

# Gestational Diabetes Mellitus

Lecture for the Academic Year 2018 – 2019  
Defined Learning Objectives

Vasilios Tanos, MD, PhD.  
Professor in Obstetrics and Gynaecology  
Team Leader ObGyn MD6

# Disclosure



G E S E A

**Chairman Gynaecological Endoscopic  
Surgery Education and Assessment**



**Womana Medical Services**  
Director  
[www.womana.com.cy](http://www.womana.com.cy)



**European Academy  
of Gynaecological Endoscopic Surgery**  
Scientific Director  
[www.europeanacademy.org](http://www.europeanacademy.org)



**ESHRE Certification of Reproductive  
Endoscopic Surgery (ECRES) committee**  
Coordinator  
[www.eshre.eu](http://www.eshre.eu)

# Presentation & Learning Objectives

- Metabolism of Carbohydrates in pregnancy
- Epidemiology of GDM
- Screening for GDM
- Clinical manifestations
- Monitoring parturients with GDM
- Treatment options
- Labour management in GDM patients

# Glucose metabolism

Normal pregnancy = diabetogenic condition

- Changes in metabolism
- Insulin resistance

Early pregnancy

- Anabolic state
- Increase in maternal fat store
- Decrease of FREE FATTY ACIDS concentration
- Decrease in insulin requirements

# Carbohydrates metabolism

## Effects of pregnancy

- Mild fasting hypoglycemia
- Post prandial hyperglycemia due to increase in plasma volume in early pregnancy
- As pregnancy advances there is a progressive increase in **tissue resistance to insulin**
- Increase insulin secretion to maintain euglycemia
- Suppress glucagon response
- Increase Prolactin and cortisol
- Increase of Human Placental Lactogen effects like Growth Hormone

# GDM prevalence

- lack of universal diagnostic criteria
- the exact figures are difficult to determine
- CDC reports prevalence rates of 4.6%-9.2%
  
- History of GDM is the most significant risk factor for GDM

(CDC 2014)

# High risk pregnant women

## During 1<sup>st</sup> antenatal visit

- Obesity
- Family History of DM
- Past History for macrosomia, stillbirth, polyhydramnio, polyuria, polydypsia frequent candidiasis, UTI, e.t.c.

### Management

- Fasting glucose
- HbA1c
- PP 2 hours after

# Risk factors

- BMI of 25 kg/m<sup>2</sup> or greater
- Diabetes in a first-degree relative
- Excessive early gestational weight gain
  - first-trimester weight gain of 2 kg
  - second-trimester 0.6 kg weight gain per week
  
- for underweight, 0.45 kg
- for normal weight, 0.32 kg
- For overweight and for obese, 0.27 kg
  
- Macrosomia in a previous pregnancy
- maternal age older than 35
- weight gain of more than 5 kg since 18 years of age

(Garrison 2015)

# Why to Screen for GDM

- Women with GDM are often asymptomatic
- In a normal pregnancy, insulin resistance develops in the second trimester and continues until birth
- The mechanism is not fully understood
- Suspected to be related to the production of hormones, cytokines, or adipokines by the placenta
- Insulin secretion also increases, resulting in normal glucose concentrations
- Gestational diabetes typically develops because of pre-existing increased insulin resistance and diminished insulin secretion
- During pregnancy, the imbalance between insulin resistance and secretion may lead to hyperglycemia.



# GDM is a disease

- Double the risk for PIH
- Macrosomia up to 40% of GDM offspring
- Significantly increased risk of shoulder dystocia in macrosomic fetuses
- Increased polyhydramnios preterm delivery and CS
- Increased admission to NICU

# Multi disciplinary management approach

- Maternal glucose levels monitoring
- Fetal development and progress
  
- Obstetrician / Ultrasonography / GDM clinic
- Dietician Nutritionist
- Endocrinologists
- Paediatrician Neonatologist

# Subclinical DM, GDM and Maternal risks

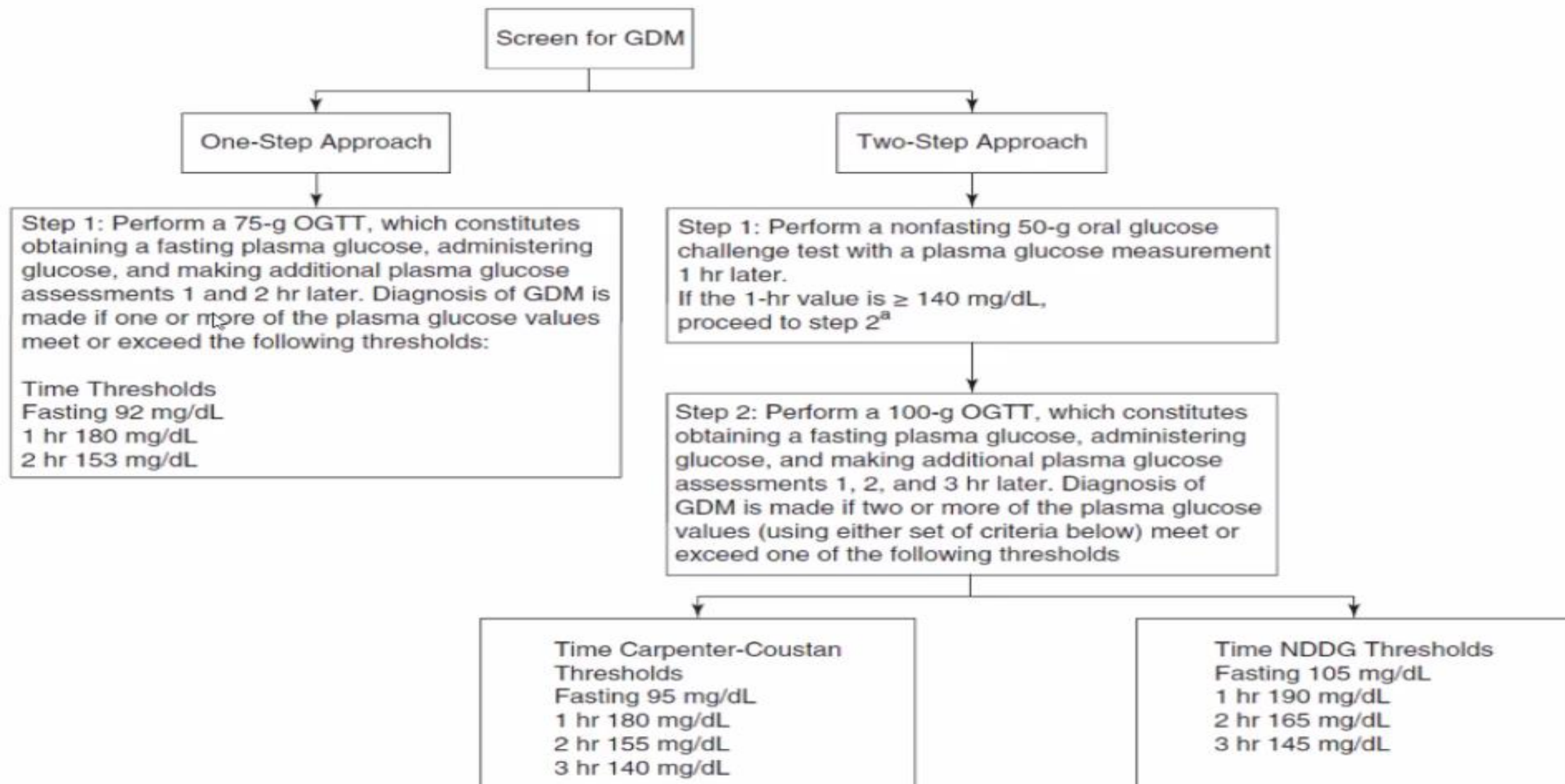
- Hypoglycaemia
- Diabetic ketoacidosis
- Retinopathy
- Nephropathy
- Hypertension
- Atherosclerosis
- Neuropathy
- Infection
- Operative Delivery

# Fetal Risks

- Congenital anomalies
- Early pregnancy loss
- Preterm delivery
- Fetal macrosomia
- Birth trauma
- Shoulder dystocia

# Screening and diagnostic criteria for gestational diabetes mellitus

Am Fam Physician 2015;91:460-7.



# One step test – screening and Dg

- 75gr oral glucose challenge test (GCT)
- 2 hours later a venous blood sample
- GDM is diagnosed if 2Hr plasma glucose is  $\geq 140\text{mg/dl}$
- Avoids multiple visits / multiple samples
- Validated by Dr Seshiah et al ACTA 2009

# Fetal and Neonatal Complications

- **Macrosomia** birthweight over 4000 g, is the most common fetal complication (15%–45%)
- **hyperbilirubinemia** in 10%–13% of neonates  
*(Esakoff 2009; Boulet 2003)*
- increased risk for neonatal **hypoglycemia, birth trauma, respiratory distress** syndrome  
*(Reece 2010)*
- **Hypoglycemia** occurs in 3%–5% of infants due to increased fetal insulin production in response to maternal hyperglycemia, which can increase the **risk of seizures**
- **Shoulder dystocia** is a rare, but serious complication can lead to **brachial plexus injury**
- Long-term complications of infants born to mothers with GDM include increased risk of
  - impaired glucose tolerance, type 2 diabetes,
  - hypertension, obesity, and dyslipidemia

*(Mitanechez 2014)*



# MANAGEMENT STRATEGIES

## Fetal Assessment

- depends on the severity of maternal hyperglycemia and the ease of glucose control
- antenatal testing for poor glycemic control (higher risk for complications eg stillbirth)  
*(ACOG 2013)*
- antenatal testing begin at 32 w (once or twice-weekly)
- fetal NSTs for 20-30 min, or modified biophysical profiles *(Garrison 2015)*
- Fetus biophysical profile: NST, AFV assessment by US
- at least one adequate pocket of amniotic fluid more than 2 cm deep, FMS
- Reactive NST, = fetal heart rate accelerates during fetal movement *(ACOG 2013)*
- antenatal testing in women who require oral drug therapy or insulin for GDM  
*(Garrison 2015)*
- no consensus regarding the use of antenatal testing in women with well controlled with nutritional therapy GDM
- Make sure that there are no complications eg HBP, HR for poor pregnancy outcomes, advanced maternal age or previous stillbirth

# Maternal Complications

- Cesarean delivery directly correlated to maternal glycaemia
- From 19.5% - to 23.7% of non-elective cesarean
- compared with 13.5% in women without diabetes (*Gorgal 2012*)
  
- HAPO study showed 5.9% had gestational hypertension and
- 4.8% had preeclampsia
- Rates of gestational hypertension and preeclampsia in the general population are 3.6%–9.1% and 1.4%–4.0%, respectively (*Roberts 2011*)
  
- up to 50% of women with GDM will develop type 2 diabetes later in life
- on average, occurs 22–28 years after pregnancy (*England 2009; O'Sullivan 1982*)
  
- Ethnicity and obesity (BMI > 30 kg/m<sup>2</sup>) may play a role in the risk and timing of the subsequent diagnosis of diabetes
- 60% of Latino women with GDM may develop diabetes within 5 years (*Kjos 1995*)
  
- 2.5- and 1.7-fold increased risk of developing metabolic syndrome and cardiovascular disease, respectively (*Gunderson 2009; Shah 2008*).

# Treatment of GDM

- Reduces the risk of maternal HBP by 40%
- A meta-analysis of 5 RCT found that treating GDM results in a 50% reduction in risk of macrosomia
- Risk of shoulder dystocia was reduced by 60%
- Rates of CS delivery are unaffected by treatment
- Evidence on maternal long-term complications, such as type 2 diabetes and obesity, is lacking

*(Hartling 2013)*

# DRUG THERAPY FOR GDM (1)

- With appropriate lifestyle modification, 70%–85% of women with GDM can achieve adequate glucose control  
*(ADA 2016)*
- Drug therapy should be considered when medical nutrition therapy and moderate physical activity fail to achieve glucose goals within 1–2 weeks
- no evidence to support that maternal and infant outcomes were affected by the glucose concentration at initiation of drug therapy for GDM  
*(Nicholson 2008)*
- initiate pharmacologic therapy if most glucose values within a 1-week period are elevated  
*(Landon 2009)*

# Oral anti glycemc drugs

- Glibenclamide (glyburide) in women intolerant of metformin therapy
- with poor glycemc control on metformin alone who refuse insulin therapy *(safe according to NICE 2015)*
- suitable first-line treatment for GDM *(ACOG 2013; Blumer 2013)*
- as an acceptable alternative to insulin therapy (Endocrine Society)
- Glyburide has potential increased risk of macrosomia and neonatal hypoglycemia,
- as well as the risk of maternal hypoglycemia
- glyburide crosses the placenta in trace amounts, and long-term safety data are lacking

# DRUG THERAPY FOR GDM

## *initiation of therapy*

- if fasting glucose are routinely greater than 95 mg/dL, or
- 1-h or 2-hour postprandial glucose are routinely 140 mg/dL and 120 mg/dL or greater, respectively *(ACOG 2013)*
- begin drug therapy if two or more values at the same meal (e.g., post-breakfast or post - lunch) in a 2-week period when desired glucose levels exceed by more than 10 mg/dL *(Moore 2010)*
- initiating drug therapy if two or more fasting glucose values exceed 100 mg/dL

# Recommended Glycemic Targets for Patients with Gestational Diabetes

Guideline	Fasting Glucose (mg/dL)	1-Hr Postprandial Glucose (mg/dL)	2-Hr Postprandial Glucose (mg/dL)
ACOG	≤ 95	< 140	< 120
ADA	≤ 95	≤ 140	≤ 120
Endocrine Society	≤ 95 <sup>a</sup>	≤ 140	≤ 120
NICE	< 95	< 140	< 115

<sup>a</sup>The Endocrine Society suggests a lower fasting glucose target of ≤ 90 mg/dL if it is attainable without significant hypoglycemia.

NICE = National Institute for Health and Care Excellence.

# Insulin Preparations Used in the Management of Gestational Diabetes

Type of Insulin Preparation	Onset of Action (hr)	Peak of Action (hr)	Duration (hr)
<b>Mealtime insulin</b>			
Insulin aspart	0.25	1–3	3–5
Insulin lispro	0.25–0.5	1–3	3–5
Regular insulin	0.5–1	2–3	5–7
<b>Basal insulin</b>			
Insulin detemir	1–2	No pronounced peak	8 to $\geq$ 24
Insulin glargine	1–2	No pronounced peak	11 to $\geq$ 24
NPH insulin	1–2	4–12	10–19 (up to 24)

# Diet and tasks

- Diet plan according to parturients
- Body weight Obese : 25 -35 Kcal /Kg
- Normal weight : 35 -40 Kcal /Kg
- Dietary compliance is evaluated and reinforced during weekly hospital visits
- Targeted values are
- Fasting < 95 mg/dl
- 1Hour post prandial < 140 mg/dl

# Glucose Monitoring

- Quality control blood glucose is occasionally measured in the laboratory
- Use glucometer and self monitor blood glucose at home

# Patient Education

- Compliance with the treatment plan highly depends on patients understanding of
- The implications of GDM on fetus and her self
- Dietary and exercise recommendations
- Self monitoring of blood glucose
- Self administration of insulin and adjustments of insulin doses

# Antepartum Management (ACOG)

- Weekly fetal surveillance since 32 w of GA for
- Clinical examination
- Growth profile
- Biophysical profile
- Non stress test

# Decision for intervention and induction of labour

Depends on

- Estimated by US Fetal Weight
- Poor glycaemic control
- On diet / insulin / macrosomia
- Non-reassuring / ominous NST
- Flat Fetal heart rate variability (non reactive NST)

# Timing of delivery

- When no complications expectant management until term
- When macrosomia induction of labour at 38 w because of high risk of shoulder dystocia
- GDM with HBP or previous stillbirth induction of labour at 37 -38 w depending on the condition of the fetus

# Conclusive remarks

- GDM 4-7 % usually well controlled with diet
- Screening with GCT at 24 -28w is essential
- Fetal monitoring EFW, NST, BPP
- Increased risk of developing Type 2 DM within 15 years
- Born children are in HR for childhood obesity and adult onset diabetes
- DM in pregnancy needs special care