Preeclampsia and Hypertension in Pregnancy

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Elevated Blood Pressure in Pregnancy

1. Chronic/Pre-existing hypertension
2. Gestational hypertension
   - With or without severe features
3. Preeclampsia/Eclampsia
   - With or without severe features
4. Preeclampsia superimposed on chronic (pre-existing) hypertension

Pregnancy Induced (Associated) Hypertension

- 6-8% of all pregnancies
- Most common medical disorder in pregnancy
- Severe features: 25%
- No "moderate"
- 10% occurs in pregnancies less than 34 weeks of gestation
1. Chronic Hypertension

- Present before the 20th week of pregnancy
- 140/90 - 160/110 (mild/moderate)
  - Tight control shows no benefit, meds may not be indicated, consider co-morbidities
  - Out-patient BP monitoring if ‘white coat HTN’
- >160/110 warrants pharmacologic intervention
- Goal of tx: BP 120/80 – 160/110
- Taper off if BP < 120/80

2. Gestational Hypertension

- Transient HTN of pregnancy
  - 10% of pregnancies
  - Detected after 20 weeks with previous normal BP
  - >140 SBP or >90 DBP
  - Measurements at least 4 hrs apart, no more than 7 days apart
  - Without significant proteinuria, end organ malfunction
  - Severe feature > 160/110

2. Gestational Hypertension

Temporary Diagnosis

- Preeclampsia, if proteinuria/ sx develop (20%)
- Chronic hypertension, if blood pressure elevation persists ≥12 weeks postpartum
- Transient PIH, if blood pressure returns to normal by 12 weeks postpartum
2. Gestational HTN Management

- No Severe Features (<160/110):
  - 2 x weekly BP checks, 1x wkly proteinuria assessment
  - Platelets and liver enzymes weekly
  - Antenatal testing
  - No bedrest, no medication
  - Watch for developing preeclampsia
  - Delivery at 37 wks

- SEVERE: same as pre-e w/ severe features

3. Preeclampsia

- Elevated blood pressure
  - \( \geq 140/90 \)
  - Seated for 5 minutes first, correct cuff size
  - 2 measurements: > 4 hours apart, < 7 days apart
- Proteinuria
  - \( \geq 0.3 \) g protein in a 24 hour specimen or
  - P/C ratio > 0.3 (mg/dL)
- **OR**: End organ malfunction
  - thrombocytopenia, liver or kidney test abnormalities, pulm edema, neuro symptoms

Preeclampsia -Risk Factors-

- Chronic hypertension (25% chance)
- Hx preeclampsia
- Elevated BMI (up to 25%)
- Family history preeclampsia
- Diabetes, insulin resistance (20-50%)
- Autoimmune disease
- Underlying renal disease
- Multi-fetal gestation
- Age \( \geq 40 \) or \( \leq 18 \)
- Limited paternal antigen exposure
- African American
- Partner history 1st degree relative with preeclampsia
- Hx of pregnancy with IUGR, abruption, demise
- IVF
- Low Vitamin D levels
The Cause of Preeclampsia
- Decreased placental perfusion leads to overproduction of anti-angiogenic proteins by the placenta which causes systemic endothelial dysfunction

Two Phase Process
1) Initial implantation incomplete
   - Trophoblastic invasion
   - Remodeling of spiral arteries 10-20wks
   - Ischemic placenta
2) Overproduction of anti-angiogenic proteins later in pregnancy
   - Placenta malfunctions
   - Over expression in maternal blood stream
   - Systemic endothelial dysfunction

The Pathogenesis of Preeclampsia
- Trophoblastic invasion of uterine spiral arteries is incomplete in women with preeclampsia
- Spiral arteries fail to remodel
- Decreased placental perfusion
Abnormal Placental Development: Why?

- Abnormal trophoblasts: differentiation
- Immunologic factors: prior exposure to fetal and paternal antigens
- Medical conditions: vascular insufficiency
  - Hypertension
  - Diabetes
  - Anti phospholipid syndrome
- Genetics: family, partner history

Placental ischemia

- Overproduction of anti-angiogenic substances made by placenta to control placental growth: sFLT, endoglin, PGM
- Causes increase in circulating maternal agents
- Multiple studies for Prediction/Screening test
  - VEGF, PIGF, soluble endoglin
- Blood or urine, 25-28 weeks?
**Endothelial dysfunction**

- Placenta growth controlled by sFLT-1 and soluble endoglin (sEng) (? others)
- Anti-angiogenic substances
- Increased levels at 3rd trimester
- Overproduction in pts with preeclampsia
- R/T endothelial damage
- Block VEGF (vascular endothelial growth factor)
- Caustive: htn, proteinuria, glomerular endotheliosis in rats

**Preeclampsia-Cause: Endothelial dysfunction**

- Hypertension
  - Disturbed endothelial control of vascular tone
  - A symptom!! (Not the cause)
- Increased vascular permeability (edema and proteinuria)
- Abnormal endothelial expression of pro-coagulants
- Changes cause ischemia of target organs
  - Brain
  - Kidney
  - Liver
  - Placenta

**Preeclampsia-Outcomes**

- Gestation at onset
- Pre-existing medical conditions
- Severe features
  - Abruption rate increased
  - Neonatal complications increased
  - 0.2% maternal mortality
  - 5% maternal morbidities (seizure, pulm edema, liver failure, DIC, stroke)
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Preeclampsia
-Prevention-

- Low dose aspirin—may delay onset in moderate/high risk pts, start 2nd tri (ACOG)
- No significant benefit:
  - Vitamins C and E
  - Calcium/magnesium
  - Fish oil
  - ASA in low risk patients
  - High protein diet
  - Anti-hypertensives DO NOT seem to prevent progression

Diagnosis: Preeclampsia with Severe Features

- BP 160/105-110
  - Either measurement
  - Technically need 2 measurements 4 hrs apart
  - Thrombocytopenia < 100,000
  - Impaired liver function: ALT or AST 2X normal
  - Serum creat > 1.1mg/dL
  - CNS symptoms
  - Pulmonary edema or cyanosis
  - Out of favor: Proteinuria ≥ 5g in 24hrs
  - Out of favor: IUGR

Eclampsia

- Preeclampsia +
  - Seizures or coma
    (that can’t be otherwise attributed)

  - 1 out of 400 w/o severe features
  - 1 out of 50 w/ severe features
4. Preeclampsia Superimposed on Preexisting HTN

- Significantly worse prognosis
- Baseline labs
- Diagnosis
  - New onset proteinuria after 20 weeks
  - Sudden increase in BP previously well controlled
  - Thrombocytopenia
  - Increase in liver enzymes
  - Fetal growth restriction

Definitive treatment for preeclampsia and eclampsia is delivery.
- Always best for mom
- Always curative

Pregnancy may be maintained to allow for fetal maturation.

Hypertensive Crisis

- BP Systolic >160 or Diastolic >105-110mmHg
  - No strong evidence on this exact threshold
- Urgent antihypertensive therapy per ACOG
- Decreases risk of CVA and heart failure
### Antihypertensive Agents for Urgent Treatment (ACOG)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosing Instructions</th>
<th>Considered 1st line agent</th>
<th>Tachycardia</th>
<th>Less adverse effects</th>
<th>Not with asthma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Labetalol</td>
<td>10-20mg IV then 20-80mg q 20-30 min to a max dose of 300mg or constant infusion 1-2mg/min IV</td>
<td>Considered 1st line agent</td>
<td>Tachycardia</td>
<td>Less adverse effects</td>
<td>Not with asthma</td>
</tr>
<tr>
<td>Hydralazine</td>
<td>5mg IV or IM, then 5-10mg IV every 20-40min or Constant infusion 0.5-1mg/hr</td>
<td>Higher/freq dose assoc with maternal hypotension, fetal distress more common than other agents</td>
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<tr>
<td>Nifedipine</td>
<td>10-20mg orally, repeat in 30min PRN then 20-60mg every 2-6 hrs</td>
<td>Reflex tachycardia possible</td>
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</tbody>
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### Maternal Eval: Lab tests
- Platelets
- Liver function: ALT, AST
- Kidney function: serum creatinine
- ≥ once a week
- Uric Acid: Not predictive
- Elevated serum LDH: sign of hemolysis, severe disease or HELLP syndrome, ? utility

### Fetal Evaluation
- Daily kick counts
- EFW at diagnosis and every 4 weeks
- NST/AFI or BPP once or twice weekly
- Corticosteroids if <37 weeks
- If IUGR suspected: Evaluation of umbilical artery Doppler indices
Antepartum Management
Preeclampsia w/o Severe Features
- Not beneficial: hospitalization, bedrest
- BP meds: Not for outpatient maintenance
- DELIVERY: 37 wks
  - Baby is near term and statistically will do well
  - Don’t wait for disease progression which adversely impacts outcomes

Delivery Indications for Preeclampsia with Severe Features <34 weeks
- Steroids administered/delivery deferred for 48 hours if:
  - AFI>5, reassuring fetal testing
  - Absence of neuro sx, oliguria, eclampsia
  - Absence of HELLP syndrome
  - Plt >100,000
  - LFT < 2x normal
  - No reverse end-diastolic flow in umbilical arteries
  - No new or increasing renal dysfunction

Antepartum Management
Preeclampsia w/ Severe Features
- Delivery if > 34 weeks
- Steroids if < 37 weeks
- MgSO4 (fetal and maternal indications)
- Consider tertiary care center/perinatologist
- Blood products available?
- If BP ≥ 160/110: anti-hypertensive med
Preeclampsia
Route of Delivery & Anesthesia

- Vaginal preferred
- Anesthesia considerations
  - Epidurals with thrombocytopenia/coagulopathies
    - Per ACOG: Plates 80,000/microL limit
    - Check before removal
  - Hypotension and uteroplacental perfusion
  - MgSO4 not to be d/c’d for C Section
  - Early consultation with anesthesiologist

Preeclampsia
Anticonvulsant Therapy

- Magnesium sulfate
  - Always indicated with severe features
  - Always indicated with eclampsia
  - Preeclampsia w/o severe features: not ‘recommended’
  - Consider with any neurological symptoms
    - Clonus, hyper-reflexia, headache, visual disturbances
  - Continue 12-48 hrs PP, or diuresis X 2-3hrs

Ehrenberg, 2006

Eclampsia

- Stabilize mother
- Self limiting: lateral position, O2, trauma prevention
- MgSO4: prevent further seizure, CVA
  - 4-6g load, 1-3g/hr
  - May re-bolus w/ 2g for recurrence
- Lorazepam 4mg over 4 min, IV push PRN
- Deliver after stabilized
- Fetal bradycardia 3-8 min following seizure common
- Consider delivery route (only 20% vaginally)
HELLP Syndrome

- Hemolysis: Increased bilirubin
- Elevated Liver enzymes: ALT, AST
- Low Platelets
- Incidence: 10-20% of women with preeclampsia
- Considered a form of preeclampsia
- 70% antepartum generally 28-36 wks
- 30% postpartum generally within 48 hrs
- Hypertension absent in 15-20% of cases
- 20% develop DIC

HELLP Syndrome Co morbidities

- Preterm delivery 70%
- Renal failure 8%
- Hepatic hematoma 1%
- Placental abruption 16%
- DIC 15-20%
- Fetal death 7-35%
- Maternal death 1%

HELLP: Antepartum Management

- Assess and stabilize mother
- Anticipate delivery
- Type and screen/cross
- Anticipate need for blood products
- MgSO4
- Consider transfer to tertiary care/ perinatologist
- Consider platelet transfusion if <20,000
- Pre-op plates transfuse to > 40-50,000
Postpartum Preeclampsia

- Sx may worsen in first 24 hrs
- Magnesium sulfate
  - new-onset hypertension and headache or blurred vision
  - or severe hypertension
- Persistent > 150/100: antihypertensive therapy
- > 160/105-110: ACOG: treat within 1 hr
- If preeclampsia dx antenatally:
  - Monitor BP for 72hrs postpartum
  - Recheck BP in office in 7-10 days
  - Discharge instructions include warning signs

Future Risk/Prevention

- Increased lifetime risk CV disease
- Recurrence rate 5-70%
- Mild, near term 5%
- Severe, delivery before 30 weeks = 70%
- Risk may be reduced with closer spaced pregnancy

Thank you