Postpartum hypertension, preeclampsia and eclampsia

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Confusing concept

- Preeclampsia only occurs in pregnancy – placenta is required
- Delivery “cures” preeclampsia
- How can preeclampsia happen postpartum?
Postpartum hypertension- preeclampsia - eclampsia

• Incidence
• Etiology and differential diagnosis
• Evaluation
• Management
• Education
Incidence

- Difficult to ascertain
- BP check at 6 weeks postpartum visit
- Mild hypertension not reported
- Usually asymptomatic
- If symptomatic, often seen and managed in ED
  - 0.3% of all PP visits to ED due to PP hypertension and preeclampsia

Clark SL et al. AJOG 2010.
Incidence

• Limitations of research studies
  – Single center
  – Inpatient, immediate PP stay (2-6 days)
  – Readmissions
• Prevalence of de novo postpartum hypertension or preeclampsia = 0.3 – 27.5%
• PP preeclampsia/eclampsia 5.7%
  – 63-66% de novo
  – ~15% eclampsia
• Morbidity and mortality

Clark SL et al. AJOG 2010.
Sibai BM. AJOG 2012.
Morbidity and mortality

- Eclampsia
- Pulmonary edema
- PP cardiomyopathy
- HELLP
- Endomyometritis
- Thromboembolism
- Maternal death (1 maternal death in each study of ~150 PP readmissions)

Sibai BM. AJOG 2012.
PP eclampsia – Incidence

- 50% developed after delivery
- 26% developed >48h after delivery
- Usually less than one week
- Most common symptom = headache
- 0.3-1% mortality
- Other complications
- Most recover, but some evidence of persistent white matter lesions and impaired cognitive function

Chames MC et al. AJOG 2002.
Aukes AM et al. AJOG 2009.
Case 1

• 32yo G2P2 PPD#6 – brought in to local hospital by ambulance after a witnessed generalized tonic-clonic seizure – she was intubated, started on a dilantin load in ED and transferred to UPMC-Presby Neuro ICU

• MRI – posterior leukoencephalopathy, ?vasculopathy

• OB called 14 hours after admission for vaginal bleeding
Case 2

• 34yo G1P1 POD#5 presented to MWH-ED with “feeling unwell” nausea/vomiting – in ED developed sudden-onset of severe headache and BP 180/110
• Course significant for being healthy
• IOL at 38w – mild preeclampsia
  – Magnesium sulfate - seizure prophylaxis
  – Misoprostil – cervical ripening
  – Pitocin - labor augmentation
  – Epidural
• Primary LTCS for arrest of dilation at 8cm
• Discharged to home on POD#3
Case 3

• 30yo G1P0101 POD#7 presents to ED with severe hypertension (on labetalol) and intermittent headache

• s/p primary LTCS for breech at 31w, severe IUGR, AEDF, oligohydramnios and severe hypertension and unrelenting headache – discharged home on POD#4

• BP in ED 170/110 – took 500mg of labetalol at home
Pathophysiology?

- Maternal endothelial dysfunction = major feature of preeclampsia
- Time course of resolution may be variable
- Most PP preeclampsia/eclampsia within 2w of delivery
- Persistent endothelial dysfunction up to 11 months post-delivery in women with early onset preeclampsia

Etiology and differential diagnosis

- New onset PP hypertension-preeclampsia
- Persistence/exacerbation of HTN in women with pre-existing GH-preeclampsia
- Preexisting HTN
  - Chronic hypertension with or without superimposed preeclampsia
  - Renal disease
- Cerebral vascular syndrome
- Cerebral venous thrombosis
- Stroke
- Post-dural puncture headache
- Other hypertensive and/or neurologic disorders (coincident with pregnancy)
<table>
<thead>
<tr>
<th>Etiology</th>
<th>Key findings to consider</th>
</tr>
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<tbody>
<tr>
<td>New-onset hypertension-preeclampsia</td>
<td>Onset 3-6 d postpartum without headaches</td>
</tr>
<tr>
<td>Volume overload</td>
<td>Large volume of fluids, regional analgesia, delayed mobilization</td>
</tr>
<tr>
<td>Medications/drugs</td>
<td>Nonsteroidal analgesics, ergot derivatives</td>
</tr>
<tr>
<td>Ibuprofen, indomethacin</td>
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<td>Vasoconstriction, headaches, nausea, vomiting, seizures</td>
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<tr>
<td>Persistence of GH-preeclampsia</td>
<td>Preexisting condition antepartum/in labor</td>
</tr>
<tr>
<td>Late-onset eclampsia</td>
<td>Headaches, visual changes, seizures, absent neurologic deficits</td>
</tr>
<tr>
<td>HELLP syndrome</td>
<td>Nausea/vomiting, epigastric pain, low platelets, increased liver enzymes</td>
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<tr>
<td>Preexisting/undiagnosed hypertension</td>
<td>Hypertension prior to pregnancy, or &lt;20 wk</td>
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<tr>
<td>Preexisting renal disease</td>
<td>Proteinuria or hematuria &lt;20 wk</td>
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<tr>
<td>Hyperthyroidism</td>
<td>Palpitations tachycardia, sweating, dry skin, heart failure</td>
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<tr>
<td>Primary hyperaldosteronism</td>
<td>Refractory hypertension, hypokalemia, metabolic alkalosis</td>
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<tr>
<td>Pheochromocytoma</td>
<td>Paroxysmal hypertension, headaches, chest pain, hyperglycemia</td>
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<tr>
<td>Renal artery stenosis</td>
<td>Hypertension that is refractory to treatment</td>
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<tr>
<td>Cerebral vasoconstriction syndrome</td>
<td>Sudden thunderclap headaches, visual changes, neurologic deficits</td>
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<tr>
<td>Cerebral venous thrombosis/stroke</td>
<td>Onset 3-7 d, gradual or acute headaches, seizures, neurologic deficits</td>
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<tr>
<td>TTP/hemolytic uremic syndrome</td>
<td>Hemolysis, severe thrombocytopenia, neurologic symptoms, normal liver enzymes</td>
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GH, gestational hypertension; HELLP, hemolysis, elevated liver enzymes, and low platelet; TTP, thrombotic thrombocytopenic purpura.
Pre-existing GH-preeclampsia

- HTN and proteinuria usually resolve within one week (data variable)
- Decrease in BP within 48h of delivery
- Increase in BP 3-6d PP
- Unrecognized preeclampsia
- Neurologic and/or laboratory abnormalities may first present PP period
- Similar for superimposed preeclampsia

Postpartum neurologic symptoms – with or without hypertension

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Central venous thrombosis
Postpartum hypertension – other causes coincident with pregnancy

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*GH, gestational hypertension; HELLP, hemolysis, elevated liver enzymes, and low platelet; TTP, thrombotic thrombocytopenic purpura.*

PP Eclampsia - Evaluation

- ABCs!!!!
- Evaluation and management - simultaneous
- History
  - Presenting symptoms/signs
  - Pregnancy history
  - Delivery and PP course
  - Medications
- Physical exam
  - BP, pulse, oxygen saturation
  - Neuro exam
  - Cardiopulmonary exam
- Laboratory studies
  - Proteinuria
  - CBC with platelets, LFTs, Cr, LDH
- Neuro-imaging
  - Consider non-contrast head CT
  - MRI/A/V
- Multi-disciplinary approach
**PP Eclampsia - Management**

- ABCs!!!!
- Magnesium sulfate IV
  - 4-6g loading dose over 20-30 minutes
  - 2g IV continuous infusion
  - Can be used IM if no IV access
  - More effective than placebo, phenytoin, diazepam, lytic cocktails
- Acute blood pressure management
- Other organ involvement with appropriate treatment
  - Pulmonary edema – diuresis
  - Renal failure – dialysis
- Neuro-imaging
  - Non contrast CT scan
  - MRI
- Multi-disciplinary approach
Posterior reversible encephalopathy syndrome (PRES)

- Sudden elevations in BP exceed normal cerebrovascular auto-regulatory capacity → regions of forced vasodilation and vasoconstriction, especially in arterial boundary zones
- Disruption of end capillary pressure → ↑hydrostatic pressure, hyperperfusion, extravasation of plasma/RBC → vasogenic edema

Evaluation

- **History**
  - Presenting symptoms/signs
  - Pregnancy history
  - Delivery and PP course
  - Medications

- **Physical exam**
  - BP, pulse, oxygen saturation
  - Neuro exam
  - Cardiopulmonary exam
    - PP cardiomyopathy (23-46% associated with HDP)

- **Laboratory studies**
  - Proteinuria
  - CBC with platelets, LFTs, Cr, LDH

- **Neuro-imaging**
  - Consider non-contrast head CT
  - MRI/A/V

- **Multi-disciplinary approach**
Common things are common

• Most common cause of hypertension beyond 48h after delivery
  – GH
  – Preeclampsia
  – Chronic HTN
  – Preexisting or de novo

• Initial management depends on history, symptoms, clinical findings, lab testing
Postpartum hypertensive disorders

PP- Hypertension Only

PP- Preeclampsia/Eclampsia
- Hypertension
- Neurologic symptoms
- Proteinuria
- Other end organ involvement
- Seizures
- HELLP

PP - Neurologic symptoms, focal deficits with or without HTN
- Central venous thrombosis
- CVA
- PRES/
- Cerebral vasoconstriction syndrome
- Hemorrhage
- Infarction
Postpartum hypertensive disorders

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  - Infarction
PP Hypertension only - management

• BP control
• Antihypertensive meds if >150/100
• Acute management (aggressive)
  – IV hydralazine
  – IV labetalol
  – Po nifedipine
• Chronic management
  – Oral nifedipine XL
  – Labetalol
  – Diuretics (furosemide, hydrochlorothiazide)
  – Methyldopa
  – Enalapril, captopril
  – (breast-feeding)
PP Hypertension only - management

- Home BPs
- Frequent visits
- Symptom monitoring
- Likely need to decrease dose or discontinue after 1-2 weeks
- Some will have persistent HTN = chronic HTN
- Consider other causes if persistent, severe elevations or other associated symptoms
  - Hyperaldosteronism
  - Renal artery stenosis
  - Pheochromocytoma
  - Hyperthyroidism
  - PP cardiomyopathy
## Drugs for the acute management of hypertension†

<table>
<thead>
<tr>
<th>Drug (FDA Category)</th>
<th>Mechanism of Action</th>
<th>Dose</th>
<th>Onset of Action</th>
<th>Comments†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Labetalol (C)</td>
<td>(\alpha) - and (\beta) - adrenergic antagonist</td>
<td>10-20mg IV, then 20-80 mg every 20-30 minutes to a maximum dose of 300mg OR continuous infusion 1-2mg/min IV*</td>
<td>5-10 min</td>
<td>Considered a first line agent during pregnancy. Less tachycardia and fewer side effects. Avoid in patients with asthma or congestive heart failure.</td>
</tr>
<tr>
<td>Hydralazine (C)</td>
<td>Arteriolar vasodilator, smooth muscle relaxant</td>
<td>5mg IV or IM, then 5-10 mg IV every 20-40 minutes OR continuous infusion 0.5 – 10 mg/hour</td>
<td>10-20 min</td>
<td>Higher or frequent dosing associated with maternal hypotension, headaches and fetal distress – may be more common than other agents.</td>
</tr>
<tr>
<td>Nifedipine (C)</td>
<td>Calcium channel blocker</td>
<td>10-20 mg orally, repeat in 30 minutes if needed; then 10-20mg every 2-6 hours</td>
<td>10-20 min</td>
<td>May observe reflex tachycardia, headaches.</td>
</tr>
<tr>
<td>Sodium Nitroprusside (C)</td>
<td></td>
<td>0.25-20 mcg/kg/min IV*</td>
<td>Within seconds</td>
<td>Relatively contraindicated and agent of last resort; longer use associated with cyanide toxicity.</td>
</tr>
</tbody>
</table>

* Continuous IV infusions should be used only in an ICU setting
† All agents are associated with headache, flushing, nausea, and tachycardia (likely due to hypotension and reflex sympathetic activation), these side effects are less with labetalol
### Oral antihypertensive drugs used for the management of chronic hypertension

<table>
<thead>
<tr>
<th>Drug (FDA Category)</th>
<th>Mechanism of Action</th>
<th>Dose</th>
<th>Maximum Dose</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Labetalol (C)</td>
<td>$\alpha$- and $\beta$-adrenergic antagonist</td>
<td>200-2400 mg/day orally in 2-3 divided doses</td>
<td>2400 mg/day</td>
<td>Well-tolerated. Potential bronchoconstrictive effects.</td>
</tr>
<tr>
<td>Nifedipine (C)</td>
<td>Calcium channel blocker</td>
<td>30-120 mg/day orally of a slow release preparation</td>
<td>120 mg/day</td>
<td>Do not use sublingual form. Side effects include headache, flushing, tachycardia; once a day dosing may improve compliance.</td>
</tr>
<tr>
<td>Methyldopa (B)</td>
<td>Centrally acting $\alpha_2$-receptor agonist</td>
<td>0.5-3g/day orally in 2-3 divided doses</td>
<td>3 g/day</td>
<td>Childhood safety data up to 7 years. May not be as effective in control of severe hypertension. Side effect profile includes lethargy.</td>
</tr>
<tr>
<td>Hydrochlorothiazide (C)</td>
<td>Thiazide diuretic</td>
<td>12.5-50 mg/day orally</td>
<td>50 mg/day</td>
<td>Not used as a primary agent in pregnancy and considered an adjunctive agent; theoretical concerns of reduced intravascular volume and decreased uterine blood flow in pregnancy; electrolytes should be monitored.</td>
</tr>
<tr>
<td>Hydralazine (C)</td>
<td>Vasodilation, smooth muscle relaxant</td>
<td>50-300 mg per day orally in 2-4 divided doses</td>
<td>300 mg/day</td>
<td>Not used as a primary agent in pregnancy and considered an adjunctive agent; may be used in combination with a sympatholytic agent (e.g., methyldopa or labetalol) to prevent tachycardia.</td>
</tr>
<tr>
<td>Angiotensin converting enzyme inhibitors/angiotensin receptor blockers</td>
<td>Associated with anomalies</td>
<td></td>
<td></td>
<td>CONTRAINDICATED IN PREGNANCY AND PRECONCEPTION PERIOD – However, captopril and enalapril are compatible with breast feeding</td>
</tr>
</tbody>
</table>
Postpartum hypertensive disorders

PP- Hypertension Only

PP- Preeclampsia/Eclampsia

Hypertension
Neurologic symptoms
Proteinuria
Other end organ involvement
Seizures
HELLP

PP -Neurologic symptoms, focal deficits with or without HTN

Central venous thrombosis
CVA
PRES/
Cerebral vasoconstriction syndrome
Hemorrhage
Infarction
PP – preeclampsia management

• Magnesium sulfate for seizure prophylaxis
  – 24-48h
• BP control
• Treatment of other associated complications
• Neuro-imaging
  – Particularly if no resolution of BP and neuro sxs
Postpartum hypertensive disorders

- PP- Hypertension Only
- PP- Preeclampsia/Eclampsia
  - Hypertension
  - Neurologic symptoms
  - Proteinuria
  - Other end organ involvement
  - Seizures
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- PP - Neurologic symptoms, focal deficits with or without HTN
  - Central venous thrombosis
  - CVA
  - PRES/
  - Cerebral vasoconstriction syndrome
  - Hemorrhage
  - Infarction
FIGURE
Recommended evaluation and management of women with postpartum hypertension

Persistent hypertension postpartum
- Detailed history & physical examination
- Presence of cerebral/gastrointestinal symptoms
- Laboratory evaluation including proteinuria

Hypertension only
- Stop vasoactive drugs
- Antihypertensive drugs
- Response to treatment

Hypertension plus
- Heart failure
- Palpitations, tachycardia
- Anxiety, short breath
- Consultation & evaluation for:
  - Thyrotoxicosis
  - Cardiomyopathy
  - Pheochromocytoma
- No further evaluation
- Evaluate for arterial stenosis & adrenal tumors
- Seek consultation

Hypertension plus
- Proteinuria
- Cerebral symptoms
- Convulsions
- Response to treatment
- Treat accordingly
- Yes
  - No further evaluation
- No
  - Neurologic consultation
  - Cerebral imaging

Hypertension plus
- Recurrent symptoms
- Neurologic deficits
- Pre/eclampsia
- Magnesium sulfate
- Antihypertensives
- Response to treatment
- RCVS
- Stroke

Hypertension plus
- Nausea/vomiting
- Epigastric pain
- Elevated liver enzymes
- Low platelets
- HELLP syndrome
- Magnesium sulfate
- Antihypertensives
- Supportive care

Hypertension plus
- Exacerbation of lupus
- TTP/HUS
- APAS
- AFLP

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AFLP, acute fatty liver of pregnancy; APAS, antiphospholipid antibody syndrome; HELLP, hemolysis, elevated liver enzymes, and low platelet; HUS, hemolytic uremic syndrome; RCVS, reversible cerebral vasoconstriction syndrome; TTP, thrombotic thrombocytopenic purpura.
Education

• Emergency departments
• Primary care providers
• Family practitioners
• Patients
  – Routine discharge instructions for all PP women
Preeclampsia

What Is It?
Preeclampsia is a serious disease related to high blood pressure. It can happen to any pregnant woman.

Risks to You
- Seizures
- Stroke
- Organ damage
- Death

Risks to Your Baby
- Premature birth
- Death

Signs of Preeclampsia
- Stomach pain
- Headaches
- Feeling nauseous; throwing up
- Seeing spots
- Swelling in your hands and face
- Gaining more than 5 pounds in a week

What Should You Do?
Call your doctor right away. Finding preeclampsia early is important for you and your baby.

For more information go to www.preeclampsia.org

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Preeclampsia is a disorder of pregnancy. Know the symptoms, trust yourself.

SIGN & SYMPTOMS
- high blood pressure
- protein in your urine
- sudden weight gain
- swelling of the hands, feet or face
- headache that won't go away
- changes in vision
- upper abdominal pain or chest pain
- breathing with difficulty, gasping, panting

If you have one or more of these signs and symptoms, you should see your doctor or go to an emergency room immediately.

My BP was ______/_______
My proteinuria was (circle one)
None Trace 1+ 2+ 3+ 4+
or ______ mg/dl
I’ve gained ______lbs in ______weeks

TODAY’S DATE

It online www.preeclampsia.org or call Toll-Free 800-665-9341
**Recommended evaluation and management of women with postpartum hypertension**

**Persistent hypertension postpartum**
- Detailed history & physical examination
- Presence of cerebral/gastrointestinal symptoms
- Laboratory evaluation including proteinuria

**Hypertension only**
- Stop vasoactive drugs
- Antihypertensive drugs
- **Response to treatment**
  - **Yes**
    - Evaluate for arterial stenosis & adrenal tumors
    - Seek consultation
  - **No further evaluation**
  - **No**
    - **Response to treatment**
      - **Yes**
        - Neurologic consultation
        - Cerebral imaging
      - **No**
        - No further evaluation

**Hypertension plus**
- Heart failure
- Palpitations, tachycardia
- Anxiety, short breath
- **Consultation & evaluation for:**
  - Thyrotoxicosis
  - Cardiomyopathy
  - Pheochromocytoma
- **Response to treatment**
  - **Yes**
    - No further evaluation
  - **Neurologic consultation**
  - Cerebral imaging

**Hypertension plus**
- Proteinuria
- Cerebral symptoms
- Convulsions
- **Response to treatment**
  - **Yes**
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  - **Neurologic consultation**
  - Cerebral imaging

**Hypertension plus**
- Recurrent symptoms
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- **RCVS**
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- **Response to treatment**
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**Hypertension plus**
- Nausea/vomiting
- Epigastric pain
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- Low platelets
- **HELLP syndrome**
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- **Supportive care**
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* AFLP, acute fatty liver of pregnancy; APAS, antiphospholipid antibody syndrome; HELLP, hemolysis, elevated liver enzymes, and low platelet; HUS, hemolytic uremic syndrome; RCVS, reversible cerebral vasoconstriction syndrome; TTP, thrombotic thrombocytopenic purpura.

Case 1

- 32yo G2P2 PPD#6 – brought in to local hospital by ambulance after a witnessed generalized tonic-clonic seizure – she was intubated, started on a dilantin load in ED and transferred to UPMC-Presby Neuro ICU
- MRI – posterior leukoencephalopathy, ?vasculopathy
- OB called 14 hours after admission for vaginal bleeding
- PP Preeclampsia management – complete recovery
Case 2

- 34yo G1P1 POD#5 presented to MWH-ED with “feeling unwell” nausea/vomiting – in ED developed sudden-onset of severe headache and BP 180/110
- Course significant for being healthy
- IOL at 38w – mild preeclampsia
  - Magnesium sulfate - seizure prophylaxis
  - Misoprostil – cervical ripening
  - Pitocin - labor augmentation
  - Epidural
- Primary LTCS for arrest of dilation at 8cm
- Discharged to home on POD#3
- PP preeclampsia management
- Neuroimaging – intracranial hemorrhage
- Neurology management
Case 3

• 30yo G1P0101 POD#7 presents to ED with severe hypertension (on labetalol) and intermittent headache
• s/p primary LTCS for breech at 31w, severe IUGR, AEDF, oligohydramnios and severe hypertension and unrelenting headache – discharged home on POD#4
• BP in ED 170/110 – took 500mg of labetalol at home
• PP preeclampsia management with aggressive diuresis and BP control
Postpartum Hypertension/Preeclampsia

For women diagnosed with gestational hypertension, preeclampsia, or superimposed preeclampsia, we suggest that blood pressure be monitored in the hospital or that equivalent outpatient surveillance be performed for at least 72 hours postpartum and again 7–10 days after delivery or earlier in women with symptoms.

Quality of evidence: Moderate
Strength of recommendation: Qualified

For all postpartum women (not just women with preeclampsia), we suggest that discharge instructions include information about the signs and symptoms of preeclampsia as well as the importance of prompt reporting of this information to their health care provider.

Quality of evidence: Low
Strength of recommendation: Qualified
Healthy Mom and healthy baby!