

A 25 years old female with hypertension getting pregnant

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Hypertension during Pregnancy: Classification

- **Pregnancy-induced hypertension**
 - Hypertension without proteinuria/edema
 - Preeclampsia
 - mild
 - severe
 - Eclampsia
- **Coincidental HTN: preexisting or persistent**
- **Pregnancy-aggravated HTN**
 - superimposed preeclampsia
 - superimposed eclampsia
- **Transient HTN: occurs in 3rd trimester, mild**

Preeclampsia: Definition

- Hypertension
 - > 140/90
 - relative ↑ no longer considered diagnostic
- Proteinuria
 - > 300 mg/24 hours or ≥ 1 or 2+ on urine dipstick
 - may occur late
- Edema (non-dependent)
 - so common & difficult to quantify it is rarely evoked to make or refute the diagnosis

Criteria for Severe Preeclampsia

- SBP > 160 mm Hg
- DBP > 110 mm Hg
- Proteinuria > 5 g/24 hr. or 3-4+ on dipstick
- Oliguria < 500 cc/24 hr.
- ↑ serum creatinine
- Pulmonary edema or cyanosis
- CNS symptoms (HA, vision changes)
- Abdominal (RUQ) pain
- Any feature of HELLP
 - hemolysis
 - ↑ liver enzymes
 - thrombocytopenia
- IUGR or oligohydramnios

Preeclampsia: Risk Factors

- Nulliparity (or, more correctly, primipaternity)
- Chronic renal disease
- Angiotensinogen gene T235
- Chronic hypertension
- Antiphospholipid antibody syndrome
- Multiple gestation
- Family or personal history of preeclampsia
- Age > 40 years
- African-American race
- Diabetes mellitus

Etiology and Prevention

- Etiology is unknown.
- Many theories:
 - genetic
 - immunologic
 - dietary deficiency (calcium, magnesium, zinc)
 - supplementation has not proven effective
 - placental source (ischemia)

Etiology and Prevention

- A major underlying defect is a relative deficiency of **prostacyclin vs. thromboxane**
- Normally (non-preeclamptic) there is an 8-10 fold ↑ in prostacyclin with a smaller ↑ in thromboxane
 - prostacyclin salutatory effects dominate
 - vasodilation, ↓ platelet aggregation, ↓ uterine tone
- In preeclampsia, thromboxane's effects dominate
 - ↑ thromboxane (from platelets, placenta)
 - ↓ prostacyclin (from endothelium, placenta)

Preeclampsia Prophylaxis: **Aspirin**

- Aspirin has been extensively studied as a targeted therapy to ↓ thromboxane production
- CLASP study, A multicenter RCT
 - [CLASP Collaborative Group, Lancet 1994;343:619-29]*
 - 9364 women, risk factors for PIH or IUGR or who had PIH or IUGR
 - 60 mg ASA daily vs. placebo
 - Small reduction (12%) in occurrence of PIH
 - Small reduction in preterm deliveries: 20 vs 22%
 - No difference in neonatal outcome

Preeclampsia: Mechanism

- At this time the most widely accepted proposed mechanism for preeclampsia is:
Global Endothelial Cell Dysfunction
- Endothelial cell dysfunction is just one manifestation of a broader intravascular inflammatory response
 - present in normal pregnancy
 - excessive in preeclampsia
 - Proposed source of inflammatory stimulus: placenta

Pathophysiology: **Cardiovascular**

- In severe preeclampsia, typically hyperdynamic with normal-high CO, normal-mod. high SVR, and normal PCWP and CVP.
- Despite normal filling pressures, intravascular fluid volume is reduced (30-40% in severe PIH)
- Variations in presentation depending on prior treatment and severity and duration of disease
- Total body water is increased (generalized edema)

Pathophysiology: Cardiovascular

- Preeclamptic patients are prone to develop **pulmonary edema** due to reduced colloid oncotic pressure (COP), which falls further postpartum:

Colloid oncotic pressure:

	Antepartum	Postpartum
Normal pregnancy:	22 mm Hg	17 mm Hg
Preeclampsia:	18 mm Hg	14 mm Hg

Pathophysiology

- **Respiratory:**
 - Airway is edematous; use smaller ET tube (6.5)
 - ↑ risk of pulmonary edema; 70% postpartum
- **Renal:**
 - Renal blood flow & GFR are decreased
 - Renal failure due to ↓ plasma volume or renal artery vasospasm
 - Proteinuria due to glomerulopathy
 - glomerular capillary endothelial swelling w/subendothelial protein deposits
 - Renal function recovers quickly postpartum

Pathophysiology: Hepatic

- RUQ pain is a serious complaint
 - warrants imaging, especially when accompanied by ↑ liver enzymes
 - caused by liver swelling, periportal hemorrhage, subcapsular hematoma, hepatic rupture (30% mortality)
- HELLP syndrome occurs in ~ 20% of severe preeclampsics.

Pathophysiology

- **Coagulation:**
 - Generally hypercoagulable with evidence of platelet activation and increased fibrinolysis
 - Thrombocytopenia is common, but fewer than 10% have platelet count < 100,000
 - DIC may occur,
 - Acutely esp. with placental abruption
- **Neurologic:**
 - Symptoms: headache, visual changes, seizures
 - Hyperreflexia is usually present
 - Eclamptic seizures may occur even w/out ↑↑BP
 - Possible causes: hypertensive encephalopathy, cerebral edema, thrombosis, hemorrhage, vasospasm

Chronic Hypertension

Defined as hypertension diagnosed

- **Before pregnancy**
- **Before the 20th week of gestation**
- **During pregnancy and not resolved postpartum**

Gestational Hypertension

- **Gestational Hypertension:**
 - Systolic >140
 - Diastolic>90
 - No Proteinuria
 - 25% Develop Pre-eclampsia

Gestational Hypertension

Diagnosis of gestational hypertension:

- Detected for first time after midpregnancy
- No proteinuria
- Only until a more specific diagnosis can be assigned postpartum

If:

- BP returns to normal by 12 weeks postpartum, diagnosis is **transient hypertension**.
- BP remains high postpartum, diagnosis is **chronic hypertension**.
- Proteinuria develops **Superimposed Preeclampsia** is diagnosed (25% incidence)

Preeclampsia-Eclampsia

- Occurs after 20th week (earlier with trophoblastic disease)
- Increased BP (gestational BP elevation) with proteinuria
- 'LL' Edema is **NOT** part of this definition

Diagnosis of Preeclampsia-Eclampsia

- **Gestational Hypertension:**
 - Systolic >140
 - Diastolic >90
- **Proteinuria is defined as urinary excretion**
 - **0.3 g protein or greater in a 24-hour**
 - **+2 or greater on urine dip specimen**

Classification of Preeclampsia-Eclampsia

- **Criteria for Severe Preeclampsia (one or more)**
 - **Blood Pressure: >160 systolic, >110 diastolic**
 - **Proteinuria: $>5\text{gm}$ in 24 hours, over 3+ urine dip**
 - **Oligurea: less than 400ml in 24 hours**
 - **CNS: Visual changes, headache, scotomata, mental status change**
 - **Pulmonary Edema**
 - **Epigastric or RUQ Pain: Usually indicates liver involvement**

Classification of Preeclampsia-Eclampsia

- **Criteria for Severe Preeclampsia (one or more)**
 - **Impaired Liver Function tests**
 - **Thrombocytopenia: <100,000**
 - **Intrauterine Growth Restriction: With or without abnormal doppler assessment**
 - **Oligohydramnios**

Classification of Preeclampsia Superimposed Upon Chronic Hypertension

- **Hypertension and no proteinuria < 20 weeks:**
New-onset proteinuria after 20 weeks
- **Hypertension and proteinuria < 20 weeks:**
 - **Sudden increase in proteinuria**
 - **Sudden increase in BP in women whose hypertension was well controlled**
 - **Thrombocytopenia (platelet count <100,000 cells/mm³)**
 - **Increase in ALT or AST to abnormal levels**

Clinical Implications of Preeclampsia

- Preeclampsia ranges from mild to severe.
- Progression may be slow or rapid – hours to days to weeks.

For clinical management, preeclampsia should be over diagnosed to prevent maternal and perinatal morbidity and mortality – primarily through timing of delivery.

Symptoms of Preeclampsia

- **Visual disturbances** typical of preeclampsia are scintillations and scotomata. These disturbances are presumed to be due to cerebral vasospasm.
- **Headache** is of new onset and may be described as frontal, throbbing, or similar to a migraine headache. However, no classic headache of preeclampsia exists.
- **Epigastric** pain is due to hepatic swelling and inflammation, with stretch of the liver capsule. Pain may be of sudden onset, it may be constant, and it may be moderate-to-severe in intensity.

Symptoms of preeclampsia

- While mild lower extremity edema is common in normal pregnancy, **rapidly increasing or nondependent edema** may be a signal of developing preeclampsia. However, this signal theory remains controversial and recently has been removed from most criteria for the diagnosis of preeclampsia.
- **Rapid weight gain** is a result of edema due to capillary leak as well as renal sodium and fluid retention.

Physical Findings in Preeclampsia

- Blood Pressure
- Proteinuria
- Retinal vasospasm or Retinal edema
- Right upper quadrant (RUQ) abdominal tenderness stems from liver swelling and capsular stretch

Differential Diagnosis

- **Documentation of HBP before conception or before gestational week 20 favors a diagnosis of chronic hypertension (essential or secondary).**
- **HBP presenting at midpregnancy (weeks 20 to 28) may be due to early preeclampsia, transient hypertension, or unrecognized chronic hypertension.**

Laboratory Tests

High-risk patients presenting with normal BP:

- **Hematocrit**
- **Hemoglobin**
- **Serum uric acid**
- **If 1+ protein by routine urinalysis (clean catch) present obtain a timed collection for protein and creatinine**
- **Accurate dating and assessment of fetal growth**
- **Baseline sonogram at 25 to 28 weeks**

Preeclampsia: Treatment

- Goal is to prevent eclampsia and other severe complications.
- Attempts to treat preeclampsia by natriuresis or by lowering BP may exacerbate pathologic changes.
- Palliate maternal condition to allow fetal maturation and cervical ripening.

Preeclampsia: Treatment

Maternal Evaluation

- **Goals:**
 - Early recognition of preeclampsia
 - Observe progression, both to prevent maternal complications and protect well-being of fetus.
 - **Early signs:**
 - BP rises in late second and early third trimesters.
 - Initial appearance of proteinuria is important.

Preeclampsia: Treatment

- Maternal Evaluation...When To Hospitalize?
 - Often, hospitalization recommended with new-onset preeclampsia to assess maternal and fetal conditions.
 - Hospitalization for duration of pregnancy indicated for preterm onset of severe gestational hypertension or preeclampsia.
 - Ambulatory management at home or at day-care unit may be considered with mild gestational hypertension or preeclampsia remote from term

Indication of Delivery

Maternal	Fetal
Gestational age \geq 38 weeks	Severe fetal growth restriction
Platelet count $<$ 100,000 cells/mm ³	Nonreassuring fetal testing results
Progressive deterioration in hepatic function	Oligohydramnios
Progressive deterioration in renal function	
Suspected abruptio placentae	
Persistent severe headaches or visual changes	
Persistent severe epigastric pain, nausea, or vomiting	

Preeclampsia

- **Antepartum Management of Preeclampsia**
 - Little to suggest therapy alters the underlying pathophysiology of preeclampsia.
 - Restricted activity may be reasonable.
 - Sodium restriction and diuretic therapy appear to have **no positive effect**.

Obstetric Management

- Classically “stabilize and deliver”



Obstetric Management

- Medical management while awaiting delivery:
 - use of steroids X 48 hours if fetus < 34 wks
 - antihypertensives to maintain DBP < 105-110
 - magnesium sulfate for seizure prophylaxis
 - monitor fluid balance, I/O, daily weights, symptoms, reflexes, HCT, plts, LFT's, proteinuria

Obstetric Management

- Indications for **expedited** delivery:
 - fetal distress
 - ↑ BP despite aggressive Rx
 - worsening end-organ function
 - development or worsening of HELLP syndrome
 - development of eclampsia

Antihypertensive Therapy

- Most commonly, for **acute control**: **hydralazine, labetalol**
- **Nifedipine** may be used, but unexpected hypotension may occur when given with MgSO_4
- For refractory hypertension: **nitroglycerin or nitroprusside** may be used
 - Nitroprusside dose and duration should be limited to avoid fetal cyanide toxicity
 - Usually require invasive arterial pressure mon
- **Angiotensin-converting enzyme (ACE) inhibitors** contraindicated due to severe adverse fetal effects

Seizure Prophylaxis & Treatment

- Magnesium sulfate vs. phenytoin for seizure prophylaxis in preeclampsia
 - Lucas, et al., N Engl J Med 1995;333:201-5.
 - 2138 patients (75% had mild PIH)
 - Maternal & fetal outcomes similar except 10 seizures in the phenytoin group (0 in MgSO_4)
- Mg vs. diazepam & Mg vs. phenytoin for preventing recurrent seizures in eclamptics
 - Eclampsia Trial Collaborative Group, Lancet 1995;345:1455
 - Mg pts were 52% or 67% less likely to have a recurrent seizure than diazepam or phenytoin pts

Preeclampsia

- **The “cure” for preeclampsia is delivery**
 - The “cure” is always beneficial for the mother, although c-section might be needed
 - The “cure” may be deleterious for the fetus

Treatment of Acute Severe Hypertension in Pregnancy

- **SBP \geq 160 mm Hg and/or DBP \geq 105 mm Hg**
 - Parenteral hydralazine is most commonly used.
 - Parenteral labetalol is second-line drug (avoid in women with asthma and CHF.)
 - Oral nifedipine used with caution. (Short-acting nifedipine is not approved by FDA for managing hypertension.)
 - Sodium nitroprusside may be used in rare cases.

Thank you