enlarged tongue
- Goitre
- Decreased sense of taste and smell
- Muscle aches and stiffness
- Dyspnea
- Deafness

- Night blindness
- Depression
- Infertility

PHYSICAL FINDINGS

A complete review of systems is required as symptoms may be subtle and involve every body system.

- Review general appearance, paying particular attention to slowed movements
- Vital signs: resting pulse (may be slow or normal), respiration rate (may be increased), temperature, BP (may be increased diastolic BP or orthostatic hypotension) and weight
- Integumentary: inspect and palpate skin, (note dry, rough, thickened skin, poor skin turgor, pallor, jaundice); inspect hair for texture and thickness (usually coarse and dry); inspect nails (usually thin and brittle) (*see “Assessment of the Integumentary System” in the chapter “Skin”*)
- Head and Neck:
 - Eyes: assess for puffiness (myxedema) of face and eyelids (*see “Assessment of the Eyes” in the chapter “Eyes”*)
 - Nose and lips (note any thickening)
 - Neck: palpate for lymphadenopathy, perform thyroid assessment including inspection (observe surgical scars), palpation (noting tenderness, firmness, fluctuance, nodule) and auscultation (noting bruits); measure size (*see “Assessment of the Ears, Nose and Throat” in the chapter “Ears, Nose and Throat”*)
- Respiratory: auscultate lungs (clear unless pleural effusion present) (*see “Assessment of the Respiratory System” in the chapter “Respiratory System”*)
- Cardiovascular: auscultate the heart, noting murmurs and rate/rhythm; point of maximal impulse (PMI) displaced if enlargement has occurred (*see “Assessment of the Cardiovascular System” in the chapter “Cardiovascular System”*)
- Gastrointestinal: auscultate bowel sounds; assess the abdomen for hepatomegaly, splenomegaly and ascites (*see “Assessment of the Gastrointestinal System” in the chapter “Gastrointestinal System”*)

- Musculoskeletal: test muscular strength, focusing on signs of proximal muscle weakness; examine fingers and toes for thickening; assess lower extremities, noting pretibial myxedema (*see “Assessment of the Musculoskeletal System” in the chapter “Musculoskeletal System”*)
- Neurologic: perform complete neurologic exam; assess tendon reflexes (may have brisk contraction then prolonged relaxation); perform mental status examination (*see “Assessment of the Central Nervous System” in the chapter “Central Nervous System”*)

Myxedema coma (life-threatening emergency):⁹⁶

- Clients with long-standing hypothyroidism, usually in elderly
- Illness precipitates myxedema coma
- Obtundation or coma with hypothermia, bradycardia, respiratory failure, possible cardiovascular collapse

DIFFERENTIAL DIAGNOSIS

- Thyroid cancer
- Euthyroid sick syndrome
- Nephrotic syndrome
- Nephritis
- Cirrhosis⁹⁷
- Depression
- Dementia from other causes
- Heart failure

COMPLICATIONS⁹⁸

- Coronary artery disease, congestive heart failure
- Constipation, megacolon
- Slow wound healing
- Anemia
- Mental disturbances including depression, organic psychosis
- Myxedema coma
- Infertility, erectile dysfunction
- Exaggerated response (toxicity) to antiepileptic, anticoagulant, hypnotic and opiate drugs (due to reduced rate of clearance)⁹⁹
- Adrenal crisis with vigorous treatment
- Bone demineralization from overtreatment for long period

DIAGNOSTIC TESTS

- Measure TSH (which will be elevated)
- Measure free T4 (per chart below)

Subclinical hypothyroidism is an elevated TSH level with a normal free T4 level.¹⁰⁰

Depending on client presentation, the physician may consider the diagnostic tests below:¹⁰¹

- Complete blood count (CBC) (hemoglobin may be reduced)
- Fasting lipid profile (dyslipidemia is common)
- Liver function tests (LFTs) (if jaundice present)
- Serum electrolytes, blood urea nitrogen (BUN), creatinine, glucose, calcium, phosphate and albumin

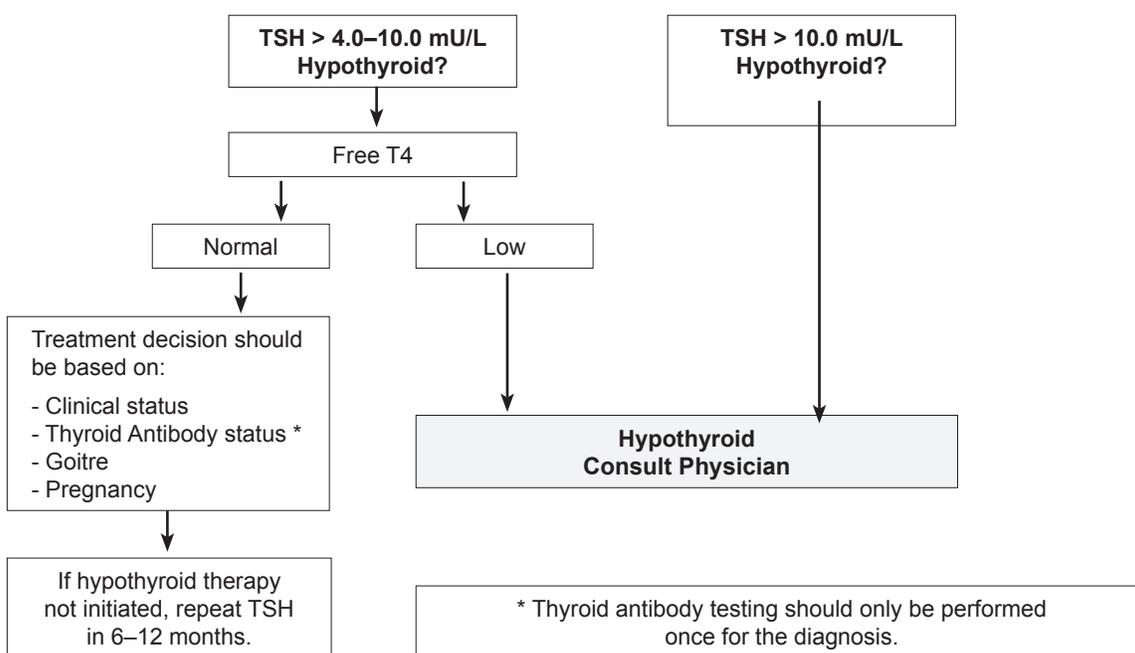
- Urine pregnancy test (women of childbearing years)
- Urinalysis (to detect proteinuria)

MANAGEMENT**Goals of Treatment**

- Identify complications (for example, cardiac, myxedema)
- Relieve symptoms
- Return to euthyroid state
- Prevent complications

Appropriate Consultation

Consult a physician if hypothyroidism is suspected or diagnosed. Drug therapy for clients with hypothyroidism is initiated by a physician.

Diagnostic Tests for Suspected Hypothyroidism

Adapted with permission from Toward Optimized Practice Clinical Practice Guideline Working Group. (2008). *Clinical Practice Guideline: Investigation and Management of Primary Thyroid Dysfunction*⁹⁸

Nonpharmacologic Interventions

Client Education

- Explain nature, course and prognosis of disease
- Counsel client about appropriate use of medications (dose, frequency, side effects, avoidance of abrupt discontinuation)
- Emphasize the need for lifelong treatment and the dangers of not taking medications
- Teach client about signs and symptoms of hyperthyroidism (indicating medication overdose) and hypothyroidism (indicating medication underdose)
- Provide dietary advice (for example, increase fibre and fluids to prevent constipation)

Pharmacologic Interventions

Therapy can be initiated by a physician prescribing the mean replacement dose of levothyroxine (1.6 µg/kg/day).^{102,103} Initial doses are lower in the elderly (for example, 50 µg/day) and in clients with coronary artery disease (for example, 25 µg/day) and may be as low as 12.5 µg/day.^{102,103} During pregnancy, requirements for levothyroxine may increase by up to 50%.

Due to differences in bioequivalence, the same brand of levothyroxine should be used throughout treatment.¹⁰⁴

The dose is titrated to the lowest dose needed to maintain a euthyroid state. The drug should be taken in the morning on an empty stomach, as food and vitamin and mineral supplements can interfere with absorption.

Subclinical hypothyroidism:¹⁰⁰

- There is insufficient evidence supporting treatment of clients with subclinical hypothyroidism except in pregnant women where aggressive case finding and treatment is justified to reduce adverse maternal and fetal outcomes

Monitoring and Follow-Up

- Follow up every 6 weeks until stabilized and after each dosage change
- Monitor weight, blood pressure and energy level
- Assess compliance with medications
- Monitor TSH and T4 levels every 6 weeks until euthyroid state is attained
- Follow up every 6–12 months after TSH level is normalized

Referral

Myxedema coma is a medical emergency. Consult physician and medivac client.

Arrange follow-up with a physician as required:

- During initial treatment phase
- Whenever symptoms are not controlled by therapy
- If there is evidence of complications

Screening Strategies

The American Thyroid Association recommends that adults be screened for thyroid dysfunction (TSH testing) at age 35 years and then every 5 years.⁸⁶

Screening may need to be done more often for clients who are at higher risk due to:^{105,106}

- Past or family history of thyroid disease
- Autoimmune disorders (diabetes mellitus)
- Goitre
- Infertility/anovulation
- Dyslipidemia
- Hypertension
- Past history of neck irradiation
- Autoimmune disorders
- Women > 50 years old or postmenopausal
- Women trying to conceive or pregnant women during the first trimester
- Postpartum women (within 6 weeks to 6 months postpartum)

METABOLIC SYNDROME

Metabolic syndrome is a cluster of unhealthy body measurements (abdominal obesity, hypertension) and laboratory results (dyslipidemia, dysglycemia) that places clients at greater risk for diabetes and cardiovascular disease.³⁹ See Table 5, “Defining Criteria for Metabolic Syndrome” for more specific information.

The worldwide prevalence of metabolic syndrome in adults is estimated at 20–25%.¹⁰⁷ In Canada, the prevalence of metabolic syndrome in the general population is estimated at 26% and age-adjusted prevalence differs between men and women and between provinces.¹⁰⁸ In an Ontario Oji-Cree community, overall prevalence of metabolic syndrome was 29.9% where 33.9% of adult females and 8.7% of adolescent females had metabolic syndrome.¹⁰⁹

CAUSES^{110,111}

- Insulin resistance (correlated with visceral fat measured by waist circumference or waist to-hip ratio)¹¹²
- Genetic factors

Risk Factors^{111,113,114,115}

- Increasing age
- Member of a high-risk group (for example, Hispanic, Asian)
- Obesity (particularly abdominal)
- Sedentary lifestyle
- High-carbohydrate intake
- Smoking
- Family history of diabetes
- Mental Illness (for example, schizophrenia, bipolar disorder)
- Pro-inflammatory state (for example, rheumatoid arthritis, systemic lupus erythematosus)
- Pro-thrombotic state
- Hormonal changes
- Polycystic ovary syndrome
- Non-alcoholic fatty liver disease

HISTORY

Signs and symptoms of:

- Type 2 diabetes mellitus (*see “History” for “Type 2 Diabetes”*)
- Dyslipidemia (*see “Dyslipidemia” in the chapter “Cardiovascular System”*)
- Hypertension (*see “Hypertension” in the chapter “Cardiovascular System”*)

PHYSICAL FINDINGS

- Obesity (BMI > 30 kg/m²)
- Abdominal obesity (“apple shape” instead of “pear shape”); measure waist circumference (place non-elastic tape measure at the level of the superior iliac crest, parallel to the floor, at the end of a patient’s relaxed expiration¹¹⁶)
- Vital signs: elevated blood pressure
- Integumentary: lipid deposits in skin (xanthomas) (*see “Assessment of the Integumentary System” in the chapter “Skin”*)

- Evidence of target organ damage (may be associated with diabetes, dyslipidemia and/or hypertension)
- Eyes: assess for retinal changes (*see “Assessment of the Eyes” in the chapter “Eyes”*)
- Cardiovascular: assess heart and peripheral pulses for bruits and hypertrophy (*see “Assessment of the Cardiovascular System” in the chapter “Cardiovascular System”*)

DIFFERENTIAL DIAGNOSIS

- Type 2 diabetes mellitus
- Dyslipidemia
- Hypertension

COMPLICATIONS

- Cardiovascular disease¹¹⁷ – while each individual component of the metabolic syndrome confers an increased risk of cardiovascular-related death, the risk is more pronounced when metabolic syndrome is present¹¹¹
- Type 2 diabetes mellitus³⁹
- Chronic kidney disease (CKD) – metabolic syndrome is associated with a 30% increased risk of developing CKD in American Indians without diabetes¹¹⁸

DIAGNOSTIC TESTS^{119,120,121}

- Fasting plasma glucose
- Fasting lipid levels (total cholesterol [TC], high-density lipoproteins [HDL-C], triglycerides [TG] and calculated low-density lipoproteins [LDL-C])
- Urine sample for albumin to creatinine ratio

There is a lack of consensus regarding the operational definition of metabolic syndrome. One of the accepted definitions, from the International Diabetes Federation (IDF) is shown on the next page.

Table 5 – Defining Criteria of Metabolic Syndrome¹²¹

Diagnostic criteria	Central obesity (using ethnic-specific values) plus ≥ 2 of the risk determinants below are present. If BMI is $> 30 \text{ kg/m}^2$, central obesity can be assumed and waist circumference does not need to be measured
Fasting plasma glucose (FPG)	FPG $\geq 5.6 \text{ mmol/L}$ (or previously diagnosed type 2 diabetes)
Blood pressure	$\geq 130/85 \text{ mm Hg}$ (or receiving treatment for previously diagnosed hypertension)
Triglycerides (TG)	$\geq 1.7 \text{ mmol/L}$ (or receiving treatment)
High-density lipoprotein cholesterol (HDL-C)	$< 1 \text{ mmol/L}$ (men) $< 1.3 \text{ mmol/L}$ (women) (or receiving treatment)
Abdominal obesity	Europids, Sub-Saharan Africans, Eastern Mediterranean and Middle East (Arab) populations: Waist Circumference: $> 94 \text{ cm}$ (men) $> 80 \text{ cm}$ (women) South Asian, Malaysian, Asian, Indian, Chinese, Japanese, Ethnic South and Central American populations: Waist Circumference: $> 90 \text{ cm}$ (men) $> 80 \text{ cm}$ (women)

Reprinted with permission from Canadian Diabetes Association. Canadian Diabetes Association 2008 clinical practice guidelines for the prevention and management of diabetes in Canada. *Can J Diabetes* 2008;32(suppl 1):S12.

MANAGEMENT

Goals of Treatment

- Prevent progression to diabetes
- Attain optimum glycemic control
- Attain target lipid levels
- Educate the client for self-care
- Prevent complications
- Attain optimum control of hypertension
- Smoking cessation

Appropriate Consultation

Consult a physician for further management if metabolic syndrome is suspected or diagnosed. Pharmacologic therapy for clients with diabetes is initiated by a physician.

Nonpharmacologic Interventions

Ley et al. (2009)¹²² found that the diagnosis of metabolic syndrome and its components was useful in communicating the increased risk of diabetes to individuals in a remote Aboriginal community where oral glucose tolerance testing was not easily accessible.

Lifestyle modification (diet and physical activity) aimed at reducing abdominal obesity is the most effective therapy for the prevention of diabetes and treatment of metabolic syndrome.^{123, 124}

Diet and Nutrition:

- In general¹²⁵:
 - Increase fruit and vegetable intake
 - Increase proportion of mono- and polyunsaturated fats in the diet while decreasing the proportion of saturated fats and trans-fatty acids to less than 7% of the total calories
 - Increase the intake of omega-3 fatty acids from fish and plant sources
 - Decrease intake of refined carbohydrates and sugar
- A Mediterranean-style diet (increased daily consumption of whole grains, vegetables, fruit, nuts and olive oil) has been shown to decrease the prevalence of metabolic syndrome at 1 year by 6.7–13.7%.¹²⁶ After 2 years, the net reduction in metabolic syndrome was 48%.¹¹⁵
- A DASH (Dietary Approach to Stop Hypertension) diet showed a decrease in the prevalence of metabolic syndrome by 35%.¹²³
- Limit alcohol consumption to no more than 2 drinks/day (men) and 1 drink/day (women)¹²⁷

Physical Activity:

- Moderate-intensity physical activity for at least 150 minutes weekly: when combined with diet changes and weight reduction have been found to reduce prevalence of metabolic syndrome by 41%¹²⁸

Weight Reduction:

- Reduce portion sizes to lower calorie intake¹²⁷ (aim to achieve a 5–10% loss of body weight in the first year which improves insulin resistance)
- Achieve and maintain a body mass index (BMI) < 25 kg/m²¹²⁵

Smoking Cessation:

- Smoking increases insulin resistance and may worsen the complications of metabolic syndrome¹³⁰

Pharmacologic Interventions

A physician must initiate drug therapy:

- Hypertension (*see “Hypertension,” “Pharmacologic Interventions” in the chapter “Cardiovascular System”*)
- Dysglycemia: if lifestyle interventions fail, a physician may consider metformin^{123,128}
- Dyslipidemia (*see “Dyslipidemia,” “Pharmacologic Interventions” in the chapter “Cardiovascular System”*)
 - Reduce low-density lipoprotein cholesterol (LDL-C) levels

Monitoring and Follow-Up

Follow-up is important to check the response to nonpharmacologic and pharmacologic treatment within 6 weeks and, if the results are satisfactory, continue follow-up at regular intervals thereafter (every 3–12 months). It is also important to provide encouragement and further education.

Dyslipidemia: *see “Dyslipidemia,” “Monitoring and Follow-up” in the chapter “Cardiovascular System”*

Hypertension: *see “Hypertension,” “Monitoring and Follow-up” in the chapter “Cardiovascular System”*

Referral

Arrange follow-up with a physician or nurse practitioner every 6–12 months if stable or more frequently as necessary.

OSTEOPOROSIS

Age-related condition characterized by deterioration in bone tissue quality and bone quality and decreased bone mass with resulting increase in bone fragility and susceptibility to fractures. The World Health Organization (WHO) definition is based on the Bone Mineral Density (BMD) as follows:¹³¹

- **Osteopenia** (low BMD): clients having a BMD between 1 and 2.5 standard deviations below the “normal” BMD (T-score -1 to -2.5)
- **Osteoporosis**: clients having a BMD more than 2.5 standard deviations below the “normal” BMD (T-score below -2.5)

NOTE: The “normal” BMD reflects the BMD of a young adult, Caucasian; the application of this definition to children, men and clients of different ethnic origins is not defined. However, this same definition used for postmenopausal women has also been used with men over 50.¹³²

In Canada, 1 in 4 women and 1 in 8 men have osteoporosis.¹³³ Prevalence in Canadian women aged 50 years and over was 12.1% at the lumbar spine, and 7.9% at the femoral neck, with a combined prevalence of 15.8%. Osteoporosis prevalence increases with age: approximately 6% at 50 years of age to over 50% over 80 years of age.¹³⁴

CAUSES

Rarely due to a single factor.

Primary Osteoporosis

Occurs in both genders and results from normal aging and decreased gonadal functioning; usually after menopause in women and later in life in men.¹³⁵

Secondary Osteoporosis^{135,136}

- Endocrine basis: glucocorticoid excess (Cushing’s syndrome), hyperthyroidism, hyperparathyroidism, hypogonadism, hyperprolactinism
- Drug-induced: corticosteroids, anticonvulsants, ethanol, tobacco, barbiturates, heparin, thyroid hormones, gonadotropin-releasing hormone agonists (for example, Lupron for prostate cancer), loop diuretics or thiazolidinediones (TZDs)
- Other causes: chronic renal failure, liver disease, malabsorption state (for example, celiac disease, inflammatory bowel disease), rheumatoid arthritis, hyperparathyroidism, multiple myeloma, organ transplant

Risk Factors¹³⁷

Major Risk Factors

- Age > 65 years
- Vertebral compression fracture
- Fragility fracture after 40 years of age (A fragility fracture is defined as any fracture that occurs spontaneously or from minor trauma – for example, a fall from a standing height.)¹³⁸
- Family history of osteoporotic fracture (especially maternal hip)
- Systemic glucocorticoid therapy (> 3 months' duration)
- Malabsorption syndrome
- Primary hyperparathyroidism
- Propensity to falls
- Osteopenia seen on x-ray
- Hypogonadism
- Early menopause (< 45 years of age)

Minor Risk Factors

- Rheumatoid arthritis
- Past history of clinical hyperthyroidism
- Chronic anticonvulsant therapy
- Low dietary calcium intake
- Smoking
- Excessive alcohol consumption
- Excessive coffee intake
- Weight < 57 kg
- Weight loss of > 10% of weight at or after age 25
- Chronic heparin therapy

HISTORY¹³⁹

- Postmenopausal female (90% of cases)
- Nontraumatic fractures, often of weight-bearing bones of the spine
- Progressive structural changes of the spine (for example, kyphosis and lordosis)
- Loss of height (> 2 cm prospectively or historical height loss of > 6 cm)
- Chronic or acute back pain
- Fall history
- Dental health (bone loss is a risk factor for periodontal disease)
- Level of physical activity (weight-bearing exercise)
- Presence of major and minor risk factors (as given above)

PHYSICAL FINDINGS^{135,140}

Perform a complete physical examination to detect secondary causes of osteoporosis (for example, thyroid nodule suggests hyperthyroidism; buffalo hump suggests Cushing's syndrome; wasting suggests malignant disease).

- Usually thin, frail elderly woman
- Measure height and compare to previous values. After achieving maximum height, a height loss of 1–1.5 cm is normal with aging; > 2 cm height loss may be related to vertebral fracture
- Musculoskeletal: assess for degrees of bony deformity; observe back for dorsal kyphosis and cervical lordosis (from multiple compression fractures); palpate spine to detect painful areas; arm span may be longer than body height (*see "Assessment of the Musculoskeletal System" in the chapter "Musculoskeletal System"*)
- Assess factors increasing risk of falls: impaired visual acuity, muscle weakness (inability to rise from a chair), coordination and balance, disability (for example, use of cane or walker) and difficulty with mobility

DIFFERENTIAL DIAGNOSIS

- In premenopausal women and in men, rule out organic disease (*see "Secondary Osteoporosis,"*)
- Osteoarthritis
- Renal or collagen disease
- Metastatic bone disease
- Multiple myeloma
- Hyperthyroidism

COMPLICATIONS

- Vertebral compression fractures
- Other fragility fractures
- Chronic pain and disability

DIAGNOSTIC TESTS^{140,141,142}

- A bone mineral density (BMD) test should be ordered to assess bone mass (and fracture risk) for all clients with one major or two minor risk factors for osteoporosis as well as for monitoring response to pharmacologic therapy. Consult with a physician prior to ordering
- X-rays are used mainly for detecting fractures. If x-ray shows osteopenia, then confirm with a bone mineral density measurement

- Other lab tests to establish baseline and exclude secondary causes of osteoporosis: complete blood count (CBC), TSH, alkaline phosphatase, liver transaminases, albumin, calcium, serum creatinine and serum protein electrophoresis
- 25-OH vitamin D level for clients with low dietary intact or poor sunlight exposure

MANAGEMENT

Goals of Treatment¹⁴³

- Reduce the risk of fracture
- Prevent disability and loss of independence
- Preserve or enhance bone mass
- Detect and manage fractures

Nonpharmacologic Interventions^{144,145,146}

Calculate 10-year Fracture Risk

The potential morbidity of osteoporosis is related to fracture risk. Individuals at risk of osteoporosis-related fracture are best identified through assessment of clinical risk factors and BMD measurement results. Therefore other factors must be considered, including smoking, alcohol intake, body mass index, glucocorticosteroid use, rheumatoid arthritis, history of fragility fracture and parental history of hip fracture. The 10-year absolute risk of fracture can be assessed by using the WHO Fracture Risk Assessment Tool (available at: <http://www.shef.ac.uk/FRAX/>).¹³²

Diet and Nutrition:

- Adequate calcium (1200–1500 mg/d) and vitamin D (\geq 800 IU/d) intake (dietary sources include salmon, sardines, green vegetables, cheeses, fortified milk, egg yolks) is essential for prevention and treatment of osteoporosis¹⁴⁷
- Maintain adequate protein intake
- Avoid excess dietary sodium ($>$ 2100 mg/day)
- Provide smoking cessation counselling (if applicable)
- Encourage limiting alcohol ($<$ 3 drinks per day; one drink is equivalent to 285 mL of beer, 120 mL of wine or 30 mL of spirits)¹⁴⁷
- Encourage limiting caffeine ($<$ 4 cups of coffee per day)

Physical Activity:

- Recommend an exercise program, particularly weight-bearing exercise (walking, jogging or aerobics 50–60 minutes three times a week provides optimum benefit)
- Exercises that increase strength and improve balance can reduce falls¹⁴⁸

Client Education

- Explain nature, course and prognosis of disease; this is a chronic condition that can be controlled but not cured; pain is often chronic
- Counsel client about appropriate use of medications (dose, frequency, side effects, importance of compliance)
- Advise client to return to clinic for assessment if character of pain changes or if pain becomes more severe
- Assess home environment for hazards to mobility; modify or provide aids as required

Pharmacologic Interventions^{141,149,150}

Preventive Therapy:

See chart for calcium and vitamin D recommendations (from all sources, diet and supplements)¹⁴⁴

Recommended Calcium and Vitamin D intake from all sources*

Calcium	
Children (4–8 years)	800 mg/day
Adolescents (9–18 years)	1300 mg/day
Premenopausal women	1000 mg/day
Men $<$ 50 years	1000 mg/day
Menopausal women	1500 mg/day
Men $>$ 50 years	1500 mg/day
Pregnant or lactating women	1000 mg/day
Vitamin D	
$<$ 50 years	400 IU/day
$>$ 50 years	800 IU/day

* 'All sources' means total diet and supplement.

Therapies for osteoporosis manipulate the normal process of bone remodeling either by reducing bone resorption (antiresorptive or anticatabolic agents) or by stimulating bone formation (anabolic).

Antiresorptive agents include: bisphosphonates, nasal calcitonin, selective estrogen receptor modulators and hormone replacement therapy (HRT).

Anabolic agents include: parathyroid hormone (PTH).

Refer to product monographs for information on dosing and side effects of specific medications.

Monitoring and Follow-Up^{151,152,153}

- Clients taking calcium supplements may be at risk for kidney stones, dyspepsia and constipation
- Clients with at least 1 major or 2 minor risk factors for osteoporosis should have a bone mineral density (BMD) test every 2–3 years to monitor changing risk
- Clients receiving pharmacologic therapy (prevention or treatment) for osteoporosis should have:
 - Initial follow-up 1–2 months after initiating therapy
 - Regular follow-up visits every 3–6 months
 - BMD test 1–2 years after initiating therapy until condition stabilizes

Referral

Refer the following clients to a physician or a nurse practitioner for assessment:

- Women in perimenopause or menopause and men > 50 years old with 1 major or 2 minor risk factors for osteoporosis

Refer the following clients to a physician for assessment:

- Anyone in whom a fracture (for example, fragility, hip, vertebral) is suspected

Arrange follow-up with a physician as required:

- During initial treatment phase
- Whenever symptoms are not controlled by therapy
- If there is evidence of complications

Screening for Osteoporosis

The *2002 Clinical Practice Guidelines for the Diagnosis and Management of Osteoporosis in Canada* recommends that all postmenopausal women and men over 50 years of age be assessed for the presence of risk factors for osteoporosis. For these clients who have at least 1 major risk factor or at least 2 minor risk factors (*see “Risk Factors,”*), then a bone mass density (BMD) test should be performed.

METABOLIC EMERGENCIES

DIABETIC KETOACIDOSIS AND HYPEROSMOLAR HYPERGLYCEMIC STATE

These two conditions are distinct, however, their initial assessment and management is the same.

Diabetic ketoacidosis (DKA) is a condition due to an absolute or relative¹⁵⁴ insulin deficiency that is characterized by hyperglycemia, ketonemia, ketonuria, acidosis, dehydration and an altered level of consciousness. The incidence of DKA is between 4.6 and 8 per 1000 person-years where 5000–10,000 clients will be admitted to hospital with DKA each year with an estimated mortality rate between 4% and 10%.¹⁵⁵ DKA typically occurs in young, lean clients with type 1 diabetes and develops within a day or so.

Hyperosmolar hyperglycemic state (HHS) is very similar to DKA as they result from the same combination of absolute or relative insulin deficiency and an excess of counter-regulatory hormones.

HHS is much less common than DKA. The incidence of HHS is less than 1 per 1000 person-years with 500–1000 patients admitted with HHS to hospital each year in Canada with a 10–50% mortality rate.¹⁵⁵ HHS is more likely to occur in older, obese clients with type 2 diabetes and older adult clients with decreased renal function; it can take several days or weeks to develop.

CAUSES¹**Risk Factors¹⁵⁶**

- New diagnosis of diabetes mellitus (DKA may be the initial manifestation seen in 15–67% of new-onset type 1 diabetics¹⁵⁷)
- Noncompliance with diet
- Failure to take insulin properly or inadequate insulin (dose, type)
- Insulin omission
- Infection or illness
- Failure to adjust diabetic regimen when ill
- Myocardial infarction
- Trauma
- Recent surgery (especially cardiac)

- Abdominal crisis
- Use of atypical antipsychotic medications¹⁵⁸
- “Brittle” diabetes¹⁵⁹ (frequent and unpredictable swings in blood glucose causing hypo- or hyperglycemia)
- Treatment failure with insulin infusion pumps
- Use of medications including glucocorticoids, higher doses of thiazide diuretics and atypical antipsychotics¹⁶⁰
- Cocaine use¹⁶⁰ (DKA only)

HISTORY

- Acute¹⁶¹ onset (DKA) vs gradual onset (HHS)
- Young, lean client with Type 1 diabetes (DKA) vs older, obese client with type 2 diabetes (HHS)
- Polyuria, polydipsia, polyphagia
- Weight loss
- Anorexia
- Nausea and vomiting
- Abdominal pain
- Malaise, weakness, marked fatigue, loss of consciousness
- Muscle aches
- Headache
- Blurred vision
- Reversible paresthesia in fingertips
- Recent infection, surgery, trauma or myocardial infarction

PHYSICAL FINDINGS

Client appears ill and may have a reduced level of consciousness. A complete examination of all body systems must be done.

- Vital signs: temperature (normal), pulse (tachycardia), respiration rate (deep and rapid [both]); Kussmaul respirations [DKA]), oxygen saturation, blood pressure (normal or may be low; postural BP drop)
- HEENT: assess for fruity odour on breath, mucous membranes dry
- Integumentary: assess for dehydration (skin warm and dry, loss of skin turgor) – usually very pronounced dehydration in HHS (*see “Assessment of the Integumentary System” in the chapter “Skin”*)
- Neurologic: assess level of consciousness and response to stimulus using Glasgow Coma Scale (*see “Assessment of the Central Nervous System” in the chapter “Central Nervous System”*)

To estimate degree of dehydration *see Table 6, “Clinical Features of Dehydration.”*

Table 6 – Clinical Features of Dehydration*¹⁶²

Feature	Mild Dehydration (< 5%)	Moderate Dehydration (5% to 10%)	Severe Dehydration (> 10%)
Heart rate	Normal	Slightly increased	Rapid, weak
Systolic blood pressure	Normal	Normal to orthostatic, > 10 mm Hg change	Hypotension
Urine output	Decreased	Moderately decreased	Markedly decreased, anuria
Mucous membranes	Slightly dry	Very dry	Parched
Axilla	Slightly dry	Dry	Dry
Skin**	Normal turgor	Decreased turgor	Tenting
Skin perfusion	Normal capillary refill (< 2 seconds)	Capillary refill slowed (2–4 seconds); skin cool to touch	Capillary refill markedly delayed (> 4 seconds); skin cool, mottled, gray
Mental status	Alert	Irritable	Lethargic, agitated or confused

*These features are not specific or reliable for all adults, particularly older adults, as they could be due to other causes. Laboratory findings are more accurate.

**Skin condition is less useful in diagnosis of dehydration for adults, particularly those > 55 years old; normal turgor does not mean that dehydration is not present in any adult.

DIFFERENTIAL DIAGNOSIS

- Hypoglycemia
- Hyperosmolar hyperglycemic state (HHS)
- Other causes of stupor or coma (for example, stroke, head injury, alcohol or drug overdose)

COMPLICATIONS¹⁶³

- Severe dehydration
- Electrolyte imbalance (for example, hyponatremia, hypokalemia, hyperkalemia, decreased serum bicarbonate)
- Cerebral edema
- Hypoglycemia related to overcorrection of hyperglycemia
- Noncardiogenic pulmonary edema

DIAGNOSTIC TESTS¹⁶⁴

- Perform urine dip to determine concentration of ketones in urine (moderate to high). Perform random blood glucose level with glucometer (≥ 14 mmol/L). Draw blood for baseline glucose level, creatinine, electrolyte levels (sodium, chloride, potassium), bicarbonate and complete blood count (CBC)
- For adult clients, draw blood for levels of cardiac enzymes to rule in/out precipitating myocardial infarction (MI)

Electrocardiography (ECG) may be helpful: look for the tall T-wave of hyperkalemia and watch for signs of silent myocardial infarction in the older diabetic client.

To differentiate between DKA and HHS, refer to *Appendix E* for the comparison of the laboratory diagnostic criteria. However, the emergency management of DKA and HHS is similar.

MANAGEMENT¹⁶⁵

The reversal of DKA should be gradual to prevent overcorrection and focus on fluid and electrolyte homeostasis. Note that there are significant differences in management of DKA in adolescents due to their significantly increased risk for cerebral edema.¹⁵⁶

Goals of Treatment⁶

- Assessment and stabilization of airway, breathing and circulation (ABC): ensure that airway is patent and protected and that ventilation is adequate in any client with reduced level of consciousness
- Restoration of normal extracellular fluid volume and tissue perfusion
- Correction of electrolyte imbalances and hyperglycemia
- Diagnosis/treatment of co-existing illness or underlying cause (precipitating factors) of DKA or HHS

Appropriate Consultation

Consult a physician immediately after stabilization of ABC.

Adjuvant Therapy

Oxygen at 4–6 L/min or more as needed; keep oxygen saturation > 97% to 98%.

Intravenous Therapy¹⁶⁶

- Start 2 large-bore IV lines with normal saline (0.9% NaCl)
- Reversing the dehydration will assist in reducing the blood glucose level. Fluid therapy is based on the degree of dehydration (*see Table 6, “Clinical Features of Dehydration”*). Initiate fluid therapy with a 0.9% NaCl bolus of 500 mL/h then consult a physician as soon as possible for further rehydration orders
- If severe fluid volume deficit (shock), then infuse 1–2 L/h to correct hypotension and shock, then continue with 500 mL/h
- Once initial stabilization is complete, further rehydration aims to correct plasma Na⁺ and K⁺ levels, however, this requires laboratory data on the client’s electrolytes

Nonpharmacologic Interventions

- Insert indwelling urinary catheter and monitor urinary output hourly, if upon consultation a physician supports its use
- Insert nasogastric tube, if upon consultation a physician supports its use. It may be useful if client is comatose or vomiting
- Clients may take fluids orally when they can be tolerated

Pharmacologic Interventions¹⁶⁷

Consult a physician immediately if DKA suspected. Start insulin therapy according to a physician's prescription.

Avoid hypoglycemia. Aim for a plasma glucose of 12–14 mmol/L. The physician may consider starting IV glucose once a plasma glucose of 14 mmol/L is reached.

Be careful giving insulin in HHS or DKA when potassium status is unknown.

Monitoring and Follow-Up¹⁶⁸

Every hour:

- Monitor vital signs (HR, RR, BP, temperature, oxygen saturation) (do more often if client condition requires it)
- Check blood glucose (also check before any insulin administration): avoid falls in glucose > 5.5 mmol per hour
- Check urine output
- Assess Glasgow Coma Scale (for 8 hours)
- Document all fluid intake and losses (for example, urine, emesis)
- Utilize cardiac monitoring if available

In addition to those things that are monitored hourly, the following measures should be done, according to the time:

0–1st hour:

- Assess Glasgow Coma Scale (GCS) on admission, check pupils
- Draw blood for CBC, electrolytes (Na, K, CL, HC03, BUN, creatinine, phosphate), venous pH, blood glucose, lactic acid level, cardiac enzymes and troponin
- Obtain urine for ketones

2nd hour:

- If feverish, suspect infection; physician to initiate antimicrobial therapy
- Draw blood for lactic acid level

3rd–8th hours:

- If abdominal pain, draw blood for amylase and lipase levels
- Draw blood for venous pH, electrolytes (as above)
- Check urine for ketones hourly

9th–24th hours:

- Check GCS every 2 hours
- Change collection of blood to every 8–12 hours at end of 24 hours

24th–48th hours:

- Continue to monitor the client and draw laboratory tests as ordered by a physician

Referral

- Medevac as soon as possible

Prevention

Any type 1 diabetic with hyperglycemia and concurrent illness should have their urine checked for ketones.

HYPOGLYCEMIA¹⁶⁹

Hypoglycemia is a cluster of symptoms related to low blood glucose levels due to exogenous, endogenous or functional causes.

CAUSES^{169,170}

- Delayed meal, inadequate caloric intake in client using antihyperglycemic agents
- Increased duration and intensity of physical exertion
- Insulin measurement error, insulin overdose
- Overdose of sulfonylurea or meglitinide antihyperglycemic agents
- Alcohol intake on an empty stomach and in malnourished clients
- Neoplasms (for example non-islet cell tumor, insulinoma)
- Hepatic, renal or cardiac failure
- Sepsis
- “Brittle” diabetes¹⁷¹ (frequent and unpredictable swings in blood glucose causing hypo- or hyperglycemia)

HISTORY¹⁷²

- Sudden onset

**Neurogenic (autonomic)
Symptoms:
[activation of sympathetic
nervous system]**

- Trembling
- Palpitations
- Sweating
- Anxiety
- Hunger
- Nausea
- Tingling

**Neuroglycopenic
Symptoms:
[abrupt cessation of
glucose in the brain]**

- Difficulty concentrating
- Confusion
- Personality changes
- Weakness
- Drowsiness
- Vision changes
- Difficulty speaking
- Headache
- Dizziness
- Change in level of consciousness

The severity of hypoglycemia may be described as:

- **Mild:** Autonomic symptoms are present; the client is able to self-treat
- **Moderate:** Autonomic and neuroglycopenic symptoms are present; the client is able to self-treat
- **Severe:** The individual requires the assistance of another person; unconsciousness may occur. Typically blood glucose < 2.8 mmol/L

PHYSICAL FINDINGS

Client may be unconscious or experiencing a seizure; if so, delay physical examination until ABCs are established and client is stabilized. Afterwards, a complete examination of all body systems must be done.

- Client will appear anxious, restless and may exhibit bizarre or aggressive behaviour
- Vital signs: pulse (tachycardia), respiration rate (elevated), oxygen saturation, blood pressure (elevated)
- Integumentary: assess skin for pallor, temperature (cold, clammy), diaphoresis (*see “Assessment of the Integumentary System” in the chapter “Skin”*)
- Neurologic: assess level of consciousness and response to stimulus with Glasgow Coma Scale, assess mental status for confusion, assess coordination, observe for a tremor (staggering gait; may appear intoxicated) (*see “Assessment of the Central Nervous System” in the chapter “Central Nervous System”*)

DIFFERENTIAL DIAGNOSIS

- Alcohol intoxication
- Alcohol-induced hypoglycemia
- Drug-induced hypoglycemia (for example, overdose)

COMPLICATIONS

- Injury due to a fall
- Hypoxia of brain
- Seizures
- Death
- Hypoglycemia unawareness¹⁷³
- If the client is taking a beta-blocker medication, then the autonomic symptoms may be blunted and the recovery from hypoglycemia may be delayed¹⁷⁴

DIAGNOSTIC TESTS

Determine blood glucose level with glucometer (< 3.3 mmol/L is the autonomic symptom warning level; if ≤ 2.8 mmol/L, client will have symptoms of neuroglycopenia).

MANAGEMENT**Goals of Treatment**

- Increase blood glucose level quickly but avoid rebound hyperglycemia¹⁷⁵
- Identify intercurrent illness or associated injury

Appropriate Consultation

Consult a physician as soon as possible after emergency interventions to discuss further care unless cause of hypoglycemia is obvious.

Adjuvant Interventions

If client is unconscious, stuporous, nauseated or unable to take oral therapy:

- Administer oxygen at 4–6 L/min or more as needed to keep O₂ saturation > 97–98%
- Start IV therapy with 5% dextrose in water (D5W) at 100–150 mL/h

Nonpharmacologic Interventions

If the client is unconscious or stuporous:

- Assessment and stabilization of airway, breathing and circulation (ABC): ensure that airway is patent and protected, and that ventilation is adequate in any client with reduced level of consciousness

If the client is conscious:¹⁷³

- Give 15 g of carbohydrate, preferably as glucose (dextrose) or sucrose tablets or as an oral solution. Examples include: glucose tablets; 3 teaspoons (15 mL or 3 packets) of table sugar dissolved in water; 175 mL of regular soft drink or fruit juice; 6 Lifesaver candies. After 15 minutes, retest blood glucose, retreat if blood glucose still < 4 mmol/L
- If the client is taking acarbose in conjunction with insulin or sulfonylureas, use glucose (dextrose) tablets (not sucrose because acarbose slows absorption of sucrose). If glucose is unavailable use milk or honey
- When client regains consciousness or recovers, obtain an accurate history (including any associated illness, previous episodes of hypoglycemia, head trauma or other injuries) and do a thorough physical examination
- To prevent repeated hypoglycemia, the client should have the usual meal or snack that is due at that time of the day. If the meal is > 1 hour away, a snack (15 g of carbohydrate + protein source) should be consumed

Pharmacologic Interventions

If client is unconscious:¹⁷³

dextrose, 50% solution, preloaded syringe,
20–50 mL IV stat over 1–3 minutes

or

glucagon, 1 mg SC, IM or IV

*NOTE: the effect of glucagon is impaired in clients who have consumed more than 2 standard alcoholic drinks in the previous few hours and in those with advanced liver disease.*¹⁷⁴

Monitoring and Follow-Up¹⁷³

- Observe response to treatment
- Recheck serum glucose level following interventions (every 15 minutes for 1 hour, then every 1–2 hours for the duration of action of the causative medication)

Referral

Medevac client if you are unable to stabilize blood glucose or if underlying cause of hypoglycemia is not clear; otherwise consider discharge home when condition has stabilized, after discussion with a physician.

Arrange referral to a physician when:

- There is no obvious cause for hypoglycemic episode
- Client has taken an oral hypoglycemic agent or long-acting insulin which resulted in hypoglycemia
- Client has persistent neurologic deficits

Discharge home may be considered after a high-carbohydrate meal if:

- Obvious cause of hypoglycemic episode has been found and treated
- Episode was rapidly reversed
- Client is able to continue frequent glucose monitoring for the duration of action of the causative medication

If recurrent hypoglycaemia, or no clear etiology is found, consult a physician about decreasing the dosage of the causative medication.

SOURCES

Internet addresses are valid as of February 2012.

BOOKS AND MONOGRAPHS

Anemia Review Panel. *Anemia guidelines for family medicine*. 2nd ed. Toronto, ON: MUMS Guideline Clearinghouse; 2008.

Bickley LS. *Bates' guide to physical examination and history taking*. 7th ed. Baltimore, MD: Lippincott Williams & Wilkins; 1999.

Crowther CL, McCance KL. *Alterations of musculoskeletal function*. In: McCance KL, Huether SE (Editors). *Pathophysiology: The biologic basis for disease in adults and children*. 5th ed. St. Louis, MO: Elsevier Mosby; 2006. p. 1497-1545.

Edmunds M, Mayhew M. *Procedures for primary care practitioners*. Baltimore, MD: Mosby; 1996.

Ferri FF. *Ferri's clinical advisor: Instant diagnosis and treatment*. St. Louis, MO: Mosby; 2004.

Fischbach FT. *A manual of laboratory and diagnostic tests*. 6th ed. Lippincott; 2000.

Goodman JJ, Uphold CR. Metabolic and endocrine problems. In: Uphold CR, Graham MV (Editors). *Clinical guidelines in family practice*. 4th ed. Gainesville, FL: Barmarrae Books, Inc.; 2003. p. 163-219.

Graham MV. (2003). Hematologic problems. In: Uphold CR, Graham MV (Editors). *Clinical guidelines in family practice*. 4th ed. Gainesville, FL: Barmarrae Books, Inc.; 2003. p. 923-32.

Gray J (Editor). *Therapeutic choices*. 5th ed. Ottawa, ON: Canadian Pharmacists Association; 2007.

Hanley DA. Osteoporosis. In: Gray J (Editor). *Therapeutic choices*. 5th ed. Ottawa, ON: Canadian Pharmacists Association; 2007. p. 972-85.

Harding SR. Common anemias. In: Gray J (Editor). *Therapeutic choices*. 5th ed. Ottawa, ON: Canadian Pharmacists Association; 2007. p. 1114-30.

Jones RE, Huether SE. Alterations of hormonal function. In: McCance KL, Huether SE (Editors). *Pathophysiology: The biologic basis for disease in adults and children*. 5th ed. St. Louis, MO: Elsevier Mosby; 2006. p. 683-734.

Karch AM. *Lippincott's 2002 nursing drug guide*. Philadelphia, PA: Lippincott; 2002.

Kasper DL, Braunwald E, Fauci A, et al. *Harrison's principles of internal medicine*. 16th ed. McGraw-Hill; 2005.

Lochnan H. Thyroid disorders. In: Gray J (Editor). *Therapeutic choices*. 5th ed. Ottawa, ON: Canadian Pharmacists Association; 2007. p. 318-29.

Mansen TJ, McCance KL. (2006). Alterations of erythrocyte function. In: McCance KL, Huether SE (Editors). *Pathophysiology: The biologic basis for disease in adults and children*. 5th ed. St. Louis, MO: Elsevier Mosby. p. 927-54.

Pagna K, Pagna T. *Diagnostic testing and nursing implications*. 5th ed. St. Louis, MO: Mosby; 1999.

Prateek L, Waddell A. *Toronto notes – MCCQE 2003 review notes*. 19th ed. Toronto, ON: University of Toronto, Faculty of Medicine; 2003.

Robinson DL, Kidd P, Rogers KM. *Primary care across the lifespan*. St. Louis, MO: Mosby; 2000.

Tierney LM Jr, McPhee SJ, Papadakis MA. *Current medical diagnosis and treatment 2001*. 40th ed., New York, NY: Lange Medical Books - McGraw-Hill; 2001.

Tintinalli J, et al. *Emergency medicine*. 5th ed. McGraw-Hill; 2000.

Tintinalli JE, Stapczynski JS, Kelen GD (Editors). *Emergency medicine plus*. CD-ROM version 2.0. New York, NY: McGraw-Hill Professional; 2001.

Uphold CR. Musculoskeletal problems. In: Uphold CR, Graham MV (Editors). *Clinical guidelines in family practice*. 4th ed. Gainesville, FL: Barmarrae Books, Inc.; 2003. p. 787-874.

JOURNAL ARTICLES

A Clear Vision. Solutions to Canada's Vision Loss Crisis. Toronto, ON: Canterbury Communications; 2004. Available at: www.costofblindness.org

American Association of Clinical Endocrinologists. Medical guidelines for clinical practice for the evaluation and treatment of hyperthyroidism and hypothyroidism. *Endocrine Practice* 2002;8(6):457-69.

Ardern CI, Katzmarzyk PT. Geographic and demographic variation in the prevalence of the metabolic syndrome in Canada. *Can J Diabetes* 2007;31(1):34-46.

Assembly of First Nations. (2007). *Quick facts – RHS 2002/03*. Selected results from RHS Phase 1 (2002/03). Available at: <http://www.rhs-ers.ca/facts>

Barton SS. Discovering the literature on Aboriginal diabetes in Canada: A focus on holistic methodologies. *Can J Nursing Research* 2008;40(4):26-54.

Brown JP, Fortier M, Osteoporosis Guidelines Committee. Canadian consensus conference on Osteoporosis, 2006 update. *Journal of Obstetrics and Gynaecology Canada* 2006;28 (Special Edition 1):s95-s112.

Brown JP, Josse RG and The Scientific Advisory Council of the Osteoporosis Society of Canada. 2002 clinical practice guidelines for the diagnosis and management of osteoporosis in Canada. *CMAJ* 2002;167(10 suppl):S1-S34. Available at: http://www.cmaj.ca/cgi/data/167/10_suppl/s1/DC1/1

Bruce SG, Kliewer EV, Young TK, Mayer T, Wajda A. Diabetes among the Métis of Canada: Defining the population, estimating the disease. *Can J Diabetes* 2003;27(4):442-48.

Canadian Diabetes Association. (2005–2009). *Diabetes facts*. Retrieved June 14, 2009, from <http://www.diabetes.ca/about-diabetes/what/facts/>

- Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. (2008). Canadian Diabetes Association 2008 clinical practice guidelines for the prevention and management of diabetes in Canada. *Can J Diabetes* 2008;32(suppl 1):S1-S201. Available at: <http://www.diabetes.ca/for-professionals/resources/2008-cpg/>
- Canadian Hypertension Education Program. (2008). *2008 CHEP recommendations for the management of hypertension*. Available at: <http://www.hypertension.ca/chep/recommendations/recommendations-overview/>
- Canadian Ophthalmological Society Clinical Practice Guideline Expert Committee. (2007). *Canadian Ophthalmological Society evidence-based clinical practice guidelines for the periodic eye examination in adults in Canada*. Available at: http://www.eyesite.ca/english/program-and-services/policy-statements-guidelines/CPG-periodic-eye-exam_e.pdf
- Chieh-Hsiang L, Yuan-Hong Y. Risperidone-associated newly diagnosed diabetes and fatal diabetes ketoacidosis in a young schizophrenic patient. *Diabetes Research and Clinical Practice* 2009;83:e66-e67.
- Chiasson JL, Aris-Jilwan N, Bélanger R, et al. Diagnosis and treatment of diabetic ketoacidosis and the hyperglycemic hyperosmolar state. *CMAJ* 2003;168(7):859-66. Available at: <http://www.cmaj.ca/cgi/content/full/168/7/859>
- Deen D. Metabolic syndrome: Time for action. *Am Fam Physician* 2004;69(12):2875-82.
- Depres JP, Poirier P, Bergeron J, Tremblay A, et al. From individual risk factors and the metabolic syndrome to global cardiometabolic risk. *European Heart Journal Supplements* 2008; 10(Suppl. 8):824-33.
- Dyck R, Klomp H, Tan LK, Turnell RW, Bockor MA. A comparison of rates, risk factors, and outcomes of gestational diabetes between Aboriginal and non-Aboriginal women in the Saskatoon health district. *Diabetes Care* 2002;25(3):487-93.
- Genest J, Frohlich J, Fodor G, McPherson R. Recommendations for the management of dyslipidemia and the prevention of cardiovascular disease: 2003 update. *CMAJ* 2003;169(9):921. Available at: <http://www.cmaj.ca/cgi/data/169/9/921/DC1/1>
- George K, Alberti MM, Zimmet P, Shaw J. The metabolic syndrome – a new worldwide definition. *The Lancet* 2005;366:1059-61.
- Guidelines & Protocols Advisory Committee. (2004). *Thyroid disease – Thyroid function tests in the diagnosis and monitoring of adults*. Available at: <http://www.bcguidelines.ca/gpac/pdf/thyroid.pdf>
- Giugliano D, Ceriello A, Esposito K. Are there specific treatments for the metabolic syndrome? *Am J Clinical Nutrition* 2008;87(8):8-11.
- Guize L, Thomas F, Pannier B, Bean K, et al. All-cause mortality associated with specific combinations of the metabolic syndrome according to recent definitions. *Diabetes Care* 2007;30(9):2381-87.
- Harris SB, et al. (1997). The prevalence of NIDDM and associated risk factors in native Canadians. *Diabetes Care* 1997;20(2):185-87.
- Health Canada. *Diabetes among Aboriginal peoples in Canada: The evidence*. Ottawa, ON: Health Canada; 2000.
- International Diabetes Federation. (2005). *The IDF consensus worldwide definition of the metabolic syndrome*. Available at: http://www.idf.org/webdata/docs/MetS_def_update2006.pdf
- Khan AA, Hodsman AB, Papaioannou A, Kendler D et al. Management of osteoporosis in men: An update and case example. *CMAJ* 2007;176(3):345-48.
- Koul PB. Diabetic ketoacidosis: A current appraisal of pathophysiology and management. *Clinical Pediatrics* 2009;48(2):135-44.
- Lau DCW, et al. 2006 Canadian clinical practice guidelines on the management and prevention of obesity in adults and children [summary]. *CMAJ* 2007;176(8):s1-s13.
- Ley S, et al. Metabolic syndrome and its components as predictors of incident type 2 diabetes mellitus in an Aboriginal community. *CMAJ* 2009;180(6):617-24.
- Lois K, Young J, Kumar S. Obesity: Epiphenomenon or cause of metabolic syndrome? *International Journal of Clinical Practice* 2008;62(6):932-38.
- Lucove J, Vupputuri S, Heiss G, North K, Russell M. Metabolic syndrome and the development of CKD in American Indians: The strong heart study. *American Journal of Kidney Diseases* 2008;51(1):21-28.
- Mayo Clinic staff. (2007, November 7). *Metabolic syndrome*. Available at: <http://www.mayoclinic.com/print/metabolic%20syndrome/DS00522/DSECTION=all&METHOD=print>

- Meigs JB. (2009, January). *The metabolic syndrome (insulin resistance syndrome or syndrome X)*. Available by subscription: www.uptodate.com
- Merck. (2007). *Lead Poisoning (Plumbism)*. The Merck Manuals Online Medical Library. Available at: <http://www.merck.com/mmpe/sec21/ch326/ch326m.html>
- Newcomer JW. Metabolic syndrome and mental illness. *American Journal of Managed Care* 2007;13(7):s170-s177.
- Olufadi R, Byrne CD. Clinical and laboratory diagnosis of the metabolic syndrome. *Journal of Clinical Pathology* 2007;61:697-706.
- Ontario Association of Medical Laboratories. (2007). *Guideline for the use of laboratory tests to detect thyroid dysfunction*. Available at: <http://www.oaml.com/PDF/FINALTSH%20Guideline%20July%2018,%2007.pdf>
- Orchard TJ, et al. The effect of metformin and intensive lifestyle intervention on the metabolic syndrome: The diabetes prevention program randomized trial. *Annals of Internal Medicine* 2005;142(8):611-19.
- Plante C, Blanchet C, Turgeon-O'Brien H. (2004). *Nunavik Inuit health survey*. Available at: http://www.inspq.qc.ca/pdf/publications/774_ESISurveyHighlights.pdf
- Pollex R L, Hanley AJG, Zinman B, Harris SB, et al. Metabolic syndrome in Aboriginal Canadians: Prevalence and genetic associations. *Atherosclerosis* 2005;184:121-29.
- Public Health Agency of Canada. (2008). *The face of diabetes in Canada*. Available at: <http://www.phac-aspc.gc.ca/cd-mc/diabetes-diabete/face-eng.php>
- Registered Nurses Association of Ontario. (2004). *Reducing foot complications for people with diabetes. Nursing Best Practice Guidelines Project*. Available at: <http://www.rnao.org/Page.asp?PageID=924&ContentID=815>
- Registered Nurses Association of Ontario. (2005). *Assessment and management of foot ulcers for people with diabetes. Nursing Best Practice Guidelines Project*. Available at: <http://www.rnao.org/Page.asp?PageID=924&ContentID=719>
- Rosenson RS. (2009 January). *Treatment of lipid disorders in secondary prevention*. Available by subscription: www.uptodate.com
- Salas-Salvado J, et al. (2008). Effect of a Mediterranean diet supplemented with nuts on metabolic syndrome status. *Archives of Internal Medicine* 2008;168(22):2449-58.
- Surks MI, et al. (2004). Subclinical thyroid disease: Scientific review and guidelines for diagnosis and management. *JAMA* 2004;291(2):228-38.
- The ADVANCE Collaborative Group. Intensive blood glucose control and vascular outcomes in patients with type 2 diabetes. *New England Journal of Medicine* 2008;358:2560-72.
- The Kidney Foundation of Canada. (2009 Winter). *Facing the facts*. Available at: <http://204.92.98.244/Document.Doc?id=102>
- Thyroid Foundation of Canada. (N.D.a). *Thyroid conditions – Diagnosis confirmation*. Available at: http://www.thyroid.ca/clinical_diagnosis.php
- Thyroid Foundation of Canada. (N.D.b). *Thyroid Conditions – Hyperthyroid*. Available at: <http://www.thyroid.ca/thyrotoxicosis.php>
- Thyroid Foundation of Canada. (N.D.c). *Thyroid Conditions – Hypothyroid*. Available at: <http://www.thyroid.ca/hypothyroidism.php>
- Toward Optimized Practice Clinical Practice Guideline Working Group. (2008). *Clinical practice guideline: Investigation and management of primary thyroid dysfunction*. Available at: http://www.topalbertadoctors.org/informed_practice/clinical_practice_guidelines/complete%20set/Thyroid%20Dysfunction/thyroid_guideline.pdf
- UK Prospective Diabetes Study Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). *Lancet* 1998;352(9131):837-53.
- Up To Date. (2009). *The patient with brittle diabetes mellitus*. Available by subscription: www.uptodate.com
- Weir E, Lipsombe L. Metabolic syndrome: Waist not want not. *CMAJ* 2004;170(9):1390-91.
- Young TK, Reading J, Elias B, O'Neil JD. (2000). Type 2 diabetes mellitus in Canada's First Nations: Status of an epidemic in progress. *CMAJ* 2000;163(5):561-66.

APPENDIX A

Summary of nutritional considerations for people with diabetes¹⁷⁶

People with diabetes should follow Eating Well with Canada's Food Guide*

- Eat at least 1 dark green and 1 orange vegetable each day; have vegetables and fruit more often than juice
- Make at least half of your grain products whole grain, each day
- Drink lower-fat milk
- Have meat alternatives such as beans, lentils or tofu often
- Eat at least 2 servings of fish each week
- Achieve and maintain a healthy body weight by being active
- Enjoy foods with little or no added fat, sugar or salt
- Satisfy thirst with water

Carbohydrate (45–60% of energy)

- Up to 60 g of added fructose (for example, fructose-sweetened beverages and foods) in place of an equal amount of sucrose is acceptable
- Intake of < 10 g/day of sugar alcohols (malitol, mannitol, sorbitol, lactitol, isomalt and xylitol) is acceptable
- The use of acesulfame potassium, aspartame, cyclamates, saccharin and sucralose is acceptable
- Include vegetables, fruit, whole grains and milk
- Within the same food category, consume low-glycemic-index foods in place of high-glycemic-index foods
- Increase dietary fibre to 25–50 g/day from a variety of sources, including soluble and cereal fibres
- Sucrose intake of up to 10% of total daily energy is acceptable

Protein (15–20% of energy)

- There is no evidence to suggest that usual recommended protein intake should be modified.

Fat (< 35% of energy)

- Restrict saturated fats to < 7% of total energy intake and restrict trans fat intake to a minimum
- Limit polyunsaturated fat to < 10% of energy intake
- Consume monounsaturated fats instead of saturated fats more often
- Include foods rich in polyunsaturated omega-3 fatty acids and plant oils

Vitamin and mineral supplements

- Routine supplementation is not necessary, except for Vitamin D in persons > 50 years and folic acid in women who could become pregnant
- In the case of an identified deficiency, limited dietary intake or special needs, supplementation may be recommended

Alcohol

- People using insulin or insulin secretagogues should be aware of the risk of delayed hypoglycemia that can occur up to 24 hours after alcohol consumption
- Limit intake to 1–2 drinks per day (\leq 14 standard drinks per week for men and \leq 9 per week for women)
- Standard drinks: 12 oz (341 mL) beer, 5 oz (142 mL) table wine, 1.5 oz (43 mL) spirits, 3 oz (85 mL) fortified wine (for example, sherry, port)

* Also see “Eating Well with Canada's Food Guide – First Nations, Inuit and Métis”. Available at: <http://www.hc-sc.gc.ca/fn-an/food-guide-aliment/fnim-pnim/index-eng.php>

APPENDIX B

Aerobic Exercise¹⁷⁷

Definition and recommended frequency	Intensity	Examples
<p>Rhythmic, repeated and continuous movements of the same large muscle group for at least 10 minutes at a time.</p> <p>Recommended for a minimum 150 minutes per week (moderate intensity); spread over at least 3 days of the week, with no more than 2 consecutive days without exercise.</p>	<p>Moderate:</p> <p>50–70% of a person's maximum heart rate</p>	<ul style="list-style-type: none"> • Biking • Brisk walking • Continuous swimming • Dancing • Raking leaves • Water aerobics
	<p>Vigorous:</p> <p>> 70% of a person's maximum heart rate</p>	<ul style="list-style-type: none"> • Brisk walking up an incline • Jogging • Aerobics • Hockey • Basketball • Fast swimming • Fast dancing

Resistance Exercise

Definition	Recommended frequency	Examples
<p>Activities that use muscular strength to move a weight or work against a resistant load.</p> <p>Initial instruction and periodic supervision of resistance exercise programs are required.</p>	<p>3 times per week</p> <ul style="list-style-type: none"> • Start with 1 set of 10–15 repetitions at moderate weight • Progress to 2 sets of 10–15 repetitions • Progress to 3 sets of 8 repetitions at heavier weight 	<ul style="list-style-type: none"> • Exercise with weight machines • Weight lifting

APPENDIX C

Diabetes and Foot Care: A Client's Checklist¹⁷⁸

DO...	DON'T...
...check your feet every day for cuts, cracks, bruises, blisters, sores, infections or unusual markings.	...cut your own corns or calluses.
...use a mirror to see the bottom of your feet if you can't lift them up.	...treat your own in-growing toenails or slivers with a razor or scissors. See your nurse, nurse practitioner, doctor or foot care specialist.
...check the colour of your legs and feet. If there is swelling, warmth or redness or if you have pain, see your doctor or foot specialist right away.	...use over-the-counter medications to treat corns and warts. They are dangerous for people with diabetes.
...clean a cut or scratch with a milk soap and water and cover with a dry dressing for sensitive skin.	...apply heat to your feet with a hot water bottle or electric blanket. You could burn your feet without realizing it.
...trim your nails straight across.	...soak your feet.
...wash and dry your feet every day, especially between the toes.	...take very hot baths.
...apply a good skin lotion every day on your heels and soles. Wipe off any excess lotion.	...use lotion between your toes.
...change your socks every day.	...walk barefoot inside or outside.
...always wear a good supportive shoe.	...wear tight socks, garters or elastics, or knee highs.
...always wear professionally fitted shoes from a reputable store. Professionally fitted orthotics may help.	...wear over-the-counter insoles – they can cause blisters if they are not right for your feet.
...choose shoes with low heels (under 5 cm high).	...sit for long periods of time.
...buy shoes in the late afternoon (since your feet swell slightly by then).	...smoke.
...avoid extreme cold and heat (including the sun).	
...exercise regularly.	
...see a foot care specialist if you need advice or treatment.	

APPENDIX D

Sample Flow Sheet for Adults with Diabetes¹⁷⁹

Care	Objective	Target
Self-monitoring of blood glucose	<ul style="list-style-type: none"> Reinforce patient's responsibility for regular monitoring as appropriate Ensure patient can use glucose meter, interpret SMBG results and modify treatment as needed Develop an SMBG schedule with patient and review record 	Preprandial (mmol/L) 4.0–7.0 for most patients 2- hour postprandial (mmol/L) 5.0–10.0 for most patients 5.0–8.0 if not achieving A1C target
Blood glucose control	<ul style="list-style-type: none"> Measure A1C every 3 months for most adults Consider testing at least every 6 months in adults during periods of treatment and lifestyle stability, and when glycemic targets are being consistently achieved 	A1C ≤ 7.0% for most patients See «Targets» , p. S29
Blood glucose meter accuracy	<ul style="list-style-type: none"> Compare meter results with laboratory measurements at least annually, and when indicators of glycemic control do not match meter 	Simultaneous fasting glucose/meter lab comparison within 20%
Hypertension	<ul style="list-style-type: none"> Measure BP at diagnostic of diabetes and at every diabetes clinic visit 	< 130/80 mm Hg
Waist circumference	<ul style="list-style-type: none"> Measure as an indicator of abdominal fat 	Target WC: M < 102 cm; F < 88 cm (see ethnic specific values in « Management of Obesity in diabetes, » p. S77)
Body mass index	<ul style="list-style-type: none"> Calculate BMI: mass in kg/(height in m)² 	Target BMI: 18.5–24.9 kg/m²
Nutrition	<ul style="list-style-type: none"> Encourage nutrition therapy (by Register Dietitian) as an integral part of treatment and self-management (can reduce A1C by 1 %–2 %) 	Meet nutritional needs by following <i>Eating Well with Canadian's Food Guide</i>
Physical activity	<ul style="list-style-type: none"> Discuss and encourage aerobic and resistance exercise Consider exercise ECG stress test for previously sedentary individuals at high risk for CAD planning exercise more vigorous than brisk walking 	Aerobic: ≥ 150 minutes/week Resistance: 3 sessions/week
Smoking	<ul style="list-style-type: none"> Encourage patient to stop at each visit; provide support as needed 	Smoking cessation
Retinopathy	<ul style="list-style-type: none"> Type 1 diabetes: Screen 5 years after diagnosis, then rescreen annually Type 2 diabetes: Screen at diagnosis, then every 1–2 years if no retinopathy present Screening should be conducted by an experienced eye care professional 	Early detection and treatment
Chronic kidney disease	<ul style="list-style-type: none"> Identification of CKD requires screening for proteinuria using random urine ACR and assessment of renal function using a serum creatinine converted to eGFR Type 1 diabetes: In adults, screen after 5 years duration of diabetes, then annually if no CKD Type 2 diabetes: Screen at diagnosis, then annually if no CKD If CKD present, perform ACR and eGFR at least every 6 months 	ACR (mg/mmol) Normal: M < 2.0; F < 2.8 Microalbuminuria: M 2.0–20.0; F 2.8–28.0 Macroalbuminuria: M > 20.0; F > 28.0 CKD if eGFRt ≤ 60 mL/min

Care	Objective	Target
Neuropathy/ foot examination	<ul style="list-style-type: none"> • Type 1 diabetes: Screen 5 years after diagnosis, then rescreen annually • Type 2 diabetes: Screen at diagnosis, then annually • Screen for neuropathy with 10-g monofilament or 128-Hz tuning fork at dorsum of great toe. In foot exam, look for structural abnormalities, neuropathy, arterial disease, ulceration, infection 	<p>Early detection and treatment</p> <p>If neuropathy present: foot care education, specialized footwear, smoking cessation</p> <p>If ulcer present: manage by multidisciplinary team with expertise</p>
CAD assessment	<ul style="list-style-type: none"> • Conduct CAD risk assessment periodically: CV history, lifestyle, duration of diabetes, sexual function, abdominal obesity, lipid profile, BP, reduced pulse, bruits, glycemic control, eGFR, ACR • Measure baseline resting ECG, then 2 years if: > 40 years, duration of diabetes > 15 years, symptoms, hypertension, proteinuria, bruits or reduced pulse • High-risk categories include: <ul style="list-style-type: none"> • Men ≥ 45 years, women ≥ 50 years or • Men < 45 years, women < 50 years with ≥ 1 of macrovascular disease microvascular disease (especially retinopathy, nephropathy), multiple additional risk factors (especially family history of premature coronary or cerebrovascular disease in 1st-degree relative), extreme single risk (for example, LDL-C > 5.0 mmol/L, systolic BP > 180 mm Hg) or duration of diabetes > 15 years and age > 30 years 	<p>Vascular protection: first priority in prevention of diabetes complications is reduction of CV risk by vascular protection through a comprehensive multifaceted approach:</p> <ul style="list-style-type: none"> • All people with diabetes: optimize BP, glycemic control and lifestyle (weight, exercise, smoking) • People with diabetes and at high risk of CV event, additional interventions: ACE inhibitor/ARB antiplatelet therapy (as indicated) and lipid lowering medication (primarily statins)
Dyslipidemia	<ul style="list-style-type: none"> • Measure fasting lipid levels (TC, HDL-C, TG and calculated LDL-C) at diagnosis of diabetes, then every 1–3 years as clinically indicated. Test more frequently is treatment initiated. 	<p>Lipid targets for those at high risk for CAD:</p> <ul style="list-style-type: none"> • Primary target: LDL-C ≤ 2.0 mmol/L • Secondary target: TC/C HDL-C < 4.0 mmol/L

Care objectives: People with diabetes will have better outcomes if primary healthcare providers: 1) identify patient with diabetes in their practice; 2) assist them by incorporating the suggested care objectives; 3) schedule diabetes-focused visits; and 4) use diabetes patient care flow sheets and systematic recall for visits.

APPENDIX E

Laboratory diagnostic criteria for Diabetic Ketoacidosis (DKA) and Hyperosmolar Hyperglycemic State (HHS)¹⁸⁰

Parameter	Normal range	DKA	HHS
Plasma glucose level, mmol/L	4.2–6.4	≥ 14	≥ 34
Arterial pH ¹	7.35–7.45	≤ 7.30	> 7.30
Serum bicarbonate level, mmol/L	22–28	≤ 15	> 15
Effective serum osmolality, mmol/kg	275–295	≤ 320	> 320
Anion gap, mmol/L ²	< 12	> 12	Variable
Serum ketones	Negative	Moderate to high	None or trace
Urine ketones	Negative	Moderate to high	None or trace

1 If venous pH is used, a correction of 0.03 must be made.

2 Calculation: $\text{Na} - (\text{Cl} + \text{HCO}_3)$

END NOTES

- 1 Anemia Review Panel. *Anemia guidelines for family medicine*. 2nd ed. Toronto, ON: MUMS Guideline Clearinghouse; 2008. p. v.
- 2 Anemia Review Panel. *Anemia guidelines for family medicine*. 2nd ed. Toronto, ON: MUMS Guideline Clearinghouse; 2008. p. 3.
- 3 Anemia Review Panel. *Anemia guidelines for family medicine*. 2nd ed. Toronto, ON: MUMS Guideline Clearinghouse; 2008. p. 49.
- 4 Anemia Review Panel. *Anemia guidelines for family medicine*. 2nd ed. Toronto, ON: MUMS Guideline Clearinghouse; 2008. p. 56.
- 5 Anemia Review Panel. *Anemia guidelines for family medicine*. 2nd ed. Toronto, ON: MUMS Guideline Clearinghouse; 2008. p. 2.
- 6 Harding SR. Common anemias. In: Gray J (Editor-in-chief). *Therapeutic choices*. 5th ed. Ottawa, ON: Canadian Pharmacists Association; 2007. p. 1120.
- 7 Anemia Review Panel. *Anemia guidelines for family medicine*. 2nd ed. Toronto, ON: MUMS Guideline Clearinghouse; 2008. p. 2-4.
- 8 Anemia Review Panel. *Anemia guidelines for family medicine*. 2nd ed. Toronto, ON: MUMS Guideline Clearinghouse; 2008. p. 34.
- 9 Plante C, Blanchet C, Turgeon-O'Brien H. (2004). *Nunavik Inuit Health Survey 2004 – Survey Highlights*. Available at: http://www.inspq.qc.ca/pdf/publications/774_ESISurveyHighlights.pdf
- 10 Mansen TJ, McCance KL. (2006). Alterations of erythrocyte function. In: McCance KL, Huether SE (Editors). *Pathophysiology: The biologic basis for disease in adults and children*. 5th ed. St. Louis, MO: Elsevier Mosby. p. 934.
- 11 Graham MV. (2003). Hematologic problems. In: Uphold CR, Graham MV (Editors). *Clinical guidelines in family practice*. 4th ed. Gainesville, FL: Barmarrae Books, Inc.; 2003. p. 926.
- 12 Graham MV. (2003). Hematologic problems. In: Uphold CR, Graham MV (Editors). *Clinical guidelines in family practice*. 4th ed. Gainesville, FL: Barmarrae Books, Inc.; 2003. p. 927.
- 13 Anemia Review Panel. *Anemia guidelines for family medicine*. 2nd ed. Toronto, ON: MUMS Guideline Clearinghouse; 2008. p. 35-36.
- 14 Harding SR. Common anemias. In: Gray J (Editor). *Therapeutic choices*. 5th ed. Ottawa, ON: Canadian Pharmacists Association; 2007. p. 1114.
- 15 Harding SR. Common anemias. In: Gray J (Editor). *Therapeutic choices*. 5th ed. Ottawa, ON: Canadian Pharmacists Association; 2007. p. 1116.
- 16 Alleyne M, et al. Individualized treatment for iron-deficiency anemia in adults. *Am J Med* 2008; 121:943-48.
- 17 Harding SR. Common anemias. In: Gray J (Editor). *Therapeutic choices*. 5th ed. Ottawa, ON: Canadian Pharmacists Association; 2007. p. 1115.
- 18 Anemia Review Panel. *Anemia guidelines for family medicine*. 2nd ed. Toronto, ON: MUMS Guideline Clearinghouse; 2008. p. 35.
- 19 Anemia Review Panel. *Anemia guidelines for family medicine*. 2nd ed. Toronto, ON: MUMS Guideline Clearinghouse; 2008. p. 51-54.
- 20 Harding SR. Common anemias. In: Gray J (Editor). *Therapeutic choices*. 5th ed. Ottawa, ON: Canadian Pharmacists Association; 2007. p. 1117.
- 21 Graham MV. (2003). Hematologic problems. In: Uphold CR, Graham MV (Editors). *Clinical guidelines in family practice*. 4th ed. Gainesville, FL: Barmarrae Books, Inc.; 2003. p. 930.
- 22 Schrier SL. (2009, September). Diagnosis and treatment of vitamin B₁₂ and folic acid deficiency. Available by subscription: www.uptodate.com
- 23 Harding SR. Common anemias. In: Gray J (Editor). *Therapeutic choices*. 5th ed. Ottawa, ON: Canadian Pharmacists Association; 2007. p. 1118.
- 24 Anemia Review Panel. *Anemia guidelines for family medicine*. 2nd ed. Toronto, ON: MUMS Guideline Clearinghouse; 2008. p. 2-4.
- 25 Mansen TJ, McCance KL. (2006). Alterations of erythrocyte function. In: McCance KL, Huether SE (Editors). *Pathophysiology: The biologic basis for disease in adults and children*. 5th ed. St. Louis, MO: Elsevier Mosby. p. 946.
- 26 Anemia Review Panel. *Anemia guidelines for family medicine*. 2nd ed. Toronto, ON: MUMS Guideline Clearinghouse; 2008. p. 46.
- 27 Anemia Review Panel. *Anemia guidelines for family medicine*. 2nd ed. Toronto, ON: MUMS Guideline Clearinghouse; 2008. p. 38.
- 28 Mansen TJ, McCance KL. (2006). Alterations of erythrocyte function. In: McCance KL, Huether SE (Editors). *Pathophysiology: The biologic basis for disease in adults and children*. 5th ed. St. Louis, MO: Elsevier Mosby. p. 938.
- 29 Mansen TJ, McCance KL. (2006). Alterations of erythrocyte function. In: McCance KL, Huether SE (Editors). *Pathophysiology: The biologic basis for disease in adults and children*. 5th ed. St. Louis, MO: Elsevier Mosby. p. 56.
- 30 Merck. (2007). *Lead Poisoning (Plumbism)*. The Merck Manuals Online Medical Library. Available at: <http://www.merck.com/mmpe/sec21/ch326/ch326m.html>

- 31 Mansen TJ, McCance KL. (2006). Alterations of erythrocyte function. In: McCance KL, Huether SE (Editors). *Pathophysiology: The biologic basis for disease in adults and children*. 5th ed. St. Louis, MO: Elsevier Mosby. p. 942-943.
- 32 Anemia Review Panel. *Anemia guidelines for family medicine*. 2nd ed. Toronto, ON: MUMS Guideline Clearinghouse; 2008. p. 4.
- 33 Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. (2008). Canadian Diabetes Association 2008 clinical practice guidelines for the prevention and management of diabetes in Canada. *Can J Diabetes* 2008;32(suppl 1):S1-201. Available at: <http://www.diabetes.ca/for-professionals/resources/2008-cpg/>
- 34 Public Health Agency of Canada. (2008). *The face of diabetes in Canada*. Available at: <http://www.phac-aspc.gc.ca/cd-mc/diabetes-diabete/face-eng.php>
- 35 Canadian Diabetes Association. (2005-2009). *Diabetes facts*. Available at: <http://www.diabetes.ca/about-diabetes/what/facts/>
- 36 Dyck R, Osgood N, Lin TH, Gao A, Stang MR. Epidemiology of diabetes mellitus among First Nations and non-First Nations adults. *CMAJ* 2010; DOI:10.1503/cmaj.090846. p. 1. Available at: <http://www.cmaj.ca/cgi/rapidpdf/cmaj.090846v1.pdf>
- 37 Health Canada. *Diabetes among Aboriginal peoples in Canada: The evidence*. Ottawa, ON: Health Canada; 2000. p. 3.
- 38 Dyck R, Klomp H, Tan LK, Turnell RW, Boctor MA. A comparison of rates, risk factors, and outcomes of gestational diabetes between Aboriginal and non-Aboriginal women in the Saskatoon health district. *Diabetes Care* 2002;25(3):488.
- 39 Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Canadian Diabetes Association 2008 clinical practice guidelines for the prevention and management of diabetes in Canada. *Can J Diabetes* 2008;32(suppl 1):S11. Available at: <http://www.diabetes.ca/for-professionals/resources/2008-cpg/>
- 40 Jones RE, Heuther SE. Alterations of hormonal function. In: McCance KL, Huether SE (Editors). *Pathophysiology: The biologic basis for disease in adults and children*. 5th ed. St. Louis, MO: Elsevier Mosby; 2006. p. 703.
- 41 Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Canadian Diabetes Association 2008 clinical practice guidelines for the prevention and management of diabetes in Canada. *Can J Diabetes* 2008;32(suppl 1):S14. Available at: <http://www.diabetes.ca/for-professionals/resources/2008-cpg/>
- 42 Canadian Diabetes Association. (2005-2009). *Diabetes facts*. Available at: <http://www.diabetes.ca/about-diabetes/what/facts/>
- 43 Goodman JJ, Uphold CR. Metabolic and endocrine problems. In: Uphold CR, Graham MV (Editors). *Clinical guidelines in family practice*. 4th ed. Gainesville, FL: Barmarrae Books, Inc.; 2003. p. 164-165.
- 44 Goodman JJ, Uphold CR. Metabolic and endocrine problems. In: Uphold CR, Graham MV (Editors). *Clinical guidelines in family practice*. 4th ed. Gainesville, FL: Barmarrae Books, Inc.; 2003. p. 166.
- 45 Goodman JJ, Uphold CR. Metabolic and endocrine problems. In: Uphold CR, Graham MV (Editors). *Clinical guidelines in family practice*. 4th ed. Gainesville, FL: Barmarrae Books, Inc.; 2003. p. 165.
- 46 Risks and side effects associated with estrogen-progestin contraceptives. (2009, September). UpToDate_online 17.3. Available by subscription: www.uptodate.com
- 47 Jones RE, Heuther SE. Alterations of hormonal function. In: McCance KL, Huether SE (Editors). *Pathophysiology: The biologic basis for disease in adults and children*. 5th ed. St. Louis, MO: Elsevier Mosby; 2006. p. 710-720.
- 48 Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Canadian Diabetes Association 2008 clinical practice guidelines for the prevention and management of diabetes in Canada. *Can J Diabetes* 2008;32(suppl 1):S10-11, S100, S112, S130.
- 49 Goodman JJ, Uphold CR. Metabolic and endocrine problems. In: Uphold CR, Graham MV (Editors). *Clinical guidelines in family practice*. 4th ed. Gainesville, FL: Barmarrae Books, Inc.; 2003. p. 168.
- 50 Barton SS. Discovering the literature on Aboriginal diabetes in Canada: A focus on holistic methodologies. *Can J Nursing Research* 2008;40(4):27.
- 51 Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Canadian Diabetes Association 2008 clinical practice guidelines for the prevention and management of diabetes in Canada. *Can J Diabetes* 2008;32(suppl 1):S30. Available at: <http://www.diabetes.ca/for-professionals/resources/2008-cpg/>
- 52 Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Canadian Diabetes Association 2008 clinical practice guidelines for the prevention and management of diabetes in Canada. *Can J Diabetes* 2008;32(suppl 1):S40-43. Available at: <http://www.diabetes.ca/for-professionals/resources/2008-cpg/>

- 53 Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Canadian Diabetes Association 2008 clinical practice guidelines for the prevention and management of diabetes in Canada. *Can J Diabetes* 2008;32(suppl 1):S37-39. Available at: <http://www.diabetes.ca/for-professionals/resources/2008-cpg/>
- 54 Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Canadian Diabetes Association 2008 clinical practice guidelines for the prevention and management of diabetes in Canada. *Can J Diabetes* 2008;32(suppl 1):S77. Available at: <http://www.diabetes.ca/for-professionals/resources/2008-cpg/>
- 55 Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Canadian Diabetes Association 2008 clinical practice guidelines for the prevention and management of diabetes in Canada. *Can J Diabetes* 2008;32(suppl 1):S32-34, S200. Available at: <http://www.diabetes.ca/for-professionals/resources/2008-cpg/>
- 56 Canadian Agency for Drugs and Technologies in Health (CADTH). (2009, December). Optimal Therapy report COMPUS – Summary report: Optimal prescribing and use of blood glucose test strips for self-monitoring of blood glucose. p. 5. Available at: http://www.cadth.ca/media/pdf/C1109_bgts_summary_report_e.pdf
- 57 Registered Nurses Association of Ontario. (2004). *Reducing foot complications for people with diabetes. Nursing Best Practice Guidelines Project*. p. 31 Available at: <http://www.rnao.org/Page.asp?PageID=924&ContentID=815>
- 58 Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Canadian Diabetes Association 2008 clinical practice guidelines for the prevention and management of diabetes in Canada. *Can J Diabetes* 2008;32(suppl 1):S25-27. Available at: <http://www.diabetes.ca/for-professionals/resources/2008-cpg/>
- 59 Lau DCW, et al. 2006 Canadian clinical practice guidelines on the management and prevention of obesity in adults and children [summary]. *CMAJ* 2007;176(8):s4.
- 60 Goodman JJ, Uphold CR. Metabolic and endocrine problems. In: Uphold CR, Graham MV (Editors). *Clinical guidelines in family practice*. 4th ed. Gainesville, FL: Barmarrae Books, Inc.; 2003. p. 169.
- 61 Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Canadian Diabetes Association 2008 clinical practice guidelines for the prevention and management of diabetes in Canada. *Can J Diabetes* 2008;32(suppl 1):S42, S46-49. Available at: <http://www.diabetes.ca/for-professionals/resources/2008-cpg/>
- 62 Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Canadian Diabetes Association 2008 clinical practice guidelines for the prevention and management of diabetes in Canada. *Can J Diabetes* 2008;32(suppl 1):S3-58. Available at: <http://www.diabetes.ca/for-professionals/resources/2008-cpg/>
- 63 Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Canadian Diabetes Association 2008 clinical practice guidelines for the prevention and management of diabetes in Canada. *Can J Diabetes* 2008;32(suppl 1):S56. Available at: <http://www.diabetes.ca/for-professionals/resources/2008-cpg/>
- 64 Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Canadian Diabetes Association 2008 clinical practice guidelines for the prevention and management of diabetes in Canada. *Can J Diabetes* 2008;32(suppl 1):S54-55. Available at: <http://www.diabetes.ca/for-professionals/resources/2008-cpg/>
- 65 Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Canadian Diabetes Association 2008 clinical practice guidelines for the prevention and management of diabetes in Canada. *Can J Diabetes* 2008;32(suppl 1):S102-05. Available at: <http://www.diabetes.ca/for-professionals/resources/2008-cpg/>
- 66 Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Canadian Diabetes Association 2008 clinical practice guidelines for the prevention and management of diabetes in Canada. *Can J Diabetes* 2008;32(suppl 1):S102. Available at: <http://www.diabetes.ca/for-professionals/resources/2008-cpg/>
- 67 Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Canadian Diabetes Association 2008 clinical practice guidelines for the prevention and management of diabetes in Canada. *Can J Diabetes* 2008;32(suppl 1):S95, S96, S107-12, S115-17. Available at: <http://www.diabetes.ca/for-professionals/resources/2008-cpg/>

- 68 Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Canadian Diabetes Association 2008 clinical practice guidelines for the prevention and management of diabetes in Canada. *Can J Diabetes* 2008;32(suppl 1):S25-27, S32-34, S82-83, S86, S99-100, S107-12, S115-16, S134-36, S140-41, S143-44, S147-48. Available at: <http://www.diabetes.ca/for-professionals/resources/2008-cpg/>
- 69 Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Canadian Diabetes Association 2008 clinical practice guidelines for the prevention and management of diabetes in Canada. *Can J Diabetes* 2008;32(suppl 1):S17. Available at: <http://www.diabetes.ca/for-professionals/resources/2008-cpg/>
- 70 Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Canadian Diabetes Association 2008 clinical practice guidelines for the prevention and management of diabetes in Canada. *Can J Diabetes* 2008;32(suppl 1):S14-16, S77, S80. Available at: <http://www.diabetes.ca/for-professionals/resources/2008-cpg/>
- 71 Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Canadian Diabetes Association 2008 clinical practice guidelines for the prevention and management of diabetes in Canada. *Can J Diabetes* 2008;32(suppl 1):S29. Available at: <http://www.diabetes.ca/for-professionals/resources/2008-cpg/>
- 72 Holman RR, Paul SK, Bethel MA, Matthews DR, Neil HAW. 10-Year follow-up of intensive glucose control in type 2 diabetes. *N Eng J Med* 2008;359:1577.
- 73 Gaede P, Vedel P, Larsen N, Jensen GvH, et al. Multifactorial intervention and cardiovascular disease in patients with type 2 diabetes. *N Engl J Med* 2003;348(5):383.
- 74 Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Canadian Diabetes Association 2008 clinical practice guidelines for the prevention and management of diabetes in Canada. *Can J Diabetes* 2008;32(suppl 1):S105, S112, S116, S128, S130, S136, S144, S148, S170, S201. Available at: <http://www.diabetes.ca/for-professionals/resources/2008-cpg/>
- 75 *A Clear Vision. Solutions to Canada's Vision Loss Crisis*. Toronto, ON: Canterbury Communications; 2004. Available at: http://www.ffb.ca/documents/Age-related%20Blindness_By%20the%20Numbers_FINAL.doc
- 76 Canadian Ophthalmological Society Clinical Practice Guideline Expert Committee. (2007). *Canadian Ophthalmological Society evidence-based clinical practice guidelines for the periodic eye examination in adults in Canada*. p. 41. Available at: http://www.eyesite.ca/english/program-and-services/policy-statements-guidelines/CPG-periodic-eye-exam_e.pdf
- 77 The Kidney Foundation of Canada. (2009 Winter). *Facing the facts*. Available at: <http://204.92.98.244/Document.Doc?id=102>
- 78 Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Canadian Diabetes Association 2008 clinical practice guidelines for the prevention and management of diabetes in Canada. *Can J Diabetes* 2008;32(suppl 1):S126, S129, S130. Available at: <http://www.diabetes.ca/for-professionals/resources/2008-cpg/>
- 79 Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Canadian Diabetes Association 2008 clinical practice guidelines for the prevention and management of diabetes in Canada. *Can J Diabetes* 2008;32(suppl 1):S201. Available at: <http://www.diabetes.ca/for-professionals/resources/2008-cpg/>
- 80 Registered Nurses Association of Ontario. (2005). *Assessment and management of foot ulcers for people with diabetes. Nursing Best Practice Guidelines Project*. Available at: <http://www.rnao.org/Page.asp?PageID=924&ContentID=719>
- 81 Toward Optimized Practice Clinical Practice Guideline Working Group. (2008). *Clinical practice guideline: Investigation and management of primary thyroid dysfunction*. Available at: http://www.topalbertadoctors.org/informed_practice/clinical_practice_guidelines/complete%20set/Thyroid%20Dysfunction/thyroid_guideline.pdf
- 82 Goodman JJ, Uphold CR. Metabolic and endocrine problems. In: Uphold CR, Graham MV (Editors). *Clinical guidelines in family practice*. 4th ed. Gainesville, FL: Barmarrae Books, Inc.; 2003. p. 193.
- 83 Goodman JJ, Uphold CR. Metabolic and endocrine problems. In: Uphold CR, Graham MV (Editors). *Clinical guidelines in family practice*. 4th ed. Gainesville, FL: Barmarrae Books, Inc.; 2003. p. 195.
- 84 Goodman JJ, Uphold CR. Metabolic and endocrine problems. In: Uphold CR, Graham MV (Editors). *Clinical guidelines in family practice*. 4th ed. Gainesville, FL: Barmarrae Books, Inc.; 2003. p. 194-195.
- 85 Lochnan H. Thyroid disorders. In: Gray J (Editor). *Therapeutic choices*. 5th ed. Ottawa, ON: Canadian Pharmacists Association; 2007. p. 320.

- 86 Goodman JJ, Uphold CR. Metabolic and endocrine problems. In: Uphold CR, Graham MV (Editors). *Clinical guidelines in family practice*. 4th ed. Gainesville, FL: Barmarrae Books, Inc.; 2003. p. 196.
- 87 Drug interactions with thyroid hormones. (2009, July). UpToDate online 17.3. Available by subscription: www.uptodate.com
- 88 Toward Optimized Practice Clinical Practice Guideline Working Group. (2008). Clinical practice guideline: Investigation and management of primary thyroid dysfunction. Available at: http://www.topalbertadoctors.org/informed_practice/clinical_practice_guidelines/complete%20set/Thyroid%20Dysfunction/thyroid_guideline.pdf
- 89 Goodman JJ, Uphold CR. Metabolic and endocrine problems. In: Uphold CR, Graham MV (Editors). *Clinical guidelines in family practice*. 4th ed. Gainesville, FL: Barmarrae Books, Inc.; 2003. p. 198.
- 90 American Association of Clinical Endocrinologists. Medical guidelines for clinical practice for the evaluation and treatment of hyperthyroidism and hypothyroidism. *Endocrine Practice* 2002;8(6):460-61.
- 91 Goodman JJ, Uphold CR. Metabolic and endocrine problems. In: Uphold CR, Graham MV (Editors). *Clinical guidelines in family practice*. 4th ed. Gainesville, FL: Barmarrae Books, Inc.; 2003. p. 197.
- 92 Bahn RS, et al. The role of propylthiouracil in the management of Graves' disease in adults: report of a meeting jointly sponsored by the American Thyroid Association and the Food and Drug Administration. *Thyroid* 2009;19(7):673-74.
- 93 Surks MI, et al. (2004). Subclinical thyroid disease: Scientific review and guidelines for diagnosis and management. *JAMA* 2004;291(2):231, 236.
- 94 Lochnan H. Thyroid disorders. In: Gray J (Editor-in-chief). *Therapeutic choices*. 5th ed. Ottawa, ON: Canadian Pharmacists Association; 2007. p. 198.
- 95 Goodman JJ, Uphold CR. Metabolic and endocrine problems. In: Uphold CR, Graham MV (Editors). *Clinical guidelines in family practice*. 4th ed. Gainesville, FL: Barmarrae Books, Inc.; 2003. p. 199.
- 96 Goodman JJ, Uphold CR. Metabolic and endocrine problems. In: Uphold CR, Graham MV (Editors). *Clinical guidelines in family practice*. 4th ed. Gainesville, FL: Barmarrae Books, Inc.; 2003. p. 200.
- 97 Goodman JJ, Uphold CR. Metabolic and endocrine problems. In: Uphold CR, Graham MV (Editors). *Clinical guidelines in family practice*. 4th ed. Gainesville, FL: Barmarrae Books, Inc.; 2003. p. 201.
- 98 Jones RE, Heuther SE. Alterations of hormonal function. In: McCance KL, Huether SE (Editors). *Pathophysiology: The biologic basis for disease in adults and children*. 5th ed. St. Louis, MO: Elsevier Mosby; 2006. p. 696.
- 99 Clinical manifestations of hypothyroidism. (2009, January). UpToDate online 17.3. Available by subscription: www.uptodate.com
- 100 Surks MI, et al. (2004). Subclinical thyroid disease: Scientific review and guidelines for diagnosis and management. *JAMA* 2004;291(2):230, 234.
- 101 Goodman JJ, Uphold CR. Metabolic and endocrine problems. In: Uphold CR, Graham MV (Editors). *Clinical guidelines in family practice*. 4th ed. Gainesville, FL: Barmarrae Books, Inc.; 2003. p. 202.
- 102 Lochnan H. Thyroid disorders. In: Gray J (Editor). *Therapeutic choices*. 5th ed. Ottawa, ON: Canadian Pharmacists Association; 2007. p. 319-320.
- 103 Treatment of hypothyroidism. (2009, September). UpToDate online 17.3. www.uptodate.com
- 104 American Association of Clinical Endocrinologists. Medical guidelines for clinical practice for the evaluation and treatment of hyperthyroidism and hypothyroidism. *Endocrine Practice* 2002;8(6):464.
- 105 Guidelines & Protocols Advisory Committee. (2004). *Thyroid disease – Thyroid function tests in the diagnosis and monitoring of adults*. Available at: <http://www.bcguidelines.ca/gpac/pdf/thyroid.pdf>
- 106 Ontario Association of Medical Laboratories. (2007). *Guideline for the use of laboratory tests to detect thyroid dysfunction*. Available at: <http://www.oaml.com/PDF/FINALTSH%20Guideline%20July%2018,%202007.pdf>
- 107 Lois K, Young J, Kumar S. Obesity: Epiphenomenon or cause of metabolic syndrome? *International Journal of Clinical Practice* 2008;62(6):932.
- 108 Ardern CI, Katzmarzyk PT. Geographic and demographic variation in the prevalence of the metabolic syndrome in Canada. *Can J Diabetes* 2007;31(1):37.
- 109 Pollex R L, Hanley AJG, Zinman B, Harris SB, et al. Metabolic syndrome in Aboriginal Canadians: Prevalence and genetic associations. *Atherosclerosis* 2005;184:124.
- 110 Pollex R L, Hanley AJG, Zinman B, Harris SB, et al. Metabolic syndrome in Aboriginal Canadians: Prevalence and genetic associations. *Atherosclerosis* 2005;184:128.
- 111 International Diabetes Federation. (2005). *The IDF consensus worldwide definition of the metabolic syndrome*. p. 9. Available at: http://www.idf.org/webdata/docs/MetS_def_update2006.pdf

- 112 Deen D. Metabolic syndrome: Time for action. *Am Fam Physician* 2004;69(12):2876.
- 113 Newcomer JW. Metabolic syndrome and mental illness. *American Journal of Managed Care* 2007;13(7):s170-s171.
- 114 Olufadi R, Byrne CD. Clinical and laboratory diagnosis of the metabolic syndrome. *Journal of Clinical Pathology* 2007;61:701-04.
- 115 Giugliano D, Ceriello A, Esposito K. Are there specific treatments for the metabolic syndrome? *Am J Clinical Nutrition* 2008;87(8):9.
- 116 Weir E, Lipscombe L. Metabolic syndrome: Waist not want not. *CMAJ* 2004;170(9):1390.
- 117 Depres JP, Poirier P, Bergeron J, Tremblay A, et al. From individual risk factors and the metabolic syndrome to global cardiometabolic risk. *European Heart Journal Supplements* 2008; 10(Suppl. 8):831.
- 118 Lucove J, Vupputuri S, Heiss G, North K, Russell M. Metabolic syndrome and the development of CKD in American Indians: The strong heart study. *American Journal of Kidney Diseases* 2008;51(1):26.
- 119 International Diabetes Federation. (2005). *The IDF consensus worldwide definition of the metabolic syndrome*. p. 1. Available at: http://www.idf.org/webdata/docs/MetS_def_update2006.pdf
- 120 George K, Alberti MM, Zimmet P, Shaw J. The metabolic syndrome – a new worldwide definition. *The Lancet* 2005;366:1059-61.
- 121 Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Canadian Diabetes Association 2008 clinical practice guidelines for the prevention and management of diabetes in Canada. *Can J Diabetes* 2008;32(suppl 1):S12. Available at: <http://www.diabetes.ca/for-professionals/resources/2008-cpg/>
- 122 Ley S, et al. Metabolic syndrome and its components as predictors of incident type 2 diabetes mellitus in an Aboriginal community. *CMAJ* 2009;180(6):623.
- 123 Giugliano D, Ceriello A, Esposito K. Are there specific treatments for the metabolic syndrome? *Am J Clinical Nutrition* 2008;87(8):10.
- 124 Meigs JB. (2009, January). *The metabolic syndrome (insulin resistance syndrome or syndrome X)*. Available by subscription: www.uptodate.com
- 125 Genest J, Frohlich J, Fodor G, McPherson R. Recommendations for the management of dyslipidemia and the prevention of cardiovascular disease: 2003 update. *CMAJ* 2003;169(9):921. Available at: <http://www.cmaj.ca/cgi/data/169/9/921/DC1/1> p. Online-7
- 126 Salas-Salvado J, et al. (2008). Effect of a Mediterranean diet supplemented with nuts on metabolic syndrome status. *Archives of Internal Medicine* 2008;168(22):2453.
- 127 Deen D. Metabolic syndrome: Time for action. *Am Fam Physician* 2004;69(12):2879.
- 128 Orchard TJ, et al. The effect of metformin and intensive lifestyle intervention on the metabolic syndrome: The diabetes prevention program randomized trial. *Annals of Internal Medicine* 2005;142(8):615.
- 129 International Diabetes Federation. (2005). *The IDF consensus worldwide definition of the metabolic syndrome*. p. 4. Available at: http://www.idf.org/webdata/docs/MetS_def_update2006.pdf
- 130 Mayo Clinic staff. (2007, November 7). *Metabolic syndrome*. Available at: <http://www.mayoclinic.com/print/metabolic%20syndrome/DS00522/DSECTION=all&METHOD=print>
- 131 Brown JP, Josse RG and The Scientific Advisory Council of the Osteoporosis Society of Canada. 2002 clinical practice guidelines for the diagnosis and management of osteoporosis in Canada. *CMAJ* 2002;167(10 suppl):S3. Available at: http://www.cmaj.ca/cgi/data/167/10_suppl/s1/DC1/1
- 132 Rahmani P, Morin S. Prevention of osteoporosis-related fracture among postmenopausal women and older men. *CMAJ* 2009;181(11):815.
- 133 Brown JP, Josse RG and The Scientific Advisory Council of the Osteoporosis Society of Canada. 2002 clinical practice guidelines for the diagnosis and management of osteoporosis in Canada. *CMAJ* 2002;167(10 suppl):S1. Available at: http://www.cmaj.ca/cgi/data/167/10_suppl/s1/DC1/1
- 134 Brown JP, Fortier M, Osteoporosis Guidelines Committee. Canadian consensus conference on Osteoporosis, 2006 update. *Journal of Obstetrics and Gynaecology Canada* 2006;28 (Special Edition 1):s96.
- 135 Uphold CR. Musculoskeletal problems. In: Uphold CR, Graham MV (Editors). *Clinical guidelines in family practice*. 4th ed. Gainesville, FL: Barmarrae Books, Inc.; 2003. p. 840.
- 136 Khan AA, Hodsman AB, Papaioannou A, Kendler D et al. Management of osteoporosis in men: An update and case example. *CMAJ* 2007;176(3):346.
- 137 Brown JP, Josse RG and The Scientific Advisory Council of the Osteoporosis Society of Canada. 2002 clinical practice guidelines for the diagnosis and management of osteoporosis in Canada. *CMAJ* 2002;167(10 suppl):S5. Available at: http://www.cmaj.ca/cgi/data/167/10_suppl/s1/DC1/1

- 138 Brown JP, Fortier M, Osteoporosis Guidelines Committee. Canadian consensus conference on Osteoporosis, 2006 update. *Journal of Obstetrics and Gynaecology Canada* 2006;28 (Special Edition 1):s99.
- 139 Uphold CR. Musculoskeletal problems. In: Uphold CR, Graham MV (Editors). *Clinical guidelines in family practice*. 4th ed. Gainesville, FL: Barmarrae Books, Inc.; 2003. p. 842.
- 140 Hanley DA. Osteoporosis. In: Gray J (Editor). *Therapeutic choices*. 5th ed. Ottawa, ON: Canadian Pharmacists Association; 2007. p. 973.
- 141 Khan AA, Hodzman AB, Papaioannou A, Kendler D et al. Management of osteoporosis in men: An update and case example. *CMAJ* 2007;176(3):347.
- 142 Rahmani P, Morin S. Prevention of osteoporosis-related fracture among postmenopausal women and older men. *CMAJ* 2009;181(11):815-16.
- 143 Hanley DA. Osteoporosis. In: Gray J (Editor). *Therapeutic choices*. 5th ed. Ottawa, ON: Canadian Pharmacists Association; 2007. p. 972.
- 144 Brown JP, Josse RG and The Scientific Advisory Council of the Osteoporosis Society of Canada. 2002 clinical practice guidelines for the diagnosis and management of osteoporosis in Canada. *CMAJ* 2002;167(10 suppl):S23. Available at: http://www.cmaj.ca/cgi/data/167/10_suppl/s1/DC1/1
- 145 Hanley DA. Osteoporosis. In: Gray J (Editor). *Therapeutic choices*. 5th ed. Ottawa, ON: Canadian Pharmacists Association; 2007. p. 974, 980.
- 146 Uphold CR. Musculoskeletal problems. In: Uphold CR, Graham MV (Editors). *Clinical guidelines in family practice*. 4th ed. Gainesville, FL: Barmarrae Books, Inc.; 2003. p. 844-45.
- 147 Rahmani P, Morin S. Prevention of osteoporosis-related fracture among postmenopausal women and older men. *CMAJ* 2009;181(11):816.
- 148 Brown JP, Josse RG and The Scientific Advisory Council of the Osteoporosis Society of Canada. 2002 clinical practice guidelines for the diagnosis and management of osteoporosis in Canada. *CMAJ* 2002;167(10 suppl):S25. Available at: http://www.cmaj.ca/cgi/data/167/10_suppl/s1/DC1/1
- 149 Brown JP, Josse RG and The Scientific Advisory Council of the Osteoporosis Society of Canada. 2002 clinical practice guidelines for the diagnosis and management of osteoporosis in Canada. *CMAJ* 2002;167(10 suppl):S13-S22. Available at: http://www.cmaj.ca/cgi/data/167/10_suppl/s1/DC1/1
- 150 Hanley DA. Osteoporosis. In: Gray J (Editor). *Therapeutic choices*. 5th ed. Ottawa, ON: Canadian Pharmacists Association; 2007. p. 974.
- 151 Brown JP, Josse RG and The Scientific Advisory Council of the Osteoporosis Society of Canada. 2002 clinical practice guidelines for the diagnosis and management of osteoporosis in Canada. *CMAJ* 2002;167(10 suppl):S6. Available at: http://www.cmaj.ca/cgi/data/167/10_suppl/s1/DC1/1
- 152 Hanley DA. Osteoporosis. In: Gray J (Editor). *Therapeutic choices*. 5th ed. Ottawa, ON: Canadian Pharmacists Association; 2007. p. 980.
- 153 Uphold CR. Musculoskeletal problems. In: Uphold CR, Graham MV (Editors). *Clinical guidelines in family practice*. 4th ed. Gainesville, FL: Barmarrae Books, Inc.; 2003. p. 848.
- 154 Jones RE, Heuther SE. Alterations of hormonal function. In: McCance KL, Huether SE (Editors). *Pathophysiology: The biologic basis for disease in adults and children*. 5th ed. St. Louis, MO: Elsevier Mosby; 2006. p. 711-712.
- 155 Chiasson JL, Aris-Jilwan N, Bélanger R, et al. Diagnosis and treatment of diabetic ketoacidosis and the hyperglycemic hyperosmolar state. *CMAJ* 2003;168(7):859, 861. Available at: <http://www.cmaj.ca/cgi/content/full/168/7/859>
- 156 Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Canadian Diabetes Association 2008 clinical practice guidelines for the prevention and management of diabetes in Canada. *Can J Diabetes* 2008;32(suppl 1):S65. Available at: <http://www.diabetes.ca/for-professionals/resources/2008-cpg/>
- 157 Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Canadian Diabetes Association 2008 clinical practice guidelines for the prevention and management of diabetes in Canada. *Can J Diabetes* 2008;32(suppl 1):S151. Available at: <http://www.diabetes.ca/for-professionals/resources/2008-cpg/>
- 158 Chieh-Hsiang L, Yuan-Horng Y. Risperidone-associated newly diagnosed diabetes and fatal diabetes ketoacidosis in a young schizophrenic patient. *Diabetes Research and Clinical Practice* 2009;83:e66-e67.
- 159 Up To Date. (2009). *The patient with brittle diabetes mellitus*. Available by subscription: www.uptodate.com
- 160 *Clinical features and diagnosis of diabetic ketoacidosis and hyperosmolar hyperglycemic state in adults*. (2008, September). Available by subscription: www.uptodate.com
- 161 Goodman JJ, Uphold CR. Metabolic and endocrine problems. In: Uphold CR, Graham MV (Editors). *Clinical guidelines in family practice*. 4th ed. Gainesville, FL: Barmarrae Books, Inc.; 2003. p. 164.

- 162 Post TW, Rose BD. (2009, January). *Clinical manifestations and diagnosis of volume depletion in adults*. UptoDate Online 17.1. Available by subscription: www.uptodate.com
- 163 Kitabchi AE, Rose BD. (2009, October 14). *Treatment of diabetic ketoacidosis and hyperosmolar hyperglycemic state in adults*. Available by subscription: www.uptodate.com
- 164 Goodman JJ, Uphold CR. Metabolic and endocrine problems. In: Uphold CR, Graham MV (Editors). *Clinical guidelines in family practice*. 4th ed. Gainesville, FL: Barmarrae Books, Inc.; 2003. p. 168.
- 165 Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Canadian Diabetes Association 2008 clinical practice guidelines for the prevention and management of diabetes in Canada. *Can J Diabetes* 2008;32(suppl 1):S67. Available at: <http://www.diabetes.ca/for-professionals/resources/2008-cpg/>
- 166 Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Canadian Diabetes Association 2008 clinical practice guidelines for the prevention and management of diabetes in Canada. *Can J Diabetes* 2008;32(suppl 1):S66. Available at: <http://www.diabetes.ca/for-professionals/resources/2008-cpg/>
- 167 Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Canadian Diabetes Association 2008 clinical practice guidelines for the prevention and management of diabetes in Canada. *Can J Diabetes* 2008;32(suppl 1):S66-67. Available at: <http://www.diabetes.ca/for-professionals/resources/2008-cpg/>
- 168 Koul PB. Diabetic ketoacidosis: A current appraisal of pathophysiology and management. *Clinical Pediatrics* 2009;48(2):139.
- 169 Jones RE, Heuther SE. Alterations of hormonal function. In: McCance KL, Huether SE (Editors). *Pathophysiology: The biologic basis for disease in adults and children*. 5th ed. St. Louis, MO: Elsevier Mosby; 2006. p. 710.
- 170 Service FJ, Cryer PE. (2009, September 9). Overview of hypoglycemia in adults. UptoDate Online. Available by subscription: www.uptodate.com
- 171 Up To Date. (2009).
- 172 Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Canadian Diabetes Association 2008 clinical practice guidelines for the prevention and management of diabetes in Canada. *Can J Diabetes* 2008;32(suppl 1):S62-63. Available at: <http://www.diabetes.ca/for-professionals/resources/2008-cpg/>
- 173 Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Canadian Diabetes Association 2008 clinical practice guidelines for the prevention and management of diabetes in Canada. *Can J Diabetes* 2008;32(suppl 1):S63. Available at: <http://www.diabetes.ca/for-professionals/resources/2008-cpg/>
- 174 Jones RE, Heuther SE. Alterations of hormonal function. In: McCance KL, Huether SE (Editors). *Pathophysiology: The biologic basis for disease in adults and children*. 5th ed. St. Louis, MO: Elsevier Mosby; 2006. p. 711.
- 175 Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Canadian Diabetes Association 2008 clinical practice guidelines for the prevention and management of diabetes in Canada. *Can J Diabetes* 2008;32(suppl 1):S62. Available at: <http://www.diabetes.ca/for-professionals/resources/2008-cpg/>
- 176 Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Canadian Diabetes Association 2008 clinical practice guidelines for the prevention and management of diabetes in Canada. *Can J Diabetes* 2008;32(suppl 1):S43. Available at: <http://www.diabetes.ca/for-professionals/resources/2008-cpg/>
- 177 Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Canadian Diabetes Association 2008 clinical practice guidelines for the prevention and management of diabetes in Canada. *Can J Diabetes* 2008;32(suppl 1):S38. Available at: <http://www.diabetes.ca/for-professionals/resources/2008-cpg/>
- 178 Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Canadian Diabetes Association 2008 clinical practice guidelines for the prevention and management of diabetes in Canada. *Can J Diabetes* 2008;32(suppl 1):S200. Available at: <http://www.diabetes.ca/for-professionals/resources/2008-cpg/>
- 179 Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Canadian Diabetes Association 2008 clinical practice guidelines for the prevention and management of diabetes in Canada. *Can J Diabetes* 2008;32(suppl 1):S195-196. Available at: <http://www.diabetes.ca/for-professionals/resources/2008-cpg/>
- 180 Chiasson, JL, et al. (2003). Diagnosis and treatment of diabetic ketoacidosis and the hyperglycemic hyperosmolar state. *CMAJ* 2003;168(7):862. Available at: <http://www.cmaj.ca/cgi/content/full/168/7/859>