
CHAPTER 17 – HEMATOLOGY, ENDOCRINOLOGY, METABOLISM AND IMMUNOLOGY

First Nations and Inuit Health Branch (FNIHB) Pediatric Clinical Practice Guidelines for Nurses in Primary Care.
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ASSESSMENT OF HEMATOLOGIC, ENDOCRINOLOGIC, METABOLIC AND IMMUNOLOGIC CONDITIONS

For this topic, history and examination of all systems are not discussed as such, because hematologic, endocrine, metabolic and immunologic disorders often manifest symptoms and signs in more than one body system, including:

- integumentary (*see pediatric Chapter 16, “Skin”*)
- eyes (*see pediatric Chapter 8, “Eyes”*)
- ears, nose, throat (*see pediatric Chapter 9, “Ears, Nose, Throat and Mouth”*)
- cardiovascular (*see pediatric Chapter 11, “Cardiovascular System”*)
- respiratory (*see pediatric Chapter 10 “Respiratory System”*)
- gastrointestinal (*see pediatric Chapter 12, “Gastrointestinal System”*)
- neurologic (*see pediatric Chapter 15, “Central Nervous System”*)

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

Iron Deficiency Anemia – Physical Findings:

- 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 section “Assessment of Integumentary System” in the pediatric Chapter 16, “Skin”*).

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

COMMON HEMATOLOGIC PROBLEMS

IRON DEFICIENCY ANEMIA

Anemia is defined as a reduction in hemoglobin level or as a decrease in circulating red blood cell mass to below age- and gender-specific limits. Iron deficiency anemia (IDA) is the most common type of microcytic, hypochromic anemia.¹

IDA is rarely found in full-term infants younger than six months and in premature infants before they have doubled their birth weight.² Iron deficiency anemia is common in toddlers (especially 9–18 months) and adolescents (especially menstruating females) due to poor iron intake and increased iron needs with rapid growth.³ Prevalence of IDA in Aboriginal infants can vary from 14% to 50% compared to 4% to 5% in the general Canadian population. A recent study of infants aged 4–18 months in two northern Ontario Cree First Nations and one Inuit community found the prevalence of all anemias to be 36%, IDA was found in 27.6% of the study population and 53.3% had depleted iron stores.⁴ IDA can have a significant negative impact on motor, cognitive and socioemotional development. These deficits may not be reversible; thus, it is a critical public health problem.⁵

See also “Iron Deficiency Anemia” under the section “Common Hematologic Problems” in the adult Chapter 10, “Hematology, Metabolism and Endocrinology”.

CAUSES^{6,7,8}

- Inadequate dietary intake of iron (common in children and adolescents and infants fed nonfortified formula)
- Increased requirements for iron without concomitant increase in intake (during growth spurts in infants, young children and adolescents)
- Poor iron stores at birth related to insufficient absorption from mother in utero, fetal and/or neonatal blood loss
- Prolonged exclusive breastfeeding
- Prolonged and early use of cow’s milk or evaporated milk prior to age of 1 year
- Nutritional deficiencies (for example, folic acid)
- Toxic effects (for example, lead poisoning)
- Bone marrow failure
- Defects in hemoglobin structure

Risk Factors^{9,10}

- Low socioeconomic status
- Member of high-risk ethnic population (Black, Aboriginal, Chinese, Latin-American)
- Pre-term and low birth weight infants (< 2500 g)
- Infants born to mothers with poorly controlled diabetes
- Perinatal bleeding, multiple pregnancy or low hemoglobin at birth
- Infection (for example, chronic childhood infections, *Helicobacter pylori*¹¹)
- Intake of cow's milk

HISTORY¹²

Infants (0 to 1 year):

- Premature birth or low birth weight (< 2500 g)
- Exclusive breastfeeding > 6 months without iron supplementation
- Intake of cow's milk as principal dietary intake (> 24 oz/day) or early intake of cow's milk (before age 9–12 months)
- Insufficient amount and frequency of feeding
- Developmental milestones not achieved

Children (> 1 to 12 years) and adolescents (> 12 to 18 years):

- Insufficient intake and/or low quality of iron-enriched foods consumed
- Low vitamin C or meat intake
- Gastrointestinal complaints (suggestive of malabsorption or GI bleeding)
- Fatigue, loss of energy

Adolescents (> 12 to 18 years):

- Severe diet restriction for weight loss
- Menstrual blood loss in females
- Fatigue, loss of energy

PHYSICAL FINDINGS¹²

- Review general appearance, paying particular attention to apparent fatigue
- Vital signs: resting pulse (increased if very anemic), respiration rate (increased if very anemic), oxygen saturation, temperature, weight for height (decreased) or obesity¹³

- 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 section "Assessment of Integumentary System" in the pediatric Chapter 16, "Skin"*)
- Head and Neck: assess eyes for pallor of conjunctiva; observe cracks at corners of mouth and glossitis (*see section "Assessment of the Eyes" in the pediatric Chapter 8, "Eyes"*)
- Respiratory: auscultate lungs (clear unless pleural effusion/heart failure present) (*see section "Assessment of the Respiratory System" in the pediatric Chapter 10 "Respiratory System"*)
- Cardiovascular: auscultate the heart for systolic flow murmurs; signs of heart failure may be present in severe cases (*see section "Assessment of the Cardiovascular System" in the pediatric Chapter 11, "Cardiovascular System"*)
- Gastrointestinal: auscultate bowel sounds; palpate for tenderness and assess the abdomen for hepatomegaly and splenomegaly (*see section "Assessment of the Gastrointestinal System" in the pediatric Chapter 12, "Gastrointestinal System"*)
- Neurologic: assess muscle strength; sensation; observe for poor concentration, irritability (*see section "Assessment of the Central Nervous System" in the pediatric Chapter 15, "Central Nervous System"*)

DIFFERENTIAL DIAGNOSIS

- Anemia of chronic disease
- Hemolytic anemia
- Anemia of acute hemorrhage
- Aplastic anemia
- Aplastic anemia
- Vitamin B₁₂ deficiency
- Folate deficiency
- Failure to thrive because of decreased nutritional intake

COMPLICATIONS^{6,14,15}

- Cognitive deficits
- Delays in psychomotor development
- Impaired growth (weight for height)
- Behavioural problems
- Depressed immune system
- Frequent infection
- Cardiac failure (only if the anemia is severe)

DIAGNOSTIC TESTS¹⁶

- Complete blood count (CBC) (includes: hemoglobin, hematocrit, complete WBC count, differential WBC count, platelets, MCV, reticulocyte count)
- If needed, to differentiate iron deficiency from other causes of anemia the following tests may be considered:
 - Peripheral blood smear
 - Serum ferritin level
 - Serum iron level
 - Total iron-binding capacity (TIBC)

Normal mean hemoglobin, hematocrit and ferritin levels vary according to the age of the child. Ferritin may be increased if infection or severe illness is present.¹⁷ See Table 1, “Hemoglobin Concentration and Hematocrit by Age” and Table 2, “Ferritin Level by Age.”^{9,16}

Table 1 – Hemoglobin Concentration and Hematocrit by Age

Age (years)	Hemoglobin Concentration (g/L)	Hematocrit (%)
1 to < 2	110	32.9
2 to < 5	111	33.0
5 to < 8	115	34.5
8 to < 12	119	35.4
Males 12 to < 15	125	37.3
Females 12 to < 15	118	35.7
Males 15 to < 18	133	39.7
Females 15 to < 18	120	35.9
Males ≥ 18	135	39.9
Females ≥ 18	120	35.7

Table 2 – Ferritin Level by Age

Age	Ferritin Level (mcg/L)
1 month to 12 months	14–400
12 months to adult	22–400

MANAGEMENT**Goals of Treatment**

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

Appropriate Consultation

- Consult a physician if hemoglobin < 110 g/L or if child appears acutely ill (for example, heart failure).

Nonpharmacologic Interventions**Client education:**^{18,19,20}

- Explain nature, course and risk of anemia related to growth and development of psychomotor, cognitive and behaviour skills
- Encourage intake of iron rich or fortified foods (for example, cereals, formula, meats)
- Counsel client about appropriate use of iron supplements:
 - dose, frequency, side effects, importance of compliance
 - follow a graduated approach to dosing to minimize GI side effects (nausea, vomiting, dyspepsia, constipation, diarrhea or dark stools) and improve compliance

- iron is best absorbed on an empty stomach (do not give within two hours after ingestion of dairy products, bran, whole grains and other substances that inhibit iron absorption)
- vitamin C enhances absorption of iron from the GI tract (advise clients to give iron supplements with citrus juices to maximize absorption)
- Oral liquid preparations may cause staining of teeth. Stains may be prevented by mixing with water or fruit juice (not milk), using a straw and then rinsing with water or juice. Stains can be removed by rubbing teeth with baking soda
- Recommend avoidance of NSAIDs (for example, ibuprofen)

Pharmacologic Interventions

There are three iron salts available in Canada, each of which differ in their elemental iron content:

- Ferrous fumarate (~33% elemental iron)
- Ferrous sulfate (~20% elemental iron)
- Ferrous gluconate (~11% elemental iron)

Treatment:¹⁸

Infants over 4 months and children:

Dosage forms suitable	Treatment dosage
Ferrous fumarate 60 mg/mL suspension (20 mg/mL elemental iron)	Mild to moderate anemia: 3 mg elemental iron/kg/day in 1–2 divided doses Severe anemia: 4–6 mg elemental iron/kg/day in 3 divided doses
Ferrous sulfate (for example, Fer-In-Sol) 75 mg/mL drops (15 mg/mL elemental iron)	
Ferrous sulfate 30 mg/mL syrup (6 mg/mL elemental iron)	

Adolescents 12 to 18 years:

Dosage forms suitable	Treatment dosage
Ferrous fumarate 300 mg tablet (100 mg elemental iron)	60–120 mg elemental iron/day
Ferrous gluconate 300 mg tablet (35 mg elemental iron)	
Sulfate ferreux, 300 mg, comprimés (60 mg elemental iron)	

Monitoring and Follow-Up¹⁸

For clients receiving iron supplements for IDA:

- Follow up 1 month after initiating therapy (assess compliance, side effects), repeat hemoglobin (should rise by 10 g/L in 1 month) and hematocrit (should rise by 3%) which confirms IDA diagnosis at this time only if original hemoglobin was < 100 g/L
- Subsequent follow-up visit at 3 months after treatment initiation to assess restoration of iron stores within age-based normal range (do CBC including hematocrit and reticulocyte count)
- Reassess hemoglobin and hematocrit 6 months after treatment is discontinued

Referral

Arrange follow-up with a physician or nurse practitioner as required:

- During initial treatment phase if there is no increased reticulocytes after 1 month of oral therapy
- During treatment phase if there is no response (hemoglobin) after 3 months of therapy
- Whenever symptoms are not controlled by therapy
- If there is evidence of complications

Prevention

Inuit and First Nations infants are at risk for iron deficiency anemia.²¹ Hemoglobin screening should occur between 6 and 12 months, optimally at 9 months of age.⁸

Pharmacologic Interventions for Prevention:²²

Infants fed evaporated milk require iron supplementation.¹³

Pre-term (< 37 weeks) and low birth weight (< 2500 g) infants 4 to 8 weeks:

Breast-fed	Ferrous fumarate 60 mg/mL suspension (20 mg/mL elemental iron)	
	Ferrous sulfate 75 mg/mL drops (15 mg/mL elemental iron)	2–4 mg elemental iron/kg/day (max 15 mg/day)
	Ferrous sulfate 30 mg/mL syrup (6mg/mL elemental iron)	
Formula +/- Breastfeeding	Iron-fortified formula	1–1.5 mg elemental iron/100 mL of formula (when ready to give formula) Do not supplement in addition to the iron-fortified formula

Term infants 0 to 6 months:

Breast-fed	No iron supplementation generally required. Should receive a Vitamin D supplement for breast-fed infants starting at birth and until diet provides a source of Vitamin D	Vitamin D (10 µg = 400 UI/day) 20 µg = 800 UI/day in northern communities Start iron-fortified cereal at 6 months
Formula +/- Breastfeeding	Iron-fortified formula or iron-fortified infant cereal	1–1.5 mg elemental iron/100 mL of formula (when ready to give formula) Do not supplement in addition to the iron fortified formula

Infants > 6 to 12 months:

Complementary foods + Breastfeeding and/or formula	Introduce complementary foods containing iron after 6 months PLUS iron-fortified formula or iron-fortified infant cereal and/or breastfeeding. Delay introduction of cow's milk until 9–12 months	1–1.5 mg elemental iron/100 mL of formula (when ready to give formula) Do not supplement iron in addition to this Iron-rich foods include: red meat, organ meat, poultry, fish, oatmeal, beans
Formula +/- Breastfeeding	Iron-fortified formula or iron-fortified infant cereal	1–1.5 mg elemental iron/100 mL of formula (when ready to give formula) Do not supplement in addition to the iron-fortified formula

Toddlers > 1 year old:

Supplemental iron NOT required unless diet lacking in iron-rich foods	Iron-rich foods include: red meat, organ meat, poultry, seafood, fish, oatmeal, beans, potato skins, raisins	
Continue iron-fortified cereals until 2 years old		

COMMON ENDOCRINE AND METABOLIC PROBLEMS

DIABETES MELLITUS²³

Diabetes mellitus is a metabolic disorder characterized by hyperglycemia, which is due to defective insulin secretion, increased tissue resistance to insulin action or both. In 2005–2006, approximately 1.9 million Canadian men and women had been diagnosed with diabetes. About 10% of people with diabetes have type 1 diabetes; the remaining 90% have type 2 diabetes²⁴.

For more detailed information, see “*Diabetes Mellitus*” under the section “*Common Endocrine and Metabolic Problems*” in the adult Chapter 10, “*Hematology, Metabolism and Endocrinology*”.

See the “*Canadian Diabetes Association 2008 Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada*” for further information, available at: <http://www.diabetes.ca/files/cpg2008/cpg-2008.pdf>.

CLASSIFICATION

There are two main types of diabetes, both associated with serious long-term complications, including cardiovascular diseases, hypertension, kidney failure, retinopathy and neuropathy.

Type 1 Diabetes

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 a younger age (< 30 years). Type 1 diabetes is rare among Aboriginal people.

Type 2 Diabetes

Type 2 diabetes mellitus occurs as a result of a defect in insulin secretion and an increase in resistance to insulin in the tissues. Age at onset is usually middle age or older. People with type 2 diabetes are much less prone to ketoacidosis.

The prevalence of type 2 diabetes is reaching epidemic proportions among First Nations people, who have a 3.6 to 5.3 times higher prevalence than the general population.²⁵ Recent evidence suggests that 19.7% of First Nations adults have been diagnosed with diabetes, including 35% of adults aged 55 years or older.²⁶ Age-adjusted prevalence rates range from 19% to 26%, which are among the highest in the world.^{27,28}

Although typically a disease of adults, type 2 diabetes often occurs in children and young adults in the First Nations population. The average age of diagnosis of diabetes among First Nations youth is 11 years.²⁹ In recent years, an increasing number of First Nations teenagers and young children have been diagnosed with type 2 diabetes.³⁰

OTHER DISORDERS OF CARBOHYDRATE METABOLISM³¹

- Impaired fasting glucose (IFG)
- Impaired glucose tolerance (IGT)

“Prediabetes” is used to describe both IFG and IGT. People with elevated fasting serum glucose levels have IFG. People with elevated serum glucose levels 2-hour post-oral glucose tolerance test (GTT) (with 75 g load) are considered to have IGT.

Individuals with prediabetes are at risk of developing diabetes and its complications. Thus, preventive interventions including lifestyle changes (for example, diet and physical activity) and more frequent screening for diabetes are a priority in these people. The focus here is on type 2 diabetes mellitus.

CAUSES³²

Potential causes of diabetes:

- Most cases of type 2 diabetes mellitus are of unknown etiology
- Genetic predisposition
- Infectious diseases (for example, cytomegalovirus, mumps, rubella, Epstein-Barr viruses)
- Autoimmune (for type 1 only)
- Drug or chemical-induced
- After pancreatitis

Risk Factors³³

- Intrauterine exposure to diabetes, or gestational diabetes³⁴
- Large-birth-weight infant
- 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)
- Abdominal obesity*
- Overweight*

- High-fat diet, high glycemic index diet
- Sedentary lifestyle
- Failure to thrive (*see section "Failure to Thrive" in this chapter*)
- Dyslipidemia
- Hypertension
- Polycystic ovarian syndrome (PCOS)
- *Acanthosis nigricans* (darkened patches on the skin)
- Medications (for example, antipsychotics, oral contraceptives, corticosteroids, thiazide diuretics)

* Obesity is a major modifiable risk factor for the development of type 2 diabetes. In 2004, 18% of Canadian children and adolescents were overweight and 8% were obese.^{35,36} In 2007, the First Nations Regional Longitudinal Health Survey (RHS) reported 22.3% of First Nations children were considered overweight while 36.2% were deemed obese.³⁷

HISTORY^{23,38}

Type 1 Diabetes (~10% of all diabetes diagnoses; highest incidence in childhood/adolescence):

- Acute onset of:
 - Polyuria, polydipsia, polyphagia
 - Weight loss
 - Blurred vision
- Nocturia
- Frequent or recurring infections (for example, persistent or recurrent candidal infection usually in the diaper area in young children)³⁹
- Ketoacidosis (rare in adults)

Type 2 Diabetes (~90% of all diabetes diagnoses):

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 history (especially any 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)
- Unresolving "flu-like" illness (ketoacidosis)

- Paresthesia of hands/fingers or feet/toes
- Medications (for example, antipsychotics, oral contraceptives, corticosteroids, thiazide diuretics)

Current Health⁴⁰

To establish diagnosis:

- Symptoms (as above) and complications associated with diabetes
- Explore family history of diabetes and other endocrine problems
- Adolescent females: gestational history (including weight and delivery details)

For patients already diagnosed:

- Frequency, severity and cause of episodes of hypoglycemia or episodes of ketoacidosis
- Symptoms and management of complications of eye, kidney, peripheral vascular and foot
- Patterns and results of glycemic control (for example, home blood glucose monitoring)

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 and alcohol intake
- Contraceptive, reproductive and sexual history
- Weight history
- Social factors (family dynamics, education, employment, lifestyle, coping skills, economic factors)

Family History

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

PHYSICAL FINDINGS

Most affected children look normal, but may appear ill if the diabetes is of sudden onset. 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.

- Measure height, weight and waist circumference; calculate body mass index (BMI)
- Vital Signs: normal unless there are complications
- Integumentary: inspect skin for infection (for example, feet or nails), assess for signs of dehydration (sunken eyes, dry mucous membranes); inspect skin for colour, temperature, bruising, wounds, hyperpigmented patches of acanthosis nigricans, sites of insulin injection (if applicable) (*see section “Assessment of the Integumentary System” in the pediatric Chapter 16, “Skin”*)
- Head and Neck:
 - Eyes: assess for fundoscopic signs of retinopathy (*see section “Assessment of the Eyes” in the pediatric Chapter 8, “Eyes”*)
 - Oral Cavity: perform a thorough mouth and dental exam (poor dental health is a risk for infection) (*see section “Assessment of the Ears, Nose, Throat and Mouth” in the pediatric Chapter 9, “Ears, Nose, Throat and Mouth”*)
 - Neck: perform a thyroid assessment
- Respiratory: perform a routine respiratory exam (*see section “Assessment of the Respiratory System” in the pediatric Chapter 10 “Respiratory System”*)
- Cardiovascular: perform a complete cardiac exam (including signs of heart failure, bruits), palpate and auscultate peripheral pulses (*see section “Assessment of the Cardiovascular System” in the pediatric Chapter 11, “Cardiovascular System”*)
- Gastrointestinal: perform abdominal exam; check for enlargement of organs (*see section “Assessment of the Gastrointestinal System” in the pediatric Chapter 12, “Gastrointestinal System”*)
- Neurologic: perform complete neurologic exam; assess feet for changes in vibrational sense, proprioception, response to light touch (with monofilament), reflexes (*see section “Assessment of the Central Nervous System” in the pediatric Chapter 15, “Central Nervous System”*)

DIFFERENTIAL DIAGNOSIS

- 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 diabetes],⁴¹ corticosteroids, thiazide diuretics)
- Diabetes insipidus (polyuria, polydipsia and nocturia but not hyperglycemia)
- Pheochromocytoma (tumour in adrenal medulla)
- Cushing’s syndrome
- Transient hyperglycemia secondary to severe stress, burns or infections

COMPLICATIONS^{38,42,43}

- Diabetic ketoacidosis (DKA) (common in type 1 diabetes) (*see “Diabetic Ketoacidosis and Hyperosmolar Hyperglycemic State” under the section “Metabolic Emergencies” in the adult Chapter 10, “Hematology, Metabolism and Endocrinology”*)
- Hypoglycemia
- Hyperosmolar hyperglycemic state (HHS) (*see “Diabetic Ketoacidosis and Hyperosmolar Hyperglycemic State” under the section “Metabolic Emergencies” in the adult Chapter 10, “Hematology, Metabolism and Endocrinology”*)
- Depression³⁹
- Eating disorder³⁹
- Retinopathy (early onset), blindness
- Peripheral neuropathy
- Nephropathy
- Other long-term complications (*see “Diabetes Mellitus” under the section “Common Endocrine and Metabolic Problems” in the adult Chapter 10, “Hematology, Metabolism and Endocrinology”*)
- Recurrent infections (for example, diaper, urinary, vaginal [yeast], skin)

DIAGNOSTIC TESTS⁴⁴**Diagnostic Blood Glucose Levels**

Fasting serum glucose level ≥ 7 mmol/L

or

or Random serum glucose level ≥ 11.1 mmol/L in the presence of symptoms

or

Serum glucose level 2 hours after oral GTT (with 75 g load) ≥ 11.1 mmol/L

NOTE: A confirmatory glucose test (any of above) must be done on another day in all cases except when client presents with symptomatic hyperglycemia at the levels described above or diabetic ketoacidosis.

Table 3 – Diagnostic Serum Glucose Levels for Impaired Fasting Glucose (IFG) and Impaired Glucose Tolerance (IGT)

Type de glycémie	Fasting serum glucose	and or or	2 hours after oral GTT (with 75 g load)
IFG	6.1–6.9		not applicable
IFG (isolated)	6.1–6.9	and	< 7.8
IGT (isolated)	< 6.1	and	7.8–11
IFG and IGT	6.1–6.9	and	7.8–11
Diabetes	≥ 7	or	≥ 11

Other Tests^{45,46}

The following tests should also be performed at the time of diagnosis for all adolescents (13–18 years old) and for children < 13 years old as indicated:

- Hemoglobin A1C (Hb_{A1C})
- Fasting lipid levels (total cholesterol [TC], high-density lipoprotein cholesterol [HDL-C], triglycerides [TG] and low-density lipoprotein cholesterol [LDL-C]) to assess for dyslipidemia
- Alanine aminotransferase (ALT) to assess for non-alcoholic fatty liver disease (NAFLD)
- Complete blood count (CBC)
- Thyroid-stimulating hormone (TSH) (20–30% of children may have associated autoimmune thyroiditis)⁴⁷
- Obtain urine sample for:
 - Urinalysis (routine and microscopy if presence of hematuria)
 - Albumin to creatinine ratio
 - Dipstick test for glucose, ketones, protein

MANAGEMENT

The management and prevention of diabetes mellitus and associated complications is a high priority in health planning and health care delivery in Aboriginal communities. Commencing at the time of diagnosis of type 2 diabetes, all children should receive intensive counselling, including lifestyle modification, from an interdisciplinary pediatric health care team.⁴⁸ Youth do not respond well to scare tactics. Positive encouragement and focusing on success are helpful in managing youth with type 2 diabetes.

Goals of Treatment

- Attain optimum glycemic control
- Educate the client (and caregivers/family) for self-care
- Prevent long-term complications

Appropriate Consultation

An urgent consultation with a physician is advisable for all children with newly diagnosed type 1 diabetes mellitus.

If a diagnosis of type 2 diabetes is confirmed and the symptoms and signs are not severe, medical treatment is not necessarily urgent. The diagnosis is more likely to constitute a medical emergency if there are moderate to large quantities of ketones in the urine and other clinical signs of ketoacidosis (for example, dehydration). However, ketoacidosis is rarely seen in type 2 diabetes.

Nonpharmacologic Interventions

Diet and Nutrition

Diet is the main focus of diabetes management. It is usually advisable to completely restructure the diet of the entire family. Starting with just cutting out juice, soda and chips can often significantly improve glycemic ranges in a youth with type 2 diabetes.

A diabetic child's diet should be low in simple carbohydrates, moderate in complex carbohydrates (starches) and high in fibre. A system of dietary exchanges, as recommended by the Canadian Diabetes Association, is useful.

Where feasible, both the parents (or caregiver) and the child should participate in a diabetes education program, including nutritional and lifestyle counselling. Where this is not possible, nurses, physicians and CHRs must work together to provide as much information as possible to affected families.

Calorie reduction for weight loss is recommended for obese children.

Physical Activity

Exercise reduces plasma glucose levels and facilitates entry of glucose into the cells. Regular exercise also decreases the risk of cardiovascular disease and promotes weight loss. All children with type 2 diabetes should be encouraged to adhere to a regular exercise program. All community resources (for example, a physical education teacher at the school and community recreation director) should be engaged in this effort.

Home Blood Glucose Monitoring (HBGM)⁴⁹

- 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 journal 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 individualized⁵⁰
- For most patients with type 2 diabetes treated with 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 benefits⁵⁰

- For women with gestational diabetes not using antidiabetes drugs, the optimal daily frequency of HBGM should be individualized⁵⁰
- 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
- 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

There are several useful reference documents available from the Canadian Paediatric Society (CPS), the Canadian Society for Exercise Physiology (CSEP), and the Public Health Agency of Canada (PHAC). These include:

- The “*Healthy Active Living for Children and Youth series*” (HAL2002-01] (CPS, 2002) available at: <http://www.cps.ca/english/statements/HAL/HAL02-01.pdf>
- “*Canadian Physical Activity Guidelines*” available at: <http://www.csep.ca/english/view.asp?x=804>
- “*Physical Activity*” available at: <http://www.phac-aspc.gc.ca/hp-ps/hl-mvs/pa-ap/index-eng.php>
- “*Physical Activity: tips to get active*” available at: <http://www.phac-aspc.gc.ca/hp-ps/hl-mvs/pa-ap/05paap-eng.php>

Community-based programs are beneficial to increase community knowledge about nutrition, physical activity, obesity and diabetes. The development of community and school recreation programs is an opportunity to collaborate with community leaders, teachers and health service providers.

Pharmacologic Interventions

Insulin is required for the treatment of type 1 diabetes.

Insulin is required in children with type 2 diabetes with severe metabolic decompensation at diagnosis (for example, DKA, severe symptoms, HbA1C $\geq 9\%$).²⁴

Data are limited on the efficacy and safety of oral antihyperglycemic agents in children; however, metformin is safe and effective when used at doses up to 1000 mg twice daily in children aged 10–16 years.⁵¹ It should be used in conjunction with nonpharmacologic management. The medications may need to be tapered or stopped after the youth has successfully adopted the lifestyle changes and the glucose remains normal. Drug treatment must be ordered by a physician.

Monitoring and Follow-Up

Children with type 2 diabetes need close, regular medical follow-up. The most useful indicators are weight (BMI) and general health. Fasting serum glucose and Hb_{A1C} levels are indicators of diabetes control, but the focus should be on lifestyle, weight loss and exercise.

Monitoring for complications should include blood pressure, eye examination, urinalysis, urine albumin creatinine ratio, renal function (eGFR), sensory function in extremities and lipid profiles.

The Canadian Diabetes Association has made the following recommendations for screening for complications of diabetes for all adolescents (13–18 years)³⁰ and for children < 13 years, as indicated:

Initial Follow-Up After Diagnosis

- There are many self-management education topics to be covered following diagnosis (diet, physical activity, home glucose monitoring, foot care, medications). Therefore, follow-up should focus on enabling the child/caregiver to be able to self-manage their diabetes and may occur every 4–6 weeks initially or more often as needed
- All clients (and their families) should be screened for symptoms of psychological distress
- All clients should be considered for influenza and pneumococcal immunizations

At diagnosis, then every 3–6 months:

- Measure BP, weight, height, waist circumference
- Measure fasting serum glucose and Hb_{A1C}
- Review compliance with drug therapy, if applicable
- Review home glucose monitoring diary
- Review compliance with nonpharmacologic therapy (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

At diagnosis, then every 1 year:

- Perform quality control of glucometer; compare venous fasting serum glucose with glucometer reading
- Measure alanine aminotransferase (ALT)
- Perform random urine for albumin:creatinine ratio (ACR) and serum creatinine for estimated glomerular filtration rate (eGFR)
- Provide influenza vaccine

- Refer for screening and evaluation for diabetic retinopathy
- Perform foot exam and screening for peripheral neuropathy (symptoms of numbness, pain, cramps, paresthesia, vibration sense, skin sensation, light touch and ankle reflexes)
- Measure androgen levels, including dehydroepiandrosterone sulphate (DHEA) and free testosterone at puberty in females with oligo/amenorrhea, acne and/or hirsutism (excessive hair growth)
- Discuss contraception and fertility issues

At diagnosis, then every 1–3 years:

- Measure fasting lipid levels (total cholesterol [TC], high-density lipoprotein cholesterol [HDL-C], triglycerides [TG] and low-density lipoprotein cholesterol [LDL C])

As needed:

- Measure fasting serum glucose
- Perform urine dipstick screening

Referral

Arrange for medevac if there is evidence of ketonuria or ketoacidosis.

- Refer all newly diagnosed clients to a physician as soon as possible for complete evaluation
- Arrange follow-up with a physician or nurse practitioner every 3–6 months if stable or more frequently with a physician if not well controlled or there is evidence of complications, as necessary
- The long-term management of type 2 diabetes is a collaborative effort between physicians, nurses, CHRs, nutritionists, educators and others

DIABETES IN ADOLESCENT PREGNANCY

There are special considerations for the management of pre-existing or gestational diabetes in pregnant adolescent girls. Good control of blood glucose is desirable to reduce the risk of a large baby with congenital malformations or stillbirth.

The higher risk pregnancy requires careful monitoring of glucose and regular care by a physician. Drug therapy is often needed. Insulin is the treatment of choice for management of type 2 diabetes in pregnant women (oral antihyperglycemic agents are not presently recommended).⁵² Many adolescent girls will require insulin during pregnancy and specialized prenatal care.

For detailed information on diabetes in pregnancy, see “Gestational Diabetes Mellitus” in the adult Chapter 12, “Obstetrics”.

PREVENTION

Risk Reduction for Type 2 Diabetes in Aboriginal Children⁵³

The Canadian Paediatric Society proposes the following initiatives to reduce the risk of type 2 diabetes in Aboriginal children and adolescents. These initiatives engage community leaders including elders, band council, women leaders, health providers (nurse practitioners, nurses, CHRs), teachers and school staff, youth groups, local businesses, etc.

- Culturally based and community-run diabetes prevention programs should be established in First Nations communities
- Traditional values (including traditional diets), activities and lifestyles, should be encouraged in an effort to prevent and/or control type 2 diabetes
- Breastfeeding should be encouraged and is a proven method of reducing obesity in children
- Daily physical activity for at least 60–90 minutes (*per “Canada’s Physical Activity Guide”*) is recommended for all children
- Schools, daycares and Head Start programs should implement at least 30 minutes of high-energy daily physical activity for all students
- Schools, daycares and Head Start programs should incorporate programs into their curriculum that explain the need for healthy living and healthy eating
- Schools should be discouraged from selling candy or other sweets for fundraising purposes
- A healthy diet, based on *“Canada’s Food Guide for First Nations, Inuit and Metis”*, is encouraged
- All Aboriginal community leaders (band councils, health care providers, teachers, etc.) should provide ample access to safe physical activity within the communities
- Local stores should be encouraged to stock healthy foods and to place high-calorie “junk” food in less obvious locations in the store (for example, not at the checkout)
- Passive activities such as watching television, playing video games and using the computer should be limited to a maximum of 1.5–2 hours per day

Screening for Type 2 Diabetes⁵⁴

The Canadian Paediatric Society recommends screening for type 2 diabetes for all children as follows:

Children who meet the criteria:

- Aboriginal descent
- Body mass index (BMI) \geq 85th percentile expected for age
- Age \geq 10 years

AND any one of the following:

- Sedentary lifestyle
- Children born to mothers who had gestational diabetes
- First- or second-degree relative with type 2 diabetes
- Acanthosis nigricans
- Dyslipidemia
- Hypertension
- Polycystic ovarian syndrome (PCOS)

FAILURE TO THRIVE

Failure to thrive (FTT) is a condition (rather than a disease) characterized by failure to gain weight or a deceleration in weight gain, low weight/height ratio and/or low weight/height/head circumference ratio.^{55,56} Weight for age falling below the third percentile on gender-appropriate growth chart or a fall in weight for age over two major percentile lines.^{57,58} Height and head circumference are affected in severe cases.

The immediate cause of this condition is inadequate nutrition⁵⁹ and may extend through a range of situations from inexperience on the part of the parents or caregiver to an organic cause and to neglect and abuse. It is recognized that the parent-child relationship may play a role in failure to thrive.⁶⁰

FTT is a common problem in pediatric practice and accounts for 1–5% of pediatric inpatient admissions.⁵⁶ It occurs more frequently among children living in poverty; one report claimed 10% of children aged < 1 year had FTT. Growth needs to be monitored carefully so that FTT is appropriately diagnosed.

CAUSES

Historically, FTT was classified as organic or non-organic. However, as most children have a mixed etiology, this classification is not useful.^{56,57} Therefore, classification of FTT according to the pathophysiologic mechanism is preferred (*see Table 4, below*).⁵⁶

Table 4 – Possible Causes of FTT**Inadequate nutrient intake**

- Inappropriate feeding technique
- Disturbed caregiver/child relationship
- Economic deprivation
- Inappropriate nutrient intake (for example, excess fruit juice consumption, factitious food allergy, inappropriate preparation of formula, inadequate quantity of food, inappropriate food for age, neglect, fad foods)
- Inappropriate parental knowledge of appropriate diet for infants and toddlers
- Insufficient lactation in mother
- Gastroesophageal reflux
- Psychosocial problems
- Maternal/infant dysfunction
- Mechanical problems (cleft palate, nasal obstruction, adenoidal hypertrophy, dental lesions)
- Sucking or swallowing dysfunction (CNS, neuromuscular, esophageal motility problems)

Inadequate appetite or inability to eat large amounts

- Psychosocial problems – apathy or rumination
- Cardiopulmonary disease
- Hypotonia, muscle weakness or hypertonia
- Anorexia of chronic infection or immune deficiency
- Cerebral palsy
- CNS pathology (for example, tumor, hydrocephalus)
- Genetic syndromes
- Anemia (for example, iron deficiency)
- Chronic constipation
- Gastrointestinal disorder (for example, pain from gastroesophageal reflux, intestinal tract obstruction)
- Craniofacial anomalies (for example, cleft lip and palate, micrognathia)

Inadequate nutrient absorption or increased losses

- Malabsorption (lactose intolerance, cystic fibrosis, cardiac disease, malrotation, inflammatory bowel disease, milk allergy, parasites, celiac disease)
- Biliary atresia, cirrhosis
- Vomiting or “spitting up” (related to infectious gastroenteritis, increased intracranial pressure, adrenal insufficiency or drugs [for example, purposeful administration of syrup of ipecac])
- Intestinal tract obstruction (pyloric stenosis, hernia, malrotation, intussusception)
- Infectious diarrhea
- Necrotizing enterocolitis or short bowel syndrome

Increased nutrient requirements or ineffective utilization

- Hyperthyroidism
- Malignancy
- Chronic inflammatory bowel disease
- Chronic systemic disease (juvenile rheumatoid arthritis)
- Chronic or recurrent systemic infection (urinary tract infection, tuberculosis, toxoplasmosis)
- Chronic metabolic problems (hypercalcemia, storage diseases and inborn errors of metabolism, such as galactosemia, methylmalonic acidemia, diabetes mellitus, adrenal insufficiency)
- Chronic respiratory insufficiency (bronchopulmonary dysplasia, cystic fibrosis)
- Congenital or acquired heart disease

Risk Factors⁵⁶

Medical risk factors:

- Premature birth (particularly when associated with intrauterine growth retardation)
- Developmental delay
- Congenital anomalies (for example, cleft lip and/or palate)
- Intrauterine exposures (for example, alcohol, anticonvulsants, infection)
- Lead poisoning
- Anemia
- Increased metabolic rate, maldigestion or malabsorption

Psychosocial risk factors:

- Poverty
- Health and nutrition beliefs (for example, fear of obesity, prolonged exclusive breastfeeding)
- Social isolation
- Life stresses
- Poor parenting skills and parent(s) or caregiver with psychosocial problems
- Disordered feeding techniques
- Unstable, dysfunctional family unit including mental illness, substance abuse, violence, domestic abuse

HISTORY⁶¹

- Record of previous weight, height and head circumference for comparison (for premature infant, adjust expected values to correct for gestational age at birth)
- Evaluation of FTT requires an extensive history including the following categories: dietary, feeding, medical, psychosocial and family

Dietary History

- Dietary intake; 24-hour log of all foods given and eaten
- Amount of food and/or formula (also consider maternal ingestion of milk suppressants [for example, alcohol, diuretic drugs, pseudoephedrine in cold remedies], inadequate milk supply, nipple problems, inadequate let-down)
- Food preparation (if formula is too diluted, then too few calories; if too concentrated, then unpalatable)
- Types of food
- Dietary restrictions related to perceived food allergies or dietary beliefs and practices
- Food preferences

- Calculate total caloric intake (for infants)
- Beverage consumption (especially, milk, juice, sodas and water) and dilution

Feeding History

- Time, location and circumstance of feedings (for example, distracted infants, inappropriate supervision, duration of meal times)
- Infrequent, brief feedings
- Poor sucking reflex
- Psychosocial events associated with feeding time
- Inappropriate feeding techniques for developmental stage
- Snack intake (type and frequency)

Medical History

- Birth history (complications, small for gestational age, premature)
- Recent infection (for example, otitis media, gastroenteritis, recurrent viral infections)
- Chronic medical condition (for example, anemia, asthma, congenital heart disease)
- Past hospitalizations, injuries, accidents
- Stool pattern (including frequency, consistency, blood, mucus)
- Vomiting, reflux or other gastrointestinal symptoms
- Infant sleeping problems
- Medications
- Review of all systems

Social History

- Number of household members
- Primary caregivers of infant/child
- Interference with adequate care-taking
- Maternal malnutrition, exhaustion or depression
- Child described as having a difficult personality or ruminating
- Family stressors (including economic, intrafamilial, major life events)
- Substance abuse
- Other children with FTT, history of neglect or abuse

Family History

- Family members with short stature
- Medical conditions or FTT in other siblings
- Mental illness

PHYSICAL FINDINGS⁶³

- General:
 - Measure weight (unclothed and no diaper), height (recumbent < 2 years; standing ≥ 2 years) and head circumference. *Note: the Canadian Paediatric Society recommends that First Nations and Inuit children should be measured using the same growth charts as the general Canadian population.*⁶⁴ See “Growth Measurement”; in the Chapter “Pediatric Prevention and Health Maintenance” for measurement tips and growth charts
 - Plot on gender- and age-appropriate growth chart. Findings: weight for age = below third percentile OR weight < 80% of median weight in relation to height OR growth chart shows significant deceleration of weight gain (line recording weight gain on growth chart crosses two major percentile lines)
 - Perform developmental screening using standardized form
 - Look for signs of abuse and neglect (minimal smiling, decreased vocalization, resistance to being held, self-stimulating rhythmic behaviours, apathetic/withdrawn and “frozen watchfulness”)
- Integumentary: poor hygiene, signs of inflicted trauma, pallor, cachexia, sparse hair, scaling skin, shape of nails, rashes, dysmorphic features (for example, small palpebral fissures, midface hypoplasia, flat philtrum, thin vermilion border) (*see section “Assessment of the Integumentary System” in the pediatric Chapter 16 “Skin”*)
- Head, Ears, Eyes, Nose and Throat: microcephaly, delayed closure of fontanelle, cataracts, papilledema, oropharyngeal lesions (for example, caries, tongue enlargement/lesions, mandibular hypoplasia, tonsillar hypertrophy, defects in soft or hard palate), delayed tooth eruption, thyroid enlargement, drooling (*see section “Assessment of the Eyes” in the pediatric Chapter 8, “Eyes” and section “Assessment of the Ears, Nose, Throat and Mouth” in the pediatric Chapter 9, “Ears, Nose, Throat and Mouth”*)
- Respiratory: auscultate noting wheezing, crackles, prolonged expiratory phase, hyperexpansion (*see section “Assessment of the Respiratory System” in the pediatric Chapter 10 “Respiratory System”*)
- Cardiovascular: auscultate the heart, noting murmurs (*see section “Assessment of the Cardiovascular System” in the pediatric Chapter 11, “Cardiovascular System”*)

- Gastrointestinal: protuberant abdomen (associated with celiac disease, malabsorption or cystic fibrosis), hyperactive bowel sounds, rectal lesions (*see section “Assessment of the Gastrointestinal System” in the pediatric Chapter 12, “Gastrointestinal System”*)
- Musculoskeletal: clubbing of nails, bone deformities, edema
- Neurologic: observe infant feeding to assess oral motor abilities (suck, gag and swallow reflexes), assess cranial nerves, deep tendon reflexes (hypotonia), muscle strength, signs of neurologic disorders (for example, fetal alcohol syndrome) (*see section “Assessment of the Central Nervous System” in the pediatric Chapter 15, “Central Nervous System”*)
- Caregiver Interaction: observe infant feeding to assess caregiver skills (observe for gagging, choking, refusal to feed, responsiveness of parent to child’s cues or unusual parent-infant interactions)

Growth Patterns**Expected Weight Gain⁵⁶**

Age	Weight Gain
0 to 3 months	26 to 31 g/day
3 to 6 months	17 to 18 g/day
6 to 9 months	12 to 13 g/day
9 to 12 months	9 to 13 g/day
1 to 3 years	7 to 9 g/day

Birth weight doubles at 4–6 months and triples at 12 months.⁶⁵

ENVIRONMENTAL FINDINGS

- Every effort should be made to observe the home setting for safety including interaction with caregivers and other family members
- Identify psychosocial or mental health problems of caregivers

DIFFERENTIAL DIAGNOSIS

Any condition identified in *Table 4, “Possible Causes of FTT,”* above.

COMPLICATIONS⁵⁶

Prognosis with respect to weight gain and growth for children with FTT is good, although between 25% and 60% of infants with FTT will remain small for age (weight or height < 20th percentile for age and sex). Cognitive function is below normal for

50% of children with FTT and a high frequency of behavioural problems and learning difficulties are found at follow-up. This is potentially due to continued adverse social circumstances.

DIAGNOSTIC TESTS⁶⁶

- Careful, detailed history and physical examination are the most valuable diagnostic tools
- Observation of infant and his or her interaction with caregivers and environment
- Accurate plotting of growth curves, including weight, height and head circumference should be done at each clinic visit
- Routine laboratory work-up should be kept to a minimum and should be done after consultation with a physician. Some tests that may be decided on include:
 - Complete blood count (CBC)
 - Urinalysis
 - Urine culture
 - Chemical profile, including sodium, potassium, chloride, blood urea nitrogen (BUN), calcium, phosphorus, liver enzymes
 - Erythrocyte sedimentation rate
 - Other studies as dictated by results of history and physical examination (for example, if there are GI symptoms such as diarrhea; stool samples for culture and sensitivity and occult blood)

MANAGEMENT

Goals of Treatment⁶³

- Identify the cause of failure to thrive
- Improve nutritional status through provision of adequate nutrition intake for catch-up growth
- Protect child from permanent sequelae
- Improve parenting skills of caregivers and caregiver/child interactions
- Manage organic disease, if present
- Ameliorate social and/or family problems
- Provide mental health support for parents

Appropriate Consultation

Consult a physician as soon as possible. Referral to a dietitian/nutrition consultant is recommended.

Admission to an inpatient setting is often the first step in sorting out the cause of this condition.

Nonpharmacologic Interventions

Diet⁶⁷

- Provision of balanced, high-calorie diet on a regular schedule for catch-up growth. The environment should be pleasant, without distractions, and not rushed. Recommended daily energy intake is:

Age	Energy (kcal/kg/day) for average replacement
10 days to 1 month	120
1 to 2 months	115
2 to 3 months	105
3 to 6 months	95
6 months to 5 years	90

- A three-day food diary should be kept to ensure that the appropriate amount of energy is given daily. Underestimation of calories is common
- During the catch-up period, discontinue all solids and liquids with fewer calories per ounce than formula or milk (that is, stop all juice and water)

Client Education

- Depends on cause (for example, provide information about preparing formula if inadequate dietary intake is the suspected cause)
- When environmental deprivation is established, attempts to engage and interact with the caregivers and family in a nonpunitive way are essential

Behavioural and Family Treatment

- Involve parents or caregiver actively in investigation and therapy
- Recognize that parents or caregiver may experience frustration and guilt
- Restore adequate caregiving
- Modify child's maladaptive learned feeding responses
- Address interactional difficulties between parents (or caregiver) and child

Other Measures

- Provision of stimulation, cuddling and affection to children in inpatient and outpatient settings
- Consult your regional policy regarding protocols to inform youth protection or social services if abuse or neglect suspected

Pharmacologic Interventions^{56,68}

- Vitamin and mineral supplementation including iron and zinc (to reduce energy cost of weight gain during catch-up growth). A physician should be consulted about appropriate dosages

Monitoring and Follow-Up

- Follow-up should be at least weekly for the first months, then at least monthly until catch-up growth is demonstrated and the positive trend is maintained^{56,69}
- When environmental deprivation is established, extremely close follow-up (weekly, both at home and in the clinic) is essential. If the family fails to comply with necessary measures, child protection authorities must be notified and foster care may be necessary

Referral

Referral for investigations to rule out organic causes is advisable. The urgency of such referral depends on the particular situation and will be determined by the physician.

Long-term, multifaceted intervention is necessary when environmental deprivation is established:

- Parenting skills training for caregivers
- Psychiatric and social services for family
- Developmental stimulation for child
- Community infant-stimulation programs for caregiver/child

COMMON IMMUNOLOGIC PROBLEMS

ALLERGIES⁷⁰

A hypersensitivity reaction where there is an altered immunologic response to an antigen that results in disease or damage to the host. To develop allergies one must have appropriate genes, contact with allergen(s) and environmental factors. There are four types of hypersensitivity reactions:

- Type I – Immediate or IgE-mediated hypersensitivity reaction (for example, food [not lactose intolerance], environmental and seasonal allergies, dust)
- Type II – Direct antibody-mediated cytotoxic (tissue specific) reaction (for example, Graves disease)
- Type III – Immune complex-mediated (for example, systemic lupus erythematosus)
- Type IV – Delayed-type or cell-mediated (for example, poison ivy and metals [jewellery])

Note: hypersensitivity reactions to drugs may be Type I (for example, hives or anaphylaxis after receipt of penicillin), Type II (for example, drug-induced hemolytic anemia, thrombocytopenia or neutropenia), Type III (for example serum sickness, vasculitis or drug fever after receipt of penicillin, amoxicillin, cefaclor or trimethoprim-sulfamethoxazole) or Type IV (for example, Stevens-Johnson syndrome or toxic epidermal necrolysis).⁷¹

Individuals who are genetically predisposed to develop allergies are called atopic. If one parent has an allergy, 40% of their children will develop allergies. If both parents have allergies, up to 80% of their children will develop allergies. Atopic individuals produce higher quantities of IgE. These individuals often present with the atopic triad: atopic dermatitis (eczema), allergic rhinitis (hay fever) and asthma.

HISTORY

- Age at onset
- Progression of symptoms
- Seasonality (for example, if an environmental allergy occurs in early spring, it is probably related to trees; if in early summer, to grass; if in fall, to ragweed)
- Exposure to animals
- Exposure to dust
- Exposure to mold in damp places, plants
- Exposure to drugs (for example penicillins, cephalosporins, quinolones)
- Complete history of environment (both indoor and outdoor)
- Record of activities
- Record of eating habits

- Complete review of systems, since allergic symptoms may involve any system
- Relation of symptoms to exertion or temperature change

MOST COMMON SYMPTOMS

- Skin: itch, rash, dryness
- Swelling of lips, eyes, ears
- Nasal symptoms: clear discharge, coryza, sneezing, snoring, congestion
- Respiratory symptoms: wheezing, difficulty breathing, cough (especially at night)
- GI symptoms: nausea, vomiting, abdominal pain (cramps), diarrhea

PHYSICAL FINDINGS

- Vital signs (change only with severe reactions): resting pulse (increased), respiration rate (increased), low blood pressure; growth failure (or failure to thrive) if food allergies
- Integumentary: angioedema (swelling caused by exudation), urticaria (hives), eczema (*see section “Assessment of the Integumentary System” in the pediatric Chapter 16, “Skin”*)
- Head and Neck: conjunctivitis (water, red, itch eyes without purulent discharge), rhinitis, allergic facies (dark circles under eyes, folds below eyes, transverse crease over bridge of nose), laryngeal edema, adenoid facies caused by chronic mouth breathing (deep nasolabial folds, high arching of palate, enlargement of tonsils and adenoids) (*see section “Assessment of the Eyes” in the pediatric Chapter 8, “Eyes” and section “Assessment of the Ears, Nose, Throat and Mouth” in the pediatric Chapter 9, “Ears, Nose, Throat and Mouth”*)
- Respiratory: auscultate lungs, wheezes from bronchospasm with asthma exacerbation, stridor (inspiratory noise), cough (especially at night) (*see section “Assessment of the Respiratory System” in the pediatric Chapter 10 “Respiratory System”*)
- Cardiovascular: auscultate the heart, noting rate/rhythm (dysrhythmias) (*see section “Assessment of the Cardiovascular System” in the pediatric Chapter 11, “Cardiovascular System”*)
- Gastrointestinal: auscultate bowel sounds, palpate for tenderness (*see section “Assessment of the Gastrointestinal System” in the pediatric Chapter 12, “Gastrointestinal System”*)

COW’S MILK ALLERGY^{72,73,74}

There are a variety of disorders related to cow’s milk allergy (CMA). CMA is an immune response to proteins in milk as opposed to lactose intolerance (*see section “Lactose intolerance” in this chapter*) which occurs when the body is missing lactase, the enzyme allowing the digestion of lactose. The reactions from lactose intolerance are related to maldigestion and include symptoms like abdominal pain and bloating, diarrhea and flatulence.

In cow’s milk allergy, the body’s immune system reacts to the protein in milk and includes both IgE-mediated reactions (for example, urticaria and wheezing) and non-IgE-mediated reactions (colic, vomiting and diarrhea) (*see Table 5, “Manifestations by System of Cow’s Milk Allergy”*). The allergy is usually seen in early infancy (first 2 months of life) and most children outgrow it by age 3, but they may develop other allergies. The reactions from cow’s milk allergy can range from an immediate response to a delayed response and is more common in infants with a family history of allergies.⁷⁵

CAUSES

- Unknown

HISTORY AND PHYSICAL FINDINGS^{73,74}

- Onset
- Duration
- Family history of atopic disease (for example, eczema, allergic rhinitis or asthma) predisposes one to CMA
- Dietary history
- Stages of reaction:
 - Immediate (within 30 minutes of exposure) (IgE-sensitized reaction)
 - Urticaria (skin rashes, perioral erythema)
 - Angioedema of the face
 - Anaphylaxis
 - Intermediate (within hours) [Non-IgE-sensitized reaction]
 - Gastrointestinal symptoms
 - Late (1 to 5 days)
 - Gastrointestinal symptoms
 - With or without respiratory symptoms
 - With or without cutaneous symptoms

Table 5 – Manifestations by System of Cow's Milk Allergy

System	Manifestations
Gastrointestinal	Nausea Abdominal pain Postprandial emesis Diarrhea (5–8 hr postprandial) Blood in stools Gastritis Gastroenteritis Enterocolitis (severe vomiting and diarrhea within hours of ingestion) Proctocolitis (blood-streaked, mucousy, loose stools and occasionally diarrhea in infants who are otherwise well-appearing) Chronic constipation Colic responsive to elimination diet
Cutaneous	Atopic dermatitis Eczema Urticaria Angioedema
Respiratory	Allergic rhinitis Asthma and/or wheezing
General	Anaphylaxis Weight loss

DIFFERENTIAL DIAGNOSIS⁷⁶

- Lactose intolerance
- Celiac disease (malabsorption syndrome)
- Gastroenteritis
- Gastroesophageal reflux
- Colic
- Pyloric stenosis
- Crohn's disease

COMPLICATIONS

- Gastric outlet obstruction
- GI blood loss leading to iron-deficiency anemia
- Protein malabsorption leading to growth retardation (for example, failure to thrive)
- Edema secondary to hypoproteinemia

DIAGNOSTIC TESTS

- Allergy testing done by an allergist, not performed before one year of age. Consult a physician for referrals. Serum IgE antibodies are examined
- CBC

MANAGEMENT

Outpatient care is appropriate except in cases of malnutrition.

Goals of Treatment

- Primary prevention
- Reduce symptoms
- Prevent complications

Nonpharmacologic Interventions⁷⁷

Allergy avoidance strategies:

- Identify the at-risk infant early (prenatally or soon after birth; document highly atopic families)
- Breastfeeding should be advocated as a means of preventing food allergy, especially in atopic families
- Delay introduction of cow's milk (not before 12 months of age)

CMA interventions:

- Breastfeeding mothers should eliminate milk and milk products from their diet
- Replace cow's milk formula with soy-based formula, extensively hydrolyzed formula or amino acid-based formula
- Arrange for a consultation with a nutritionist

Pharmacologic Interventions

For those with a true CMA: epinephrine autoinjector (prescribed by a physician).

Monitoring and Follow-Up

- Monitor as necessary until symptoms are under control
- Monitor growth to ensure that child is gaining weight

Referral

Refer to a physician for evaluation if:

- symptoms are not controlled by dietary measures (for example, elimination of cow’s milk from the diet of a breastfeeding mother or a change in infant formula),
or
- there are concerns about an underlying pathologic condition, such as inflammatory bowel disease, or
- the child is not thriving.

LACTOSE INTOLERANCE⁷⁸

Inability to digest lactose (milk sugar, a disaccharide) into its constituent sugars, (glucose and galactose) because of low levels of lactase enzyme in the brush border of the duodenum. The amount of lactose that causes symptoms varies from individual to individual, depending on the amount of lactose consumed, the degree of lactase deficiency and type of lactose-containing food that is ingested. In contrast to lactose intolerance, cow’s milk allergy (CMA) is distinct and involves the immune system and varying degrees of injury to the intestinal mucosa.

FORMS OF LACTOSE INTOLERANCE

Lactose Malabsorption

- Physiologic problem that manifests as lactose intolerance
- Imbalance between the amount of ingested lactose and the amount of lactase available to hydrolyze the disaccharide

Primary Lactase Deficiency

- Age at presentation usually adolescence or adulthood
- Gradual onset that progresses over many years
- Prevalence and age of onset varies according to ethnic background^{79,80}

Secondary Lactase Deficiency

- Caused by any injuries to the intestinal mucosa (for example, acute gastroenteritis, persistent diarrhea, small bowel overgrowth) or a reduction in mucosal surface (for example, because of resection)
- Usually transient, with duration of intolerance determined by the nature and course of the primary condition
- 50% or more of infants with acute or chronic diarrhea (especially those with rotavirus disease) have lactose intolerance. Breast milk contains a large quantity of lactose but does not seem to worsen diarrhea associated with viral or bacterial diseases
- Also common in individuals with giardiasis, cryptosporidiosis and ascariasis, inflammatory bowel disease (Crohn’s disease) and AIDS malabsorption syndrome
- Age at presentation varies with underlying condition

Congenital Lactase Deficiency

- Very rare

Developmental Lactase Deficiency

- Relative lactase deficiency observed among preterm infants of less than 34 weeks’ gestation

CAUSES

Primary Form⁷⁹

- Racial or ethnic lactose malabsorption (genetically regulated deficiency in lactase activity)
- Developmental lactase deficiency (premature infants born before 34 weeks’ gestation)
- Congenital lactase deficiency (rare autosomal recessive disorder)

Secondary Form⁸¹

- Bacterial overgrowth causing increased fermentation of dietary lactose in small bowel
- Mucosal injury to GI tract
- Inflammatory bowel disease (including Crohn’s disease)

Note: Lactase activity is normal in all healthy children of any racial or ethnic group until approximately 5 years of age. Thus, lactose intolerance detected in younger children usually indicates an underlying mucosal lesion or bacterial overgrowth syndrome.

HISTORY AND PHYSICAL FINDINGS

- Bloating
- Cramping (primarily in periumbilical area or lower abdomen)
- Abdominal pain
- Diarrhea or loose stools
- Flatulence
- Audible rumbling (borborygmus)
- Vomiting is common in adolescents
- Frothy, bulky, watery stool in children
- Malnutrition may occur (*see Table 4, “Physical Signs of Nutritional Deficiency Disorders” in the pediatric Chapter “Nutrition”*)
- Inadequate weight gain

Degree of symptoms varies with osmolality, fat content in which the sugar is ingested, the rate of gastric emptying, the sensitivity to intestinal distention of the upper small bowel, the rate of intestinal transit and the response of the colon to the carbohydrate load.

DIFFERENTIAL DIAGNOSIS

- Diseases mentioned under “*Secondary Lactase Deficiency*”
- Cystic fibrosis
- Malnutrition
- Failure to thrive

COMPLICATIONS

- Calcium deficiency
- Vitamin D deficiency and rickets
- Failure to thrive

DIAGNOSTIC TESTS^{79,82}

- Lactose tolerance test (50 g test dose is taken with blood glucose levels measured at 0, 60, 120 minutes plus the assessment of GI symptoms)
- Lactose breath hydrogen test (measures lactose non-absorption) is especially useful in children (to be ordered only by a physician)

MANAGEMENT

Outpatient care, except in severe cases of malnutrition.

Nonpharmacologic Interventions⁷⁹**Dietary adjustments:**

- Reduce or restrict intake of dietary lactose to control symptoms
- Yogurt and fermented products such as hard cheeses are tolerated better than milk
- Calcium-fortified juices for children > 1 year old who cannot drink milk
- Ensure adequate calcium and vitamin D supplementation

Client education:

- Suggest that parents (or caregiver) and child learn what level of lactose is tolerable
- Stress that parents or caregiver must read labels on commercial products, because milk sugar is used in many products and therefore may cause symptoms
- Lactose-intolerant children may tolerate whole milk or chocolate milk or ice cream better than skim milk due to the high sugar and fat content
- Lactose is tolerated better when it is consumed with other food products than when it is consumed alone

Pharmacologic Interventions⁸³

- Enzyme replacement therapy with “lactase” (beta galactosidase). When added to food (as drops) or taken with a meal (as tablets or capsules) lactase lowers, but does not completely eliminate, dietary lactose intake
- Lactase (for example, Lactaid, Lacteeze, Dairyaid, others) is a nonprescription drug that is available in different strengths and dosage forms (tablets, capsules, drops). The efficacy in preventing symptoms varies with a given product; thus it is necessary to individualize the dose
- Start with 1 or 2 tablets or capsules with lactose-containing foods or meals

These agents vary in effectiveness at preventing symptoms. In some areas, milk with added lactase is available.

Supplementary calcium and vitamin D is necessary if the dietary intake of milk and milk products is insufficient. See chart below for calcium and vitamin D recommendations (from all sources, diet and supplements).⁸⁴

Recommended Calcium and Vitamin D intake from all sources*

Calcium

Children (4–8 years)	800 mg/day
Adolescents (9–18 years)	1 300 mg/day
Premenopausal women	1 000 mg/day
Men < 50 years	1 000 mg/day
Pregnant or lactating women	1 000 mg/day

Vitamin D

< 50 years	40 IU/day
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* 'All sources' means total diet and supplement.

Monitoring and Follow-Up

- Monitor as necessary until symptoms are under control
- Monitor growth to ensure that the child is gaining weight

Referral

Refer to a physician for evaluation if:

- symptoms are not controlled by dietary or pharmacologic (lactase) measures
- there are concerns about an underlying pathology (for example, inflammatory bowel disease)
- the child is not thriving.

URTICARIA (HIVES)^{85,86}

White, raised, palpable areas (wheals) in the superficial dermis surrounded by areas of redness (flares) accompanied by itching. A classic finding of urticaria is the effervescent rash – a rash that resolves in one area and starts in another.

Acute urticaria is a common condition affecting up to 20% of the population at some point in their lives. It is characterized by a rapid onset and resolution within several hours but may be recurrent. Many have a trigger but most are idiopathic.

CAUSES^{85,86}

Mechanism is the localized release of histamine with dilatation of the blood vessels in the skin and leakage of fluid into the surrounding tissue.

The following are frequent causes of urticaria:

- Drugs
- Foods
- Infections (viral, streptococcal)

- Inhaled allergens (for example, pollen, animal dander)
- Insect bites and stings
- Contact with latex (for example, balloons)
- Systemic diseases (for example, rheumatoid disease, malignant lesions, endocrine problems)
- Hereditary causes
- Physical causes (for example, exercise, cold, heat, exposure to sun)

HISTORY⁸⁶

- History of previous anaphylaxis/allergies
- Onset
- Duration
- Frequency (if recurrent)
- Diet
- Exposure to inhalants
- Family history of atopic disease (for example, asthma, allergic rhinitis or eczema)
- Fever
- Sore throat
- Other systemic symptoms (for example, heart racing, difficulty breathing)
- Exposure to drugs
- Recent travel
- Changes in health status

PHYSICAL FINDINGS

- Vital signs: temperature (normal), heart rate (normal or increased), respiration rate (normal), blood pressure (normal or decreased)
- Integumentary: urticarial rash (*see section "Assessment of the Integumentary System" in the pediatric Chapter 16, "Skin"*)

If swelling of the lips, eyes or ears or if there is any respiratory difficulty or stridor/wheezing, emergency treatment is immediately required. *See "Anaphylaxis" in the pediatric Chapter 20, "General Emergencies and Major Trauma"*.

DIFFERENTIAL DIAGNOSIS⁸⁶

- Insect bites
- Erythema multiforme
- Vasculitis (Henoch-Schönlein purpura)
- Viral exanthems
- Atopic dermatitis
- Contact dermatitis
- Maculopapular drug eruptions
- Pityriasis rosea

COMPLICATIONS

None related to urticaria.

If urticaria is associated with anaphylaxis, respiratory failure and death could ensue. If urticaria is due to an underlying disease, treatment must be directed to the specific disease.

DIAGNOSTIC TESTS

– None

In an older child (> 1 year), allergy testing may be useful if urticaria is recurrent. Consult a physician for referrals.

MANAGEMENT**Goals of Treatment**

- Identify and eliminate trigger
- Provide symptomatic relief (this may take several days to weeks)

Appropriate Consultation

Consult a physician if urticaria is extensive and/or acute respiratory symptoms are involved. For severe urticaria, a short course of systemic corticosteroids may be required if prescribed by physician.

Nonpharmacologic Interventions

Avoid contact with identified trigger.

Pharmacologic Interventions

If symptoms are mild, some degree of symptomatic relief can be obtained from common antihistamines:

For example: diphenhydramine hydrochloride (Benadryl), 1.25 mg/kg PO q6h prn, maximum dose 300 mg/day

For urgent treatment of anaphylaxis, give epinephrine 1:1000 0.01 mg/kg (maximum 0.3 mg) IM prior to calling a physician. *See also “Anaphylaxis” in the pediatric Chapter 20 “General Emergencies and Major Trauma”.*

Monitoring and Follow-Up

Follow up in 24 hours to ensure that symptoms are diminishing. Complete resolution may take several days to weeks.

Referral

Prepare for medevac if symptoms are severe or anaphylaxis is involved. Otherwise, refer child electively to a physician (or nurse practitioner) for evaluation.

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