Hypertensive Disorders of Pregnancy

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Learning Objectives

- Review the most current guidelines for diagnosis of hypertensive disorders in pregnancy
- Outline management and treatment strategies
- Discuss recent recommendations for use of aspirin and magnesium sulfate
Hypertensive disorders of pregnancy is a major health issue for women and their infants.

- Preeclampsia is a leading cause of maternal and perinatal morbidity and mortality, complicating 2-8% of pregnancies worldwide.
  - Accounts for ~15% of preterm births.
  - Accounts for 10-15% of maternal deaths.
Beyond Pregnancy

Preeclampsia is a risk factor for future cardiovascular disease and metabolic disease in women

- According to the American Heart Association women who have preeclampsia have twice the risk for stroke and a four-fold risk of high blood pressure later in life
### Cardiovascular Changes

<table>
<thead>
<tr>
<th>Preconception</th>
<th>Pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>First Trimester</td>
</tr>
<tr>
<td>Hemodynamic</td>
<td></td>
</tr>
<tr>
<td>CO</td>
<td>↑</td>
</tr>
<tr>
<td>SVR</td>
<td>↓</td>
</tr>
<tr>
<td>HR</td>
<td>↑</td>
</tr>
<tr>
<td>BP</td>
<td>↓</td>
</tr>
<tr>
<td>Neurohormonal</td>
<td></td>
</tr>
<tr>
<td>Renin/angiotensin</td>
<td>Plasma volume*</td>
</tr>
<tr>
<td>RBC changes</td>
<td>RBC mass</td>
</tr>
<tr>
<td>Structural changes</td>
<td>LV wall mass</td>
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<tr>
<td></td>
<td>Chamber sizes</td>
</tr>
<tr>
<td></td>
<td>Aorta</td>
</tr>
</tbody>
</table>

BP indicates blood pressure; CO, cardiac output; HR, heart rate; LV, left ventricular; RBC, red blood cell; and SVR systemic vascular resistance. ↑ and ↓ reflect relative changes in parameters from preconception values.

*The greater increase in plasma volume relative to the increase in RBC mass results in the physiological anemia of pregnancy.

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Cardiovascular Changes

ACOG Task Force on Hypertension in Pregnancy

- 17 clinician-scientists from fields of OB, MFM, HTN, internal medicine, nephrology, anesthesiology, physiology and patient advocacy

Provides evidence-based recommendations for the management of patients with hypertension during and after pregnancy.

- Recommendations are graded as strong or qualified based on evidence of effectiveness weighed against evidence of potential harm.
Hypertensive Disorders of Pregnancy

- Gestational hypertension
- Preeclampsia
- Eclampsia
- Superimposed preeclampsia
- Chronic hypertension
- Preeclampsia-eclampsia
- Chronic HTN (any cause)
- Chronic HTN with superimposed preeclampsia
- Gestational hypertension
Key Differences

Eliminated dependency on proteinuria to diagnose preeclampsia.
Eliminates:

- recommendations for bed rest
- delivery prior to 37 0/7 weeks of gestation
- magnesium sulfate for mild gestational hypertension or for preeclampsia without severe features
- eliminates massive proteinuria and/or FGR as indicators of severe preeclampsia
Proteinuria

Assessment

- ≥ 300 mg in a 24-h urine specimen (gold standard)

- Urine protein:creatinine ratio in a single voided urine
  - > 0.3 mg/dL correlates to > 300 mg/dL

- Qualitative dipstick reading ≥ 1+
  - quick
  - inconsistent- use only if other methods not available
Gestational Hypertension
Diagnosis

- SBP ≥ 140 mm Hg or DBP ≥ 90 mm Hg after 20 weeks in a previously normotensive women
- Absence of proteinuria or other systemic abnormalities
- BP returns to normal <12 weeks postpartum
  - Final diagnosis made only postpartum
Gestational Hypertension

Management

- BP assessment at least 2x weekly (office/home)
- Urine protein assessment weekly
- No antihypertensive medications if SBP <160 mm Hg or DBP <110 mm Hg
- Regular activity (no bedrest)
Gestational Hypertension

Management

- Antenatal testing
- Conservative management until 37 0/7 weeks of gestation
- BP monitoring for 72 hours postpartum (in hospital or outpatient) and again 7-10 days after delivery
Chronic Hypertension

- Predates conception or is detected prior to 20 weeks of gestation
- Complicates 1-5% of pregnancies
- 45% of AA women, 28% of Hispanic women, 31% of Caucasian women
- Higher rates seen with AMA, obesity, metabolic syndrome
Chronic Hypertension Management

- Antihypertensive medications as per prepregnancy, titrated between BP 120/80 and 160/105 mm Hg
- Labetalol, nifedipine or methyldopa for persistent SBP ≥ 160 mm Hg or DBP ≥ 105 mm Hg
- Baseline assessment of proteinuria, liver function
- Serial sonography for growth
Antenatal testing

Delivery recommendations:

- No medication: 38 0/7-39 6/7 weeks of gestation
- On medication: 37 0/7-39 6/7 weeks of gestation
- Poorly controlled: 36 0/7-37 6/7 weeks of gestation

ACOG Committee Opinion No. 560, April 2013
Superimposed Preeclampsia

**Diagnosis**

- CHTN in association with preeclampsia

- With or without severe features
  - Management is guided by subcategory
    - If only HTN exacerbation with SBP < 160 mm Hg or DBP < 110 mm Hg then treatment is as per “preeclampsia without severe features”
    - If HTN exacerbation warrants treatment or organ dysfunction manifests, the treat as per “preeclampsia with severe features”
Usually occurs after 20 weeks of gestation
  - Early-onset: <34 weeks

New-onset HTN: SBP $\geq 140$ mm Hg or DBP $\geq 90$ mm Hg occurring 4 hours apart with either
  - + new-onset proteinuria
  - presence of any severe feature
Thrombocytopenia (<100K)

Impaired liver function as indicated by: (transaminases 2x normal, severe persistent right upper quadrant or epigastric pain unresponsive to medication and not accounted for by alternative diagnoses or both)

New development of renal insufficiency (serum creatinine >1.1 mg/dL or doubling of serum creatinine in absence of other renal disease)

Pulmonary edema

New onset cerebral or visual disturbances
Preeclampsia/Eclampsia

Risk Factors

- Pre-gestational diabetes
- Autoimmune disease
- Multifetal gestation
- CHTN
- History of preeclampsia
- Renal disease
- Abnormal serum analytes
  - (low PaPP-A (<5%ile),
  - elevated MSAFP,
  - increased Inhibin A (2.0 or >)
- ART
- African American race
- Overweight or obese ***
# Preeclampsia/Eclampsia

## Risk Factors

<table>
<thead>
<tr>
<th>Exposure</th>
<th>Preeclampsia in the Exposed Group</th>
<th>Preeclampsia in the Nonexposed Group</th>
<th>RR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic hypertension (n=165)</td>
<td>53 (32.1)</td>
<td>184 (7.4)</td>
<td>4.32 (3.32–5.61)</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Pregestational diabetes (n=57)</td>
<td>23 (40.4)</td>
<td>214 (8.3)</td>
<td>4.86 (3.46–6.84)</td>
<td>&lt;.01</td>
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<tr>
<td>Smoking (n=95) (missing data)</td>
<td>10 (10.5)</td>
<td>214 (9.0)</td>
<td>1.17 (0.64–2.13)</td>
<td>.61</td>
</tr>
<tr>
<td>Multiple gestation (n=148)</td>
<td>35 (23.7)</td>
<td>202 (8.1)</td>
<td>2.91 (2.12–4.01)</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>African American race (n=598)</td>
<td>85 (14.2)</td>
<td>152 (7.5)</td>
<td>1.91 (1.49–2.45)</td>
<td>&lt;.01</td>
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<tr>
<td>Family history of preeclampsia (n=147)</td>
<td>21 (14.3)</td>
<td>216 (8.7)</td>
<td>1.65 (1.09–2.50)</td>
<td>.02</td>
</tr>
<tr>
<td>Prior preeclampsia (n=176)</td>
<td>45 (25.6)</td>
<td>192 (7.8)</td>
<td>3.28 (2.46–4.36)</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Nulliparity (n=1,157)</td>
<td>113 (9.8)</td>
<td>124 (8.4)</td>
<td>1.17 (0.91–1.49)</td>
<td>.22</td>
</tr>
<tr>
<td>Assisted reproductive techniques (n=312)</td>
<td>52 (16.7)</td>
<td>185 (8.0)</td>
<td>2.09 (1.58–2.78)</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Maternal age 35 y or older (n=758)</td>
<td>79 (10.4)</td>
<td>158 (8.4)</td>
<td>1.24 (0.96–1.60)</td>
<td>.10</td>
</tr>
<tr>
<td>Maternal age 40 y or older (n=157)</td>
<td>21 (13.4)</td>
<td>216 (8.7)</td>
<td>1.54 (1.01–2.33)</td>
<td>.05</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td></td>
<td>68 (4.8)</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>25 or less (n=1,409)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Greater than 25–30 (n=652)</td>
<td>59 (9.1)</td>
<td></td>
<td>1.88 (1.34–2.62)</td>
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<td>Greater than 30–35 (n=323)</td>
<td>44 (13.6)</td>
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<td>2.82 (1.97–4.04)</td>
<td>&lt;.01</td>
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<tr>
<td>Greater than 35–40 (n=146)</td>
<td>29 (19.9)</td>
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<td>4.11 (2.76–6.14)</td>
<td>&lt;.01</td>
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<tr>
<td>Greater than 40 (n=107)</td>
<td>37 (34.6)</td>
<td></td>
<td>7.17 (5.06–10.16)</td>
<td>&lt;.01</td>
</tr>
</tbody>
</table>

RR, risk ratio; CI, confidence interval; BMI, body mass index.
Data are n (%) unless otherwise specified.

• Clinical Risk Factors for Preeclampsia in the 21st Century. Emmanuelle Paré, MD, MSCE, Samuel Parry, MD, Thomas F. McElrath, MD, PhD, Dominick Pucci, PhD, Amy Newton, and Kee-Hak Lim, MD (Obstet Gynecol 2014;0:1–8)
Preeclampsia/Eclampsia

Pathophysiology

- Pregnancy specific syndrome of reduced tissue perfusion due to vasospasm and endothelial activation
- Glomerular lesions and proteinuria typically occur late in gestation
- Clinical manifestation may be months after presumed onset
Key placental lesion in preeclampsia

Failure of spiral arteries to dilate, lose their endothelium smooth muscle and inner elastic lamina which normally would result in flaccid large diameter.


Preeclampsia without severe features

**Management**

- No antihypertensive medications if SBP $<160$ mm Hg or DBP $<110$
- Regular activity/ no strict bed rest
- Sonography
- Antenatal testing
- At diagnosis $\geq 37\,0/7$ weeks of gestation
- No magnesium sulfate if SBP $<160$ mm Hg or DBP $<110$ mm Hg
Severe Preeclampsia

- New-onset HTN: SBP $\geq 140$ mm Hg or DBP $\geq 90$ mm Hg occurring 4 hours apart with proteinuria OR any of the following:
  - Thrombocytopenia (<100K)
  - Impaired liver function as indicated by: (transaminases 2x normal, severe persistent right upper quadrant or epigastric pain unresponsive to medication and not accounted for by alternative diagnoses, or both)
  - New development of renal insufficiency (serum creatinine $>1.1$ mg/dL or doubling of serum creatinine in absence of other renal disease)
  - Pulmonary edema
  - New onset cerebral or visual disturbances
Early vs Late-onset Preeclampsia

- Prior to 34 weeks
  - Increased fetal death
  - 0.38 incidence
  - AA race, CHTN, congenital anomalies

- After 34 weeks
  - Rate increases with increasing gestational age
  - 2.72 incidence
  - Younger maternal age, nulliparity, DM


<table>
<thead>
<tr>
<th>Exposure</th>
<th>Adjusted OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic hypertension</td>
<td>17.58</td>
<td>7.15–43.26</td>
</tr>
<tr>
<td>Multiple gestation</td>
<td>12.72</td>
<td>5.04–32.01</td>
</tr>
<tr>
<td>History of preeclampsia</td>
<td>6.84</td>
<td>1.75–26.68</td>
</tr>
<tr>
<td>Nulliparity</td>
<td>5.02</td>
<td>1.66–15.18</td>
</tr>
</tbody>
</table>

OR, odds ratio; CI, confidence interval.
* Controlling for variables listed in this table.
Preeclampsia with severe features

**Management**

- < 33 6/7 weeks and stable maternal/fetal conditions with:
  - PPROM
  - Labor
  - Thrombocytopenia
  - Persistently elevated liver transaminases
  - FGR (<5%ile)
  - Severe oligohydramnios (AFI < 5 cm)

- **Postpone delivery** 48 hours to allow corticosteroid completion
Preeclampsia with severe features

Management

- Before fetal viability (23 0/7 weeks)
  - Maternal stabilization
  - Delivery

- < 34 0/7 weeks with stable maternal and fetal conditions
  - Conservative management only at appropriate facilities with adequate maternal and neonatal intensive care resources
  - Corticosteroids for FLM
  - Delivery at diagnosis after 34 0/7 weeks of gestation
  - Magnesium sulfate intra- and postpartum

- ≥34 weeks gestation
  - Maternal stabilization
  - Delivery
  - Magnesium sulfate intra- and postpartum
Preeclampsia with severe features

Management

- Delivery after maternal stabilization and regardless of gestational age for:
  - Uncontrollable severe hypertension
  - Eclampsia
  - Pulmonary edema
  - DIC
  - Nonreassuring fetal status
  - IUFD
- Administer corticosteroids if viable, but do not delay delivery
Eclampsia

- New onset of generalized tonic-clonic seizures in a woman with gestational HTN or preeclampsia who did not have a preexisting seizure disorder
  - incidence 0-1.8%, and as high as 14% in developing countries.
  - tertiary referral centers, in multifetal gestation, and in populations with no prenatal care

- Antepartum (38-53%)
  - 91% develop after 28 weeks
  - 7.5% between 21-28 weeks
  - 1.5% at 20 weeks gestation or less

- Postpartum (11-44%)
  - PP>48 hours <4 weeks
  - May develop despite use of magnesium sulfate within the first 24 hours of delivery
Magnesium sulfate 6gm over 15-20 minutes
  
  - 2gm/hr continuous IV infusion
  - 10% will seize after initial Mg load
    - Give another 2gm over 3-5 minutes
    - Recurrence treated with sodium amobarbital 250 mg IV over 3-5 minutes
    - Ca gluconate 1 gm IV usually reverses mild to moderate respiratory depression

Delivery
  
  - Vaginal delivery if SROM or in labor with no contraindications
  - Cesarean section <30 weeks if not in labor
Eclampsia

Maternal Morbidities

- HELLP 10-15%
- Abruption 7-10%
- DIC 7-11%
- Pulmonary edema 3-5%
- ARF 5-9%
- Aspiration pneumonia 2-3%
- Liver hematoma 1%
Eclampsia

*Maternal Mortality*

- 0-2% in developed countries
- 14% in developing world
- Approximately 20% of USA pregnancy related deaths attributable to preeclampsia/eclampsia
- No prenatal care, AA women at greater risk
- Highest mortality associated with onset prior to 28 weeks
Before viability - stabilize then deliver

<33 6/7 weeks of gestation and stable maternal/fetal condition:

› Administer corticosteroids
› Delay delivery for 24-48 hours
HELLP Syndrome

Sibai criteria

- All of the following:
  - Plt < 100k
  - AST > 70 IU/L (> 2x upper limit of normal)
  - Abnormal peripheral smear
  - LDH > 600 IU/L (>2x upper limit of normal) OR bilirubin > 1.2 mg/dL.
  - Considered partial HELLP syndrome if all parameters are not met.
Postpartum Management

- Treat with magnesium sulfate for new-onset hypertension associated with HA, blurred vision or preeclampsia with severe HTN

- Begin antihypertensive therapy:
  - Persistent (2 occasions 4-6 hours apart) SBP $\geq 150$ mm Hg or DBP $\geq 100$ mm Hg
  - Within 1 hour if persistent and SBP $\geq 160$ mm Hg or DBP $\geq 110$ mm Hg
Task force concludes with “moderate certainty” that there is a substantial net benefit of daily low-dose aspirin (60-150 mg/d) use to reduce the risk for preeclampsia, PTB, and IUGR in women at high risk for preclampsia.

Recurrence risk is inversely related to gestational age at first delivery.
Low-dose aspirin after 12 weeks for women at greatly increased risk of adverse pregnancy outcomes

- ACOG, World Health Organization, National Institute for Health and Clinical Excellence, American Heart Association, American Stroke Association, American Academy of Family Physicians, etc.
# Prevention

<table>
<thead>
<tr>
<th>Risk level</th>
<th>Risk Factors</th>
<th>Recommendation</th>
</tr>
</thead>
</table>
| High       | History of preeclampsia, especially when accompanied by an adverse outcome  
            Multifetal gestation  
            Chronic hypertension  
            Type 1 or 2 diabetes  
            Renal disease  
            Autoimmune disease (SLE, antiphospholipid syndrome) | Low-dose aspirin if patient has ≥ of these high-risk factors |
| Moderate   | Nulliparity  
            Obesity (BMI > 30 kg/m²)  
            Family history of preeclampsia  
            African American, low socioeconomic status  
            Age ≥ 35 years  
            Personal history (LBW, SGA, previous adverse outcome, >10-year pregnancy interval | Low-dose aspirin if patient has several of these moderate-risk factors |
| Low        | Previous uncomplicated full-term delivery | No low-dose aspirin |

Maternal Safety Bundle for Severe Hypertension in Pregnancy

http://www.acog.org/~/media/Districts/District%20II/PDFs/SMI/v2/SevereHTNinPregnancyAugust2014PDF.pdf  Kelly Gilchrist
Diagnostic Criteria: Severe Hypertension

- Severe hypertension that is accurately measured using standard techniques and is persistent for > 15 minutes is considered a **hypertensive emergency**.

Severe hypertension is defined as:
- *systolic blood pressure* ≥ 160 mm Hg  
  or  
- *diastolic blood pressure* ≥ 110 mm Hg

- Severe hypertension can occur during the antepartum, intrapartum, or postpartum period.
Agents to Use: First Line

First line medications for the management of severe hypertension in pregnant and postpartum women are:

- Intravenous labetalol
- Intravenous hydralazine

**Note:** Magnesium Sulfate

- **Is not recommended as an antihypertensive agent**
- Remains the **drug of choice for seizure prophylaxis and for controlling seizures** in eclampsia
- Unless contraindicated, **should be given** when managing a hypertensive crisis
  - IV bolus of 4-6 grams in 100 ml over 15 minutes followed by IV infusion of 1-2 grams per hour
  - continue for 24 hours postpartum
Algorithm: First Line Management with Labetalol*

1. SBP ≥ 160 or DBP ≥ 110
   - Notify a provider and institute fetal surveillance if viable

2. Labetalol 20 mg IV over 2 minutes
   - Repeat BP in 10 minutes
   - If SBP ≥ 160 or DBP ≥ 110, administer labetalol 40 mg IV over 2 minutes; if BP is below threshold, continue to monitor BP closely

3. Repeat BP in 10 minutes
   - If SBP ≥ 160 or DBP ≥ 110, administer labetalol 80 mg IV over 2 minutes; if BP is below threshold, continue to monitor BP closely

4. If SBP ≥ 160 or DBP ≥ 110, administer hydralazine 10 mg IV over 2 minutes; if below threshold, continue to monitor BP closely
   - Repeat BP in 10 minutes and again in 20 minutes
   - If SBP ≥ 160 or DBP ≥ 110 at 20 minutes, obtain emergency consultation from specialist in MFM, internal medicine, anesthesiology, or critical care

5. If SBP ≥ 160 or DBP ≥ 110
   - Give additional antihypertensive medication per specific order as recommended by specialist

6. Once BP thresholds are achieved, repeat BP:
   - every 10 minutes for 1 hour
   - then every 15 minutes for 1 hour
   - then every 30 minutes for 1 hour
   - then every hour for 4 hours

    Institute additional BP monitoring per specific order

    *Maximum cumulative IV administered doses should not exceed the following: hydralazine 25 mg; labetalol 220 mg in 24 hours.

*Hold IV labetalol for maternal pulse under 60

Safe Motherhood Initiative
Algorithm: First Line Management with Hydralazine

- **SBP ≥ 160 or DBP ≥ 110**
  - Notify a provider and institute fetal surveillance if viable
  - Administer hydralazine 5 mg or 10 mg IV over 2 minutes
  - Repeat BP in 10 minutes and again in 20 minutes
  - If SBP ≥ 160 or DBP ≥ 110 at 20 minutes, administer hydralazine 10 mg IV over 2 minutes; if below threshold, continue to monitor BP closely
  - If SBP ≥ 160 or DBP ≥ 110 at 20 minutes, administer labetalol 20 mg IV over 2 minutes; if below threshold, continue to monitor BP closely
  - If SBP ≥ 160 or DBP ≥ 110, administer labetalol 40 mg IV over 2 minutes and obtain emergency consultation from specialist in MFM, internal medicine, anesthesiology, or critical care
  - Repeat BP in 10 minutes
  - Give additional antihypertensive medication per specific order as recommended by specialist
  - Once BP thresholds are achieved, repeat BP
    - every 10 minutes for 1 hour
    - then every 15 minutes for 1 hour
    - then every 30 minutes for 1 hour
    - then every hour for 4 hours
  - Institute additional BP monitoring per specific order

*Maximum cumulative IV administered doses should not exceed the following: hydralazine 25 mg; labetalol 220 mg in 24 hours.*

Safe Motherhood Initiative
Postpartum Surveillance: Inpatient

Once a hypertensive emergency is treated and the patient is delivered, additional monitoring, follow-up, and education is necessary to prevent additional morbidity.

- Preeclampsia and eclampsia can develop postpartum
- Blood pressure should be measured every 4 hours after delivery until stable.
- Nonsteroidal anti-inflammatory agents may increase blood pressure in some patients and should not be used in women with elevated blood pressure
- Patient should not be discharged until blood pressure is well controlled for at least 24 hours
- Blood pressure peaks 2-6 days after delivery so discharge planning should include repeat blood pressure measurements as outpatient and a review of the signs and symptoms that should prompt the patient to seek medical care
References

- The uterine spiral arteries in human pregnancy: facts and controversies. Pijnenborg R, Vercruysse L, Hanssens M
  Placenta. 2006 Sep-Oct; 27(9-10):939-58
HYPERTENSION

- Blood pressure
- High BP
- Vessels
- Diastolic
- Systolic
- Men
- Women
- Obesity
- Stroke
- Headache
- White coat syndrome
- Awareness
- Help
- Factors
- Heredity
- Genetic
- Hospital
- Lab tech
- Medical
- Blood
- Test
- Diet
- Health
- Arteries
- Cost
- Nurse
- Blood
- Doctor
- Diuretics
- Prevention
- Research
- Risk
- Care
- Normal
- Condition
- Exercise
- Stress
- BMI
- Medication
- Cuff