Document History:

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#	Details of Revisions:	Approval:	Date:
1	New document		
2	Revised		
3	Revised		
4	Added Appendix II for laboratories capable of promptly reporting venous blood; Comment for limitations of glucometer testing: do NOT use venous blood; Delphic LIS comments; Delphic LIS comments Corrections to LIS comments	C. Oleschuk	2 April 2009 28 May 2009 8 June 2009
5	General revision with 2013 CDA Criteria	A. Sokoro	3 Dec 2013
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6.1	Delay in centrifugation vs analysis clarification (p.6).	E Petryayeva	4 Jan 2023
7	Clarified definition of 'time zero' (p. 6). Mentioned addition of calculator for pediatric patients (JA110-10-17B). Included product information for graduated disposable cups in Appendix 2. Corrected that patient weight for pediatric protocol should be <42kg (93 lbs)	N Landry	14 May 2024

1.0 PURPOSE AND SCOPE

To provide a procedure for provincial standardization of oral glucose tolerance testing for diagnosis of diabetes and screening/diagnosis of Pre-Diabetes and Type 2 diabetes mellitus (T2DM) according to 2018 Diabetes Canada Clinical Practice Guidelines.

2.0 RELATED DOCUMENTS

SOP Number	Title
110-10-18	Gestational Diabetes Mellitus (GDM) - 50g and 75g Oral Glucose Testing
100-10-79	Phlebotomy Collection Manual
JA110-10-18	Job Aid for 50g Gestational Diabetes Glucose Challenge Test
JA110-10-17	Job Aid for 75g Oral Glucose Tolerance Testing (T2DM and GDM)
JA110-10-17B	OGTT Calculator for Pediatric Patients
F110-10-17A	Oral Glucose Tolerance Testing (OGTT) Record Form
PB110-10-17	Oral Glucose Tolerance Testing - Patient Brochure
110-20-06	Fasting Protocols

3.0 BACKGROUND

3.1 Definition of Diabetes and Prediabetes

Diabetes mellitus is a heterogeneous metabolic disorder characterized by the presence of hyperglycemia due to impairment of insulin secretion, defective insulin action or both. The chronic hyperglycemia of diabetes is associated with relatively specific long-term microvascular complications affecting the eyes, kidneys and nerves, as well as an increased risk for cardiovascular disease (CVD). The diagnostic criteria for diabetes are based on thresholds of glycemia that are associated with microvascular disease, especially retinopathy. “Prediabetes” is a practical and convenient term referring to impaired fasting glucose (IFG), impaired glucose tolerance (IGT) (1) or a glycated hemoglobin (A1C) of 6.0% to 6.4%, each of which places individuals at high risk of developing diabetes and its complications.

3.2 Classification of Diabetes

The majority of cases of diabetes can be broadly classified into 2 categories: type 1 diabetes and type 2 diabetes, although some cases are difficult to classify. Gestational diabetes (GDM) refers to glucose intolerance with onset or first recognition during pregnancy. Monogenic diabetes is a rare disorder caused by genetic defects of beta cell function that typically presents in young people (<25 years of age), is noninsulin dependent and is familial, with an autosomal dominant pattern of inheritance. Differentiating between type 1, type 2 and monogenic diabetes is important but can be difficult at the time of diagnosis in certain situations. 1 highlights the main features of type 1 diabetes, including LADA form, type 2 diabetes and monogenic diabetes. No diagnostic test or clinical criteria can reliably make this distinction, but additional testing may be helpful in atypical presentations if knowing the specific diagnosis may alter management.

Table 1. Classification of diabetes

Type 1	encompasses diabetes that is primarily a result of pancreatic beta cell destruction with consequent insulin deficiency, which is prone to ketoacidosis. This form includes cases due to an autoimmune process and those for which the etiology of beta cell destruction is unknown.
Type 2	may range from predominant insulin resistance with relative insulin deficiency to a predominant secretory defect with insulin resistance. Ketosis is not as common.
GDM	refers to glucose intolerance with onset or first recognition during pregnancy.
Other	**specific types** include a wide variety of relatively uncommon conditions, primarily specific genetically defined forms of diabetes or diabetes associated with other diseases or drug use

Obesity and physical signs of insulin resistance (e.g. acanthosis nigricans) are more common in children and adolescents with type 2 diabetes than type 1 diabetes. In adults, a systematic review of clinical indicators identified age at diagnosis of diabetes <30 to 40 years, and time to needing insulin <1 to 2 years as more predictive of type 1 diabetes than body mass index (BMI).

The presence of autoimmune markers, such as anti-glutamic acid decarboxylase (GAD) or anti-islet cell (ICA) autoantibodies, may be helpful in identifying type 1 diabetes and rapid progression to insulin requirement, but levels wane over time and they do not have sufficient diagnostic accuracy to be used routinely. In cases where it is difficult to distinguish between type 1, type 2 and monogenic diabetes, presence of 1 or more autoantibodies (GAD and ICA) indicates type 1 diabetes with a need for insulin replacement therapy; however, the absence of autoantibodies does not rule out type 1 diabetes. If the person has clinical features suggestive of monogenic diabetes (familial diabetes with autosomal dominant pattern of inheritance >2 generations, onset <25 years, not having obesity), genetic testing for monogenic diabetes may be performed.

3.3 Diagnostic Criteria

3.3.1 Diabetes

Table 2. Diagnosis of Diabetes

FPG ≥ 7.0 mmol/L
Fasting = no caloric intake for at least 8 hours
or
A1C ≥ 6.5% (in adults)
Using a standardized, validated assay in the absence of factors that affect the accuracy of the A1C and not for suspected type 1 diabetes
or
2hPG in a 75g OGTT ≥11.1 mmol/L
or
Random PG ≥11.1 mmol/L
Random = any time of the day, without regard to the interval since last meal

2hPG, 2-hour plasma glucose; *AlC,* glycated hemoglobin; *FPG,* fasting plasma glucose; OGTT, oral glucose tolerance test; *PG,* plasma glucose.

In the absence of symptomatic hyperglycemia, if a single laboratory test result is in the diabetes range, a repeat confirmatory laboratory test (FPG, A1C, 2hPG in a 75 g OGTT) must be done on another day. It is preferable that the same test be repeated (in a timely fashion) for confirmation, but a random PG in the diabetes range in an asymptomatic individual should be confirmed with an alternate test.

In the case of symptomatic hyperglycemia, the diagnosis has been made and a confirmatory test is not required before treatment is initiated. If results of 2 different tests are available and both are above the diagnostic thresholds, the diagnosis of diabetes is confirmed.

Other measures of glycemia, such as fructosamine, glycated albumin and 1,5-anhydroglucitol have not been validated for the diagnosis of diabetes.

In individuals in whom type 1 diabetes is likely (younger or lean or symptomatic hyperglycemia, especially with ketonuria or ketonemia), confirmatory testing should not delay initiation of treatment to avoid rapid deterioration. If results of 2 different tests are available and both are above the diagnostic cut points, the diagnosis of diabetes is confirmed. When the results of more than 1 test are available (among FPG, A1C, 2hPG in a 75 g OGTT) and the results are discordant, the test whose result is above the diagnostic cut point should be repeated and the diagnosis made on the basis of the repeat test.

3.3.2 Prediabetes

The term "prediabetes" refers to impaired fasting glucose (IFG), impaired glucose tolerance (IGT) or a HbA1c of 6.0% to 6.4%. Not all individuals with prediabetes will necessarily progress to diabetes. However, they are at higher risk for developing diabetes in addition to cardiovascular disease. Prediabetes id diagnosed according to the criteria and tests shown in table 3.

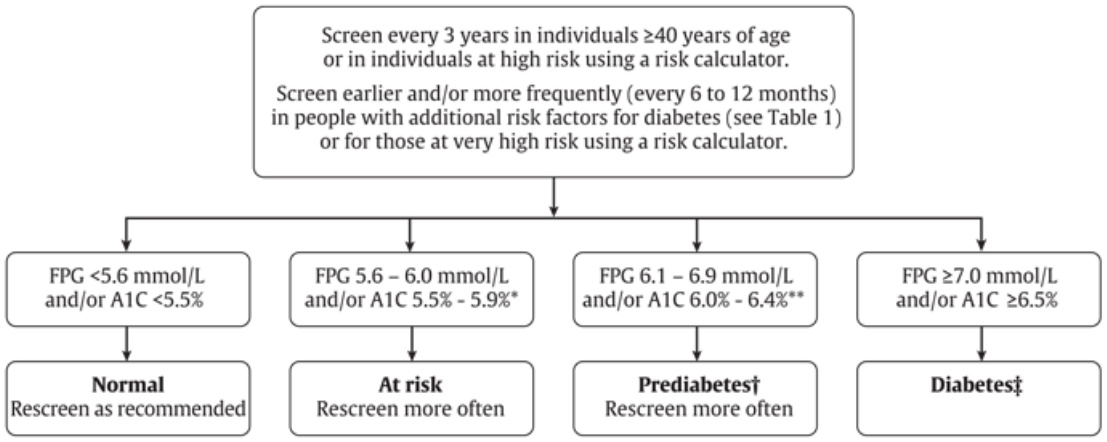
Table 3. Diagnosis of Prediabetes

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

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

3.4 Screening for Type 2 Diabetes in Adults

In the absence of evidence for interventions to prevent or delay type 1 diabetes, routine screening for type 1 diabetes is not recommended.
Screen for type 2 diabetes using a fasting plasma glucose and/or glycated hemoglobin (A1C) every 3 years in individuals ≥40 years of age or in individuals at high risk on a risk calculator (33% chance of developing diabetes over 10 years).
While fasting plasma glucose (FPG) and/or A1C are the recommended screening tests, a 75 g oral glucose tolerance test (OGTT) may be considered when the FPG is 6.1 to 6.9 mmol/L (19) and/or A1C is 6.0% to 6.4%.



If both FPG and A1C are available, but discordant, use the test that appears furthest to the right side of the algorithm.

*Consider 75 g OGTT if ≥1 risk factors; ** Consider 75 g OGTT (see Tables 3 and 5 in the Definition, Classification and Diagnosis of Diabetes, Prediabetes and Metabolic Syndrome chapter, p. S10 for interpretation of 75 g OGTT).

†Prediabetes = IFG or A1C 6.0 to 6.4% (see Table 5 in the Definition, Classification and Diagnosis of Diabetes, Prediabetes and Metabolic Syndrome chapter, p. S10).

‡In the presence of symptoms of hyperglycemia, a single test result in the diabetes range is sufficient to make the diagnosis of diabetes. In the absence of symptoms of hyperglycemia, if a single laboratory test result is in the diabetes range, a repeat confirmatory laboratory test (FPG, A1C, 2hPG in a 75 g OGTT) must be done on another day. It is preferable that the same test be repeated (in a timely fashion) for confirmation, but a random PG in the diabetes range in an asymptomatic individual should be confirmed with an alternate test. If results of two different tests are available and both are above the diagnostic cut points the diagnosis of diabetes is confirmed.

A1C, glycated hemoglobin; *FPG,* fasting plasma glucose; *IFG,* impaired fasting glucose

Figure 1. Screening and diagnosis algorithm for type 2 diabetes

Table 4. Risk factors for type 2 diabetes

- Age ≥40 years
- First-degree relative with type 2 diabetes
- Member of high-risk population (e.g. African, Arab, Asian, Hispanic, Indigenous or South Asian descent, low socioeconomic status)
- History of prediabetes (IGT, IFG or A1C 6.0%–6.4%)*
- History of GDM
- History of delivery of a macrosomic infant
- Presence of end organ damage associated with diabetes:
  - >Microvascular (retinopathy, neuropathy, nephropathy)
  - CV (coronary, cerebrovascular, peripheral)
- Presence of vascular risk factors:
  - HDL-C <1.0 mmol/L in males, <1.3 mmol/L in females*
  - >TG ≥1.7 mmol/L*
  - Hypertension*
  - Overweight*
  - Abdominal obesity*
  - Smoking
- Presence of associated diseases:
  - History of pancreatitis
  - Polycystic ovary syndrome*
  - Acanthosis nigricans*
  - Hyperuricemia/gout
  - Non-alcoholic steatohepatitis
  - Psychiatric disorders (bipolar disorder, depression, schizophrenia†
  - HIV infection‡
  - Obstructive sleep apnea§
  - Cystic fibrosis
- Use of drugs associated with diabetes:
  - Glucocorticoids, atypical antipsychotics, statins, anti-rejection drugs
  - Highly active antiretroviral therapy‡

4.0 75g ORAL GLUCOSE TOLERANCE TESTING (OGTT) – LIS Code: GTT2

IMPORTANT:

- **Procedure below is only applicable to adults and children with body weight greater than 42 kg (93 lbs).**
- **Please refer to Appendix 2 and JA110-10-17B for details on glucose dose for children with body weight less than 42 kg.**

4.1 Materials

Reagents	• 75 g glucose drink (75g/300mL bottle; 0.25 g/mL) • Graduated disposable measuring cup (for patients <42 kg)
Equipment	• Core lab chemistry analyzer • Do not use POCT devices to measure glucose

4.2 Patient preparation (adult or child ≥42 kg/93 lbs)

- Patient should be healthy and ambulatory
- Patient should fast for 8-14 h (only water permitted) prior to test
- Patient should not be dehydrated
- Patient should not be on any medication affecting glucose levels for at least 3 days: atypical antipsychotics, beta-adrenergic agonists, diazoxide, glucocorticoids, interferon alpha, nicotinic acid, pentamidine, phenytoin, protease inhibitors, thiazide diuretics
- This test should be performed after three days of unrestricted diet and physical activity
- Some laboratories may only perform this test by appointments

4.3 Glucose Drink Dose

Adult	Glucose drink is supplied as a 75 g dose in 300 mL and full dose should be given to adult.
Child (<18y.o. and <42kg)	Children should receive adjusted glucose dose: 1.75g/kg body weight to a max of 75g. The child's weight should be indicated on the requisition. Use JA110-10-17B OGTT Calculator for Pediatric Patients to determine the volume of drink to be administered. See Appendix 2 for calculation details.

4.4 Testing Procedure

- Confirm patient identity as per Phlebotomy Collection Manual 100-10-79
- Provide patient a copy of patient brochure for OGTT testing SOP PB110-10-17
- Order test ***GTT2*** in Delphic
    - Create separate lab ID# from any other blood work on the same requisition.

- Add entry to "Glucose Tolerance Testing Record Form" F110-10-17A
- Collect fasting plasma glucose sample. Indicate on the tube label "fasting".
- Administer drink:
    - Adult: 75 g glucose drink in 250 mL
    - Child <18yo and <42kg: dose calculated in Section 4.3

- **Time zero (t = 0) is when the patient has finished consuming the drink**. **The entire drink must be consumed within 5 minutes.**
    - Notify physician/nursing staff if patient is unable to drink entire contents or should they become sick.
    - Discontinue test if patient becomes sick. Do not proceed to collect next blood sample. Report glucose results collected prior to patient vomiting and cancel other(s) with comment:

"Patient got sick, test is cancelled."

- Update Record Form F110-10-17A with time zero and scheduled 2 hour time.
- Inform the patient about the time for 2-hour collection.
    - Clearly state that it must be within 10 minutes or test will be cancelled.
    - Patient must remain seated throughout the test. No exercise or walking. Food and drinks are not permitted, except water

- Collect a plasma blood sample 2 h post the start of consuming of the drink. Indicate on the label of the tube "2 hour"
    - If *Collected* sample time exceeds *Scheduled* time by more than 10 minutes, cancel the test using ***REJS*** and add comment:

      "Specimen collected outside of acceptable time window (10 min) for timed collection."

- Forward samples to the laboratory. On the GTT format, report the fasting and 2 hour glucose.

Note: All collected plasma samples must be sent to the lab immediately to be centrifuged and analyzed. Delay in separation from cells (>30 min) causes decrease in glucose levels and potentially missed diagnosis of diabetes.

4.5 Interpretation of 75g OGTT for diagnosis of prediabetes and diabetes

Sample	Prediabetes	Diabetes
Fasting PG	6.1-6.9 mmol/L	≥ 7.0 mmol/L
2 h PG	7.8-11.0 mmol/L	≥ 11.1 mmol/L

PG, plasma glucose

5.0 COMMENT FOR REPORTING 75g OGTT (GTT2) IN DELPHIC:

Interpretation of 75 g oral glucose tolerance test (non-gestational)

5.1 For the diagnosis of diabetes mellitus

Fasting plasma glucose (FPG) **≥ *7.0 mmol/L***
AND/OR
Hemoglobin A1c (HbA1c) **≥ 6.5%**
OR
Plasma glucose 2-hr post challenge **≥ *11.1 mmol/L***

5.2 For the diagnosis of impaired fasting glucose (IFG)

Fasting plasma glucose **= 6.1 - 6.9 mmol/L**
AND/OR
Hemoglobin A1c (HbA1c) **= 6.0% - 6.4%**
AND
Plasma glucose2-hr post-challenge **< 7.8 mmol/L**

5.3 For the diagnosis of impaired glucose tolerance (IGT)

Fasting plasma glucose = **6.1 - 6.9 mmol/L**
AND/OR
Hemoglobin A1c (HbA1c) **= 6.0% - 6.4%**
AND
Plasma glucose 2-hr post-challenge **= 7.8 – 11.0 mmol/L**

5.4 For the diagnosis of combined impaired fasting glucose (IFG) and impaired glucose tolerance (IGT)

Fasting plasma glucose **= 6.1 - 6.9 mmol/L**
AND/OR
Hemoglobin A1c (HbA1c) **= 6.0% - 6.4%**
AND
Plasma glucose 2-hr post-challenge **= 7.8 - 11.0 mmol/L**

Appendix 1: Oral Glucose Tolerance Testing for GDM and T2DM

	Gestational Diabetes (GDM) (24-28 weeks of gestation)			Type 2 Diabetes Mellitus (T2DM)		
	Preferred Approach		**Alternative Approach**			
Test	50g glucose challenge test (GCT) *Pregnant* *1st tier test*	75g OGTT for GDM *Pregnant* *2nd tier test*	75g OGTT for GDM *pregnant*	75g OGTT for T2DM *non-pregnant*		
LIS code	GT50	GTTP	Not available	GTT2		
Preparation	Non-fasting	Fasting	Fasting	Fasting		
Drink	75g in 300 mL, give 200 mL only 50g in 300 mL	75g in 300 mL	75g in 300 mL	75g in 300 mL (adult) 1.75g/kg weight (child <18y.o ***and*** <42 kg)		
Sample(s) collected	1 hour	Fasting plasma 1 hour 2 hours	Fasting plasma 1 hour 2 hours	Fasting plasma 2 hours		
Interpretation	PG<7.8 mmol/L → normal • *repeat at 24-28 weeks of gestation if done earlier* PG≥11.1 mmol/L → GDM • *No further testing needed* PG 7.8-11.0 mmol/L • *Perform 75g OGTT for GDM (code:GTTP)*	If ≥1 value is met → GDM: ▪ FPG ≥ 5.3 mmol/L ▪ 1h ≥ 10.6 mmol/L ▪ 2h ≥ 9.0 mmol/L	If ≥1 value is met → GDM: ▪ FPG ≥ 5.1 mmol/L ▪ 1h ≥ 10.0 mmol/L ▪ 2h ≥ 8.5 mmol/L		**Prediabetes**	**Diabetes**
				FPG	6.1-6.9 mmol/L	≥ 7.0 mmol/L
				2h PG	7.8-11.0 mmol/L	≥ 11.1 mmol/L

PG, plasma glucose; *FPG*, fasting plasma glucose

References:

Diabetes Canada Clinical Practice Guidelines Expert Committee. *Diabetes Canada 2018 Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada*. Can J Diabetes. 2018;42(Suppl 1):S1-S325.

Appendix 2: Administering OGTT to children <18 y.o. AND body weight <42 kg (93 lbs)

For children, please contact the **Pediatric Provincial Diabetes Program at Diabetes Education Resource for Children and Adolescents** (204-787-3011) or Pediatric Endocrine Clinic (204-787-7435) if body weight was not indicated on the requisition or there are other questions about the request.

Fasting

Fasting periods for pediatric patients should be determined on an individual basis; however, in general, the guidelines used for adults can be followed. For infants, the fasting period is typically shortened to less than 4 hours.

Glucose Drink Dose

Child (<18y.o. and <42kg)	Should receive adjusted glucose dose: 1.75g/kg body weight to a max of 75g. **Calculations:** 1) Convert pounds to kg: $$\boldsymbol{weight(kg) = \frac{weight\ (lbs)}{2.2}}$$ 2) Volume of drink to give: $$\boldsymbol{Adjusted\ dose\ (mL) = 7 \times weight\ (kg)}$$ • Measure the mL of calculated dose from the 75g dose into graduated disposable cup. • Discard the remainder of the 75g drink.

Graduated Disposable Cups

- 250 mL (8 oz.) measuring cups can be purchased through Avantor Sciences (formerly VWR):

  Catalog #470003-346
  Supplier #2046400

  Example: