

Common Obstetric Complications: What Every Health Care Provider Should Know

Molly Siegel, MD

Maternal Fetal Medicine
Massachusetts General Hospital

Disclosures

Neither I nor my spouse/partner has a relevant financial relationship with a commercial interest to disclose

I will be discussing some difficult topics including pregnancy loss

Learning Objectives

- Demonstrate a general understanding of common obstetric complications
 - Miscarriage
 - Stillbirth
 - Preterm birth
 - Hypertensive disorders of pregnancy
 - Gestational Diabetes
- Discuss opportunities for preconception optimization and medication counseling peri conception and in pregnancy

Miscarriage

- 11-22% of clinically recognized pregnancies before 20 weeks end in miscarriage
 - Many may be asymptomatic: consider a 6-8 week ultrasound
- Risk factors and etiologies
 - Fetal: 50% have a chromosomal abnormality
 - Maternal: infection, medical disorders (diabetes, hypertension, vascular disease), age
 - Controversial: cancer, malnutrition, substance use, environmental toxin, occupational exposures



Massachusetts General Hospital
Founding Member, Mass General Brigham
Psychiatry Academy

OPINION

MEGHAN, THE DUCHESS
OF SUSSEX

The Losses We Share

Perhaps the path to healing
begins with three simple words:
Are you OK?

Recurrent Pregnancy Loss

- Definitions- depends on who you ask
 - Generally 2 or 3+ consecutive losses before 20-24 weeks
- 1% of fertile couples
- Etiologies:
 - Idiopathic (40-50%): the majority will go on to have a normal pregnancy
 - Parental chromosome abnormalities (2-4%, translocations)
 - Antiphospholipid antibody syndrome
 - Structural uterine anomalies
 - Endocrine disorders: suboptimally controlled diabetes or thyroid disease

Miscarriage Management

- Expectant management
 - 80% of first trimester pregnancies pass in 8 weeks
- Medical management
 - First trimester losses can be managed at home with mifepristone followed by misoprostol 24hrs later (or misoprostol alone)
 - Later in second trimester done in hospital
 - 5-20% require procedure for retained products of conception
 - Benefits: avoid procedure, at home
 - Risks/disadvantages: slightly unpredictable timing, pain, traumatic to miscarry at home, may need procedure
- Surgical management (D+C)
 - Benefits: time selected, in office or OR with anesthesia, completion without requiring follow up
 - Risks: uterine perforation, bleeding, infection, recurrent D+Cs can lead to uterine scarring

Stillbirth

- Definition: fetal death after 20 weeks gestation
- Epidemiology:
 - 5.7/1000 US births
 - Early stillbirth (20-27 weeks) decreased over the last decade but late stillbirth (after 28 weeks) relatively stable
 - Despite substantial reductions in infant and childhood mortality over this time period
 - Disparities: Non-Hispanic Black individuals have stillbirth rate >2x that of other groups (up to 10/1000)

Stillbirth

- Risk factors
 - Maternal: exposure to racism, age, tobacco use, medical conditions (diabetes, hypertension, lupus, antiphospholipid antibody syndrome, obesity, substance use disorders), nulliparity, prior adverse outcome, infections
 - Fetal: genetic and structural anomalies
 - Pregnancy/placenta: ART, abruptoin
- Most stillbirths do not have risk factors, and routine surveillance based on risk factors does not effectively prevent occurrence

[Home](#) | [JAMA](#) | [Vol. 335, No. 5](#)

JAMA Insights | Women's Health

Stillbirth

Adina R. Kern-Goldberger, MD, MPH, MSCE^{1,2}; Uma M. Reddy, MD, MPH³; Jennifer L. Bailit, MD, MPH¹

» [Author Affiliations](#)

Stillbirth Workup

- Autopsy and placental pathology
 - Option for external evaluation only plus MRI, XR, US, tissue sampling
- Genetics: microarray +/- karyotype
- Maternal evaluation
 - Fetal-maternal hemorrhage screen
 - Syphilis serology
 - Antiphospholipid antibodies
 - A1c, TSH
 - Maternal history: arrhythmias/sudden death, consanguinity

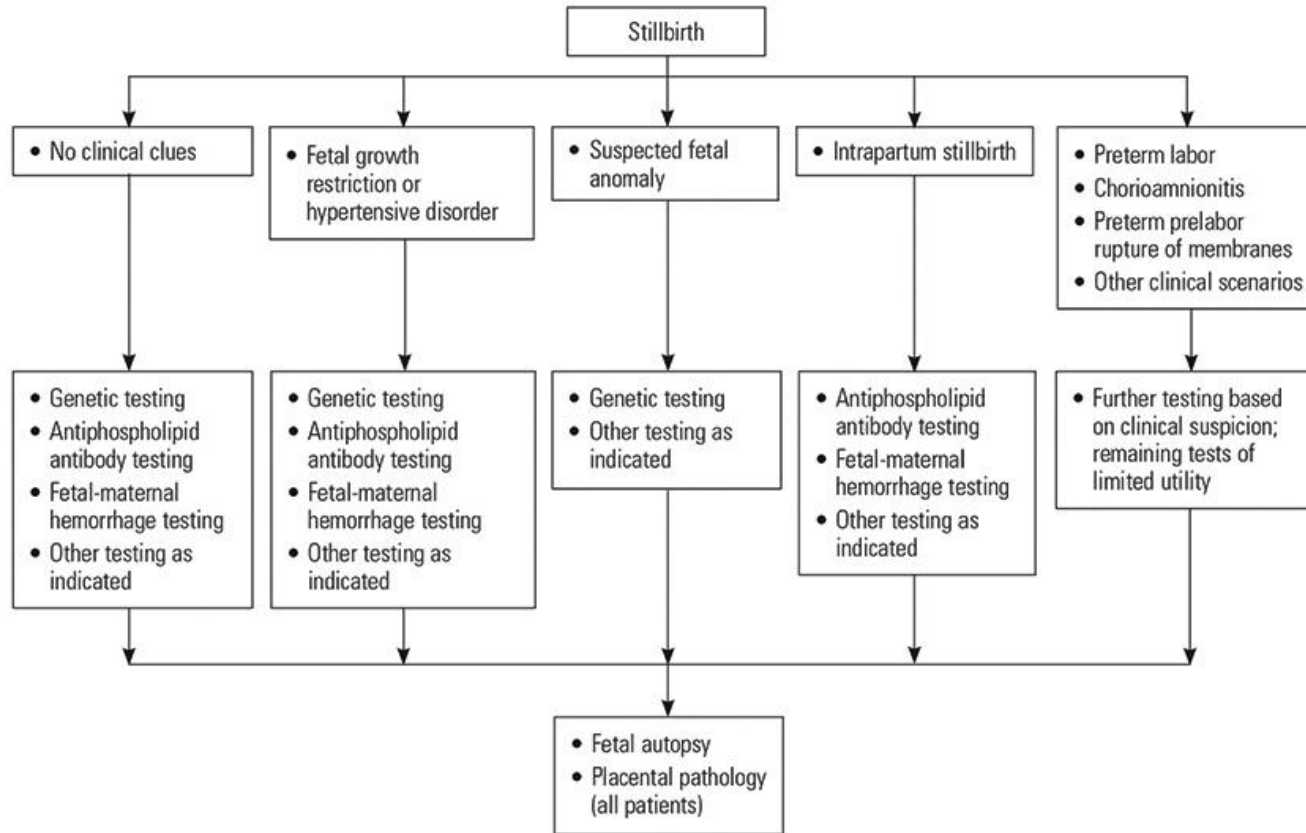


Figure 3. Evaluation of stillbirth based on test utility in a variety of clinical scenarios. (Adapted from Page JM, Christiansen-Lindquist L, Thorsten V, Parker CB, Reddy UM, Dudley DJ, et al. Diagnostic Tests for Evaluation of Stillbirth: Results From the Stillbirth Collaborative Research Network. *Obstet Gynecol* 2017;129:699–706.)

Stillbirth Management

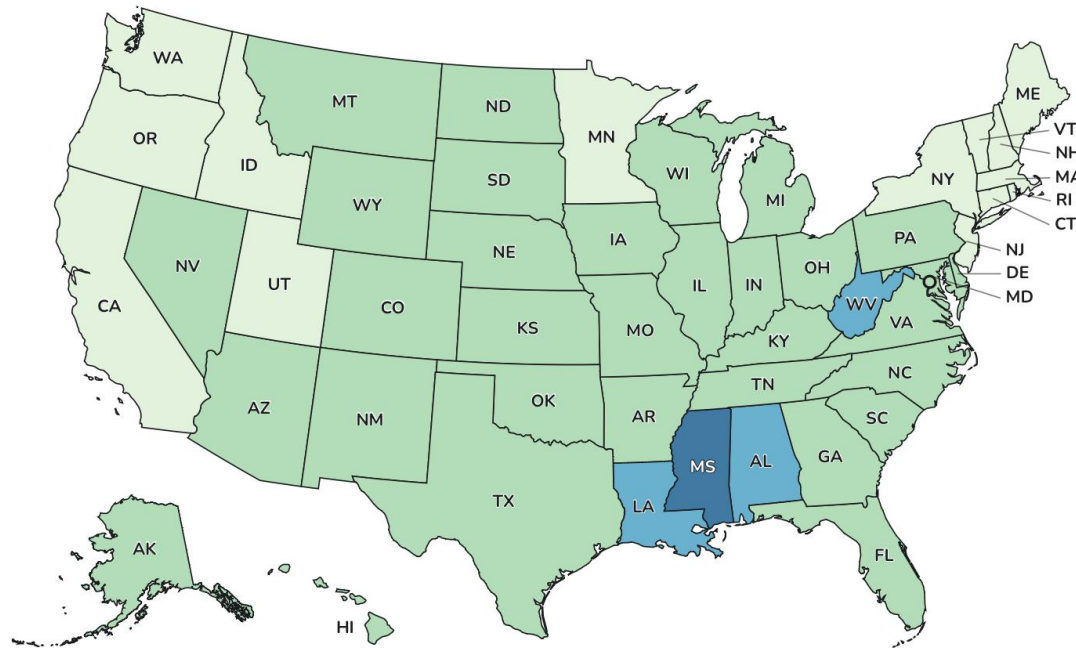
- Delivery timing:
 - If counseled appropriately and medically stable, delivery can be delayed for short period of time
 - Risks: infection, bleeding, DIC, VTE
 - Spontaneous labor will occur in 1-2 weeks of demise in most pregnancies but increases risks of complications
- Route
 - Induction of labor
 - Dilation and evacuation

Dilation and Evacuation	Induction of Labor
Surgical environment	Labor and Delivery environment
Unable to see or hold intact fetus	Can hold fetus after delivery
Autopsy less informative	Full autopsy possible
Brief same day procedure	Hospitalization can be prolonged

Preterm Birth

- Definition: delivery prior to 37 weeks gestation
- US rate: ~10%
- Classifications
 - Late preterm: 34.0-36.6
 - Early preterm: <34 weeks
 - Periviable: 20-25 weeks





Prediction and Prevention of Spontaneous Preterm Birth

Practice Bulletin ⓘ | Number 234 | August 2021

Management of Preterm Labor

Practice Bulletin ⓘ | Number 171 | October 2016

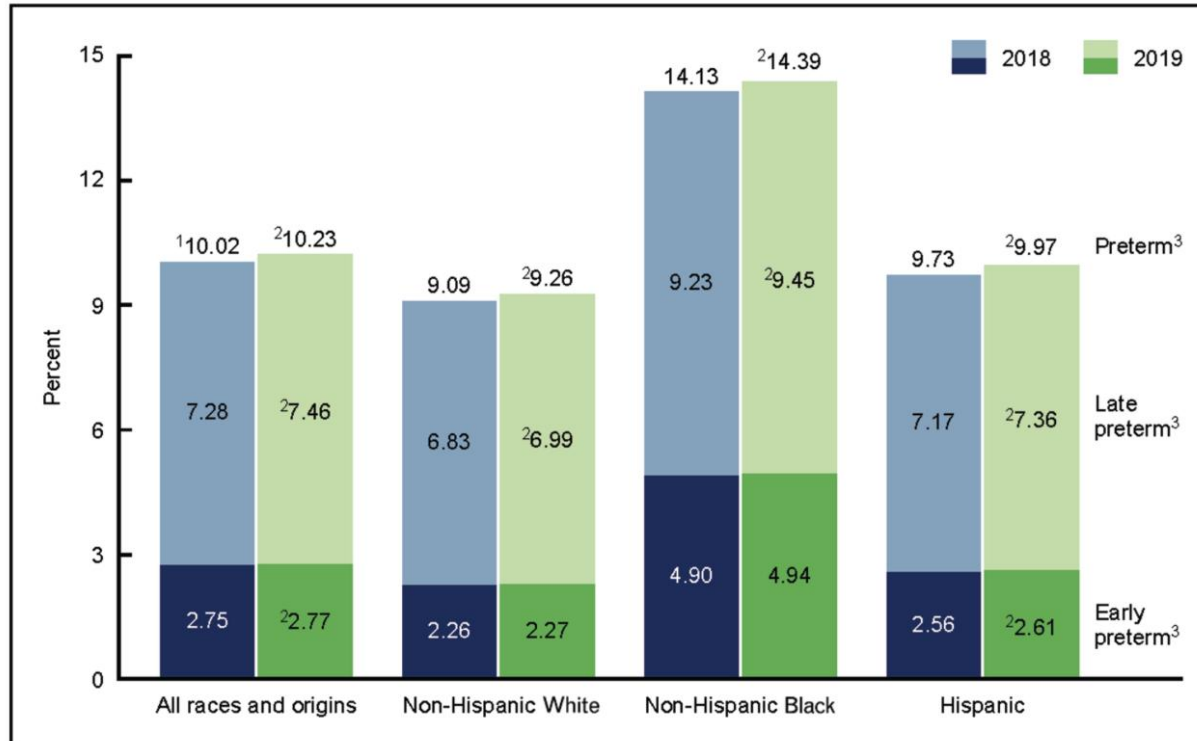
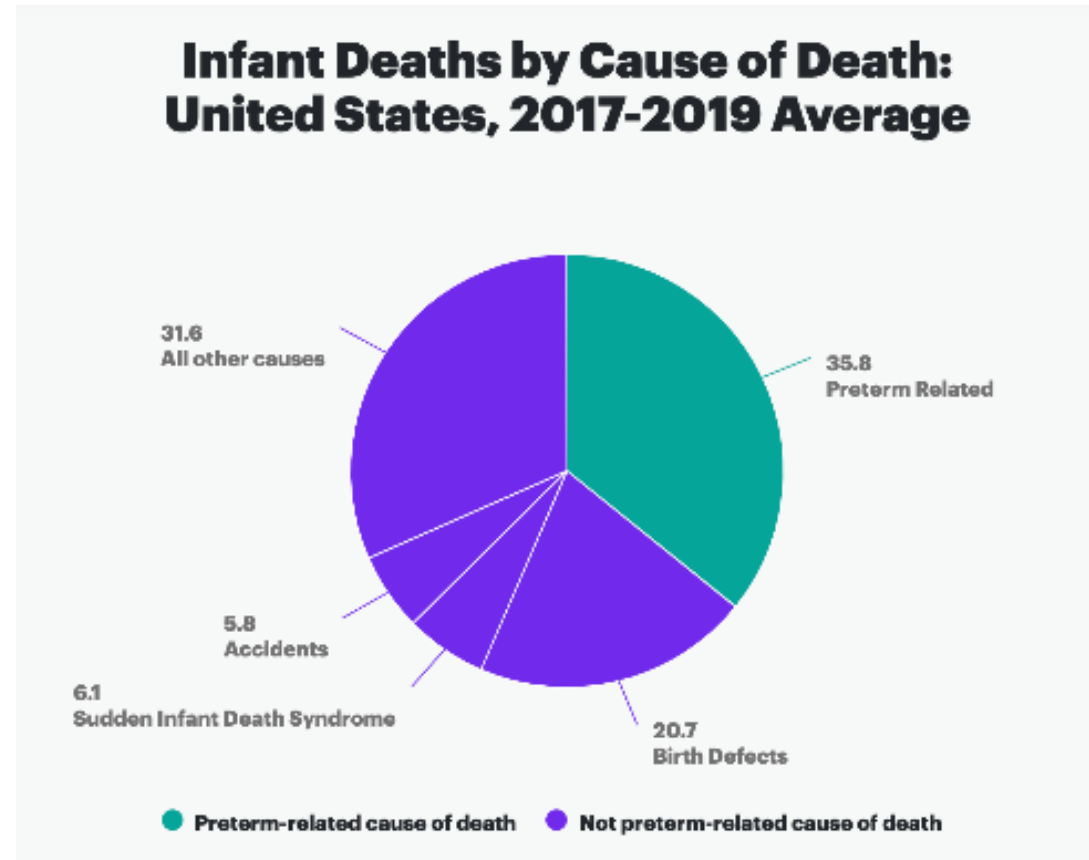


Figure 1. Preterm birth rates, by race and Hispanic origin of the mother: United States, 2018 and 2019. Reprinted from Martin JA, Hamilton BE, Osterman MJK. Births in the United States, 2019. NCHS Data Brief 2020 Oct(387):1–8. ¹Data do not add to totals due to rounding. ²Significant increase from 2018 ($P < .05$). ³Significant difference between all race and Hispanic-origin groups ($P < .05$). NOTES: Preterm is less than 37 weeks of gestation, late preterm is 34–36 weeks of gestation, and early preterm is less than 34 weeks of gestation. Access data table for Figure 4 at: <https://www.cdc.gov/nchs/data/databriefs/db387-tables-508.pdf#4>. SOURCE: National Center for Health Statistics, National Vital Statistics System, Natality.

Preterm Birth: Risks



Preterm Birth: Risks

- Leading cause of neonatal mortality
 - 70% of neonatal deaths and 36% of infant deaths
 - 25-50% of long-term neurologic impairment
- Leading cause of antenatal hospitalization in the US
- Large cost to healthcare system
 - 2022 IOM: \$25.2 billion in the US, \$51,000 per premature infant

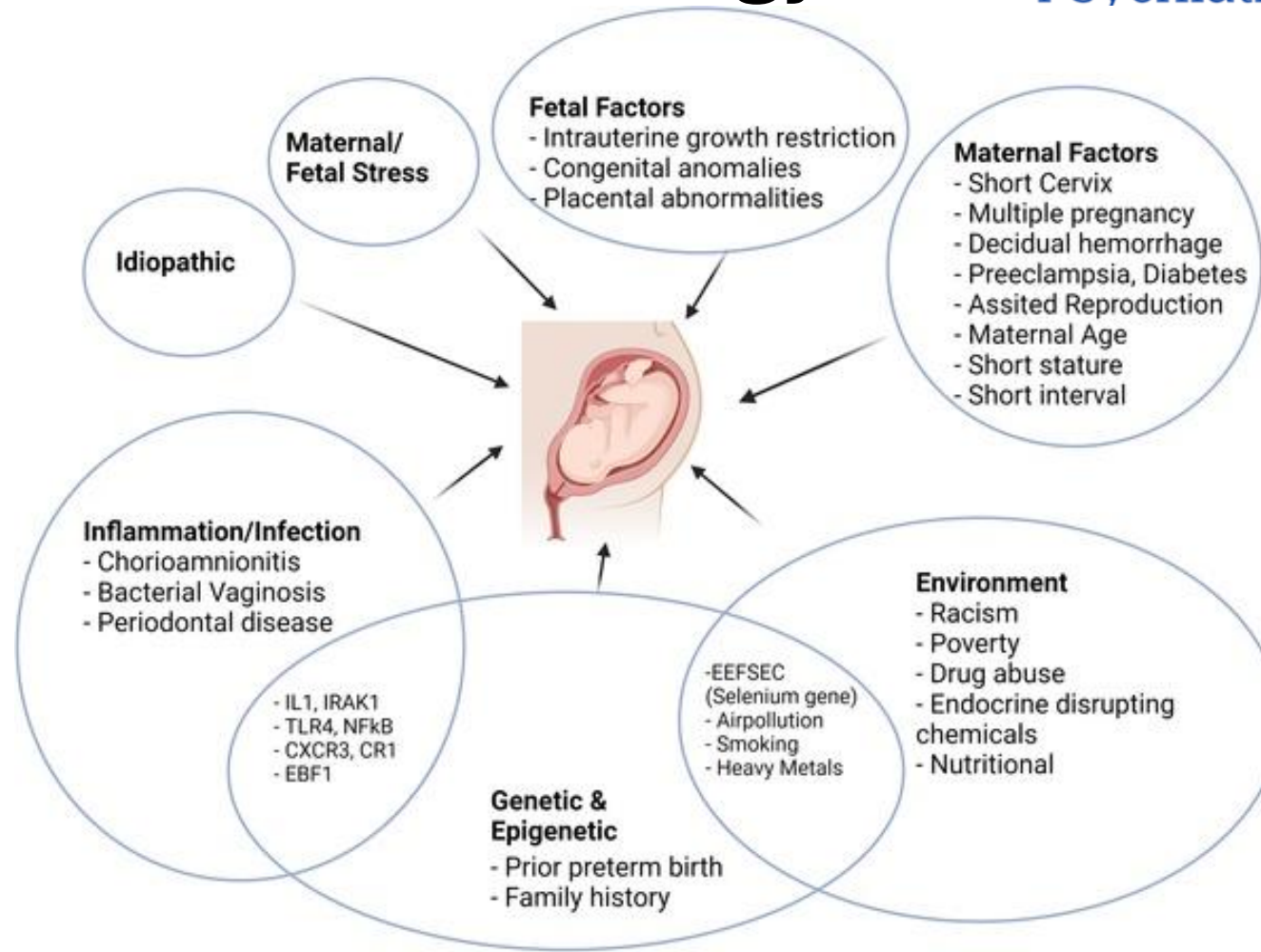
Preterm Birth: Risks

- Short term:
 - Pulmonary: RDS, bronchopulmonary dysplasia, apnea of prematurity
 - GI: hyperbilirubinemia, feeding intolerance, necrotizing enterocolitis, growth abnormalities
 - Immunological: infections (perinatal and hospital acquired), immune deficiencies
 - CNS: intraventricular hemorrhage, periventricular leukomalacia, hydrocephalus
 - Ophthalmological: retinopathy of prematurity
 - CV: hypertension, patent ductus arteriosus, pulmonary hypertension
 - Renal: water/electrolyte imbalance, acid-base disturbances
 - Hematological: iatrogenic anemia, transfusions, anemia of prematurity
 - Endocrine: hypoglycemia, transient low thyroxine, cortisol deficiency

Preterm Birth: Risks

- Long term:
 - Pulmonary: bronchopulmonary dysplasia, reactive airway disease, asthma
 - GI: failure to thrive, short bowel syndrome, cholestasis
 - Immunological: RSV, bronchiolitis
 - CNS: CP, hydrocephalus, developmental delay, hearing loss
 - Ophthalmological: blindness, retinal detachment, myopia, strabismus
 - CV: Pulmonary hypertension, hypertension in adulthood
 - Endocrine: impaired glucose regulation and insulin resistance

Preterm Birth: Etiology



Preterm Birth: Management

- Corticosteroids
 - 2 doses of betamethasone or 4 doses of dexamethasone at 24 (maybe lower?) – 34 (or sometimes later?) weeks
 - Lower rates of: perinatal/neonatal death, respiratory distress, intraventricular hemorrhage, necrotizing enterocolitis, need for mechanical ventilation, systemic infection in first 48hrs of life
- Tocolysis: indomethacin or nifedipine to try to slow uterine activity in order to complete course of steroids
- Magnesium: to reduce cerebral palsy in pregnancies < 32 weeks (also given for preeclampsia)
- Antibiotics: if GBS unknown or concern for chorioamnionitis

Hypertensive Disorders of Pregnancy

- Diagnoses: gestational hypertension, preeclampsia with and without severe features, HELLP syndrome, eclampsia
- Definitions: new onset hypertension after 20 weeks (versus before = chronic hypertension) with or without end organ dysfunction
- Incidence: 5% of pregnancies

Hypertensive Disorders of Pregnancy

- Risk factors:
 - Nulliparity
 - Prior pregnancy with preeclampsia, stillbirth, or growth restriction
 - Extremes of maternal age (>40 or <18)
 - Chronic medical conditions (obesity, diabetes, renal or vascular disease, autoimmune disease)
 - Multiple gestation
 - Exposure to racism
 - New partner

Diagnostic Criteria for Preeclampsia

Blood Pressure (BP)

- New onset systolic BP of ≥ 140 mmHg or diastolic BP of ≥ 90 mm Hg on two occasions at least 4 hours apart after 20 weeks' of gestation in a patient without preexisting hypertension
- OR-
- Systolic BP of ≥ 160 mmHg or diastolic BP of ≥ 110 mm Hg (severe range hypertension) on 2 occasions at least 15 minutes apart after 20 weeks' of gestation in a patient without preexisting hypertension

AND

Proteinuria

- ≥ 300 mg of protein per 24-hour urine collection or increased from baseline
- OR-
- Urine protein/creatinine ratio of ≥ 0.3 mg/dL

OR in the absence of proteinuria with new-onset hypertension:

- Thrombocytopenia: Platelet count less than 100,000/microliter
- Renal insufficiency: Serum creatinine concentrations > 1.1 mg/dL or a doubling of the serum creatinine concentration in the absence of other renal disease
- Impaired liver function: Elevated serum liver transaminases to twice normal concentration
- Pulmonary edema
- Severe persistent right upper quadrant or epigastric pain unresponsive to medication and not accounted for by alternative diagnosis
- New-onset headache unresponsive to medication and not accounted for by alternative diagnoses or visual disturbances

adapted from reference 1



Massachusetts General Hospital
Founding Member, Mass General Brigham
Psychiatry Academy

Hypertensive Disorders of Pregnancy

- Pathophysiology: poorly understood, maternal vascular malperfusion at placental interface
- Prevention: low dose (81 or 162mg) aspirin starting at 12 weeks
- Typical presentation: third trimester (or late second) with new onset hypertension +/- symptoms (headache, scotomata, RUQ pain), proteinuria, lab abnormalities, fetal growth restriction
- Management: delivery versus expectant management based on disease severity and gestational age
 - Maternal monitoring: BP, labs, symptoms
 - Fetal monitoring: growth, antenatal testing



Hypertensive Disorders of Pregnancy

- Long term risks of:
 - Chronic hypertension (3-4x risk of those normotensive in pregnancy)
 - Heart failure (4.2x risk)
 - Stroke (81% increased risk)
 - End stage renal disease (5-12x risk)
 - Atrial arrhythmias, coronary heart disease, mortality (2x risk)
- Very important to ask about hypertensive disease in pregnancy at healthcare visits outside of pregnancy!

Gestational Diabetes

- Definition: glucose intolerance diagnosed in pregnancy, typically in third trimester
- Epidemiology: 6% of US pregnancies
- Risk factors:
 - History of GDM, family history of Type 2 DM, age > 35, exposure to racism, prior macrosomic infant, prior adverse obstetric outcomes, high parity, obesity, prediabetes, PCOS, excessive gestational weight gain, diet/lifestyle
- Etiology: placental hormones causing insulin resistance + predisposing risk factors

Gestational Diabetes

- Screening: universal, timing depends on institution and patient risk factors
- Monitoring:
 - BG checks 4x/day (fasting and 1-2hr postprandial)
 - Fetal growth monitoring
 - Antenatal testing
- Treatment
 - First line: diet and activity modification
 - Medication: insulin or metformin

Gestational Diabetes

- Maternal risks
 - Preeclampsia
 - Weight gain
 - Cesarean section, birth trauma
 - Type 2 DM later in life (50% risk)
- Fetal risks
 - Macrosomia (BW >4kg)
 - Shoulder dystocia, birth injuries
 - Neonatal hypoglycemia, hyperbilirubinemia
 - Long term risk of metabolic syndrome

Preconception Care

- Core Interventions
 - Folic acid/prenatal vitamins
 - Update vaccinations (especially live vaccines)
 - Lifestyle modifications: optimize BMI, nicotine and THC cessation, avoid alcohol and non-prescribed substances, disease optimization (ie A1c <7, hypertension management)
 - Discuss/change potentially teratogenic medication
- Consider maternal fetal medicine or OB preconception to review medications, disease, and potential teratogens
- Contraception



Risk-Risk Framework for Medications in Pregnancy

What are the risks to the patient (and the fetus) of being off of (or on reduced dose of) the medication?

What are the risks (theoretical or known) to the fetus of exposure to the medication?

Medications in Pregnancy

1979-2014

FDA Pregnancy Risk Categories

CATEGORY A	Adequate, well-controlled studies in pregnant women have not shown an increased risk of fetal abnormalities.
CATEGORY B	Animal studies have revealed no evidence of harm to the fetus; however, there are no adequate and well-controlled studies in pregnant women. OR Animal studies have shown an adverse effect, but adequate and well-controlled studies in pregnant women have failed to demonstrate a risk to the fetus.
CATEGORY C	Animal studies have shown an adverse effect and there are no adequate and well-controlled studies in pregnant women. OR No animal studies have been conducted and there are no adequate and well-controlled studies in pregnant women.
CATEGORY D	Adequate well-controlled or observational studies in pregnant women have demonstrated a risk to the fetus. However, the benefits of therapy may outweigh the potential risk.
CATEGORY X	Adequate well-controlled or observational studies in animals or pregnant women have demonstrated positive evidence of fetal abnormalities. The use of the product is contraindicated in women who are or may become pregnant.
CATEGORY NA	A US Food and Drug Administration pregnancy rating is not available.



2015-present

“Pregnancy and Lactation Labeling Rule”

- Replaced categories with narrative
- Drugs marketed after 2001 do not have categories

Medications in Pregnancy

Definitive Risk

- Renin-angiotensin Blockers
- **Certain antiepileptics**
- Systemic antimycotics
- Antineoplastics
- Isotretinoin
- Sulfamethoxazole
- Warfarin

Potential Risk

- NSAIDS
- **Systemic antivirals**
- **Beta Blockers**
- Aminoglycosides
- Antiarrhythmics
- **Immunosuppressants**
- **Duloxetine**
- **Gabapentin**
- Teriflunomide

Sarayani A et al. Prenatal Exposure to teratogenic medications in the era of Risk Evaluation and Mitigation Strategies. AJOG Aug 2022.

Medications in Pregnancy

- 70% of pregnant individuals are prescribed 1 or more medications during pregnancy
- Only 9 medications have been approved and marketed in the US for obstetrical indications
- No other specialty in medicine has such a short list of drug approvals with so few indications
- The TERIS expert advisory board members were unable to determine the teratogenic risks associated with 97.7% of drugs approved by the FDA between 2000 and 2010
 1. Eunice Kennedy Shriver NIHHD Task Force on Research Specific to Pregnant Women and Lactating Women. 2018.
 2. Wesley B, et al. Prescription Medications for Use in Pregnancy- Perspective from the US Food and Drug Administration. AJOG July 2021

Words Matter

2% Risk of a Malformed
Newborn

98% chance of an
unaffected infant

Tripling or a 200%
increase in Risk

1 per 1000 to 3 per 1000
increase risk or 99.7
percent likelihood of no
affect

Words Matter

- Review risks and benefits of untreated disease vs. medication exposure
- Chose words carefully
 - Consider framing in a positive rather than negative way
 - Site the **absolute risk** rather than the **odds ratio**
- Remember most drugs are low risk teratogens that produce anomalies in 10 per 1000 maternal exposures
- All pregnant persons have a 3% risk of having a newborn with a congenital abnormality

Medications in Pregnancy

- Sources for information on medication:
 - Briggs Drugs in Pregnancy and Lactation
 - Reprotox
 - IBM Micromedex
 - Mother to Baby

Thank you!