Preeclampsia -
The new guidelines and recommendations for management

Robert S. Egerman, MD

<table>
<thead>
<tr>
<th>CLASSIFICATION</th>
<th>SYSTOLIC BLOOD PRESSURE (SBP)</th>
<th>DIASTOLIC BLOOD PRESSURE (DBP)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LOW**</td>
<td>&lt;90</td>
<td>&lt;60</td>
</tr>
<tr>
<td>NORMAL</td>
<td>&lt;120</td>
<td>&lt;80</td>
</tr>
<tr>
<td>PREHYPERTENSION</td>
<td>120 - 139</td>
<td>80 - 89</td>
</tr>
<tr>
<td>HIGH: STAGE 1 HYPERTENSION</td>
<td>140 - 159</td>
<td>90 - 99</td>
</tr>
<tr>
<td>HIGH: STAGE 2 HYPERTENSION</td>
<td>≥160</td>
<td>≥100</td>
</tr>
</tbody>
</table>
Impact of high normal blood pressure on the risk of cardiovascular disease

Chobanian, Hypertension 2003

Benefits of Rx hypertension

Neal, Lancet 2000
JNC VIII

• Age 18 – 59
• GOALS:
  • Systolic < 140 mm Hg
  • Diastolic < 90 mm Hg - demonstrable benefit
• Completeness
• Age > 60
• Systolic < 150 mm Hg
• Diastolic < 90 mm Hg

JAMA 2014
Causes of hypertension

- Chronic kidney disease or obstructive uropathy
- Renovascular hypertension
- Coarctation of the aorta
- Drug-induced or drug-related
- Cushing syndrome and other glucocorticoid excess states including chronic steroid therapy
- Pheochromocytoma
- Primary aldosteronism and other mineralocorticoid excess states
- Sleep apnea
- Thyroid or parathyroid disease
At a minimum

• **Why is the patient hypertensive?**
  – History
    • Prior medical history, alcohol, smoking, drugs
  – Physical
    • Look at the patient (proptosis, nervous, Cushingoid)
    • BP in both arms
    • Chest, Abdominal bruits, Edema, Pulses
  – Lab
    • CMP, TSH, Urinalysis, Protein/Creatinine

Learning objectives

• **Contrast new guidelines** from prior categorizations of preeclampsia
• **Determine appropriate delivery** timing for those diagnosed with preeclampsia
• **Review treatment of hypertension** and hypertensive urgencies during pregnancy
• **Construct plans for future cardiovascular risk reduction** in women affected with preeclampsia
Overview

• Perspective
• New changes in definitions and management
  – Preeclampsia
  – Gestational hypertension
  – Chronic hypertension and superimposed preeclampsia
• Managing hypertensive emergencies
• Prevention of preeclampsia
• Reducing long term cardiovascular risk

HYPERTENSION IN PREGNANCY
The American College of OB/GYN sponsored a task force through 2011 and 2012 to address hypertensive disease in pregnancy with 17 experts from various specialties.

Case 1

- 40 yo caucasian female at 33 weeks
- No antecedent hypertension
- BP 157/98
- No proteinuria
- Creatinine 1 mg/dL, AST 60 U/L
- EFW 1480 grams (<5%), normal doppler
- Diagnosis and Management?
- When would you deliver?
Case 2

- 31 yo African American female at 35 weeks
- No antecedent hypertension
- BP 156/100
- Protein/Creatinine 370
- Creatinine 0.9 mg/dL, AST 45 U/L
- Normal fetal growth and testing
- Diagnosis and Management?
- When would you deliver?

The new guidelines

- “You’ll be exhilarated”
- “You find hope where before none”
- “You’ll ride the emotional roller coaster”
- “You’ll laugh, you’ll cry”
- “You’ll learn some things”
- “You’ll realize some of the advice is good (and some probably not so good)”
The new guidelines

“There is enough poor advice here to have the whole thing rescinded, refined and re-released along with the entirety of the new ASCCP guidelines.”

Perspective

• Incidence of preeclampsia has increased by 25% in the past 20 years
• Preeclampsia causes an estimated 60,000 maternal deaths yearly worldwide
• A rigid diagnosis is not helpful
• There are 50 –100 near misses for every maternal death
• Preeclampsia is a risk for future cardiovascular disease
A Re-naming

No more mild preeclampsia

Only preeclampsia with severe features or without

The skinny on this

- Preeclampsia is hypertension with either
  - Thrombocytopenia (< 100,000 /µL)
  - Transaminases 2 fold higher than normal
  - Doubling of creatinine or > 1.1 mg/dL
  - Pulmonary edema
  - New onset cerebral or visual disturbances
- AND proteinuria is not necessary for the diagnosis
- Gestational hypertension is the absence of above
- Chronic hypertension
- Chronic hypertension with superimposed preeclampsia
Proteinuria

- 300 mg in a 24 hour period or
- Protein/creatinine 0.3 (mg/dL/mg/dL)
- The old 5 grams of protein has gone away . . .
- Dipsticks are discouraged [1+ could be used]

Hypertension

- Systolic 140 mm Hg or higher or
- Diastolic 90 mm Hg or higher
- Systolic 160 mm Hg or higher or
- Diastolic 110 mm Hg or higher
- On two caissons 4 hours apart on bed rest
- Unless treatment before this time
Fetal growth restriction

Antenatal assessment

- Preeclampsia without severe features
  - Weekly liver and platelet assessment
  - Twice weekly BP assessment
  - Daily fetal movement counts/symptoms
  - No Rx unless severe range > 160 syst or 110 dias

- Gestational hypertension
  - Weekly BP and protein assessment
  - No Rx unless severe range > 160 syst or 110 dias
  - Bed rest not needed for either group
Antenatal assessment

• Sonography for fetal growth is recommended and umbilical doppler assessment if there is growth restriction

Antenatal steroids

• **Defer delivery for 48 hours** if < 33 6/7 weeks and severe preeclampsia and any of:
  – pPROM
  – Thrombocytopenia
  – Abnormal transaminases or creatinine
  – Growth restriction (< 5%)
  – Reversed end diastolic flow on umbilical doppler
  – Gestational hypertension
  – Oligohydramnios (AFI < 5 cm)
Antenatal steroids

- **No delay for delivery after steroids** if \( < 33 \frac{6}{7} \) weeks and severe preeclampsia and any of:
  - Uncontrolled hypertension
  - Eclampsia
  - Pulmonary edema
  - Abruptio placenta
  - Disseminated intravascular coagulation
  - Non reassuring fetal status
  - Fetal demise

Magnesium sulfate

- “For women with systolic BP of less than 160 mm Hg and a diastolic BP less than 110 mm Hg and no maternal symptoms, it is suggested that magnesium sulfate not be administered universally for the prevention of eclampsia.”
  
  **Quality of evidence: Low**

- When using magnesium sulfate continue intraoperatively if a cesarean section is performed
Magnesium sulfate **Alternatives**

**ANTICONVULSANT MEDICATIONS**

(for recurrent seizures or when magnesium is contraindicated):

- **Lorazepam** (2-4 mg IV x 1, may repeat x 1 after 10-15 minutes)
- **Diazepam** (5-10 mg IV every 5-10 minutes to maximum dose of 30 mg)
- **Phenytoin** (15-20 mg/kg IV x 1, may repeat 10 mg/kg IV after 20 minutes if no response); avoid with hypotension, may cause cardiac arrhythmias
- **Keppra** (500 mg IV or orally, may repeat in 12 hours); dose adjustment needed if renal impairment

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**Antihypertensives**

- **Labetalol** (20, 40, 80 mg IV* over 2 minutes, escalating doses, repeat every 10 minutes or 200 mg orally if no IV access); avoid in asthma or heart failure, can cause neonatal bradycardia
- **Hydralazine** (5-10 mg IV* over 2 minutes, repeat in 20 minutes until target blood pressure is reached)
- Repeat blood pressure every 10 minutes during administration

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

If first line agents are unsuccessful, recommend emergency consultation with a specialist (e.g., MFM, internal medicine, OB anesthesiology, critical care) for second line management decisions
Delivery

- 37 weeks without severe features of preeclampsia (including gestational hypertension)
- 34 weeks or if unstable maternal or fetal condition, earlier in those with preeclampsia with severe features
- This includes HELLP syndrome (& no expectant management if below viability)

Delivery: fetal conditions

- with severe preeclampsia < 34 weeks
- AFI < 5 or maximal pocket < 2 cm
- IUGR < 5%
- Reversal diastolic flow
- Recurrent variable or late decelerations
- BPP 4/10 on at least 2 occasions 6 hours apart
Hypertension

- Systolic 160 mm Hg or higher or
- Diastolic 110 mm Hg or higher
- Use an antihypertensive agent

Pregnancy-Related Deaths Florida 1999-2010:
Opportunities to make pregnancy safer

Courtesy of Anthony Gregg, MD
How Do Women Die Of Preeclampsia in CA?

CA-PAMR Final Cause of Death Among Preeclampsia Cases, 2002-2004 (n=25)

<table>
<thead>
<tr>
<th>Final Cause of Death</th>
<th>Number</th>
<th>%</th>
<th>Rate/100,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke</td>
<td>16</td>
<td>64.0%</td>
<td>1.0</td>
</tr>
<tr>
<td>Hemorrhagic Hemorrhagic</td>
<td>14</td>
<td>(87.5%)</td>
<td></td>
</tr>
<tr>
<td>Thrombotic Hemorrhagic</td>
<td>2</td>
<td>(12.5%)</td>
<td></td>
</tr>
<tr>
<td>Hepatic (liver) Failure</td>
<td>4</td>
<td>16.0%</td>
<td>.25</td>
</tr>
<tr>
<td>Cardiac Failure</td>
<td>2</td>
<td>8.0%</td>
<td></td>
</tr>
<tr>
<td>Hemorrhage/DIC</td>
<td>1</td>
<td>4.0%</td>
<td></td>
</tr>
<tr>
<td>Multi-organ failure</td>
<td>1</td>
<td>4.0%</td>
<td></td>
</tr>
<tr>
<td>ARDS</td>
<td>1</td>
<td>4.0%</td>
<td></td>
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Factors Contributing to Pregnancy-Related Deaths, CA-PAMR 2002-2004

<table>
<thead>
<tr>
<th>Contributing Factor</th>
<th>Preeclampsia N (%)</th>
<th>TOTAL N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>OVERALL</td>
<td>25 (100%)</td>
<td>129 (89%)</td>
</tr>
<tr>
<td>PATIENT FACTORS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Underlying significant medical conditions</td>
<td>8 (50%)</td>
<td>40 (39%)</td>
</tr>
<tr>
<td>Delay or failure to seek care</td>
<td>10 (63%)</td>
<td>27 (26%)</td>
</tr>
<tr>
<td>Lack of understanding the importance of a health event</td>
<td>9 (56%)</td>
<td>16 (15%)</td>
</tr>
<tr>
<td>HEALTHCARE PROFESSIONALS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Delay in diagnosis</td>
<td>22 (92%)</td>
<td>62 (54%)</td>
</tr>
<tr>
<td>Use of ineffective treatment</td>
<td>19 (79%)</td>
<td>48 (42%)</td>
</tr>
<tr>
<td>Misdiagnosis</td>
<td>13 (54%)</td>
<td>36 (31%)</td>
</tr>
<tr>
<td>Failure to refer or seek consultation</td>
<td>6 (25%)</td>
<td>26 (23%)</td>
</tr>
<tr>
<td>HEALTHCARE FACILITY</td>
<td>12 (48%)</td>
<td>72 (50%)</td>
</tr>
</tbody>
</table>
Preeclampsia, BP, Stroke

Martin, Obstet Gynecol 2005

Preeclampsia, BP, Stroke

28 pts, 12 antepartum, 8 eclampsia, 53% death

Martin, Obstet Gynecol 2005
Postpartum

• Recognize NSAIDs contribute to hypertension
• Avoid these if bp is elevated > 1 day postpartum
• With either preeclampsia, gestational hypertension or superimposed preeclampsia:
  – BP monitoring 72 hours after delivery in the hospital or at home
  – Reassess in the office in 7-10 days
  – Earlier in patients with symptoms
Postpartum

• New onset hypertension associated with headache or blurred vision or preeclampsia, parenteral magnesium is suggested
• Treat persistent BP over 150 mm Hg Syst or 100 mm Hg Diastolic. Persistent BP over 160 mm Hg Syst or 110 mm Hg Diast should be treated within 1 hour

Postpartum

• Discharge instructions should include awareness of the signs or symptoms of preeclampsia
Chronic hypertension

- Treat if persistent BP over 160 mm Hg Syst or 105 mm Hg Diastolic unless end organ involvement
- Sonography for fetal growth (and umbilical doppler assessment if there is growth restriction)
- Delivery not before 38 weeks unless problems
- Delivery at 37 weeks if superimposed preeclampsia (SIP) and no severe features and 34 weeks with severe features
- Use intrapartum magnesium sulfate if SIP

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Less Than 140/90 (n=478)</th>
<th>140–150/90–99 (n=221)</th>
<th>151–159/100–109 (n=60)</th>
<th>P trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>Composite outcome</td>
<td>51 (10.7)</td>
<td>42 (19.0)</td>
<td>18 (30.0)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Perinatal death</td>
<td>15 (3.1)</td>
<td>16 (7.2)</td>
<td>6 (10.0)</td>
<td>.003</td>
</tr>
<tr>
<td>Severe preeclampsia</td>
<td>2 (0.4)</td>
<td>3 (1.4)</td>
<td>0 (0)</td>
<td>.726</td>
</tr>
<tr>
<td>Abruption</td>
<td>7/473 (1.5)</td>
<td>3/220 (1.4)</td>
<td>1 (1.7)</td>
<td>&gt;.999</td>
</tr>
<tr>
<td>Indicated preterm birth less than 35 wk of gestation</td>
<td>37 (7.7)</td>
<td>36 (16.3)</td>
<td>16 (26.7)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>SGA less than 10%</td>
<td>41/464 (8.8)</td>
<td>26/212 (12.3)</td>
<td>14/59 (23.7)</td>
<td>.001</td>
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SGA, small for gestational age.
Data are n (%) or n/N (%) unless otherwise specified.

Ankumah, Obstet Gynecol 2014
### Chronic Hypertension

#### Table 2. Incidence of Adverse Pregnancy Outcomes by Blood Pressure Category

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SGA, small for gestational age. Data are n (%) or n/N (%) unless otherwise specified.

Ankumah, Obstet Gynecol 2014
Chronic hypertension with SIP

- Development of proteinuria after 20 weeks gestation
- **Sudden exacerbation of hypertension or need to escalate therapy when previously well controlled**
- Manifestation of signs symptoms or increased liver enzymes
- Decreased platelet count less than 100,000 /µL
- Right upper quadrant pain, headaches
- Pulmonary edema or congestion
- Renal insufficiency
- Sudden substantial and sustained increases in protein

Postpartum and beyond

- **If preeclampsia then yearly:**
  - BP
  - Lipids
  - Fasting glucose
  - Assessment of body mass index
Long term risk for CVD
- Hypertension increased 6 fold
- Ischemic heart disease 2 fold
- Cerebrovascular disease 2 fold
- Diabetes 2 fold
- Hypothyroidism
- End stage renal disease
- Above risks are on the low end
- Earlier onset of preeclampsia the greater risk
- Mechanism-? Vascular damage, dyslipidemia

Table 2: HDP and Death from CVD.

<table>
<thead>
<tr>
<th>Author</th>
<th>No. Participants</th>
<th>Years to Follow-up</th>
<th>Outcome</th>
<th>RR/OR/HR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chesley et al. (1968)</td>
<td>270</td>
<td>22-45</td>
<td>Death</td>
<td>3.0</td>
</tr>
<tr>
<td>Jonsholt et al. (1966)</td>
<td>7543</td>
<td>50</td>
<td>Death</td>
<td>1.90 (1.02-3.52)</td>
</tr>
<tr>
<td>Irgens et al. (2001)</td>
<td>626272</td>
<td>13</td>
<td>Death</td>
<td>1.65 (1.01-2.70)</td>
</tr>
<tr>
<td>Funai et al. (2005)</td>
<td>37061</td>
<td>24-36</td>
<td>CVD Death</td>
<td>3.07 (2.18-4.34)</td>
</tr>
<tr>
<td>Bellamy et al. (2007)</td>
<td>198252</td>
<td>10-14</td>
<td>Overall Death</td>
<td>1.49 (1.05-2.14)</td>
</tr>
<tr>
<td>McDonald et al. (2008)</td>
<td>2,375,751</td>
<td>Na</td>
<td>CVD Death</td>
<td>2.29 (1.73-3.04)</td>
</tr>
<tr>
<td>Mongrew-Chaffin et al.</td>
<td>14403</td>
<td>37</td>
<td>CVD Death</td>
<td>2.14 (1.29-3.57)</td>
</tr>
</tbody>
</table>

Charlton, Heart Lung Circulation 2013
Postpartum assessment
Hypertensive disease

Table 4. Comparative Risk Ratios for the Main Causes of CVD.

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Risk Ratio for Coronary Artery Disease</th>
<th>95% Confidence Interval for Risk Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoking</td>
<td>2.1</td>
<td>1.50–2.90</td>
</tr>
<tr>
<td>Hypertension</td>
<td>2.1</td>
<td>1.40–3.00</td>
</tr>
<tr>
<td>LDL (&gt;4.1 mmol/L)</td>
<td>1.7</td>
<td>1.17–2.40</td>
</tr>
<tr>
<td>Preeclampsia</td>
<td>2.2</td>
<td>1.86–2.52</td>
</tr>
</tbody>
</table>

Charlton, Heart Lung Circulation 2013
Prevention of preeclampsia

- **USPHTF**
- 15 RCT high risk patients
- 6 RCT and 2 observational average risk
- **Low dose asa** beginning in 2nd trimester
- Preeclampsia  \( RR = 0.76 \) [95% CI, 0.62-0.95]
- IUGR  \( RR = 0.80 \) [95% CI, 0.66-0.99]

Henderson, Ann Int Med 2014

- {Chronic hypertension, diabetes, renal disease, prior preeclampsia, autoimmune, multiples}
- Less risk is obesity and AMA}
Hospital efforts

- Recognition in Ob triage areas
  - Admission
  - Discharge
- Timely treatment of hypertension
- Recognition when treatment is not adequate
- Post partum management
  - Before discharge
  - Discharge
  - Readmission
- Patient information and follow up