

Screening, Diagnosis and Management of Diabetes in Pregnancy

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Objectives

- Epidemiology of GDM
- Screening of GDM
 - Universal vs. selective screening
 - Screening thresholds
- Diagnosis of GDM
 - GTT: diagnostic thresholds
- Management of GDM
 - Oral hypoglycemic agents vs. insulin injections
- Postpartum follow-up



Epidemiology of Diabetes during Pregnancy in the U.S.

- 154,000 (4%) of all pregnancies
 - 135,000 (88%) due to GDM
 - 12,000 (8%) due to Type 2 DM
 - 7,000 (4%) due to Type 1 DM

ACOG practice bulletin. Gestational Diabetes. Obstet Gynecol 2001;93:525-34
ADA position statement. Standards of Medical Care in Diabetes. Diabetes Care 2006;29:S4-42



GDM: Obstetric Considerations

- GDM associated with
 - Gestational hypertension
 - Preeclampsia
 - Operative deliveries
 - Postpartum development of Type 2 DM

Crowther CA et al. N Engl J Med 2005;352:2477-86.
Casey BM et al. Obstet Gynecol 1997;90:867-73.
Yang X et al. Diabetes Care 2002;9:1619-24.



GDM: Perinatal Considerations

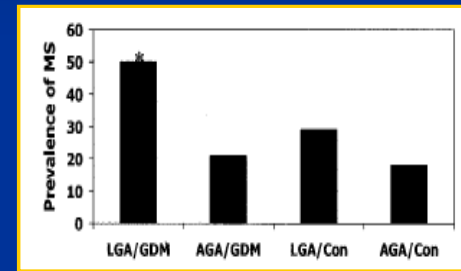
- GDM associated with
 - Fetal macrosomia
 - Birth trauma
 - Metabolic abnormalities
 - Hypoglycemia
 - Hyperbilirubinemia/polycythemia
 - Hypocalcemia
 - Respiratory distress syndrome
 - Preterm delivery
 - Perinatal mortality

Crowther CA et al. N Engl J Med 2005;352:2477-86
 Casey BM et al. Obstet Gynecol 1997;90:867-73
 Yang X et al. Diabetes Care 2002;9:1619-24



GDM: Postnatal Considerations

- Metabolic syndrome evaluated in a longitudinal cohort of 179 children (at age 6,7,9,11)



Boney CM et al. Metabolic syndrome in childhood: Association with birthweight, maternal obesity and GDM. Pediatrics 2005;115:e290-6



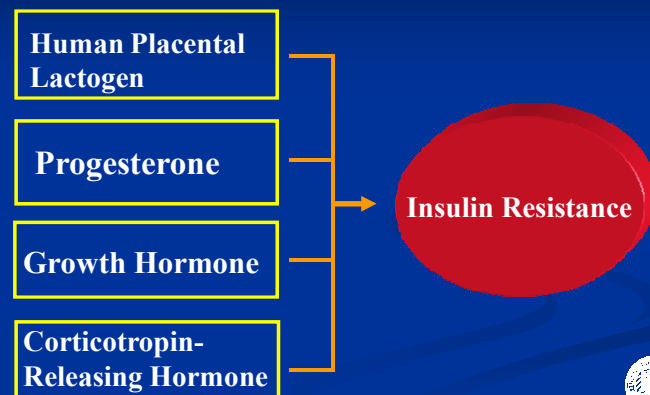
Gestational Diabetes Mellitus

- Insulin resistance first recognized during pregnancy
 - Prevalence: 1-14% of all pregnancies

ACOG practice bulletin. Gestational Diabetes. Obstet Gynecol 2001;93:525-34
 ADA position statement. Standards of Medical Care in Diabetes. Diabetes Care 2006;29:S4-42



GDM: Diabetogenic hormones



Risk Factors of GDM

- Maternal age >25 years
- Body mass index >25 kg/m²
- Ethnicity
 - Latina
 - Native American
 - South or East Asian, Pacific Island ancestry
 - ? African American
- Personal/Family history of DM
- History of macrosomia
- Glycosuria

ACOG practice bulletin. Gestational Diabetes. Obstet Gynecol 2001;93:525-34
 ADA position statement. Standards of Medical Care in Diabetes. Diabetes Care 2006;29:S4-42



Screening of GDM

- ACOG: Universal screening
 - Clinical history
 - Laboratory testing
- ADA: Selective screening
 - Risk assessment at first visit
 - High risk: GCT as soon as feasible
 - Average risk: GCT at 24-28 weeks GA
 - Low risk: No GCT

ACOG practice bulletin. Gestational Diabetes. Obstet Gynecol 2001;93:525-34
 ADA position statement. Standards of Medical Care in Diabetes. Diabetes Care 2006;29:S4-42



Screening of GDM

- U.S. Preventive Service Task Force:
 - Insufficient evidence for universal screening
 - Screening of high-risk women may be beneficial

U.S. Preventive Services Task Force. Guide to clinical preventive services. 2nd ed. Baltimore: Williams & Wilkins 1996;193-208



Low Risk for GDM

- Maternal age < 25 years
- Weight normal before pregnancy
- Members of an ethnic group with a low prevalence of GDM
- No known DM in 1st degree relatives
- No history of abnormal glucose tolerance
- No history of poor obstetric outcome

ADA position statement. Standards of Medical Care in Diabetes. Diabetes Care 2006;29:S4-42



Universal vs. Selective Screening

- Naylor et al: prospective study n=3,131

TABLE 5. Rates of Detection and of False Positive Tests with Chem Case and with Selective Testing.*

Screening	Detection Point	Accuracy	FPR	Gain	Accuracy	FPR
	%	% (95% CI)	%	% (95% CI)	% (95% CI)	%
Used case (no 100% of patients, 1 threshold of 140 mg/dL)	76.3 (54)	—	—	17.9 (20)	—	—
Moore screening: use risk of patient						
Two threshold rules						
Strategy A: 140 mg/dL for scores 2-3, 120 mg/dL for scores 0-2	81.9 (37)	+4.3 (-4.3 to +13.2)	8.26	18.8 (20)	-1.9 (-3.9 to +0.1)	0.00
Strategy B: 140 mg/dL for scores 2-4, 130 mg/dL for scores 0-2	81.2 (36)	+2.8 (-3.0 to +11.5)	8.41	18.4 (20)	-2.3 (-4.3 to -0.9)	0.00
Strategy C: pruned threshold rules by scores 2-3, 120 mg/dL for scores 0-2	79.7 (48)	+1.4 (-6.8 to +11.4)	8.74	13.6 (20)	-4.2 (-6.8 to -1.4)	<0.001
Strategy D: pruned threshold rules by scores 2-3, 120 mg/dL for scores 0-3	76.1 (54)	0 (-0.5 to +0.1)	1.86	13.8 (20)	-4.7 (-6.9 to -1.1)	<0.001

Naylor CD et al. Selective screening for GDM. NEJM 1997;337:1591-6



Universal vs. Selective Screening

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Naylor CD et al. Selective screening for GDM. NEJM 1997;337:1591-6



Screening of GDM

- Screening test
 - 50gm 1-hour glucose challenge test (GCT)
- Screening thresholds
 - 130mg/dL: 90% sensitivity (23% screen +)
 - 140mg/dL: 80% sensitivity (14% screen +)

ACOG practice bulletin. Gestational Diabetes. Obstet Gynecol 2001;93:525-34
 ADA position statement. Standards of Medical Care in Diabetes. Diabetes Care 2006;29:S4-42



Screening Thresholds by Ethnicity: GCT 130 - 150 mg/dL

GCT	130 mg/dL sensitivity (specificity) %	135 mg/dL sensitivity (specificity) %	140 mg/dL sensitivity (specificity) %	145 mg/dL sensitivity (specificity) %	150 mg/dL sensitivity (specificity) %
White	99.5 (82.5)	93.9 (87.1)	89.2 (90.7)	75.6 (92.9)	66.2 (95.0)
African American	98.8 (88.4)	96.5 (91.1)	92.9 (93.8)	81.2 (96.0)	70.6 (97.0)
Latina	98.3 (80.9)	94.1 (85.5)	89.9 (88.7)	78.2 (91.1)	65.6 (93.5)
Asian	98.5 (75.9)	93.0 (81.1)	88.8 (86.0)	79.8 (89.0)	69.0 (91.8)

Esakoff et al. Screening for gestational diabetes. Am J Obstet Gynecol 2005;193:1040-4



Screening Thresholds by Ethnicity: Sensitivity of GCT 130 - 150 mg/dL

GLT	130 mg/dL sensitivity (specificity) %	135 mg/dL sensitivity (specificity) %	140 mg/dL sensitivity (specificity) %	145 mg/dL sensitivity (specificity) %	150 mg/dL sensitivity (specificity) %
White	99.5 (82.5)	93.9 (87.1)	89.2 (90.7)	75.6 (92.9)	66.2 (95.0)
African American	98.8 (88.4)	96.5 (91.1)	92.9 (93.8)	81.2 (96.0)	70.6 (97.0)
Latina	98.3 (80.9)	94.1 (85.5)	89.9 (88.7)	78.2 (91.1)	65.6 (93.5)
Asian	98.5 (75.9)	93.0 (81.1)	88.8 (86.0)	79.8 (89.0)	69.0 (91.8)

Esakoff et al. Screening for gestational diabetes. Am J Obstet Gynecol 2005;193:1040-4



Screening Thresholds by Ethnicity: False Positive Rates of GCT 130 - 150 mg/dL

GCT	130 mg/dL	135 mg/dL	140 mg/dL	145 mg/dL	150 mg/dL
White	17.5%	12.9%	9.3%	7.0%	5.0%
African American	11.6%	9.0%	6.3%	4.0%	3.1%
Latina	19.4%	14.7%	11.5%	9.1%	6.6%
Asian	24.2%	19.1%	14.1%	11.2%	8.4%

Esakoff et al. Screening for gestational diabetes. Am J Obstet Gynecol 2005;193:1040-4



Is GCT Ever Diagnostic for GDM

■ GCT, GDM diagnosis & Perinatal outcomes

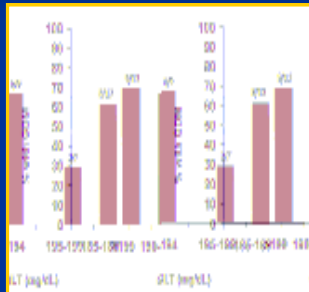


Table III. Multivariate analysis in women with GCT ≥ 200 mg/dL.*

	No GDM (OR) (95% CI)	GDM (OR) (95% CI)
Mode of delivery [†]		
Operative vaginal	-	8.37 (0.18-8.95)
Cesarean section	4.18 (1.16-6.15)	2.25 (1.58-4.21)
Preeclampsia	2.62 (0.50-11.7)	0.40 (0.12-1.37)
Birth weight:		
>4000 g	0.99 (0.13-7.82)	1.87 (0.86-4.07)
>4500 g	-	1.14 (0.60-2.61)
Parturition delivery:		
<37 weeks gestation	1.26 (0.91-11.7)	1.80 (0.97-3.44)
<34 weeks gestation	4.07 (0.52-31.5)	2.67 (0.93-7.64)
~32 weeks gestation	8.68 (1.62-91.9)	2.92 (0.87-9.76)
Shoulder dystocia	15.18 (1.66-4.88)	2.08 (0.82-18.3)
5-minute Apgar <7	6.41 (1.23-33.5)	0.57 (0.10-3.31)
Birth trauma [‡]	-	1.12 (0.25-5.00)
Neonatal morbidity [§]	0.75 (0.15-3.78)	0.80 (0.40-1.63)

Altiano LC et al. Alternative methods of diagnosing GDM. Am J Obstet Gynecol 1999;181:1158-61
Cheng et al. Markedly elevated GLT & perinatal outcomes. JMFNM 2006;19:729-34



Diagnosis of GDM

■ Diagnostic test

- FS >126mg/dL or random BG >200mg/dL
- 100gm 3-hour glucose tolerance test (GTT)
 - 2 or more abnormal values

	Carpenter and Coustan	National Diabetes and Data Group
Fasting	95 mg/dL	105 mg/dL
1hr	180 mg/dL	190 mg/dL
2hr	155 mg/dL	165 mg/dL
3hr	140 mg/dL	145 mg/dL

ADA position statement. Standards of Medical Care in Diabetes. Diabetes Care 2006;29:S4-42



Diagnosis of GDM

Diagnostic test

- 75gm 2-hour glucose tolerance test (GTT)
 - 2 or more values exceeding threshold (ADA)
 - Fasting or 2-hr value exceeds threshold (WHO)

	WHO	ADA
Fasting	126mg/dL	95 mg/dL
1hr	--	180 mg/dL
2hr	140mg/dL	155 mg/dL

ADA position statement. Standards of Medical Care in Diabetes. Diabetes Care 2006;29:S4-42
 WHO: Prevention of diabetes mellitus. Geneva, WHO 1994



Diagnosis of GDM

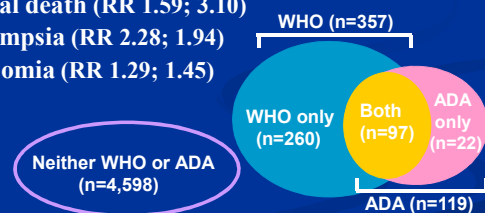
- 75gm 2-hr GTT vs. 100gm 3-hr GTT
 - Poor concordance: kappa index 0.18-0.21
 - 16-20 weeks: 15/277 (2hrGTT) vs. 41/277 (3hrGTT), 11 concordant
 - 26-31 weeks: 25/484 (2hrGTT) vs 60/484 (3hrGTT), 13 concordant
 - Omission of the 3rd hr value (100mg GTT):
 - 87% sensitivity (Atilano et al 1999)
 - 26.4 vs. 28.4% GDM, no difference in perinatal outcomes of 18 omitted cases (Jakobi 2004)

Mello G et al. Lack of concordance between 75g and 100g GTT for diagnosis of GDM. Clin Chem 2006; 52:1679-82.
 Atilano LC et al. Alternative methods of diagnosing GDM. Am J Obstet Gynecol 1999;181:1158-6
 Jakobi et al. A 2-hr vs. 3-hr 100gm GTT for diagnosis of GDM. J Perinatal Med 2004; 32:320-2



Diagnosis of GDM: 75gm GTT

- ADA vs. WHO diagnostic criteria
- Cohort study: 4,977 women with 2-hr 75gGTT
- GDM by either diagnostic criteria associated with:
 - Perinatal death (RR 1.59; 3.10)
 - Preeclampsia (RR 2.28; 1.94)
 - Macrosomia (RR 1.29; 1.45)

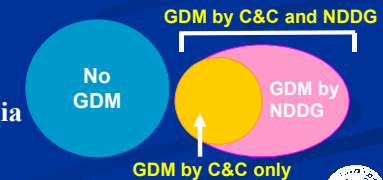


Schmidt MI et al. GDM diagnosed with a 75gm-2-hr OGTT and adverse perinatal outcomes. Diabetes care 2001;24:1151-5.



Diagnosis of GDM

- ADA and the 4th International Workshop-Conference on GDM:
 - Carpenter & Coustan diagnostic criteria
- Carpenter & Coustan vs. NDDG:
 - Women with GDM by Carpenter and Coustan only have higher odds of
 - Macrosomia
 - Hypoglycemia
 - Hyperbilirubinemia



ADA position statement. Standards of Medical Care in Diabetes. Diabetes Care 2006;29:S4-42
 Metzger EB et al. Diabetes Care 1998;21:Suppl 2: B161-7
 Ferrara A et al. Diabetologia 2006;



Diagnosis of GDM

- Women with false-positive GCT
 - Retrospective cohort study (Stamilio 2004)
 - Cesarean delivery
 - Macrosomia
 - Shoulder dystocia
 - Composite morbidity
 - Retrospective cohort study (McLaughlin 2006)
 - Cesarean delivery
 - Preeclampsia
 - Macrosomia
 - ICN admission

Stamilio et al. False positive 1-hour GCT and adverse perinatal outcomes. *Obstet Gynecol* 2004;103:148-56
 McLaughlin et al. Women with one-elevated GTE. *Am J Obstet Gynecol* 2006;194:e16-9.



Diagnosis of GDM

- Continuous relationship between carbohydrate intolerance and adverse outcome
- No single cutoff can separate
 - those with high risk
 - those with no risk at all
- GDM diagnostic criteria validated by
 - Predictive value for subsequent diabetes in the mother
 - Rather than ability to identify risk to the fetus/newborn
- Diagnostic criteria appropriate but arbitrary

Constan DR, Carpenter MW. The diagnosis of gestational diabetes. *Diabetes Care* 1998;21 Suppl 2:B5-8



Management of GDM

- Nutrition therapy
- Home self glucose monitoring
- Medical therapy if glycemic control not achieved with diet/exercise
 - Subcutaneous insulin
 - Oral hypoglycemic agents
 - Glyburide
 - Metformin
- Antenatal monitoring

ACOG practice bulletin. Gestational Diabetes. *Obstet Gynecol* 2001;93:525-34
 Gabbe SG. Management of diabetes mellitus by ObGyn. *Obstet Gynecol* 2004;103:1229-34

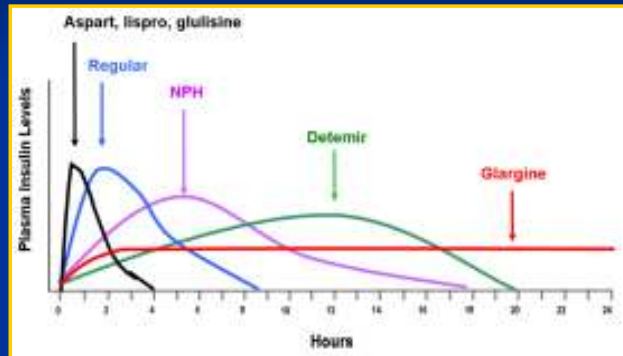


Goals of Glycemic Control

- Blood glucose goals during pregnancy
 - Fasting < 95mg/dL
 - 1-hr postprandial < 130-140mg/dL
 - 2-hr postprandial am < 120mg/dL
 - 2am < 120mg/dL



Treatment of GDM



Adapted from ADA: Clinical Education Program "Insulin Therapy for the 21st Century"



Treatment of GDM

Table 2. Primary Clinical Outcomes among the Infants and Their Mothers.*

Outcome	Intervention Group no. (%)	Routine Care Group no. (%)	Unadjusted Relative Risk (95% CI)	Unadjusted P Value	Adjusted Relative Risk (95% CI)†	Adjusted P Value†	Step-Down Side P Value
Infants							
Totals: 506 524							
Any serious perinatal complication‡	7 (1)	23 (4)	0.32 (0.11–0.78)	0.004	0.33 (0.14–0.75)	0.01	0.04
Death	2	5 (1)		0.86		0.67	
Stillbirth	0	1 (0.1)		0.76		0.76	
Neonatal death	0	2 (0.4)		0.70		0.50	
Shoulder dystocia§	7 (1)	14 (3)	0.46 (0.24–0.90)	0.07	0.44 (0.19–1.04)	0.08	
Birth fractures	0	1 (0.1)		1.00		0.39	
Neuro palsy	0	3 (0.5)		0.28		0.21	
Admission to neonatal nursery**	237 (47)	321 (61)	0.63 (0.56–0.70)	0.000	0.63 (0.53–0.75)	0.00	0.04
Jaundice requiring phototherapy	44 (9)	40 (8)	0.95 (0.67–1.40)	0.79	0.92 (0.62–1.37)	0.72	0.16
Mothers							
Totals: 492 510							
Induction of labor††	239 (49)	270 (53)	0.81 (0.70–0.94)	0.002	0.74 (0.55–1.00)	<0.001	0.005
Cesarean delivery	134 (27)	144 (28)	0.96 (0.80–1.14)	0.60	0.91 (0.71–1.16)	0.77	0.08
Bedside	72 (15)	81 (16)	0.72 (0.49–1.09)	0.20	0.77 (0.55–1.09)	0.13	
Emergency	40 (8)	30 (6)	0.81 (0.62–1.05)	0.11	0.82 (0.64–1.13)	0.11	

Crowther et al. Effect of treatment of GDM on pregnancy outcomes. NEJM 2005;256:2277-86



Treatment of GDM

Table 4. Secondary Outcomes among the Infants.*

Outcome	Intervention Group (N=506)	Routine Care Group (N=524)	Adjusted Treatment Effect (95% CI)†	Adjusted P Value†
Birth weight — g	3335±351	3402±360	-245 (-219 to -70)	<0.001
Large for gestational age — no. (%)‡	65 (13)	115 (22)	0.62 (0.47 to 0.81)	<0.001
Macrosomia (≥4 kg) — no. (%)	49 (10)	110 (21)	0.47 (0.34 to 0.64)	<0.001
Small for gestational age — no. (%)§	33 (7)	38 (7)	0.88 (0.58 to 1.39)	0.59
5-Min Apgar score <7 — no. (%)	6 (1)	11 (2)	0.57 (0.21 to 1.53)	0.26
Hypoglycemia requiring IV therapy — no. (%)¶	35 (7)	27 (5)	1.42 (0.87 to 2.32)	0.16
Neonatal convulsions — no. (%)	1 (0.1)	2 (0.4)	0.52 (0.05 to 5.89)	1.00
Respiratory distress syndrome — no. (%)	27 (5)	19 (4)	1.52 (0.86 to 2.71)	0.15

Crowther et al. Effect of treatment of GDM on pregnancy outcomes. NEJM 2005;256:2277-86



Insulin vs. Oral Agents

- Langer et al 2000
 - Randomized controlled trial (n=404)
 - Similar glycemic control

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±6	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	98±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

Langer O et al. A comparison of glyburide and insulin in women with GDM. N Engl J Med 2000;242:1134-8



Langer 2000: Insulin vs. Glyburide

- Similar neonatal outcomes

TABLE 4. NEONATAL OUTCOMES.*

OUTCOME	GLYBURIDE (N=261)	INSULIN (N=263)	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 — µU/ml‡	18±13	18±21	0.84
Intravenous glucose therapy — no. (%)	28 (14)	22 (11)	0.36
Hypoglycemia — no. (%)	18 (9)	12 (6)	0.25
Hypokalemia — no. (%)	2 (1)	2 (1)	0.99
Hyperbilirubinemia — no. (%)	12 (6)	8 (4)	0.36
Polythemia — 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

Langer O et al. A comparison of glyburide and insulin in women with GDM. N Engl J Med 2000;242:1134-8



Langer 2000: Insulin vs. Glyburide

- Similar neonatal outcomes

Neonatal Outcome	Glyburide % (n)	Insulin % (n)	p-value
Birth weight > 4000 gms	7% (14)	4% (9)	0.26
Lung complications	8% (16)	6% (12)	0.43
Hypoglycemia	9% (18)	6% (12)	0.25
Hyperbilirubinemia	6% (12)	4% (8)	0.36
Composite morbidity	30%	20%	0.05

Langer O et al. A comparison of glyburide and insulin in women with GDM. N Engl J Med 2000;242:1134-8



Insulin vs. Oral Agents

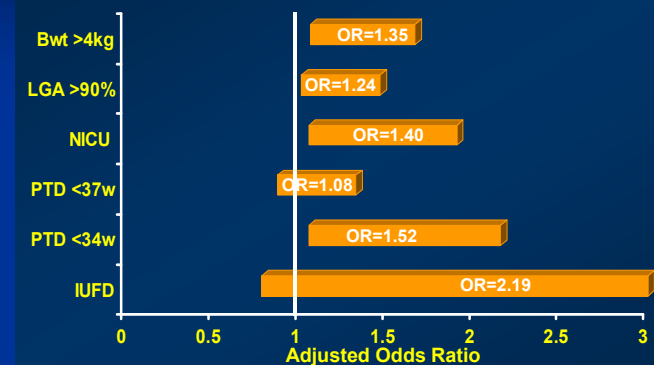
- Jacobson et al 2005
- Retrospective cohort study (n=504)

Neonatal Outcome	Glyburide % (n)	Insulin % (n)	p-value
Preeclampsia	12 % (28)	6 % (16)	<0.05
Birth wt > 4000 gms	24 % (63)	25 % (60)	NS
Mean birth weight	3661 gms	3599 gms	NS
Birth injury	3 % (8)	1 % (3)	0.08
Phototherapy	9 % (21)	5 % (12)	<0.05

Jacobson GF et al. Comparison of glyburide and insulin for the management of GDM. AJOG 2005;193:118-24



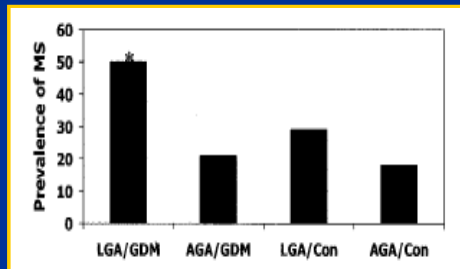
GDM: Medical Therapy vs. Insulin



Multivariable logistic regression adjusting for maternal age, ethnicity, parity, education level, GA at delivery, GA at GDM diagnosis, BMI, and gestational weight gain

GDM: Postnatal Considerations

- Metabolic syndrome evaluated in a longitudinal cohort of 179 children (at age 6,7,9,11)



Boney CM et al. Metabolic syndrome in childhood: Association with birthweight, maternal obesity and GDM. *Pediatrics* 2005;115:e290-6



Medical Management of GDM

- ACOG Practice Bulletin:
 - No oral agents other than glyburide has been shown to be safe and effective in GDM
 - Further study recommended before use of newer oral hypoglycemic agents can be supported for use in pregnancy

ACOG practice bulletin. *Gestational Diabetes. Obstet Gynecol* 2001;93:525-34



Postpartum Follow-up

- Diagnosis of DM in non-pregnant state:

Normal Values	Impaired fasting glucose or impaired glucose tolerance	Diabetes Mellitus
FPG <110mg/dL	FPG 110-125mg/dL	FPG ≥126mg/dL
75g 2hr GTT 2hr PG <140mg/dL	75g 2hr GTT 2hr PG 140-199mg/dL	75g 2hr GTT 2hr PG ≥200mg/dL Symptoms of DM & random PG ≥200mg/dL

ACOG practice bulletin. *Gestational Diabetes. Obstet Gynecol* 2001;93:525-34



Postpartum Follow-up

- Cost-effective screening:
 - Fasting PG, 2hr GTT, Hgb A1c
 - Annually, every 2 years, every 3 years
 - Assume negative 6-week screen progress to DM 8% per year
 - Each positive FPG, Hgb A1c followed by confirmatory GTT
 - GTT every 3 years: lowest cost per case DM detected

Kim C et al. Efficacy and cost of postpartum screening strategies for diabetes among women with histories of GDM. *Diabetes Care* 2007;30:1102-6



Diabetes and Pregnancy: Summary

■ Gestational Diabetes

■ Screening and Diagnosis

- Universal screening
- GCT Thresholds: 130 mg/dl vs. 140 mg/dl
- GTT diagnostic criteria: Carpenter and Coustan

■ Management

- Diet/exercise, nutritional consult
- Self-monitoring of blood glucose
- Insulin vs oral hypoglycemic agents if indicated

■ Postpartum screening

