

PREGNANCY RELATED HYPERTENSION AND DIABETES

Therapeutic Management

August 2021

Collaborators









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Course Overview

- Hypertensive Disorders of Pregnancy
 - Prevalence
 - Risk and screening
 - Management
 - Medications
- Gestational Diabetes
 - Prevalence
 - Risk and screening
 - Management
 - Medications



Presenters

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Conflicts of Interest

• None of the speakers or advisors have a conflict of interests to declare.



Important Information



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The video can be paused and resumed later.







Hypertensive Disorders of Pregnancy

August 2021
Rita W. Driggers, MD

Medical Director, Maternal Fetal Medicine

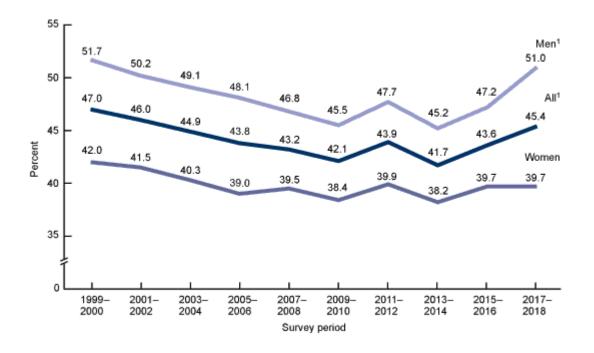
Sibley Memorial Hospital, Johns Hopkins Medicine

Objectives

- At the completion of this module, the learner should possess the knowledge to:
 - Recognize and properly diagnose pregnancies complicated by chronic hypertension, gestational hypertension, and preeclampsia
 - Counsel patients about the complications and risks associated with hypertensive disorders of pregnancy
 - Manage or describe the management of and make appropriate referrals for pregnancies complicated by chronic hypertension, gestational hypertension, and preeclampsia
 - Manage or describe the management of and make appropriate referrals for pregnancies complicated by hypertensive emergencies, and eclampsia

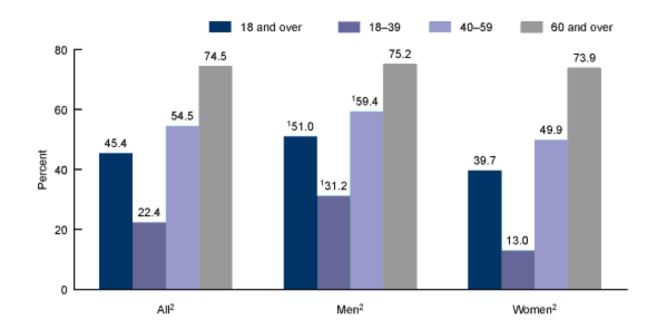


 Age-adjusted trend in hypertension prevalence among adults aged 18 and over, by sex: United States, 1999 -2018





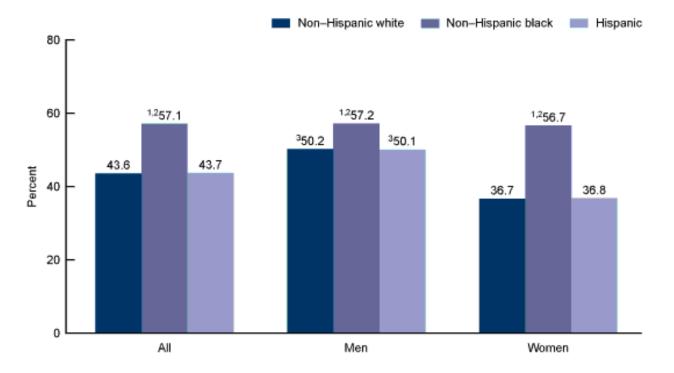
 Prevalence of hypertension among adults aged 18 and over, by sex and age: United States, 2017-2018





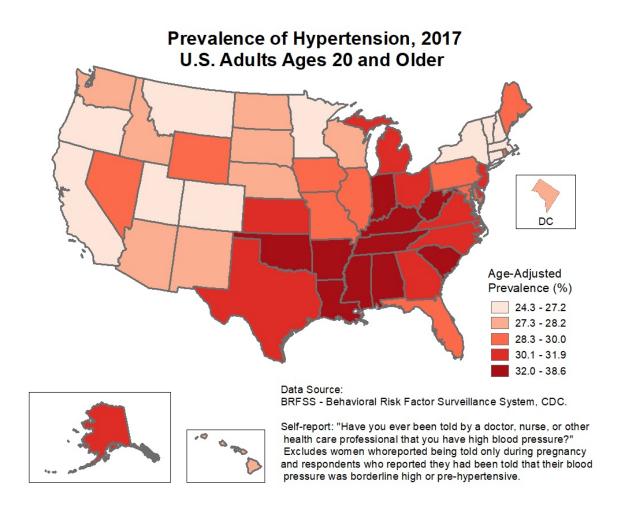
NCHS Data Brief No. 364, April 2020

 Age-adjusted prevalence of hypertension among adults aged 18 and over, by race and Hispanic origin: United States, 2017-2018





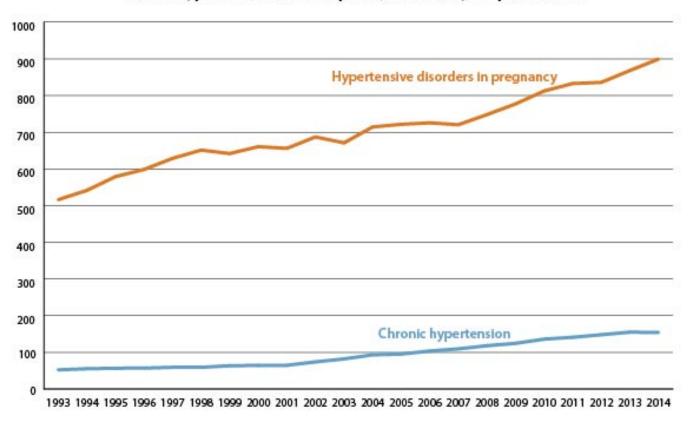




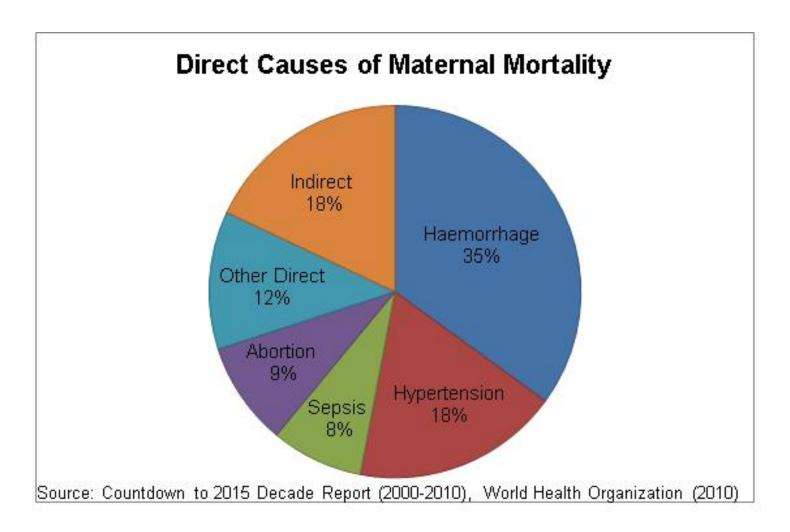


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Rate of hypertensive disorders per 10,000 delivery hospitalizations







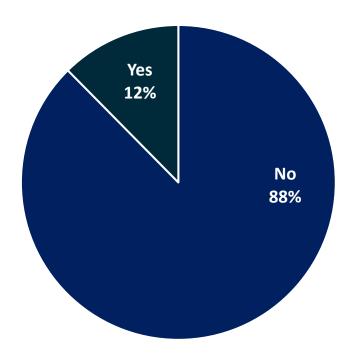


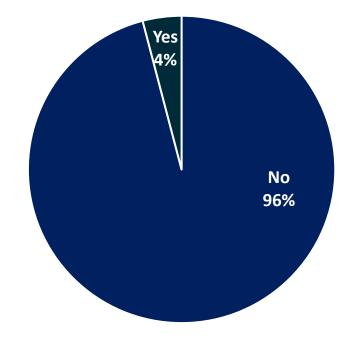
Deliveries by maternal health conditions

Distribution of DC-resident delivery hospital discharges by mother's health conditions that complicated the pregnancy or delivery, 2016-2019

GESTATIONAL HYPERTENSION

PREEXISTING HYPERTENSION





Data Source: Hospital Discharge Data for 2016-2019, DC Hospital Association



Knowledge Check

Which of the following groups has the highest prevalence of hypertension

- A. Non-Hispanic white adults
- B. Non-Hispanic black adults
- C. Hispanic adults



- Chronic hypertension
 - 2017 America College of Cardiology and the American Heart Association modified blood pressure categories:
 - Normal: Less than 120/80 mmHg
 - Elevated: Systolic between 120-129 and diastolic less than 80 mmHg
 - Stage 1: Systolic between 130-139 or diastolic between 80-89 mmHg
 - Stage 2: Systolic at least 140 or diastolic at least 90 mmHg
 - Resulted in increase in prevalence of hypertension from ~32% to ~46% in the US adult population



Muntner P. J Am Coll Cardiol 2018;71:109-18.

- Chronic hypertension in pregnancy
 - Defined as hypertension diagnosed or present before pregnancy or before 20 weeks of gestation
 - Hypertension that is diagnosed for the first time during pregnancy and that does not resolve in the typical postpartum period
 - Traditional BP criteria:
 - Systolic BP of 140 mmHg or higher
 - Diastolic BP of 90 mmHg or higher
 - Requires at least two readings at least 4 hours apart



Am J Obstet Gynecol 2000;183:S1–22 ACOG Practice Bulletin #203, Jan 2019

- Preeclampsia
 - Systolic BP of 140 mmHg or higher or diastolic BP of 90 mm Hg or higher on two occasions at least 4 hours apart after 20 weeks in a woman with a previously normal blood pressure, and
 - Proteinuria
 - 300mg or higher on 24-hour urine collection
 - Protein: Creatinine ratio of 0.3 or more
 - Dipstick reading of 2+ protein
 - Preeclampsia may be diagnosed without proteinuria if severe features are present

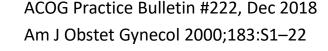


- Preeclampsia with severe features
 - Systolic blood pressure of 160 mm Hg or higher, or diastolic blood pressure of 110 mm Hg or higher on two occasions at least 4 hours apart
 - Thrombocytopenia: Plt < 100k
 - Renal insufficiency: Cr > 1.1mg/dl or doubled
 - Impaired liver function: Liver transaminases twice upper limits of normal or severe persistent RUQ or epigastric pain
 - Pulmonary edema
 - Headache unresponsive to medication and not explained by alternative diagnosis
 - Visual disturbances

ACOG Practice Bulletin #222, Dec 2018



- Gestational hypertension
 - Defined as systolic BP 140 mmHg or higher OR diastolic BP 90 mmHg or higher on two occasions at least 4 hours apart after 20 weeks with previously normal BP
 - Considered severe when systolic BP reaches 160 mmHg or diastolic BP reaches 110 mmHg
 - Occurs without proteinuria or lab abnormalities
 - Develops after 20 weeks and resolves in the postpartum period
 - May not truly be distinct entity from preeclampsia





- Hemolysis, elevated liver enzymes, and low platelets (HELLP) syndrome
 - More severe form of preeclampsia
 - Associated with increased rates of maternal morbidity and mortality
 - Suggested diagnostic criteria:
 - AST or ALT more than twice upper limits of normal
 - Platelets < 100k
 - LDH > 600 IU/L

ACOG Practice Bulletin #222, Dec 2018 Clin Perinatol 2004;31:807-33 Am J Obstet Gynecol 1991;164:1500-9 Am J Obstet Gynecol 1990;162:311-16 Am J Obstet Gynecol 1999;180:1373-84 Am J Obstet Gynecol 1995;172:1876-8



- Eclampsia
 - Most severe manifestation of hypertensive disorders of pregnancy
 - New-onset seizures in absence of other causes
 - Significant cause of maternal mortality, especially in low-resource settings
 - Occurs in small proportion of patients:
 - 1.9% with preeclampsia
 - 3.2% with severe features

ACOG Practice Bulletin #222, Dec 2018 J Repro Med 1987;32:499-503 Lancet 2002;359:1877–90 Br J Obstet Gynaecol 1998;105:300-3



- Eclampsia
 - Often preceded by signs of cerebral irritation
 - Severe occipital or frontal headache
 - Blurred vision/photophobia
 - Altered mental status
 - May occur before, during, or after labor
 - Up to 38% do not have hypertension or proteinuria prior to seizure



Knowledge Check

The primary difference between gestation hypertension and preeclampsia is:

- A. Blood pressure levels
- B. Whether proteinuria is present
- C. Gestational age at diagnosis
- D. Whether blood pressure levels return to normal in the postpartum period



Risk factors for chronic hypertension

- Age, sex, race/ethnicity
- Elevated BP: Systolic between 120-129 and diastolic less than 80 mmHg
- Diabetes
- Unhealthy diet
- Physical inactivity
- Obesity
- Too much alcohol
- Tobacco use
- Genetics and family history



Risk factors for preeclampsia

- Nulliparity
- Multifetal gestations
- Preeclampsia in a previous pregnancy
- Chronic hypertension
- Pregestational diabetes
- Gestational diabetes
- Thrombophilia



Risk factors for preeclampsia

- Systemic lupus erythematosus
- Prepregnancy body mass index greater than 30
- Antiphospholipid antibody syndrome
- Maternal age 35 years or older
- Kidney disease
- Assisted reproductive technology
- Obstructive sleep apnea



Knowledge Check

Which of the following is NOT a risk factor for BOTH chronic hypertension AND preeclampsia:

- A. Advancing age
- B. Diabetes
- C. Obesity
- D. Thrombophilia



Maternal complications of chronic hypertension

- If poorly controlled:
 - Maternal mortality
 - Cerebrovascular accidents
 - Pulmonary edema
 - End-organ damage (heart, brain, kidneys)
- Gestational diabetes
- Superimposed preeclampsia
- Cesarean delivery
- Postpartum hemorrhage

ACOG Practice Bulletin #203, Jan 2019
J Reprod Med 2007;52:1046–51
Am J Perinatol 2016;33:745–50
Int J Gynaecol Obstet 2004;86:7–11
Ultrasound Obstet Gynecol 2017;50:228–35



Maternal complications of preeclampsia

- Progression to eclampsia
 - Seizures may lead to
 - Maternal hypoxia
 - Trauma
 - Aspiration pneumonia
 - Residual neurologic damage is rare
- Increased risk of chronic hypertension and cardiovascular disease



Fetal/neonatal complications of maternal chronic hypertension

- Stillbirth or perinatal death
 - Independent of other possible contributors
- Growth restriction (17%)
- Preterm birth (28%)
 - Indicated, not spontaneous
- Congenital anomalies
 - Cardiac, hypospadias, esophageal atresia
- Placental abruption

ACOG Practice Bulletin #203, Jan 2019 J Perinatol 1997;17:425–7 BJOG 2008;115:1436–42 BMJ 2014;348:g2301 BJOG 2015;122:1002–9



Fetal/neonatal complications of maternal preeclampsia

- Fetal growth restriction
- Oligohydramnios
- Placental abruption
- Non-reassuring fetal heart rate monitoring
- Preterm birth
 - Spontaneous or indicated





Knowledge Check

Fetal/neonatal risks of BOTH chronic hypertension and preeclampsia include all of the following EXCEPT:

- A. Fetal growth restriction
- B. Placental abruption
- C. Congenital anomalies
- D. Preterm birth



- Preconception
 - Evaluate for end-organ damage
 - Optimize maternal co-morbidities
 - Optimize BP control
 - Medication review
 - Explain maternal and fetal/neonatal risks
 - Evaluate for causes of secondary hypertension

ACOG Practice Bulletin #203, Jan 2019 Obstet Gynecol 2015;126:e112–26 Obstet Gynecol 2009;113:1405–13 Obstet Gynecol 2005;105:675–85



Box 3. Historical Features Favoring Hypertension Cause

Primary Hypertension

- Gradual increase in BP, with slow rate of rise in BP
 BP lability, episodic pallor, and dizziness
- Lifestyle factors that favor higher BP (eg, weight gain, high-sodium diet, decreased physical activity, job change entailing increased travel, excessive consumption of alcohol)
- Family history of hypertension

Secondary Hypertension

- BP lability, episodic pallor, and dizziness (pheochromocytoma)
- Snoring or hypersomnolence (obstructive sleep apnea)
- Muscle cramps or weakness (hypokalemia from primary aldosteronism or secondary aldosteronism due to renovascular disease)
- Weight loss, palpitations, heat intolerance (hyperthyroidism)
- Edema, fatigue, frequent urination (kidney disease or failure)
- History of coarctation repair (residual hypertension associated with coarctation)
- Central obesity, facial rounding, easy bruisability (Cushing syndrome)
- Medication or substance use (eg, alcohol, NSAIDS, cocaine, amphetamines)
- Absence of family history of hypertension

Abbreviations: BP, blood pressure; NSAIDs, nonsteroidal antiinflammatory drugs.

Reprinted from: Whelton PK, Carey RM, Aronow WS, Casey DE Jr, Collins KJ, Dennison Himmelfarb C, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines [published erratum appears in] Am Coll Cardiol 2018;71:2275-9]. J Am Coll Cardiol 2018;71:e127–248.



- Baseline evaluation
 - Serum aspartate aminotransferase and alanine aminotransferase
 - Serum creatinine
 - Serum electrolytes (specifically potassium)
 - Blood urea nitrogen
 - Complete blood count
 - Spot urine protein/creatinine ratio or 24-hour urine for total protein and creatinine
 - Electrocardiogram or echocardiogram as appropriate
- Usual BP changes in pregnancy
- Low-dose aspirin (81mg)



ACOG Practice Bulletin #203, Jan 2019 Ann Intern Med 2014;161:819–26

- BP treatment goals during pregnancy
 - Studies evaluating tight versus less tight control of BPs
 - Tight control of hypertension
 - Conferred no benefit to the fetus
 - Had only marginal effects for the woman(reduced frequency of progression to severe hypertension)
- Initiate antihypertensive therapy for persistent chronic hypertension:
 - Systolic BP \geq 160mmHg
 - Diastolic BP ≥ 110mmHg
- Treat at lower blood pressure thresholds with comorbidities



ACOG Practice Bulletin #203, Jan 2019 N Engl J Med 2015;372:407–17

- BP treatment goals during pregnancy
 - Limited data on ideal BP
 - Lowering BP too much may compromise uteroplacental blood flow
 - Current recommendations:
 - Systolic BP at or above 120mmHg but less than 160mmHg
 - Diastolic BP at or above 80mmHg but less than 110mmHg
 - Lower BPs for women with comorbid conditions



- Maternal and fetal monitoring
 - Close monitoring of BPs
 - Assessment of fetal growth
 - Antenatal fetal surveillance
- Delivery timing
 - Delivery by 38+0-39+6 weeks with CHTN on no meds
 - Delivery by 37+0-39+6 weeks with CHTN controlled on meds
 - Delivery by 36+0-37+6 weeks with CHTN difficult to control
 - Delivery by 34 weeks or sooner with superimposed preeclampsia



- Postpartum considerations
 - BP control continues to be an issue postpartum
 - After initial decline immediately after delivery, BPs rise
 - Severe hypertension or superimposed preeclampsia may develop
 - Outpatient follow up the first 1-2 weeks
 - Home BP monitoring
 - Goal BP postpartum:
 - Systolic BP ≤ 150mmHg
 - o Diastolic BP < 100mmHg

ACOG Practice Bulletin #203, Jan 2019
Obstet Gynecol 2018;131:e140–50
Obstet Gynecol 2018;131:e140–50
Cochrane Database of Systematic Reviews 2013, Issue 4. Art. No.: CD004351
Hypertens Pregnancy 2010;29:294–300



Knowledge Check

Which of the following is TRUE about chronic hypertension during pregnancy?

- A. Blood pressure goals during pregnancy are lower than when not pregnant
- B. Blood pressure normally decreases in the 2nd trimester and this decrease may be more profound in patients with chronic hypertension
- C. Very tight control of blood pressures improves fetal outcomes
- Blood pressure goals immediately postpartum are the same as during pregnancy



- Delivery is the only cure for GHTN/preeclampsia
- Delaying delivery increases likelihood that preeclampsia will progress (to severe preeclampsia, HELLP, or eclampsia)
- Initial evaluation:
 - Labs (CBC, Cr, LDH, AST, ALT, testing for proteinuria)
 - Ultrasound for estimated fetal weight and amniotic fluid index
 - Fetal monitoring
- Subsequent management depends on gestational age and test results
 - Must balance maternal and fetal risks

ACOG Practice Bulletin #222, Dec 2018



- Mild preeclampsia or gestational hypertension
 37 weeks
 - Delivery is recommended
 - Administration of intrapartum-postpartum magnesium sulfate to prevent eclampsia is not recommended as long as BPs are in mild range (SBP<160mm Hg and DBP <110mm Hg) and the patient is without symptoms
 - Monitor BPs in the hospital for at least 72 hours postpartum and again 7-10 days after delivery, earlier in women with symptoms



- Mild preeclampsia or gestational hypertension
 <37 weeks
 - Close monitoring as follows:
 - Serial assessment of maternal symptoms and fetal movement (daily by the patient)
 - Twice weekly BP checks (at least once in office, once at home by patient)
 - Weekly assessment of platelet counts and liver enzymes
 - Once or twice weekly fetal monitoring



- Mild preeclampsia or gestational hypertension
 <37 weeks
 - Do not treat SBP <160mm HG or DBP <110mm Hg (if BPs are greater than this, patient now has severe disease)
 - Strict bedrest is NOT recommended, but decreased activities may be indicated
 - Serial growth assessments every 3-4 weeks



- Mild preeclampsia or gestational hypertension
 <37 weeks
 - Delivery is recommended at 37 weeks if not indicated prior for severe disease
 - Administration of intrapartum-postpartum magnesium sulfate to prevent eclampsia is not recommended as long as BPs are in mild range (SBP<160mm Hg and DBP <110mm Hg) and the patient is without symptoms
 - Monitor BPs in the hospital for at least 72 hours postpartum and again 7-10 days after delivery, earlier in women with symptoms



- Severe preeclampsia or gestational hypertension >34 weeks
 - Delivery is recommended after maternal stabilization
 - Administration of intrapartum-postpartum magnesium sulfate to prevent eclampsia is recommended
 - For women undergoing cesarean delivery, the intraoperative administration of parenteral magnesium sulfate to prevent eclampsia is recommended
 - Monitor BPs in the hospital for at least 72 hours postpartum and again 7-10 days after delivery, earlier in women with symptoms



- Severe preeclampsia or gestational hypertension <34 weeks
 - If stable maternal and fetal conditions, expectant management with close observation is recommended
 - Treat sustained systolic BPs > 160mmHg or diastolicBPs > 110mmHg
 - Give corticosteroids to decrease morbidities associated with prematurity



- Severe preeclampsia or gestational hypertension <34 weeks
 - Give corticosteroids to decrease morbidities associated with prematurity and deliver after 48 hours with any of the following:
 - o PPROM
 - Labor
 - Platelets < 100,000 per microliter
 - Transaminases persistently twice or more the upper normal values
 - IUGR (EFW<5th percentile)
 - Severe oligohydramnios (AFI < 5cm)
 - Umbilical artery reversed end diastolic flow
 - New onset renal insufficiency (doubling of Cr or Cr > 1.1mg/dl)



- Severe preeclampsia or gestational hypertension <34 weeks
 - Give corticosteroids but DO NOT delay delivery (after initial maternal stabilization) regardless of gestational age for any of the following:
 - Uncontrollable severe hypertension
 - Eclampsia
 - o Pulmonary edema
 - Abruptio placentae
 - Disseminated intravascular coagulation
 - Non-reassuring fetal status
 - o IUFD



- Severe preeclampsia or gestational hypertension <34 weeks
 - Mode of delivery need not be cesarean delivery (determine by presentation, cervical exam, and maternal/fetal conditions)
 - Administration of intrapartum-postpartum magnesium sulfate to prevent eclampsia is recommended
 - For women undergoing cesarean delivery, the intraoperative administration of parenteral magnesium sulfate to prevent eclampsia is recommended
 - Monitor BPs in the hospital for at least 72 hours postpartum and again 7-10 days after delivery, earlier in women with symptoms



- Severe preeclampsia or gestational hypertension prior to viability
 - Delivery after maternal stabilization is recommended
 - Monitor BPs in the hospital for at least 72 hours postpartum and again 7-10 days after delivery, earlier in women with symptoms



- HELLP syndrome
 - If prior to fetal viability or ≥34 weeks, delivery should be undertaken shortly after initial maternal stabilization
 - If after viability but < 34 weeks, delay delivery for 24-48 hours (to administer corticosteroids) if maternal and fetal condition remains stable
 - Monitor BPs in the hospital for at least 72 hours postpartum and again 7-10 days after delivery, earlier in women with symptoms



- Postpartum gestational hypertension/preeclampsia
 - For women in the postpartum period who present with new-onset hypertension associated with headaches or blurred vision or preeclampsia with severe hypertension, the parental administration of magnesium sulfate is recommended
 - For women with persistent postpartum hypertension, SBP > 150 mmHg or DBP > 100mmHg, on at least 2 occasions 4-6 hours apart, anti-hypertensive therapy is as needed for BP elevations above the cut off
 - SBP > 160mmHg or DBP > 110mmHg should be treated within 1 hour
 - Monitor BPs in the hospital for at least 72 hours postpartum and again 7-10 days after delivery, earlier in women with
 symptoms

 ACOG Practice Bulletin #222, Dec 2018



- Counseling for future pregnancies
 - Prone to hypertensive complications in future pregnancies
 - At increased risk of later life cardiovascular disease
 - The earlier preeclampsia occurred, the more likely it is to recur
 - Risk of recurrence:
 - 15% for women who had preeclampsia in one previous pregnancy
 - 30% for women who had preeclampsia in previous two pregnancies
 - 40% for nulliparous women who were diagnosed prior to 30 weeks
 - 5-7% for women with one episode of HELLP



- Counseling for future pregnancies
 - With subsequent development of preeclampsia, there is high incidence of:
 - Preterm delivery
 - Fetal growth restriction
 - Placental abruption
 - Cesarean delivery
 - Initiate daily low-dose aspirin (81mg) beginning in the late first trimester is suggested
 - Therapy should be initiated prior to 16 weeks in order to improve trophoblast invasion which is typically complete by 20 weeks gestation



Knowledge Check

Which of the following statements is FALSE about the management of preeclampsia and gestational hypertension:

- A. Mild preeclampsia or gestational hypertension prior to 37 weeks may be managed expectantly with close follow up
- B. Delivery is indicated for severe preeclampsia at or beyond 34 weeks
- C. If HELLP syndrome is diagnosed at 32 weeks, delivery is indicated after maternal stabilization
- D. If preeclampsia with severe features is diagnosed prior to fetal viability, delivery is recommended after maternal stabilization



Conclusions/Summary

- Prevalence of hypertensive disorders of pregnancy is increasing
- Pregnancies complicated by hypertensive disorders of pregnancy are at increased risk for maternal and fetal/neonatal complications
- Recognizing and properly diagnosing pregnancies complicated by chronic hypertension, gestational hypertension, and preeclampsia is vital to reducing these complications



Conclusions/Summary

- Counseling patients about the complications and risks associated with hypertensive disorders of pregnancy will empower patients to seek medical advice when appropriate
- Appropriate management of pregnancies complicated by chronic hypertension, gestational hypertension, and preeclampsia decreases maternal and fetal/neonatal complications





Pharmacologic Management of Hypertension in Pregnancy

August 2021

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Objectives

- Determine first line options for the treatment of hypertension in pregnancy
- Describe benefits and risks of therapies in the treatment of hypertension in pregnancy
- Recognize antihypertensive medications to be avoided during pregnancy
- Identify major patient counseling points on appropriate administration of medications and strategies to improve adherence



Is Pharmacotherapy Necessary?

- The American College of Obstetricians and Gynecologists (ACOG) recommends not initiating medication for mild chronic hypertension (>140/90 mmHg and <160/110mmHg)
 - Consider discontinuing medication in women with mild hypertension who become pregnant and recommend lifestyle modifications
- Pharmacotherapy is recommended for pregnant women with severe hypertension (systolic BP >160mmHg or diastolic BP ≥105-110mmHg)
 - Initiate medications at BP ≥150/100 mmHg in women with end-organ involvement, such as cardiac or renal disease



1st Line Preferred Agents

	Labetalol	Nifedipine ER
Class	Combined Alpha and Beta blocker	Calcium Channel Blocker
Dosing	 Initial: 100mg twice daily, increase by 100mg twice daily every 2 to 3 days as needed Usual effective dose: 200 to 800mg in 2 divided doses Max total daily dose: 2400mg 	 Initial: 30 to 60mg once daily, increase at 7-14 day intervals Usual effective dosage: 30 to 90mg once daily Max total daily dose: 120mg
Side effects	Bronchoconstriction	 Flushing, peripheral edema, heartburn, nausea, dizziness
Data in pregnancy	 Crosses the placenta May be associated with fetal growth restriction and neonatal bradycardia 	 Crosses the placenta Increase in perinatal asphyxia, cesarean delivery, prematurity, and intrauterine growth retardation have been reported



2nd Line Preferred Agents

	Hydrochlorothiazide	Methyldopa
Class	Diuretic	Central acting alpha agonist
Dosing	12.5 to 25mg daily	 Initial: 250mg 2 to 3 times daily, increase every 2 days as needed Usual effective dosage: 250 to 1000mg in 2 to 3 divided doses Max total daily dose: 3000mg
Side effects	Volume depletionElectrolyte disorders	SedationDepression
Data in pregnancy	 Crosses the placenta May cause neonatal jaundice, thrombocytopenia, or other adverse events observed in adults 	 Crosses the placenta Data shows use in pregnancy does not cause fetal harm and improves fetal outcomes



Alternative Agents

	Hydralazine	Clonidine
Class	Vasodilator	Alpha2-Adrenergic Agonist
Dosing	 Initial 10mg orally 4 times daily, titrating 10 to 25mg/day every 2 to 5 days Usual Effective Dose: 50-100mg orally in 2 to 4 divided doses Max total daily dose: 200mg 	 Initial 0.1mg twice daily, titrating in increments of 0.1mg/day weekly as needed/tolerated Usual Effective Dose: 0.2 to 0.6mg/day in 2 divided doses Max total daily dose: 2.4mg
Side effects	Reflex tachycardiaEdemaNausea/Vomiting/Diarrhea	 Rebound hypertension if stopped suddenly Orthostatic hypotension Nausea/GI pain/Constipation
Data in pregnancy	 Crosses the placenta Pharmacokinetics may be altered due to pregnancy-induced physiologic changes and maternal acetylator status (NAT2 genotype) 	 Crosses the placenta Pharmacokinetics may be altered due to increase in nonrenal clearance in pregnancy, possibly regulated by CYP2D6 genotype



Preferred Agents in Hypertensive Emergency

	Labetalol	Hydralazine	
Class	Combined Alpha and Beta Blocker	Vasodilator	
Dosing	 20mg IV gradually over 2 minutes Continuous infusion of 1 to 2mg/minute can be used instead of intermittent therapy, or started after initial 20mg dose 	5mg IV gradually over 1 to 2 minutes	
Monitoring	 Reassess BP at 10 minute intervals If BP remains above target at 10 minutes, give 40mg IV over 2 minutes Reassess BP every 10 minutes thereafter. If continuously above target, then give 80mg IV over 2 minutes Cumulative max dose-300mg. 	 Reassess BP at 20 minute intervals If BP remains above goal at 20 minutes, give 5 or 10mg IV over 2 minutes If BP remains above goal at 40 minutes, give 10mg IV over 2 minutes Cumulative max dose- 30mg 	



Alternative Agents in Hypertensive Emergency

	Nifedipine ER	Nicardipine
Class	Calcium Channel Blocker	Calcium Channel Blocker
Dosing	 Initial 30mg orally Repeat dose of 30mg if target dose is not achieved in 1-2 hours 	 Initial dose of 5mg/hour IV by infusion pump, can be increased to max of 15mg/hour Onset of action 5-15 minutes Avoid rapid titration to minimize risk of overdosing
Monitoring	 If goal BP is not achieved after 2 doses, consider administering a different class of agents 	Adjust dose within above range to achieve targeted BP



Magnesium Sulfate

- Prevent convulsions in the setting of eclampsia/preeclampsia
- Initial IV: 4 to 6 g loading dose over 15-30 minutes at onset of labor or induction/cesarean delivery
 - 1 to 2g/hour continuous infusion for at least 24 hours after delivery (max infusion rate 3g/hour)
 - Administer bolus of 2 to 4g over at least 5 minutes if seizure occurs while administering magnesium
 - Max dose: 40g/24hours
- Calcium gluconate should be available to treat magnesium toxicity if needed



Antihypertensive Agents to Avoid

- ACEI, ARBs
 - Crosses the placenta
 - Increased risk of fetal malformations
- Mineralocorticoid receptor antagonists (eplerenone, spironolactone)
 - Crosses the placenta
 - May cause feminization of male fetus (spironolactone)
 - High doses have been associated with intrauterine growth restriction



Knowledge Check

JP has now become pregnant. Her provider does not want to further increase labetalol due to fear of further decreasing HR, however, her BP is not sufficiently controlled. Which medication would be the best to add on?

- A. Thiazide
- B. Nifedipine ER
- C. Clonidine
- D. Losartan



Conclusions

- Labetalol and nifedipine are the preferred antihypertensive agents in pregnancy
- Pharmacists are a valuable resource to ensure patients stay adherent to their medications for optimal outcomes for both mother and baby and to assist in choosing the safest medications



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Gestational Diabetes

August 2021 Rita W. Driggers, MD

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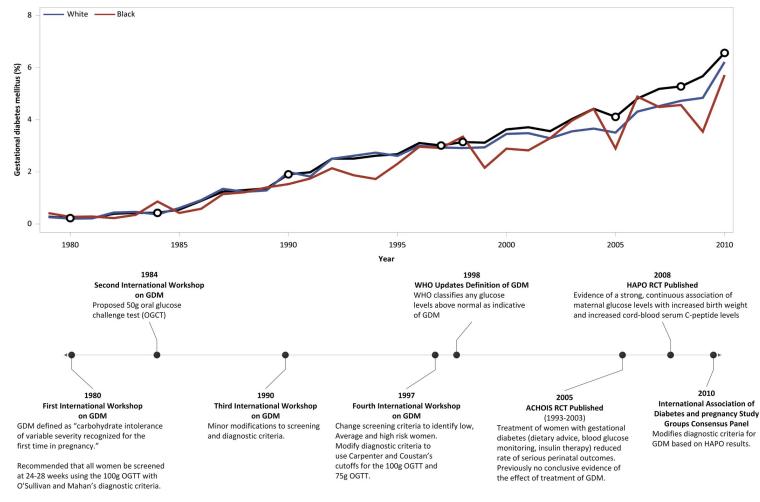
Sibley Memorial Hospital, Johns Hopkins Medicine

Objectives

- At the completion of this module, the learner should possess the knowledge to:
 - Identify patients at increased risk for the development of gestational diabetes
 - Describe the most frequently used gestational diabetes testing protocols
 - Counsel patients about the risks of gestational diabetes to the mom and the baby
 - Properly manage a pregnancy complicated by gestational diabetes



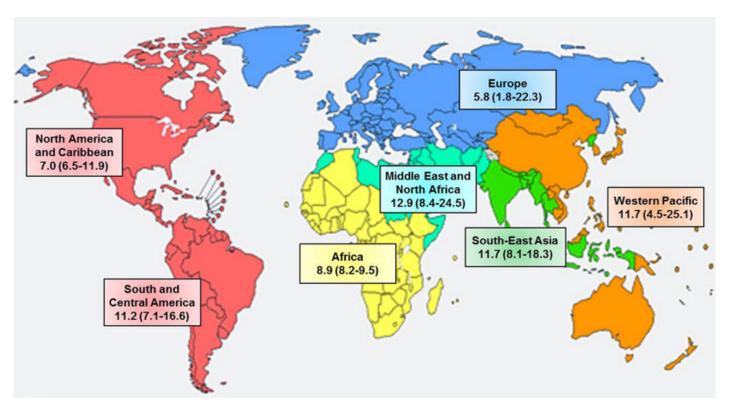
Impact/Prevalence



Lavery BJOG 2017



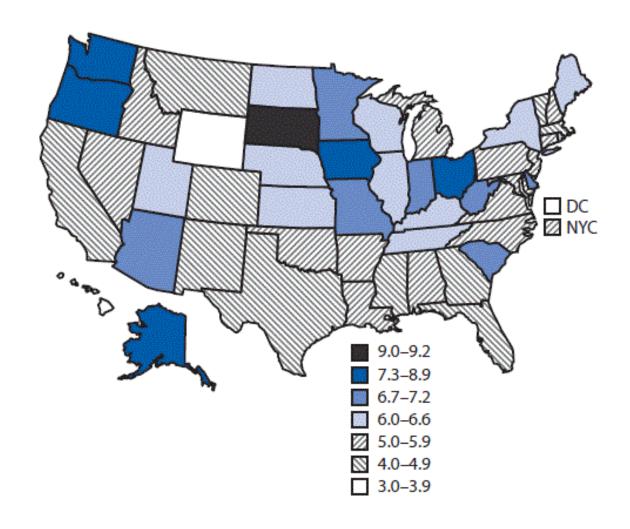
Country-specific Prevalence of GDM



Median (interquartile range) prevalence (%) of GDM by World Health Organization region, 2005-2015



Prevalence of GDM Among Women with Live Birth in 2016



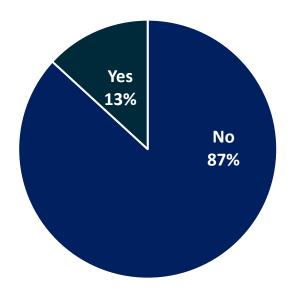


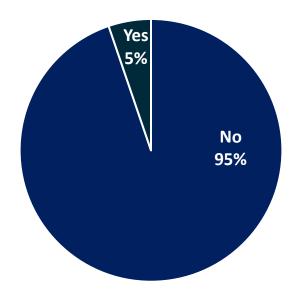
Deliveries by maternal health conditions

Distribution of DC-resident delivery hospital discharges by mother's health conditions that complicated the pregnancy or delivery, 2016-2019

OBESITY

GESTATIONAL DIABETES





Data Source: Hospital Discharge Data for 2016-2019, DC Hospital Association



Knowledge Check

Which of the following states/areas has the highest prevalence of gestational diabetes?

- A. District of Columbia
- B. South Dakota
- C. Alabama
- D. Georgia



Risk Factors

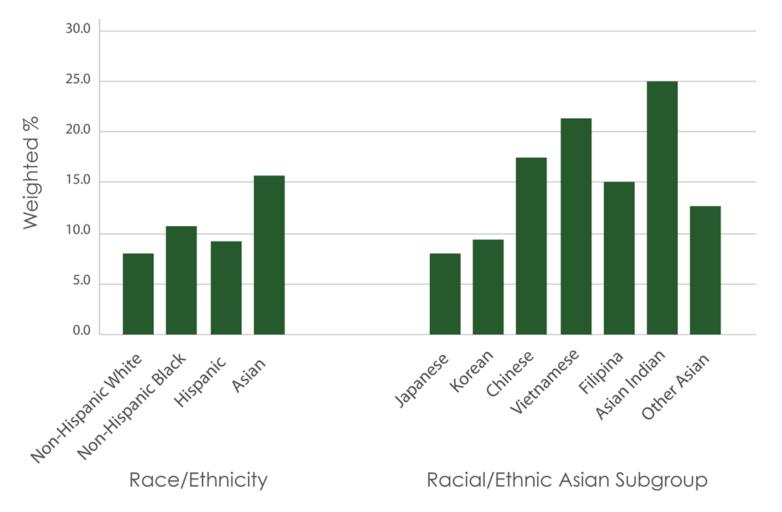
- Personal history of GDM
- Personal history of baby weighing > 9lb
- Family history of Type 2 DM
- Polycystic ovarian syndrome (PCOS)
- Obesity
- Glycosuria
- Age
- Race/ethnicity





https://www.cdc.gov/diabetes/basics/gestational.html

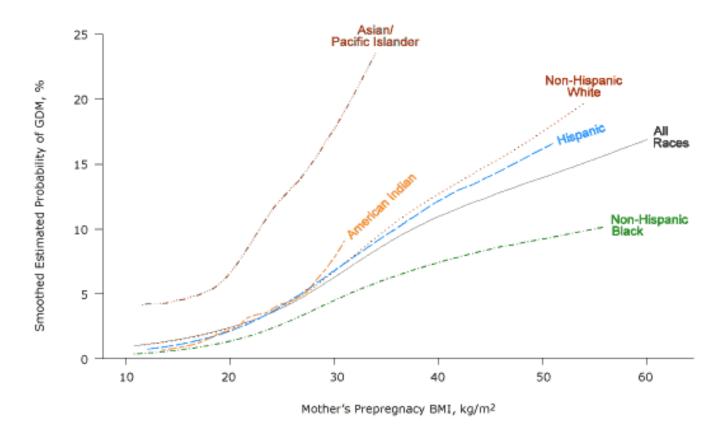
Risk Factors – Race/Ethnicity





CDC.gov

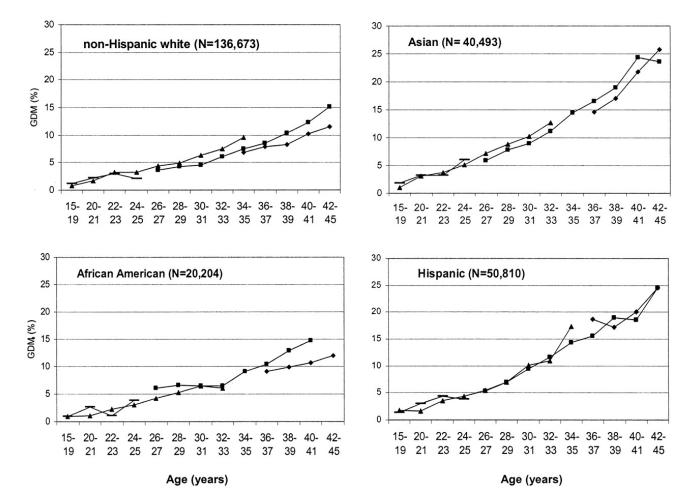
Risk Factors – Prepregnancy BMI







Risk Factors - Age





Care.diabetesjournals.org

Knowledge Check

Which of the following race/ethnicities has the highest prevalence of gestational diabetes with a normal BMI?

- A. American Indian
- B. Asian/Pacific Islander
- C. Hispanic
- D. Non-Hispanic Black



Screening/Diagnosis

- Universal versus risk-based screening
- Screening based on historic factors will fail to identify
 ½ of women with GDM
- Only 10% of pregnant women are low-risk
- In 2014, the US Preventive Services Task Force recommended screening all pregnant women for GDM at or beyond 24 weeks of gestation
- 1973 study proposed the use of the 50gm, 1-hour oral glucose tolerance test (OGTT) followed by 100gm 3hour OGTT if abnormal
 - Most widely accepted screening test in US
 - Used by 95% of obstetricians in the US

ACOG Practice Bulletin #190, February 2018 Coustan DR. Obstet Gynecol 1989 O'Sullivan JB. Am J Obstet Gynecol 1973 Gabbe SG. Obstet Gynecol 2004 Moyer VA. Ann Intern Med 2014



Indications for early screening

- Overweight or obese (BMI > 25 or BMI > 23 in Asian Americans)
 with one or more of the following additional risk factors:
- Physical inactivity
- First-degree relative with diabetes
- High-risk race or ethnicity
- Previously infant weighing 4,000g (approximately 9lbs) or more
- Previous gestational diabetes mellitus
- Hypertension
- History of cardiovascular disease

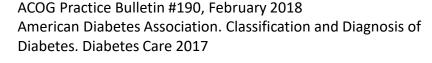
- HDL cholesterol level less than 35 mg/dL, a triglyceride level greater than 250 mg/dL
- Polycystic ovarian syndrome
- A_{1C} greater than or equal to 5.7%, impaired glucose tolerance, or impaired fasting glucose on previous testing
- Other clinical conditions associated with insulin resistance



ACOG Practice Bulletin #190, February 2018
American Diabetes Association. Classification and Diagnosis of Diabetes. Diabetes Care 2017

Screening/Diagnosis

- Two-step approach most commonly used
- Thresholds for the 1-hour glucose challenge vary by institution
 - 130 to 140 mg/dl
 - Using 130 mg/dl
 - Higher screen positive rate, higher sensitivity but higher false positive rates.
 - Using 140mg/dl
 - Lower screen positive rate, lower sensitivity but also lower false positive rates.





Screening/Diagnosis

Table 1. Proposed Diagnostic Criteria for Gestational Diabetes Mellitus* \leftarrow

Status	Plasma or Serum Glucose Level Carpenter and Coustan Conversion		Plasma Level National Diabetes Data Group Conversion	
	mg/dL	mmol/L	mg/dL	mmol/L
Fasting	95	5.3	105	5.8
1 hour	180	10.0	190	10.6
2 hours	155	8.6	165	9.2
3 hours	140	7.8	145	8.0

^{*}A diagnosis generally requires that two or more thresholds be met or exceeded, although some clinicians choose to use just one elevated value.

Adapted with permission from the American Diabetes Association. Classification and Diagnosis of Diabetes. Diabetes Care 2017;40 (Suppl. 1):S11–S24. Copyright 2017 American Diabetes Association.



Knowledge Check

Risk-based screening rather than universal screening for gestational diabetes is recommended because the majority of patients with gestational diabetes have risk factors.

- A. True
- B. False



Complications: Maternal

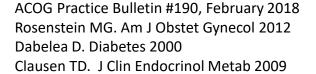
- Preeclampsia
- Cesarean delivery
- Developing Type 2 DM later in life
 - Up to 70% of women with GDM will develop diabetes within 22-28 years after pregnancy
 - Influenced by race, ethnicity, and obesity
 - 60% of Latin American women may develop Type 2 DM within 5 years

ACOG Practice Bulletin #190, February 2018 Yogev Y. Am J Obstet Gynecol 2004 Ehrenberg HM. Am J Obstet Gynecol 2004 England LJ. Am J Obstet Gynecol 2009 O'Sullivan JB. JAMA 1982 Kim C. Diabetes Care 2002 Kjos SL. Diabetes 1995



Complications: Fetal/Neonatal

- Macrosomia
- Shoulder dystocia
- Birth trauma
- Neonatal hypoglycemia
- Hyperbilirubinemia
- Stillbirth
- Childhood and adult-onset obesity and diabetes





Management - Benefits of treatment

- 2005 Australian Carbohydrate Intolerance Study in Pregnant Women trial
 - Reduction in rate of composite of serious newborn complications
 - o perinatal death
 - shoulder dystocia
 - o birth trauma
 - Preeclampsia
 - Large for gestational age
 - Birth weight greater than 4,000 g



Management - Benefits of treatment

- US Preventive Task Force systematic review
 - Preeclampsia
 - Shoulder dystocia
 - Macrosomia
- Treatment in most studies consisted of dietary counseling and exercise



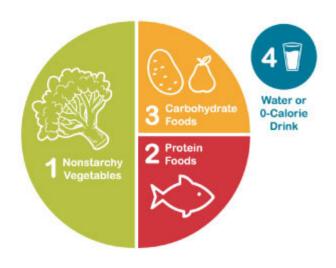
Knowledge Check

Maternal complications of gestational diabetes that have been shown to be reduced with adequate treatment include:

- A. Cesarean delivery
- B. Preeclampsia
- C. Developing Type 2 DM later in life



Management - Diet/nutrition counseling



- Little evidence evaluating different GDM diets
- Most recommend 3 meals and 2-3 snacks daily



Management - Diet/nutrition counseling

• Limit carbohydrate intake to 33-40% of calories, with the remaining calories divided between protein (20%) and fat (40%)

Breakfast: 10-20% (30 g carb)

Lunch: 20-30% (30 g carb)

Dinner: 30-40% (45 g carb)

–Snacks: up to 30% (15 g carb)



Management - Exercise

- Women with uncomplicated pregnancies and without a medical reason to avoid pregnancy should be encouraged to exercise
- Physical inactivity is a risk factor for GDM
- Additional benefits of exercise, lower incidence of:
 - Excessive gestational weight gain
 - Gestational hypertensive disorders
 - Preterm birth
 - Cesarean birth



Management - Exercise

Table 3. Characteristics of a Safe and Effective Exercise Regimen in Pregnancy

When to Start	First Trimester, More Than 12 Weeks of gestation		
Duration of a session	30–60 minutes		
Times per week	At least 3-4 (up to daily)		
Intensity of exercise	Less than 60-80% of age-predicted maximum maternal heart rate*		
Environment	Thermoneutral or controlled conditions (air conditioning; avoiding prolonged exposure to heat)		
Self-reported intensity of exercise (Borg scale)	Moderate intensity (12–14 on Borg scale)		
Supervision of exercise	Preferred, if available		
When to end	Until delivery (as tolerated)		

^{*}Usually not exceeding 140 beats per minute.

Modified from Berghella V, Saccone G. Exercise in pregnancy! Am J Obstet Gynecol 2017;216:335-7.



Management - Blood sugar monitoring and goals

- 4 times per day blood glucose monitoring
- American Diabetes Association suggests the following targets:
 - Fasting: 95 mg/dl or less
 - One hour after a meal (postprandial): 140 mg/dl or less
 - Two hours after a meal (postprandial): 120 mg/dl or less
- When targets cannot be achieved with diet and exercise, pharmacologic treatment is recommended



Knowledge Check

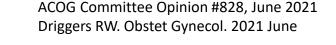
Which of the following are correct goals for carbohydrate intake and blood sugar values?

- A. Fastings < 95mg/dl, 30gm of carbohydrates with snacks
- B. 1 hour postprandial < 120mg/dl, 45gm of carbohydrates with dinner
- C. 2 hour postprandial < 140mg/dl, 30gm of carbohydrates with lunch
- D. 1 hour postprandial < 140mg/dl, 30gm of carbohydrates with breakfast



Management - Fetal monitoring

- BPP, modified BPP, growth assessments
- GDM well controlled with diet and exercise
 - No indication for antenatal testing prior to 40 weeks
- GDM controlled with medications
 - Once or twice weekly antenatal testing starting at 32 weeks
- Poorly controlled GDM
 - Twice weekly antenatal testing starting at 32 weeks





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Management - Delivery

- Delivery timing
 - GDM well controlled with diet and exercise
 - 39-0/7 to 40-6/7 weeks
 - GDM well controlled on medications
 - 39-0/7 to 39-6/7 weeks
 - GDM poorly controlled
 - Individualized
- Mode of delivery
 - Women with GDM and estimated fetal weight 4500gm or more should be counseled regarding risks/benefits of cesarean delivery



Management - Delivery

- Rates of shoulder dystocia in pregnancies complicated by diabetes:
 - 8.4% for infants between 4000 and 4250 gm
 - 12.3% for infants between 4250 and 4500 gm
 - 19.9% for infants between 4500 and 4750 gm
 - 23.5% for infants between 4750 and 5000 gm
- If delivery was assisted by forceps or vacuum
 - 12.2% for infants between 4000 and 4250 gm
 - 16.7% for infants between 4250 and 4500 gm
 - 27.3% for infants between 4500 and 4750 gm
 - 34.8% for infants between 4750 and 5000 gm



Management - Postpartum screening

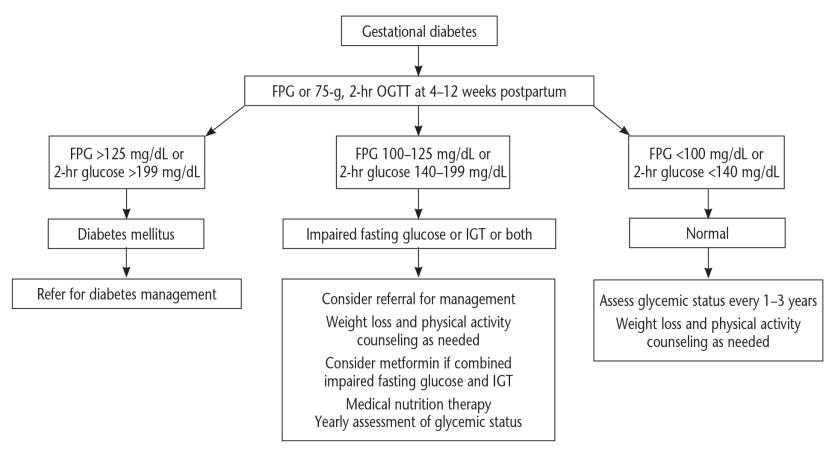


Figure 1. Management of postpartum screening results. Abbreviations: FPG, fasting plasma glucose; OGTT, oral glucose tolerance test; IGT, impaired glucose tolerance. \Leftarrow



Management - Counseling for future health and pregnancies

- Up to 70% will develop diabetes later in life
 - ACOG and ADA recommend repeat testing every
 1-3 years
 - Maintain healthy weight and diet
- Increased risk of recurrent GDM
 - Can reduce risk by maintain healthy weight and diet
 - Early screening in subsequent pregnancies
 - Repeat at 24-28 weeks if early screening normal



All patients with gestational diabetes should be screened with either a fasting plasma glucose level or a 75gm, 2hr OGTT at 4-12 weeks postpartum

- A. True
- B. False



Summary

- US is seeing an increase in prevalence of pregnancies complicated by GDM
- Universal screening for GDM is recommended
- Poorly controlled GDM is associated with increased risk of maternal and fetal/neonatal complications
- Adequate control of blood sugars may decrease these risks
- Postpartum screening is recommended
- Regular screening by PCP every 1-3 years





Pharmacologic Management of Gestational Diabetes

August 2021

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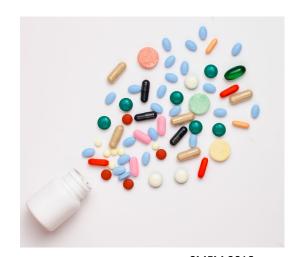
Objectives

- Determine first line options for the treatment of gestational diabetes (GDM)
- Describe benefits and risks of therapies in the treatment of GDM
- Recognize diabetes medications to be avoided during pregnancy
- Identify key areas for patient counseling



Is Pharmacotherapy Necessary?

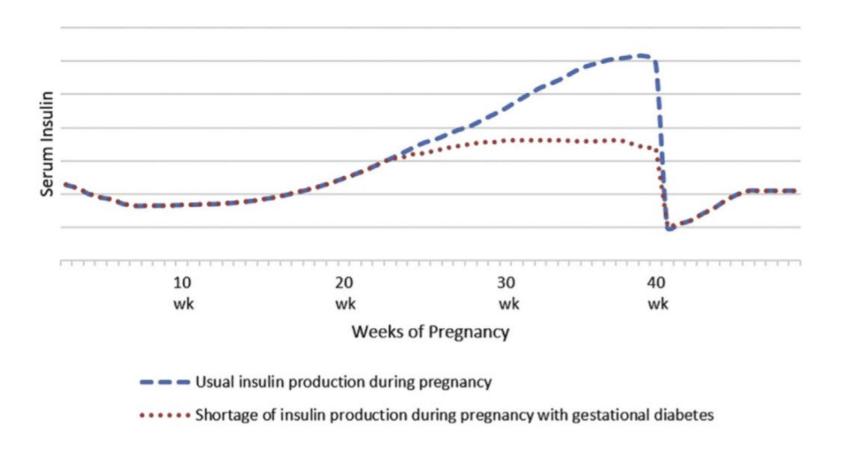
- Lifestyle modifications are crucial component
- Initiation of pharmacotherapy for GDM has been shown to improve outcomes if the patient is unable to maintain blood glucose at goal with diet and lifestyle modifications
- 30% of women diagnosed with GDM require pharmacologic therapy



SMFM 2018



Insulin Production During Pregnancy





Insulin

- Preferred first line therapy for GDM
- Does not cross the placenta
- Highly effective



- Type of insulin and regimen used should be based on blood glucose patterns
 - Fasting hyperglycemia: Starting dose ~0.2 units/kg/day basal insulin
 - Fasting and post-prandial hyperglycemia: Starting total daily dose ~0.7-1.0 units/kg/day split between basal and bolus insulins and given in divided doses
- Side effects: hypoglycemia, weight gain



Basal Insulin

	NPH	Detemir	Glargine
Туре	Intermediate	Long	Long
Onset	1-3 hours	1-3 hours	1-2 hours
Duration	13-18 hours	18-26 hours	24 hours
Peak	5-7 hours	Minimal peak at 8- 10 hours	No peak
Data in pregnancy	 Most well studied for safety and effectiveness 		 Acceptable safety Similar outcomes to NPH
Usual Frequency	Once-twice daily	Once-twice daily	Once daily
Formulations	Vial, pen	Vial, pen	Vial, pen



Bolus Insulin

	Lispro	Aspart	Regular
Туре	Rapid	Rapid	Short
Onset	1-15 min	1-15 min	30-60 min
Duration	3-5 hours	3-5 hours	6-8 hours
Peak	1-2 hours	1-2 hours	2-4 hours
Data in pregnancy	 Acceptable safety Lower risk of delayed hypoglycemia when compared to regular 	 Acceptable safety Lower risk of delayed hypoglycemia when compared to regular 	 Least immunogenic Most well studied for safety and effectiveness
Usual Frequency	Daily- 3 times daily (With meals)	Daily- 3 times daily (With meals)	Daily- 3 times daily (With meals)
Formulations	Vial, pen	Vial, pen	Vial



Non-Insulin Options

- Metformin
- Glyburide
 - declining use
- Higher patient acceptance
- Up to 30% of patients may require insulin in conjunction





Oral Agents

	Metformin	Glyburide
Class	Biguanide	Sulfonylurea
Dosing	Initial: 500 mg once or twice daily Max total daily dose: 2,550 mg (IR, as two divided doses) 2,000 mg (XR)	1.25 to 20 mg/day given as single or divided doses
Side effects	GI upset	HypoglycemiaWeight gain
Data in pregnancy	 Crosses placenta Less maternal weight gain and neonatal hypoglycemia Not associated with an increase in birth defects, but long-term safety data not available 	 Crosses placenta Neonatal hypoglycemia, macrosomia Outcomes not equivalent to insulin or metformin Long-term safety data not available



Patient LS is 25 weeks pregnant and newly diagnosed with GDM. She has reservations about administering insulin injections. Which of the following could be considered for management of her GDM?

- A. liraglutide
- B. metformin
- C. glipizide
- D. empagliflozin



How Do We Choose?

- Cost
- Timing of hyperglycemia
- Side effects
- Health literacy



Patient LS has been taking metformin 1000 mg twice daily, but as she progresses in her pregnancy, her fasting blood glucose has been running in the 160s-180s despite good adherence to medications and diet/lifestyle modifications. What would your next step be?

- A. Discontinue metformin and initiate regular insulin
- B. Discontinue metformin and initiate linagliptin
- C. Add glyburide
- D. Add NPH insulin



Pharmacist's Role

- Address patient barriers to medication adherence
 - Complexity of regimen
 - Patient concerns about harm to baby
 - Adverse effects
 - Cost
- Proper administration and storage of medication
- Management of hypoglycemia
- Accessible follow-up





With the addition of NPH to her regimen, review of Patient LS' blood glucose log reveals that her readings are now at goal. Which of the following should be included in the counseling provided to patient LS?

- A. Since blood glucose is now at goal, patient will need minimal follow up as she can continue the same maintenance dose for the remainder of her pregnancy.
- B. Patient will need careful follow up after delivery as insulin requirements usually increase rapidly post-partum.
- C. Patient should continue to return for frequent follow-ups as insulin requirements can rapidly change as her pregnancy progresses.
- D. If she experiences an episode of hypoglycemia, insulin should be discontinued.



Conclusion

- Insulin is the preferred first line option for management of GDM
- Metformin can be considered as an alternative if patient is unable to use insulin
- Due to potential risks, would consider use of therapies other than glyburide until additional data is available
- Other usual agents for DM management are generally not recommended for GDM due to limited safety data



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