

Gestational Diabetes

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CDA CLASSIFICATION OF DIABETES:

- TYPE 1 DIABETES is primarily a result of pancreatic beta cell destruction and is prone to ketoacidosis.
- TYPE 2 DIABETES may range from predominant insulin resistance with relative insulin deficiency to a predominant secretory defect with insulin resistance.
- GESTATIONAL DIABETES MELLITUS (GDM) refers to glucose intolerance with onset or first recognition during pregnancy.
- OTHER forms consist mainly of specific genetically defined forms of diabetes or diabetes associated with other diseases or drug use.



GDM: Gestational Diabetes

- ❖ GDM is defined as any degree of glucose intolerance with onset or first recognition during pregnancy
 - ❖ Insulin or no insulin
 - ❖ Pre-conceptual glucose intolerance?
 - ❖ Condition persists after pregnancy
 - ❖ Reclassification postpartum

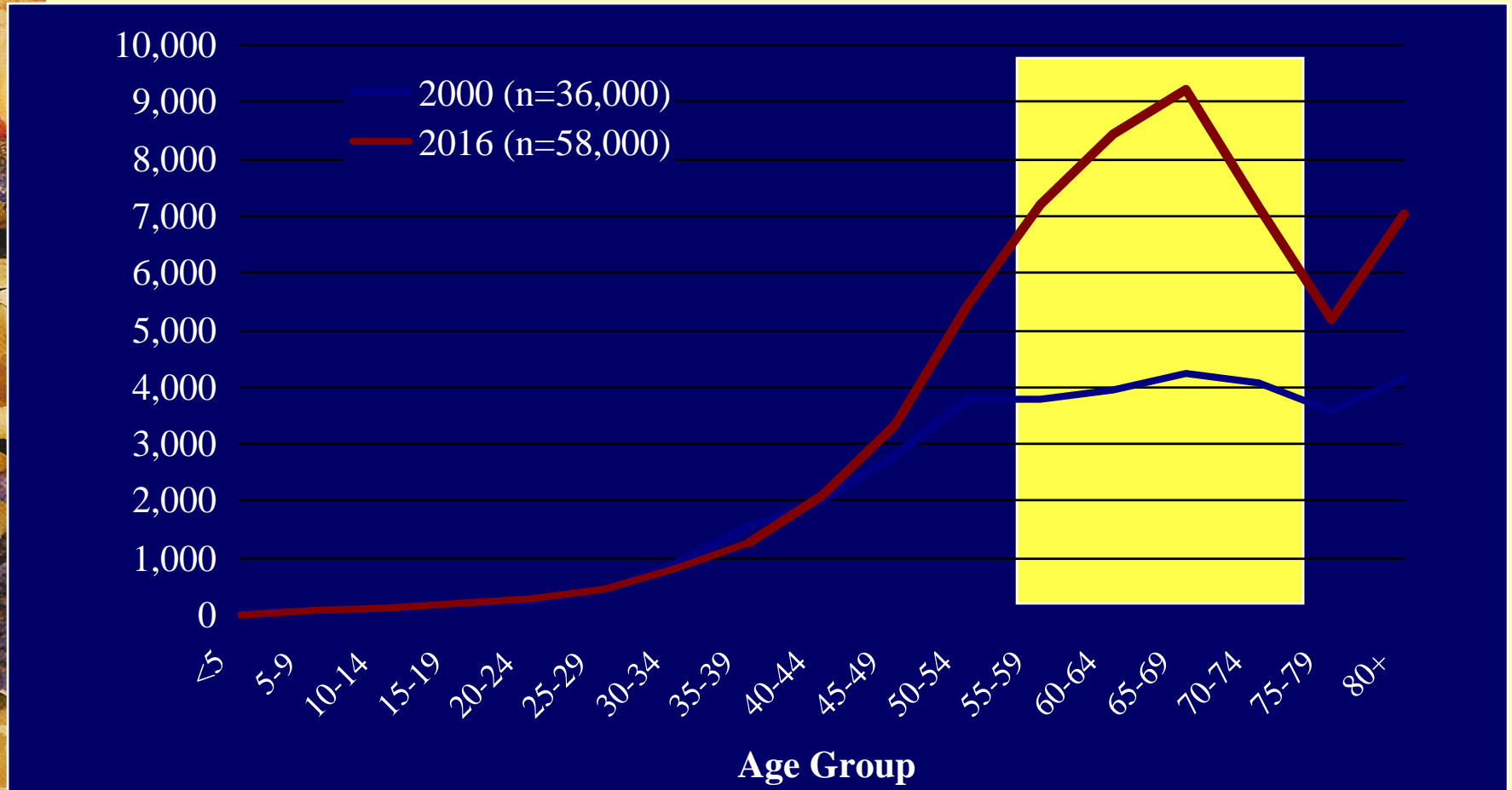
WHY?

- ❖ GDM results from the inability to secrete sufficient insulin to compensate for the increased nutritional needs of mom and baby, increased adiposity, and the increased levels of diabetogenic hormones:
 - ❖ Human placental lactogen
 - ❖ Prolactin, cortisol, and progesterone

Prevalence:

- ❖ American Diabetes Association- 7%
- ❖ Canadian Diabetes Association -
3.8% non-aboriginal and 18% aboriginal

Estimated Diagnosed Diabetes Cases in New Brunswick by Age Group, 2000 and 2016



RISK FACTORS FOR GDM

- Previous diagnosis of GDM
- Previous delivery of a macrosomic infant
- Member of a high-risk population (Aboriginal, Hispanic, South Asian, Asian or African descent)
- Age \geq 35 years
- Obesity (BMI \geq 30 kg/m²)
- Polycystic ovarian syndrome and / or hirsutism
- Acanthosis nigricans
- Corticosteroid use

GDM and adolescents:

- ❖ Retrospective case control study of 4822 women - 68% BMI <25; 32% with BMI>25

Outcome for BMI>25	Odds Ratio
Cesarean Delivery	1.6
Pregnancy induced Hypertension	1.8
Gestational Diabetes	3.0

MATERNAL EFFECTS:

- ❖ Hypertensive disorders
- ❖ Preeclampsia
- ❖ Operative Delivery
- ❖ Increased monitoring and health care resources
- ❖ Increased risk for subsequent type 2 diabetes
- ❖ Cardiovascular disease

GDM increases risk of cardiovascular disease in women with family history.

- ❖ Retrospective chart review and survey of ~900 women with or without GDM obese with family history of DM2
- ❖ Average age 49 years, avg BMI 34
- ❖ 86% women with GDM had Metabolic Syndrome
- ❖ 15.5 % with self reported cardiovascular disease
- ❖ Cardiovascular disease occurring at average age 45 years

FETAL EFFECTS:

- ❖ Macrosomia and associated birth injury
- ❖ Perinatal mortality
- ❖ Hypoglycemia
- ❖ Hyperbilirubinemia
- ❖ Hypocalcemia
- ❖ Congenital malformations
- ❖ Risk for diabetes and obesity

SCREENING & DIAGNOSIS

- In 2003, screening, diagnosis and management of gestational diabetes mellitus is controversial.
- Screening all pregnant women for GDM between 24 and 28 weeks is recommended.
- Screening in the first trimester should be considered for women with multiple risk factors, and if negative, these women should be reassessed during subsequent trimesters.
- Women with GDM are at higher risk of postpartum diabetes, prediabetes and lipid abnormalities.

DIAGNOSTIC CRITERIA FOR DIABETES

	Fasting plasma glucose (mmol/L)		75-g OGTT 2-hr plasma glucose (mmol/L)
IFG	6.1 - 6.9		Not applicable
IFG (isolated)	6.1 - 6.9	and	< 7.8
IGT (isolated)	< 6.1	and	7.8 – 11.0
IFG and IGT	6.1 – 6.9	and	7.8 – 11.0
Diabetes	≥ 7.0	or	≥ 11.1

SCREENING AND DIAGNOSIS GDM

All pregnant women between 24 and 28 weeks
If multiple risk factors are present, assess during each trimester.

1hPG following 50-g glucose load at any time of day

1hPG ≥ 10.3

GDM

1hPG = 7.8-10.2

75-g OGTT. Measure FPG, 1hPG, 2hPG

If 2 values are met or exceeded

FPG ≥ 5.3
1hPG ≥ 10.6
2hPG ≥ 8.9

IGT of pregnancy

If 1 value is met or exceeded

SCREENING & DIAGNOSIS

- The screening test for GDM is a 1-hour plasma glucose measurement following a 50-gram oral glucose load given at any time of day.
- If the 1hPG is ≥ 10.3 mmol/L GDM is confirmed.
- If the 1hPG is 7.8 - 10.2 mmol/L, a 75-g OGTT should be conducted and 1hPG and 2hPG values obtained.
- In view of the controversies about diagnostic tests, other accepted methods may be used.

Why not screen?

- ❖ *In 2003, screening, diagnosis and management of gestational diabetes mellitus is controversial.....*
- ❖ 1998: don't screen low risk
- ❖ Maternal anxiety?
- ❖ changing from 50-75-100 g tests -what is an abnormal blood glucose?
- ❖ No randomized control trial that compares treatment with no treatment and showing benefit of treatment

75 or 100g OGTT vs FPG

- ❖ 75g more cost effective
- ❖ ADA, CDA and WHO endorse 75g OGTT - but all have different criteria for abnormal glucose
- ❖ *Clin Chem 2006 Sep(52)1679-84:*
 - ❖ Only weak correlation between diagnosis with 100g vs 75g - 3X more diagnosed in early pregnancy with 100g and 2X in late pregnancy.

75g OGTT vs fasting plasma glucose

- ❖ Chart review of 300 women with OGTT at 24-28 weeks
- ❖ Glucose (fasting or pc) only poorly correlated with birth weight
- ❖ Fasting glucose better than pc glucose for predicting LGA
- ❖ (*HEY BUT....WE COULD ALWAYS SCREEN FOR DIABETES IN PRECONCEPTION WITH FASTING GLUCOSE!*)

MANAGEMENT - TARGETS

- The glycemic targets associated with the best pregnancy outcome in GDM are:

Preprandial < 5.3 mmol/L

1-hour postprandial < 7.8 mmol/L

2-hour postprandial < 6.7 mmol/L

- Women with GDM should carry out frequent fasting and postprandial home blood glucose monitoring in order to achieve glycemic targets.

When should they test?

- ❖ Before meals or postprandial?
- ❖ *Postprandial vs preprandial blood glucose monitoring in women with gestational diabetes mellitus requiring insulin therapy. NEJM 1995(19)1237-1241*
 - ❖ pc: Increased insulin
 - ❖ pc: A1c 3x lower
 - ❖ pc: 70% reduction in C-section

MANAGEMENT - LIFESTYLE RECOMMENDATIONS

- Nutrition therapy is the primary treatment of GDM, although evidence on the optimal diet is lacking.
- Carbohydrate intake should be distributed over 3 meals and at least 3 snacks (one of which should be at bedtime).
- Hypocaloric diets are not recommended.
- Physical activity should be encouraged.

MANAGEMENT

- ▶ If women with GDM do not achieve glycemic targets by nutrition therapy alone within 2 weeks of initiation, insulin therapy should be prescribed.
- ▶ A variety of protocols can be used, with multiple injections of up to 4 injections per day being most effective. Insulin should be adjusted based on fasting and postprandial glucose values.
- ▶ Early third trimester assessment of fetal growth may help determine a need for more aggressive therapy to reduce the risk of macrosomia.
- ▶ Oral hypoglycemic agents should not routinely be used.

2X daily vs 4X daily insulin

- ❖ 270 GM and 110 pregestational DM
- ❖ More insulin in 4X daily (22-28 units)
- ❖ Reduction in A1c by 0.3%
- ❖ No increase in hypoglycemia
- ❖ No difference in macrosomia, C-sections
- ❖ Lower rate neonatal morbidity (hypoglycemia, hyperbilirubinemia)

A comparison of glyburide and insulin in GDM

TABLE 1. CHARACTERISTICS OF 404 WOMEN WITH GESTATIONAL DIABETES.*

CHARACTERISTIC	GLYBURIDE (N=201)	INSULIN (N=203)
Age — yr	29±7	30±6
BMI ≥27.3 before pregnancy — no. (%)†	141 (70)	132 (65)
Nulliparity — no. (%)	56 (28)	59 (29)
Family history of diabetes — no. (%)	86 (43)	91 (45)
Previous gestational diabetes — no. (%)	24 (12)	22 (11)
Previous delivery of infant with macrosomia — no. (%)	36 (18)	45 (22)
Screening plasma glucose — mg/dl‡	169±28	169±31
Wk of gestation	24±7	25±7
Wk of gestation at delivery	38.7±1.6	38.5±2.1
Results of oral glucose-tolerance test — mg/dl‡		
Fasting	97±14	98±16
At 1 hr	197±31	201±30
At 2 hr	174±31	174±29
At 3 hr	140±37	134±37
Serum C peptide — ng/ml§	3.8±2.3	3.4±1.5
Dose of glyburide — mg/day	9±6	—
Dose of insulin — units/day¶	—	85±48
No. of clinic visits attended	11±5	12±6
No. of clinic visits missed	1.5±2.1	1.2±2.2
No. of measurements of blood glucose/day	4±2	4±2
Weight gain — lb	21±17	21±15

*Plus-minus values are means ±SD. There were no significant differences between the two groups in any characteristics by the chi-square test or Student's t-test.

†The body-mass index (BMI) is the weight in kilograms divided by the square of the height in meters.

‡Values shown are for plasma glucose. To convert values for glucose to millimoles per liter, multiply by 0.056.

§To convert values for C peptide to nanomoles per liter, multiply by 0.331.

¶Mean insulin doses were calculated from diagnosis to delivery.

||The mean values were calculated from the weight before pregnancy to the last weight measured within a week before delivery. To convert values for weight gain to kilograms, divide by 2.2.

Randomly assigned to receive SU or insulin (0.7u/kg)

Blood Glucose Concentrations and A1c Values in Women with GDM

TABLE 2. BLOOD GLUCOSE CONCENTRATIONS MEASURED AT HOME AND GLYCOSYLATED HEMOGLOBIN VALUES BEFORE TREATMENT IN WOMEN WITH GESTATIONAL DIABETES.*

VARIABLE	GLYBURIDE (N=201)	INSULIN (N=203)	P VALUE†
Blood glucose (mg/dl)‡			
Fasting	104±25	108±26	0.12
Preprandial	104±20	107±23	0.16
Postprandial	130±25	129±27	0.69
Mean	114±19	116±22	0.33
Glycosylated hemoglobin (%)	5.7±1.3	5.6±1.2	0.42

*Values are means ±SD.

†P values were calculated by a two-tailed t-test.

‡Blood glucose was measured at home during a one-week period. To convert values for glucose to millimoles per liter, multiply by 0.056.

Langer O et al. N Engl J Med 2000;343:1134-1138



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Blood Glucose and A1c During Treatment

TABLE 3. BLOOD GLUCOSE CONCENTRATIONS MEASURED AT HOME AND GLYCOSYLATED HEMOGLOBIN VALUES DURING TREATMENT IN WOMEN WITH GESTATIONAL DIABETES.*

VARIABLE	GLYBURIDE (N=201)	INSULIN (N=203)	P VALUE†
Week of gestation when blood glucose testing started	28±6	27±8	0.22
No. of weeks of testing	10±6	11±7	0.12
Blood glucose (mg/dl)‡			
Fasting	98±13	96±16	0.17
Preprandial	95±15	97±14	0.17
Postprandial	113±22	112±15	0.60
Mean	105±16	105±18	0.99
Glycosylated hemoglobin (%)§	5.5±0.7	5.4±0.6	0.12

*Values are means ±SD.

†P values were calculated by a two-tailed t-test.

‡Blood glucose values are means of measurements obtained throughout pregnancy. To convert values for glucose to millimoles per liter, multiply by 0.056.

§The test was performed late in the third trimester.

Langer O et al. N Engl J Med 2000;343:1134-1138



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Neonatal Outcomes

TABLE 4. NEONATAL OUTCOMES.*

OUTCOME	GLYBURIDE (N=201)	INSULIN (N=203)	P VALUE
Neonatal features			
Large size for gestational age — no. (%)	24 (12)	26 (13)	0.76
Birth weight — g	3256±543	3194±598	0.28
Ponderal index >2.85 — no. (%)†	18 (9)	24 (12)	0.33
Macrosomia — no. (%)	14 (7)	9 (4)	0.26
Metabolic outcomes			
Cord-serum insulin — $\mu\text{U}/\text{ml}\ddagger$	15±13	15±21	0.84
Intravenous glucose therapy — no. (%)	28 (14)	22 (11)	0.36
Hypoglycemia — no. (%)	18 (9)	12 (6)	0.25
Hypocalcemia — no. (%)	2 (1)	2 (1)	0.99
Hyperbilirubinemia — no. (%)	12 (6)	8 (4)	0.36
Polycythemia — no. (%)	4 (2)	6 (3)	0.52
Lung complications — no. (%)	16 (8)	12 (6)	0.43
Respiratory support — no. (%)	4 (2)	6 (3)	0.52
Admission to neonatal intensive care unit — no. (%)	12 (6)	14 (7)	0.68
Congenital anomaly	5 (2)	4 (2)	0.74
Perinatal mortality — no. (%)§			
Stillbirth	1 (0.5)	1 (0.5)	0.99
Neonatal death	1 (0.5)	1 (0.5)	0.99

*Plus-minus values are means \pm SD.

†The ponderal index was calculated as 100 times the weight in grams divided by the cube of the length in centimeters.

‡To convert values for insulin to picomoles per liter, multiply by 6.0.

§Numbers include infants with congenital anomalies

Langer O et al. N Engl J Med 2000;343:1134-1138



Can we use glyburide?

- ❖ Doesn't cross the placenta - works as well as insulin and causes no adverse effects...
- ❖ Does this population apply to ours?
- ❖ Pretreatment glucose better than most post-treatment glucose!
- ❖ Started in week 24-25 - safety less of a concern after organogenesis

POST-PARTUM FOLLOW-UP

- Within 6 months of delivery, a fasting plasma glucose or a 75-g OGTT should be done to screen for diabetes and prediabetes.
- Breastfeeding, life-long healthy eating and regular physical activity should be encouraged.
- Women with GDM should be monitored for development of type 2 diabetes according to the screening guidelines.

PLANNING NEXT PREGNANCY

- ▶ Women with previous GDM, impaired fasting glucose or impaired glucose tolerance should plan future pregnancies in consultation with their healthcare providers.
- ▶ Glucose tolerance should be assessed prior to conception.

GDM - RECOMMENDATIONS

All pregnant women should be screened for GDM between 24 and 28 weeks gestation [*Grade D, Consensus*]. Plasma glucose (PG) should be measured 1 hour after a 50-g glucose load [*Grade B, Level 1*]. Women with multiple risk factors should be screened during the first trimester and, if negative, should be reassessed during subsequent trimesters [*Grade D, Consensus*].

If the 1hPG in the 50-g glucose screening test is 7.8 to 10.2 mmol/L, a 75-g OGTT should be conducted, and FPG, 1hPG and 2hPG levels obtained [*Grade D, Consensus*]. In view of the controversies about diagnostic tests in this area, other accepted methods may be used [*Grade D, Consensus*].

GDM - RECOMMENDATIONS

→ Women with GDM should strive to attain the following glycemic targets, as these are associated with the best pregnancy outcomes:

preprandial PG < 5.3 mmol/L [*Grade D, Consensus*];

1-hour postprandial PG < 7.8 mmol/L [*Grade A, Level 1*];
and

2-hour postprandial PG < 6.7 mol/L [*Grade D, Consensus*].

GDM - RECOMMENDATIONS

If women with GDM do not achieve glycemic targets within 2 weeks with nutrition therapy alone, insulin therapy should be initiated [*Grade D, Consensus*]. When insulin therapy is initiated, up to 4 injections/day should be considered [*Grade A, Level 1A*].

Women with GDM should conduct frequent FBG and postprandial home BG monitoring [*Grade C, Level 3*].

GDM - RECOMMENDATIONS

As women who have had GDM have an elevated risk of subsequent type 2 diabetes, they should be re-evaluated within 6 months of delivery with a 2hPG in a 75-g OGTT (preferred test) or an FPG test, and be counselled on a healthy lifestyle [*Grade D, Consensus*].

The Hyperglycemia and Adverse Pregnancy Outcome (HAPO) Study

- ❖ 1. to examine glucose tolerance in a large, heterogeneous, multinational, multicultural, ethnically diverse cohort of women in the third trimester of gestation with medical caregivers "blinded" to status of glucose tolerance (except in those instances where fasting and/or two hour OGTT plasma glucose concentration exceeds a predefined cutoff value); and
- ❖ 2. to derive internationally acceptable criteria for the diagnosis and classification of gestational diabetes mellitus (GDM) based on the specific relationships between maternal glycemia and the risk of specific adverse outcomes that are established through this study.

Effect of treatment of Gestational Diabetes Mellitus on Pregnancy outcomes

- ❖ ~1000 women enrolled after diagnosis IGT of pregnancy at 24-24 weeks
- ❖ RCT of routine care VS insulin
- ❖ Reduction in “Any serious perinatal complication”. (3% absolute reduction)
- ❖ Increased macrosomia, LGA in routine care
- ❖ Improvement in quality of life scales and Edinburgh Postnatal Depression Scale with insulin.